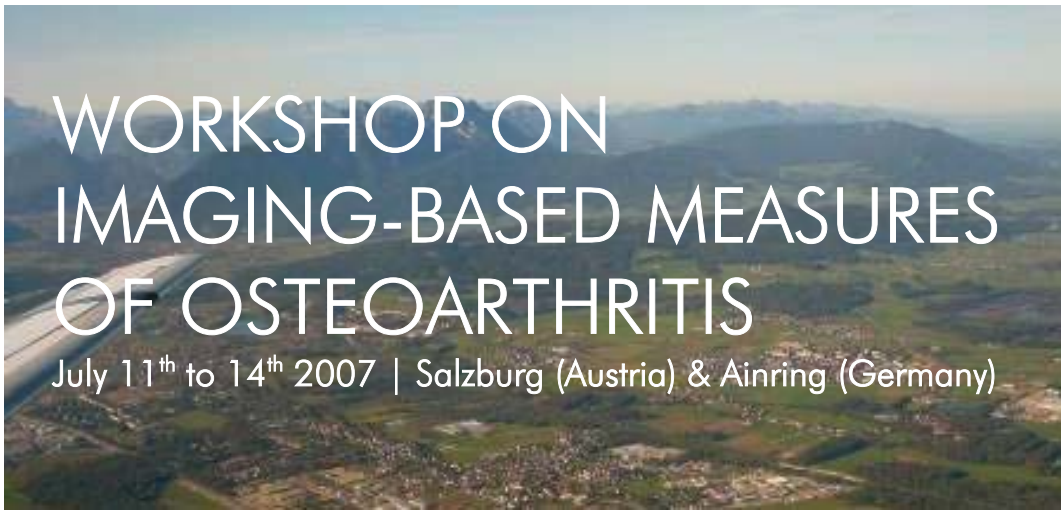

WORKSHOP ON IMAGING-BASED MEASURES OF OSTEOARTHRITIS

July 11th to 14th 2007 | Salzburg (Austria) & Ainring (Germany)

www.pmu.ac.at/imagingworkshop

PARACELSUS MEDIZINISCHE PRIVATUNIVERSITÄT

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Final Program

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

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WELCOME

Dear Workshop Participant,

Welcome to the 1st Workshop on "Imaging-based Measures of Osteoarthritis". We are excited that the community of researchers working on imaging methods in OA is coming together in their own workshop for the first time. Given the many large epidemiological studies now under way, for example the OA Initiative, we feel that the right time has come.

We were very pleasantly surprised with the large number of registrations and the high quality of the submitted abstracts. To date we have 115 registered participants from Australia, Austria, Belgium, Canada, England, Germany, Ireland, Italy, Japan, the Netherlands, Sweden, Switzerland, and the US. Eight invited lectures will be presented on key topics of OA imaging. A total of 62 abstracts were submitted; 23 will be presented orally, 27 as posters, and 12 as late-breaking posters. We hope you will enjoy both the focus and the comprehensiveness of the program.

Our thanks go to the program committee: Erika Schneider, David Hunter, Thomas Link and Tim Mosher for their diligent work on the program and their thoroughness in rating the abstracts despite the short timeframe. We would also like to thank the sponsors, who have made this workshop possible. Special thanks and recognition go to the two organizations supporting the meeting: the Osteoarthritis Research Society International (OARSI) and the Paracelsus Medical University (PMU). The 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, PMU admits only 42 medical students per year who go through an intense 5 year study. The first students will graduate in 2008. As the PMU is currently under reconstruction, we are not able to hold the conference there, but you will get a chance to visit it during the poster session, which takes place in its library.

This workshop will be different from larger conferences in that it will provide more time for meeting people and for discussion. We have invited you to the slightly remote "Reiter Alm", overlooking Salzburg and the Alps, because we hope this will provide exactly the right atmosphere. We are confident that the "beauty and peace" of this place will make the transfers between here and the hotels in Salzburg worthwhile. The Reiter Alm is located in an area called the "Rupertiwinkel". A major Roman street, the Via Giulia Augusta II, crossed the river Saalach here. Today, this provides the demarcation of the Austrian/German border. Historically, however, the Rupertiwinkel and Salzburg Land always belonged together and share a common heritage. In the Vienna Congress of 1816, they were politically divided with Salzburg becoming part of Austria and the Rupertiwinkel a part of Bavaria (Germany).

Reiter Alm was built in 2000 on the site of an old farm in the community of Ainring. Today it serves various purposes: it is a show room for spa devices produced by a local company (Haslauer GmbH), it is a spa hotel, it has a very nice restaurant, and it contains a small convention center which we hope will be ideal for our purposes. Because of its multifunctionality, please do not be shocked if you see someone in bathing suit.

We hope you will travel safely and enjoy your time. It is our wish that the workshop will provide ample opportunity for building bridges between scientists working here in Europe and those working across the ocean; between those working in academia and those working in industry; between all those who are working with the various imaging methodologies; and between those developing imaging methods and those applying them. We hope that this workshop will be a good place to form new collaborations for combating osteoarthritis for the betterment of patients suffering from this disease. Most of all, we hope this workshop will be a place to form new friendships which are usually at the core and an important driving force of fruitful scientific collaboration.

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

OVERVIEW

TRAVEL INFORMATION

When going to the conference site by taxi, please tell the taxi driver that you need to go to:

Reiter Alm, 83404 Ainring / Ulrichshögl, Germany

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

We provide transportation from Salzburg to the conference site by bus.

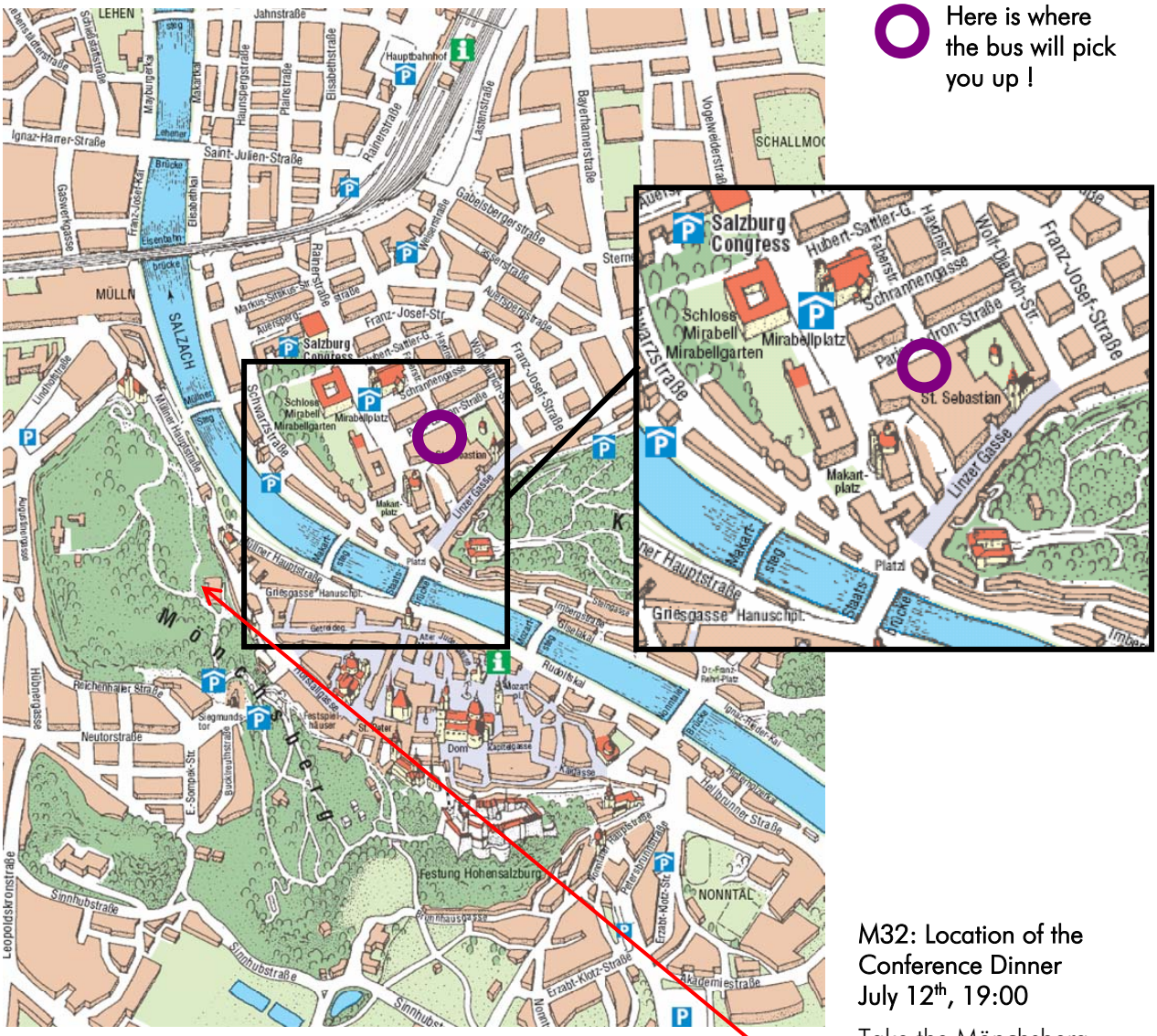
For pick up place and times, please see next page

BUS PICK UP POINT AND TIMES IN SALZBURG

Please be there 10 mins early. If you have problems finding the spot, please call + 43 664 4408153

Pick up times in Salzburg:

Wednesday,	11th July 2007	12:15 p.m.
Thursday,	12th July 2007	8:15 a.m.
Friday,	13th July 2007	8:15 a.m.
Saturday,	14th July 2007	9:00 a.m.



M32: Location of the Conference Dinner July 12th, 19:00

Take the Mönchsberg Elevator up the Mönchsberg to the Modern Art Museum and the M32 at Anton Neumayr Platz

PROGRAM AT A GLANCE

Wednesday, July 11th, 2007 – Reiter Alm

12:30 Registration Open, Lunch

14:00 – 14:10	Welcome by Felix Eckstein, Conference Organizer	
14:10 – 14:20	Welcome by Felix Sedlmayer, Vice-Rector, Paracelsus Medical University	
14:20 - 15:20	**Invited Speaker Session 1:**	**Diarthroidal Joint Anatomy & Pathology**
14:20-14:50	Reinhard Putz	DIARTHROIDAL JOINT ANATOMY
14:50-15:20	Thomas Aigner	DIARTHROIDAL JOINT PATHOLOGY
16:00 to 18:00	**Submitted Abstracts Session 1:**	**Joint Pathophysiology in OA**

Thursday, July 12th, 2007 – Reiter Alm

9:00 to 10:30	**Invited Speaker Session 2:**	**The Osteoarthritis Initiative (OAI)**
9:00-9:40	Michael Nevitt	THE OAI DESIGN, COHORT CHARACTERISTICS, AND OPPORTUNITIES FOR RESEARCH
9:40-10:00	Gayle Lester	NIH OPPORTUNITIES FOR USE OF OAI DATA
10:00-10:30	Erika Schneider	RESULTS OF THE OAI PILOT STUDIES
11:15 to 12:55	**Submitted Abstracts Session 2:**	**The OAI and other Multicenter Studies**
14:45 to 17:00	**Poster Session – *Library of the Paracelsus Medical University***	
14:45 – 15:30	Poster Session 1	(Presenters of Posters No. 1 to 14 at posters)
15:30 – 16:15	Poster Session 2	(Presenters of Posters No. 15 to 27 at posters)
16:15 – 17:00	Late Breaking Abstract Posters	(Presenters of Posters No. 28 to 39 at posters)
17:00 – 17:30	Tour of the University (for those interested)	
19:00	**Conference Dinner at the M32, Salzburg**	
	http://www.moenchsberg32.at/de-m32.shtml	

Friday, July 13th, 2007 – Reiter Alm

9:00 to 10:30	**Submitted Abstracts Session 3:**	**MRI Techniques and Animal Models**
11:00 to 13:00	**Submitted Abstracts Session 4:**	**Clinical Studies**
14:30 to 16:00	**Invited Speaker Session 3:**	**Regulatory Aspects of Imaging Biomarkers in OA**
14:30-15:00	Frits Lekkerkerker	EMEA PERSPECTIVE ON IMAGING MARKERS IN OA: LESSONS TO LEARN FROM THE USE OF DXA IN REGULATORY STUDIES ON OSTEOPOROSIS
15:00-15:30	Phil Conaghan	CLINICAL ENDPOINTS IN OA FOR THE VALIDATION OF IMAGING BIOMARKERS
15:30-16:00	Sarah Okada	FDA REGULATORY PERSPECTIVE ON IMAGING BIOMARKERS FOR OSTEOARTHRITIS
16:30 – 18:00	**Podium Discussion:**	**Where Do We Go From Here ?**
19:00	**Dinner at the Hahnei Huaba Beergarden, Ainring**	http://www.hahnei-huaba.de/

Saturday, July 14th, 2007

9:00 to 16:00	**Post Workshop Hiking Trip**	
21:00	**Chill out in the May Day Bar @ Hangar 7**	http://www.hangar-7.com/

PROGRAM IN DETAIL | WEDNESDAY JULY 11TH

- Reiter Alm -

12:15
Transfer Bus Leaving Salzburg to Reiter Alm
Bus Terminal at Paris Lodron Strasse (p. 5)
St. Sebastian Building

12:30 Registration Open, Lunch

14:00 – 14:10: Welcome by Felix Eckstein, Conference Organizer
Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University

14:10 – 14:20: Welcome by Felix Sedlmayer,
Vice-Rector, Paracelsus Medical University

Invited Speaker Session 1: Diarthroidal Joint Anatomy & Pathology

14:20 to 15:20 Session Chair: Felix Eckstein
(20 min presentation + 10 min discussion)

14:20- 14:50	**Reinhard Putz** Ludwig-Maximilians Universität, München DIARTHROIDAL JOINT ANATOMY
14:50- 15:20	**Thomas Aigner** Universität Leipzig DIARTHROIDAL JOINT PATHOLOGY

15:20 – 15:50 Coffee

Submitted Abstracts Podium Session 1: Joint Pathophysiology in OA

16:00 to 18:00 Session Chair: David Hunter

(12 min presentation + 8 min discussion)

16:00-16:20	*Conaghan P.G., **Rhodes L., *Hensor E.M.A., *Thomas C., *Emery P., ***Grainger A.J. *Academic Unit of Musculoskeletal Disease, University of Leeds, **Academic Units of Medical Physics, University of Leeds, ***Department of Radiology, Chapel Allerton Hospital, Leeds UK. OSTEOARTHRITIS WAS THE CORRECT NAME!
16:20-16:40	*/**Lammentausta E., *Kiviranta P., ***Töyräs J., *Hyttinen M.M., ****Kiviranta I., *Jurvelin J.S., **Nieminen M.T. * University of Kuopio, Kuopio, Finland, ** Oulu University Hospital, Oulu, Finland, *** Kuopio University Hospital, Kuopio, Finland, **** Jyväskylä Central Hospital, Jyväskylä, Finland QUANTITATIVE MRI OF PARALLEL CHANGES OF ARTICULAR CARTILAGE AND TRABECULAR BONE
16:40-17:00	*/**Roemer F.W., **Guermazi A, ***Hunter D.J., ***Niu J., ***Zhang Y., *** Felson D.T. * Department of Radiology, Klinikum Augsburg, Augsburg, Germany, ** Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A., *** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A. PREVALENCE OF MRI-DETECTED RELEVANT MENISCAL ABNORMALITIES AND ITS RELATION TO JOINT EFFUSION IN KNEES WITHOUT RADIOGRAPHIC OSTEOARTHRITIS
17:00-17:20	*Frobell R.B., *Roos H.P., *Roos E.M., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., *** Tamez J., * Lohmander L.S. * Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden, ** Pfizer Global Research & Development, Ann Arbour, MI, USA,*** VirtualScopics Inc ,NY, USA THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – DEVELOPMENT OF POST TRAUMATIC BONE MARROW LESIONS, JOINT FLUID AND CARTILAGE VOLUME IN KNEES TREATED SURGICALLY OR NON-SURGICALLY
17:20-17:40	*Li X., *Bolbos R.I., **Ma C.B., *Link T.M., *Majumdar S. * Musculoskeletal Quantitative Imaging Research (MQIR) group, Department of Radiology, University of California, San Francisco (UCSF), San Francisco, CA, USA, ** Department of Orthopaedic Surgery, UCSF, San Francisco, CA, USA QUANTITATIVE ASSESSMENT OF BONE MARROW EDEMA PATTERN AND OVER-LYING CARTILAGE IN OSTEOARTHRITIC AND ACL-INJURED KNEES USING HIGH FIELD MR IMAGING AND SPECTROSCOPY
17:40-18:00	* Frobell R.B., *Roos E.M., *Roos H.P., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., ***Tamez J., * Lohmander L.S. * Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden, ** Pfizer Global Research & Development, Ann Arbor, MI, USA,*** VirtualScopics Inc ,NY, USA THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – ASSOCIATED ANATOMI-CAL LESIONS AND BONE MARROW LESIONS SUGGEST DIFFERENCES IN TRAUMA SEVERITY.

18:15 Bus transfer to Salzburg

PROGRAM IN DETAIL | THURSDAY JULY 12TH

- Reiter Alm -

8:15 Transfer Bus Leaving Salzburg / Bus Terminal at Paris Lodron Strasse (see page 5)

Invited Speaker Session 2: The Osteoarthritis Initiative (OAI)

9:00 to 10:30 Session Chair: Tim Mosher

(12-25 min presentation, 8-15 min discussion)

9:00- 9:40	Michael Nevitt UCSF, San Francisco THE OAI DESIGN, COHORT CHARACTERISTICS, AND OPPORTUNITIES FOR RESEARCH
9:40- 10:00	Gayle Lester NIH; Bethesda NIH OPPORTUNITIES FOR USE OF OAI DATA
10:00- 10:30	Erika Schneider The Cleveland Clinic Foundation, Cleveland RESULTS OF THE OAI PILOT STUDIES

10:30 – 11:10 Coffee Break

Submitted Abstracts Oral Session 2: The OAI and other Multicenter Studies

11:15 to 12:55 Session Chair: Michael Nevitt

12 min presentation + 8 min discussion

11:15- 11:35	*Hunter DJ, *Niu J, *Zhang YQ, **Totterman S, **Tamez J, ***Dabrowski C, ***Davies R, ****Hellio Le Graverand-Gastineau MP, *****Luchi M, ******Tymofyeyev Y, ******Beals CR for the OAI Investigators Group. *BUSM, Boston, U.S.A.,**VirtualScopics, Rochester, NY, USA.,***GSK, Collegeville, PA, USA., ****Pfizer, Ann Arbor, Michigan, USA.,*****Novartis, East Hanover, NJ, USA., ******MERCK, Rahway, NJ, USA. CHANGE IN CARTILAGE MORPHOMETRY: A SAMPLE OF THE PROGRESSION COHORT OF THE OSTEOARTHRITIS INITIATIVE (OAI)
11:35- 11:55	*Maschek S., *Wirth W., **Hellio-Le Graverand M.P., **Wyman B.,*Hudelmaier M., ***Nevitt M., *Eckstein F., and the Osteoarthritis Initiative (OAI) Investigators group * Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Pfizer Global Research and Development, Ann Arbor MI, USA, *** Dept. of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA CHANGE IN FEMOROTIBIAL CARTILAGE VOLUME AND SUBREGIONAL CARTILAGE THICKNESS OVER 1 YEAR, DATA FROM THE OSTEOARTHRITIS INITIATIVE PROGRESSION SUBCOHORT

11:55- 12:15	*Lo G.H., *McAlindon T.E., **Niu J., **Zhang Y., ***Beals C., ****Dabrowski C., *****Graverand-Gastineau M., ******Luchi M, **Hunter DJ * Tufts-New England Medical Center, Boston, MA; ** Boston University Medical Center, Boston, MA; *** Merck Pharmaceuticals, Rahway, NJ; **** GlaxoSmithKline, Collegeville, PA; ***** Pfizer, Ann Arbor, MI; ****** Novartis, East Hanover, NH, USA STRONG ASSOCIATION OF BONE MARROW LESIONS AND EFFUSION WITH PAIN IN OSTEOARTHRITIS
12:15- 12:35	*Hellio-Le Graverand M.P., *Wyman B., *Buck R., **Wirth W., *Hudelmaier M., *Eckstein F. for the A 9001140 Investigators * Pfizer Global Research and Development, Ann Arbor MI, USA, ** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany TWELVE MONTH LONGITUDINAL CHANGE IN REGIONAL CARTILAGE MORPHOLOGY IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY
12:35- 12:55	*Krishnan, N., **Wyman, B. **Buck, R., **Hellio, M-P, ***Tamez, J. ***Totterman S. * McKenzie, C., *Burstein, D., for the A9001140 Investigators * Beth Israel Deaconess Medical Center, Boston MA, USA, ** Pfizer Global Research and Development, Groton, CT, USA, *** VirtualScopics, Rochester, NY, USA CROSS SECTIONAL ANALYSIS of dGEMRIC MEASUREMENTS IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY

13:00 Lunch at the Reiter Alm

14:15 Bus transfer to Paracelsus Medical University

Poster Session

- Library of Paracelsus Medical University -

All posters will be mounted throughout the entire afternoon – for titles see pages 16 ff.

14:45 – 15:30 Poster Session 1 (Presenters of Posters No. 1 to 14 at posters)

15:30 – 16:15 Poster Session 2 (Presenters of Posters No. 15 to 27 at posters)

16:15 – 17:00 Late Breaking Posters (Presenters of Posters No. 28 to 39 at posters)

Refreshments kindly sponsored by Synthes

SYNTHES®

17:00 – 17:30 Tour of the University (for those interested)

19:00 Conference Dinner

Restaurant M32, Salzburg

http://www.moenchsberg32.at/de-m32.shtml

Dinner kindly sponsored by MerckSerono

(how to get there *see page 5* and ticket)

MERCK SERONO

PROGRAM IN DETAIL | FRIDAY JULY 13TH

- Reiter Alm -

8:15 Transfer Bus Leaving Salzburg / Bus Terminal at Paris Lodron Strasse (see page 5)

Submitted Abstracts Oral Session 3: MRI Techniques and Animal Models

9:00 to 10:30 Session Chair: Erika Schneider

(10 min presentation + 5 min discussion)

9:00- 9:15	*Li W, *Scheidegger R, *Wu Y, **Vu AT, and *Prasad PV *Department of Radiology, Evanston Northwestern Healthcare, Evanston, IL, USA., **GE Healthcare, Waukesha, WI, USA. VALIDATION OF 3D LOOK-LOCKER TECHNIQUE FOR DGEMRIC
9:15- 9:30	*Nishii T., **Kuroda K., **Matsuoka Y., *Yoshikawa H. * Osaka University Medical School, Suita, Osaka, Japan, ** Institute of Biomedical Research and Innovation, Kobe, Hyogo, Japan ASSESSMENT OF KNEE CARTILAGE T2 IN RESPONSE TO MECHANICAL LOADING AT 3.0 T MR IMAGING
9:30- 9:45	*/**Lammentausta E., *Kiviranta P., ***Töyräs J., ****Kiviranta I., */***Jurvelin J.S. , **Nieminen M.T. * University of Kuopio, Kuopio, Finland,** Oulu University Hospital, Oulu, Finland, *** Kuopio University Hospital, Kuopio, Finland,**** Jyväskylä Central Hospital, Jyväskylä, Finland DEGENERATION-INDUCED DEPTH-WISE VARIATION IN T2 OF HUMAN PATELLAR CARTILAGE
9:45- 10:00	*,**Wang C., *Borthakur A., *Witschey W.R.T., *Reddy R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA ** Depts. Of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA T1RHO RELAXATION EVALUATION OF KNEE OA IN A GUINEA PIG MODEL
10:00- 10:15	Piscaer T.M., Waarsing J.H.., Kops N., Pavljasevic P., Verhaar J.A.N., van Osch G.J.V.M., Weinans H. Erasmus University Medical Center, the Netherlands IN-VIVO IMAGING OF CARTILAGE DEGENERATION IN SMALL ANIMAL MODELS USING MICRO-CT-ARTHROGRAPHY.
10:15- 10:30	*Gassner R., ** Ferretti M., **Deschner J., **Srinivasan A., **Wang Z., **Perera P., Sowa G., ***Piesco N., ****Salter R., **Agarwal S. * Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria, ** Division of Oral Biology, Ohio State University, Columbus, OH, USA , *** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA, **** Department of Orthopaedic Surgery, Hospital for Sick Children, Toronto, Ontario, Canada BIOMECHANICAL SIGNALS SUPPRESS PRO-INFLAMMATORY RESPONSES IN ARTICULAR CARTILAGE IN VIVO

10:30 – 11:00 Coffee Break

Submitted Abstracts Oral Session 4: Clinical Studies

11:00 to 13:00 Session Chair: Thomas Link

(12 min presentation + 8 min discussion)

11:00- 11:20	***Mamisch, T.C., *Welsch G.Z., * Szomolanyi P, **Marlovits S, *Trattnig S * AKH Vienna, Department of Radiology, Vienna, Austria, ** AKH Vienna, Department of Trauma Surgery, Vienna, Austria, *** University Bern, Department of Orthopedic Surgery, Bern, Switzerland BIOCHEMICAL IMAGING OF CARTILAGE REPAIR: COMPARISON OF NON-CONTRAST AND CONTRAST TECHNIQUES FOR ASSESSMENT OF CARTILAGE REPAIR TISSUE COMPOSITION AND MATURATION OVER TIME.
11:20- 11:40	*Hunter DJ, *Niu J, *Zhang YQ, *McLennan C, *LaValley M, **Hudelmaier M, **Eckstein F, *Felson DT. *BUSM, Boston, MA, **Institute of Anatomy & Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria. MEASURES OF CARTILAGE MORPHOMETRY BY RADIOGRAPHIC OA STATUS; THE FRAMINGHAM STUDY
11:40- 12:00	*Kim, Y.-J., *Jessel, R., *Dudda, M., **Mamisch, T.C., *Millis, M.B. * Children's Hospital-Boston, Harvard Medical School, Boston, MA, USA, ** University of Bern, Bern, Switzerland APPLICATION OF DGEMRIC IN ASSESSING CARTILAGE DAMAGE IN HIP DYSPLASIA AND FEMOROACETABULAR IMPINGEMENT
12:00- 12:20	*Guermazi A, *, **Roemer F.W., ***Hunter D.J., *** Neogi T., ***Niu J., *** Felson D.T. * Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A., ** Department of Radiology, Klinikum Augsburg, Augsburg, Germany, *** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A. OSTEOPHYTOSIS AND RADIOGRAPHIC OSTEOARTHRITIS IN KNEES WITH MODERATE TO ADVANCED CHONDROPATHY ASSESSED BY MRI
12:20- 12:40	*Oka H., *Yoshimura N., *Muraki S., *Mabuchi A., **Nakamura K., **Kawaguchi H *22nd Century Medical Center, **Sensory & Motor System Medicine, The University of Tokyo, Tokyo, Japan FULL-AUTOMATIC MEASUREMENT OF KNEE OSTEOARTHRITIS PARAMETERS BY A NOVEL COMPUTER-ASSISTED SYSTEM ON STANDARD RADIOGRAPHS
12:40- 13:00	*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Pettersen P., ***Christiansen C. * Department of Computer Science, University of Copenhagen, Denmark,** Nordic Bioscience (NB), Herlev, Denmark *** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark LONGITUDINAL CHANGES IN CARTILAGE SURFACE INCONGRUITY: A MARKER OF PREDISPOSITION FOR OA?

13:00 Lunch at the Reiter Alm

Invited Speaker Session 3: Regulatory Aspects of Imaging Biomarkers in OA

14:30 to 16:00 Session Chair: Gayle Lester

(20 min presentation + 10 min discussion)

14:30-15:00	**Frits Lekkerkerker** Medicines Evaluation Board Netherlands EMEA PERSPECTIVE ON IMAGING MARKERS IN OA: LESSONS TO LEARN FROM THE USE OF DXA IN REGULATORY STUDIES ON OSTEOPOROSIS
15:00-15:30	**Phil Conaghan** University of Leeds CLINICAL ENDPOINTS IN OA FOR THE VALIDATION OF IMAGING BIOMARKERS
15:30-16:00	**Sarah Okada** Food and Drug Administration (FDA), Rockville, MD FDA REGULATORY PERSPECTIVE ON IMAGING BIOMARKERS FOR OSTEOARTHRITIS (RECORDED PRESENTATION AND TELECONFERENCE DISCUSSION)

16:00 – 16:30 Coffee Break

Podium Discussion: Where Do We Go From Here ?

16:30 – 18:00 Podium: Gayle Lester, Erika Schneider, Phil Conaghan, David Hunter, Frits Lekkerkerker, Thomas Link, Tim Mosher, Michael Nevitt

18:00 Closing Remarks

18:15 Bus transfer or walk (depending on weather) to the Hahnei Huaba Beergarden or to Salzburg (for those who cannot stay)

19:00 Dinner at the Hahnei Huaba Beergarden (at own cost)

Rupertiweg 13a 83404 Ainring http://www.hahnei-huaba.de/

23:00 Bus transfer to Salzburg

PROGRAM IN DETAIL | SATURDAY JULY 14TH

Post Workshop Hiking Tour

9:00 Bus Leaving Salzburg / Bus Terminal at Paris Lodron Strasse (see page 4)
9:30 Bus Leaving Reiter Alm (for those who stay there)

We encourage all participants of the workshop – fit or unfit, with or without family - to join us for the "Post Workshop Hiking Trip". This will give us the opportunity to discuss and solve all unresolved issues of imaging in osteoarthritis well above sea level.

There will be a bus pick up at 9 a.m. from the bus terminal at Paris Lodron Strasse in central Salzburg, with the bus taking us to either the Untersberg cable car (picture below middle) or the Predigtstuhl cable car (picture below left)
http://members.aon.at/untersbergbahn/Untersbergbahn_e.htm
http://www.predigtstuhl-bahn.de/

The decision will be made on Friday depending on weather conditions. With sunny weather, little winds, and clear sky, Untersberg provides the most spectacular views that you will have experienced, looking down over Salzburg on the one side and over the Austrian and German alpine peaks on the other side.

The cable car (18 € return ticket) takes you from 456 to 1776 m in altitude in only 8.5 min. At about 3 min walking distance from the station there is the "Hochalm" where great Austrian dishes are served. There is a relatively easy walk to the "Salzburger Hochthron" summit that takes about 45 minutes. However, good shoes are recommended. We plan to take an easy stroll on the summit, but those who like to take it easy can simply stay at the "Hochalm" and wait for the more ambitious ones to return. Those who are very competitive can continue from the summit to the Mittagsscharte for another 45 mins or so and then return. At the end, we will all meet back at the "Hochalm" near the cable car station.

If the weather is less favourable, Predigtstuhl is less exposed, but nevertheless offers splendid views onto Bad Reichenhall, Salzburg and the alps.

Predigtstuhl is the oldest cable car in the world, built in 1927 and still existing in its original form. The return trip is 17 € per adult. Directly at the the top you will find Germany's highest hotel at 1600 m altitude with a wonderful panorama terrace. From there it only is an easy, flat 15 min walk to the Almhütte Schlegelmulde, where you can enjoy Bavarian dishes and beer.

Those who would like to move on can follow the path for another 30 min to the first peak with a more splendid view, then continue hiking as long as they like towards the South, and return when they feel it is time to join the others at Schlegelmulde.

We plan to return from the top at 3:30 p.m. to catch the bus at 4 p.m. and to be back in Salzburg no later than 5:00 p.m. However, you can leave any time earlier, and may take a taxi, either directly to the airport or back to your hotel.

16:00 Bus transfer to airport hotel and to Salzburg (Paris Lodron Strasse)

Chill out in the May Day Bar @ Hangar 7 (for those who never like to stop)

21:00 Those who want to have a great time on the last evening in one of the most scenic bars in the world, meet in the "May Day Bar" on the 2nd floor @ Hangar 7 @ the airport. Enjoy a spectacular view onto Dietrich Mateschitz's (Red Bull) private airplane, helicopter and Formula 1 car collection. If you are still around, don't miss it: if you haven't seen it, you haven't seen Salzburg. http://www.hangar-7.com/

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POSTER SESSIONS | THURSDAY JULY 12TH

- Library of Paracelsus Medical University –

14:45 – 15:30 Poster Session 1 (Presenters of Posters No. 1 to 14 at posters)

1	Bouchgua M., Alexander K., Carmel E.N., Beauchamp G., Richard H, Laverty S. Faculty of Veterinary Medicine, University of Montreal, St-Hyacinthe, QC, Canada. BONE MINERAL DENSITY ASSESSED BY COMPUTED TOMOGRAPHY IN AN IN VIVO RABBIT MODEL OF OSTEOARTHRITIS
2	*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A. * Chemistry Department, New York University, New York, NY, ** Radiology Department, New York University, New York, NY. CHEMICAL EXCHANGE SATURATION TRANSFER FOR ASSESSING PROTEOGLYCANS IN CARTILAGE
3	*Gassner R., **Long P., ***Evans C., ****Deschner J., **Piesco N., ****Agarwal S. * Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria, ** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA, *** Department of Orthopedic Surgery - Brigham & Women's Hospital, Harvard Medical School, Boston, USA, **** Division of Oral Biology, Ohio State University, Columbus, OH, USA CHONDROCYTES SENSING MECHANICAL STRAIN DISPLAY ANTI-INFLAMMATORY ACTIONS IN VITRO
4	*Anandacoomarasamy A., *Giuffre B., **Stanwell P., ***Fransen M., *Sambrook P., *March L. * Royal North Shore Hospital, Sydney, Australia, ** University of Sydney, Sydney, Australia, *** The George Institute, Sydney, Australia COMPARISON OF DGEMRIC USING CORONAL AND SAGITTAL IMAGE ACQUISTION IN AN OBESE POPULATION UNDERGOING WEIGHT LOSS
5	*,**Winalski C.S., *Schneider E., **Yoshioka H., ***Shortkroff S., ****Rosen G.M. * Division of Radiology, Cleveland Clinic Foundation, Cleveland, OH, USA, ** Department of Radiology, Brigham & Women's Hospital, Boston, MA, USA, *** Orthopedic Research Laboratory, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, USA, ****Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, and NitroSci, Baltimore, MD, USA DENDRIMER-LINKED NITROXIDE MR CONTRAST AGENTS FOR CARTILAGE IMAGING: DISTRIBUTION IN CARTILAGE, PH AND CHARGE DEPENDENCE OF SOLUTE DIFFUSION
6	Fleming B.C., Bowers M.E., Tung G.A., Leventhal E.L., Trinh N., Crisco J.J., Kimia B.B. Brown Medical School, Providence, RI, USA EFFECTS OF ACL INTERFERENCE SCREWS ON FEMOROTIBIAL CARTILAGE THICKNESS MEASUREMENTS USING 1.5T AND 3T MRI
7	*Bangerter N.K., **Staroswiecki E., **Gurney P.T., *Hargreaves B.A., *Gold G.E. * Department of Radiology, Stanford University, Stanford, CA, USA, ** Department of Electrical Engineering, Stanford University, Stanford, CA, USA HIGH RESOLUTION IN VIVO SODIUM MRI OF ARTICULAR CARTILAGE AT 7T

8	*Hudelmaier M., *Wirth W., ** Charles C.H., ***Kraus V.B., ****Wyman B., ****Hellio Le Graverand-Gastineau M.-P., *Eckstein F. * Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Duke Image Analysis Laboratory, Durham NC, USA, *** Division of Rheumatology & Immunology, Duke University Medical Center, Durham NC, USA, **** Pfizer Global Research and Development, Ann Arbor MI, USA HOW DOES CHOICE OF COMPUTATIONAL ALGORITHM AND FEMORAL REGION OF INTEREST AFFECT MEASURES OF CARTILAGE MORPHOLOGY IN THE KNEE
9	Joyce M., Ryan J., Rainford L.A., Last J., Brennan P.C. University College Dublin, Dublin, Ireland IMPACT OF VARYING THE X-RAY SOURCE DETECTOR DISTANCE IN X-RAY EXAMINATION OF THE ARTHRITIC CERVICAL SPINE
10	*Wirth W., **Kunz M.,***Inglis D., ***Adachi R., ***Beattie K., **Hudelmaier M., *Eckstein F. * Chondrometrics GmbH, Ainring, Germany, ** Institute of Anatomy & Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria, *** Center for Appendicular MRI Studies, McMaster University, Hamilton, ON, Canada IMPACT ON REGION SIZE ON THE TEST-RETEST PRECISION OF REGIONAL CARTILAGE THICKNESS MEASUREMENTS IN THE FEMOROTIBIAL JOINT
11	*Marijnissen A.C.A., **Vincken K.L., *Vos P.A.J.M., ***Saris D.B.F., **Viergever M.A., *Bijlsma J.W.J., **Bartels L.W., *Lafeber F.P.J.G. *Rheumatology & Clin. Immunology, UMC Utrecht, The Netherlands, **Image Sciences Institute, UMC Utrecht, The Netherlands, ***Orthopaedics, UMC Utrecht, The Netherlands KNEE IMAGES DIGITAL ANALYSIS (KIDA): A NOVEL METHOD TO QUANTIFY INDIVIDUAL RADIOGRAPHIC FEATURES OF KNEE OSTEOARTHRITIS IN DETAIL.
12	*Kunz M., **Cahue S., **Marshall M., *Wirth W, *Hudelmaier M., **Sharma L., *Eckstein F. * Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA LONGITUDINAL CHANGE AND PATTERN OF PATELLAR CARTILAGE LOSS IN OA PATIENTS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT
13	*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Pettersen P., ***Christiansen C. * Department of Computer Science, University of Copenhagen, Denmark, ** Nordic Bioscience (NB), Herlev, Denmark *** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark LONGITUDINAL CHANGES IN CARTILAGE SURFACE SMOOTHNESS: A MARKER OF PROGRESSION DURING MODERATE OA?
14	*Williams T.G., ***Bowes M., *Taylor C.J., *Hutchinson C.E, **Waterton J.C., **Maciewicz R.A., **Holmes A.P. * Imaging Science and Biomedical Engineering, University of Manchester, UK. ** AstraZeneca, Macclesfield, UK. *** Imorphics, Manchester, UK. MORE SENSITITVE ANALYTICAL MEASURES CANNOT COMPENSATE FOR PATIENT HETEROGENEITY WITH RESPECT TO ANNUALISED CARTILAGE LOSS

15:30 – 16:15 Poster Session 2 (Presenters of Posters No. 15 to 27 at posters)

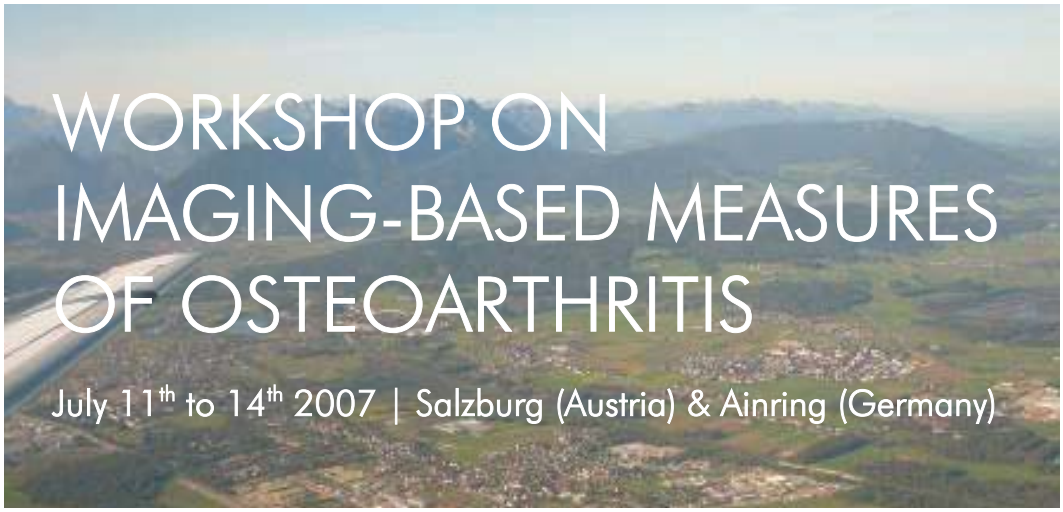
15	*Tamez-Pena J., * Barbu-McInnis M., * Totterman S. *VirtualScopics, Rochester, NY, USA MRI BASED METHDOLOGY FOR THE QUANTITATIVE EVALUATION OF SUBCHONDRIAL BONE PLATE SURFACE CHANGES
16	*Fischer K.J., *Thoomakuntla B.R., *Waller A.A., **Bilgen M., **McIff T.E., **Toby E.B. * University of Kansas, Lawrence, KS, USA, ** University of Kansas Medical Center, Kansas City, KS, USA MRI-BASED MODELING OF RADIOCARPAL JOINT CONTACT PRESSURE DISTRIBUTIONS DURING FUNCTIONAL LOADING: CURRENT VALIDATION DATA
17	Bouchgua M., Alexander K., d'Anjou M.A., Girard C., Beauchamp G., Richard H., Laverty S. Faculty of Veterinary Medicine, University of Montreal, St Hyacinthe, QC, Canada. MULTIMODALITY IMAGING OF TEMPORAL CHANGES IN KNEE OSTEOARTHRITIS LESIONS IN AN IN VIVO RABBIT MODEL
18	*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A. * Chemistry Department, New York University, New York, NY, ** Radiology Department, New York University, New York, NY. NA-MRI: AN EARLY MARKER FOR CARTILAGE DEGENERATION
19	*Stok K.S., **Pelled G., **Zilberman Y., **Kallai I., **Gazit D., *Müller R. * Institute for Biomedical Engineering, University and ETH Zürich, Zürich, Switzerland , ** Skeletal Biotech Lab, Hebrew University, Jerusalem, Israel OSTEOARTHRITIS IMAGING USING CONFOCAL MICROSCOPY AND MICRO-COMPUTED TOMOGRAPHY – A MURINE STUDY
20	*Sochor, M.A., *,**Witschey II, W.R.T., *,**Borthakur, A., *,**Reddy, R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA USA ** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA OSTEOARTHRITIS PACKAGE: AN MRI PROTOCOL FOR DETECTION OF EARLY OA.
21	*Wlk MV, *Chochole M, **Landsiedl F * Herz-Jesu Hospital Vienna, Orthopedic Dep., Austria, ** Orthopedic Hosp. Speising Vienna, 1. Dep., Austria PATHOLOGY OF THE DISCUS TRIANGULARIS OF THE WRIST IN MRI AND ARTHROSCOPY: A COMPARISON
22	*Haslam J., *Lacey T., *Brett A., **Tengowski M.W. * Optasia Medical Ltd, Manchester, UK, ** Pfizer Global Research & Development, Ann Arbor, MI, USA REPRODUCIBILITY OF AUTOMATED RADIOGRAPHIC JOINT SPACE WIDTH AND FRACTAL SIGNATURE ANALYSIS MEASUREMENTS IN THE MEDIAL TIBIOFEMORAL COMPARTMENT OF THE KNEE
23	*Sasho T., *Nakagawa K., *Ochiai N., *Ogino S., *Nagashima R., *Matsuki K., ** Wada Y., **Watanabe A., *Moriya H. * Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University. Japan, ** Department of Orthopaedic Surgery, Teikyo University Chiba Medical Center, Japan SEMI-AUTOMATIC EVALUATION OF DISEASE SEVERITY OF OSTEOARTHTITIS OF THE KNEE FROM MRI USING NEWLY DEVELOPED SOFTWARE

24	*Qazi A.A., **Karsdal M.A., ***Christiansen C., **Dam E.B. * Image Group, Department of Computer Science, University of Copenhagen, Denmark, ** Nordic Bioscience (NB), Herlev, Denmark, *** Center for Clinical and Basic Research, Ballerup, Denmark SEPARATION OF HEALTHY AND EARLY OA BY QUANTIFICATION OF CARTILAGE HOMOGENEITY FROM MRI: A LONGITUDINAL STUDY
25	*Wyman, B. *Buck, R.,*Hellio, M-P, **Krishnan, N.,** McKenzie, C., ***Totterman S. ****Charles, C. **Burstein, D, ***Tamez, J., for the A9001140 Investigators * Pfizer Global Research and Development, Groton, CT, USA, ** Beth Israel Deaconess Medical Center, Boston MA, USA, *** VirtualScopics, Rochester, NY, USA, ****Duke Image Analysis Laboratory, Durham, NC, USA SIX MONTH LONGITUDINAL CHANGE IN DGEMRIC MEASUREMENTS IN A MULTI-CENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY
26	*,**Witschey II W.R.T., *,**Borthakur A., *,** Elliott M.A., *Sochor M.A., *,**Reddy R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA, ** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA SLIPS: AN MRI PULSE SEQUENCE FOR RAPID AND QUANTITATIVE 3D T1RHO MRI OF CARTILAGE IN A CLINICAL SETTING.
27	*Waarsing JH, **Rozendaal RM, **Bierma-Zeinstra SM, *Weinans, H. * Dept. of orthopedics, Erasmus Medical Center, Rotterdam, The Netherlands, ** Dept. of General Practice, Erasmus Medical Center, Rotterdam, The Netherlands STATISTICAL APPEARANCE MODELS OF THE PROXIMAL FEMUR IN DXA SCANS ASSOCIATE WITH STATE AND PROGRESSION OF CLINICAL OA.

16:15 – 17:00 Late Breaking Poster Session (Presenters of Posters No. 28 to 39 at posters)

28	*Bolbos R.I., *Zuo J., *Banerjee S., *Cheng J., *Link T.M., **Ma B.C., *Li X., *Majumdar S. *Musculoskeletal and Quantitative Imaging Research Group, Department of Radiology, University of California San Francisco, CA, USA, ** Department of Orthopaedic Surgery, University of California San Francisco, CA, USA INTERRELATIONSHIP BETWEEN TRABECULAR BONE AND ARTICULAR CARTILAGE OF THE KNEE JOINT IN EARLY OA USING PARALLEL MRI AT 3T
29	*Carballido-Gamio J., *Link T.M., *Majumdar S. * University of California, San Francisco, San Francisco, CA, USA NEW TECHNIQUES FOR CARTILAGE MRI RELAXATION TIME ANALYSIS
30	*Eckstein F., *Stein V., *Lengfelder V., *Hudelmaier M., *Wirth W., **Cahue S., **Marshall M., **Sharma L. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA REGIONAL CARTILAGE LOSS IN PATIENTS WITH FEMOROTIBIAL OSTEOARTHRITIS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT
31	*Wong A.K.O., **Inglis D. Ph.D., ***Beattie K.A. Ph.D., ***Adachi J.D. M.D. FRCP(C) * Department of Biology, McMaster University, Hamilton, ON, Canada, ** Department of Civil Engineering, McMaster University, Hamilton, ON, Canada, *** Department of Medicine, McMaster University, Hamilton, ON, Canada *(continues on next page)*

	REPRODUCIBILITY OF COMPUTER-ASSISTED JOINT ALIGNMENT MEASUREMENT IN KNEE RADIOGRAPHS
32	*Kennan R.P., **Rasa C., **Loewrigkeit C., **Lowitz K., *Liu H., **Ronan, J. ,**Wickham L. A, **Visco D. * Merck & Co Inc, *Imaging, ** Laboratory of Animal Resources, Rahway, NJ, USA IN VIVO HIGH FIELD T2 MAPPING OF CARTILAGE DEGRADATION IN A RAT MODEL OF OSTEOARTHRITIS INDUCED BY PARTIAL MENISCAL TRANSECTION.
33	*Koo S., **Hargreaves B.A., **Bangerter N.K., *,***Andriacchi T.P., **Gold G.E. * Department of Mechanical Engineering, Stanford University, Stanford, California, USA, ** Department of Radiology, Stanford University, Stanford, California, USA, *** Department of Orthopaedic Surgery, Stanford University, Stanford, California, USA AUTOMATIC SEGMENTATION OF KNEE ARTICULAR CARTILAGE FROM MRI: A MULTI-CONTRAST AND MULTI-DIMENSIONAL APPROACH
34	*Losina E., **Emrani P.S., **Kessler C.L., **Reichmann W.M., **Wright E.A., ***McAlindon T.E., **Katz J.N. * Brigham and Women's Hospital & Boston Univ. School of Public Health, Boston, MA, USA, ** Brigham and Women's Hospital, Boston, MA, USA, *** Tufts-New England Med. Center, Boston, MA, USA. INFLUENCE OF RADIOGRAPHIC VIEW AND FOLLOW-UP TIME ON THE ANNUAL RISK OF PROGRESSION OF AT LEAST ONE K-L GRADE IN KNEE OSTEOARTHRITIS (OA): AN ANALYTIC LITERATURE SYNTHESIS
35	*Losina E., **Meredith D.S., ***Neumann G., ***Yoshioka H., ***Lang P., ***Katz J.N. *Brigham and Women's Hospital, Boston, MA & Boston Univ. School of Public Health, Boston, MA, USA, **Harvard Medical School, Boston, MA, USA, ***Brigham and Women's Hospital, Boston, MA, USA. USING MRI FOR EMPIRICAL EVALUATION OF THE WHOLE JOINT HYPOTHESIS FOR THE PATHOGENESIS OF KNEE OSTEOARTHRITIS
36	*Hunter DJ, *Niu J, **Totterman S, **Tamez J, ***Hellio Le Graverand-Gastineau MP, ****Beals C, *****Maschek S, ***** Hudelmaier M, ***** Eckstein F. *BUSM, Boston, U.S.A, **VirtualScopics, Rochester, NY, USA, ***Pfizer, Ann Arbor, Michigan, USA. ****MERCK, Rahway, NJ, USA, ***** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany COMPARISON OF TWO MRI-BASED TECHNIQUES FOR MEASURING CHANGE IN CARTILAGE MORPHOLOGY OVER ONE YEAR IN THE OAI PROGRESSION SUBCOHORT
37	*Sonka M., **Zhang X., ***Millington S. * The University of Iowa. Iowa City IA, USA, ** Medical Imaging Applications, LLC, Coralville IA, USA, *** Royal London Hospital, Whitechapel, London, UK THREE-DIMENSIONAL SEGMENTATION AND ANALYSIS OF ARTICULAR CARTILAGE
38	*Stahl R., *Li, X., *Majumdar, S., **Luke, A., *Link, T.M. * Department of Radiology, University of California, San Francisco, CA, U.S.A., ** Department of Orthopedic Surgery, University of California, San Francisco, CA, U.S.A. T1RHO, T2 AND FOCAL CARTILAGE PATHOLOGY IN PHYSICALLY ACTIVE AND SEDENTARY HEALTHY SUBJECTS VERSUS EARLY OA PATIENTS
39	*Wiener E., *Settles M., *Weirich G., *Rummeny E.J. *Klinikum rechts der Isar, Technische Universität München, München, Germany THE QUANTIFICATION OF RELAXATION EFFECTS, DYNAMICS AND SPATIAL DISTRIBUTIONS OF IONIC AND NON-IONIC CONTRAST AGENTS IN ARTICULAR CARTILAGE AT 1.5 T



WORKSHOP ON IMAGING-BASED MEASURES OF OSTEOARTHRITIS

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Abstract Book

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SUBMITTED ABSTRACTS PODIUM SESSION 1: JOINT PATHOPHYSIOLOGY IN OA

Wednesday, July 11th, 2007: 16:00 to 18:00 Session Chair: David Hunter

(12 min presentation + 8 min discussion)

16:00-16:20	*Conaghan P.G.,**Rhodes L.,*Hensor E.M.A.,*Thomas C.,*Emery P.,***Grainger A.J. *Academic Unit of Musculoskeletal Disease, University of Leeds, **Academic Units of Medical Physics, University of Leeds, ***Department of Radiology, Chapel Allerton Hospital, Leeds UK. OSTEOARTHRITIS WAS THE CORRECT NAME!
16:20-16:40	*/**Lammentausta E., *Kiviranta P., ***Töyräs J., *Hyttinen M.M., ****Kiviranta I., *Jurvelin J.S., **Nieminen M.T. * University of Kuopio, Kuopio, Finland, ** Oulu University Hospital, Oulu, Finland, *** Kuopio University Hospital, Kuopio, Finland, **** Jyväskylä Central Hospital, Jyväskylä, Finland QUANTITATIVE MRI OF PARALLEL CHANGES OF ARTICULAR CARTILAGE AND TRABECULAR BONE
16:40-17:00	*/**Roemer F.W., **Guermazi A, ***Hunter D.J., ***Niu J., ***Zhang Y., *** Felson D.T. * Department of Radiology, Klinikum Augsburg, Augsburg, Germany,** Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A.,*** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A. PREVALENCE OF MRI-DETECTED RELEVANT MENISCAL ABNORMALITIES AND ITS RELATION TO JOINT EFFUSION IN KNEES WITHOUT RADIOGRAPHIC OSTEOARTHRITIS
17:00-17:20	*Frobell R.B., *Roos H.P., *Roos E.M., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., *** Tamez J., * Lohmander L.S. * Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden,** Pfizer Global Research & Development, Ann Arbour, MI, USA,*** VirtualScopics Inc ,NY, USA THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – DEVELOPMENT OF POST TRAUMATIC BONE MARROW LESIONS, JOINT FLUID AND CARTILAGE VOLUME IN KNEES TREATED SURGICALLY OR NON-SURGICALLY
17:20-17:40	*Li X., *Bolbos R.I., **Ma C.B., *Link T.M., *Majumdar S. * Musculo-skeletal Quantitative Imaging Research (MQIR) group, Department of Radiology, University of California, San Francisco (UCSF), San Francisco, CA, USA,** Department of Orthopaedic Surgery, UCSF, San Francisco, CA, USA QUANTITATIVE ASSESSMENT OF BONE MARROW EDEMA PATTERN AND OVERLYING CARTILAGE IN OSTEOARTHRITIC AND ACL-INJURED KNEES USING HIGH FIELD MR IMAGING AND SPECTROSCOPY
17:40-18:00	* Frobell R.B., *Roos E.M., *Roos H.P., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., ***Tamez J., * Lohmander L.S. * Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden,** Pfizer Global Research & Development, Ann Arbor, MI, USA,*** VirtualScopics Inc ,NY, USA THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – ASSOCIATED ANATOMICAL LESIONS AND BONE MARROW LESIONS SUGGEST DIFFERENCES IN TRAUMA SEVERITY.

OSTEOARTHRITIS WAS THE CORRECT NAME!

*Conaghan P.G.,**Rhodes L.,*Hensor E.M.A.,*Thomas C.,*Emery P.,***Grainger A.J.

*Academic Unit of Musculoskeletal Disease, University of Leeds
**Academic Units of Medical Physics, University of Leeds
***Department of Radiology, Chapel Allerton Hospital, Leeds UK.

INTRODUCTION: The importance of synovitis in clinical osteoarthritis (OA) remains somewhat controversial and there is a paucity of information on its frequency and its relevance to clinical symptoms. These concepts have important implications for OA therapies. The most sensitive tool for detecting synovitis is contrast-enhanced MRI, but few OA cohorts have used contrast agents.

OBJECTIVE: This study used gadolinium (Gd) enhanced MRI to examine the extent of synovitis and its relation to patient symptoms.

METHODS: Subjects with ACR OA knee and varying degrees of pain were enrolled. Standard demographic data and clinical symptoms were recorded including global pain by VAS scale, WOMAC pain and patient-reported location of pain around the knee. The knee was examined using a 1.5T Gyroscan ACS-NT whole-body scanner (Philips Medical Systems, Best, The Netherlands) with quadrature receive knee coil and with the patient in the supine position. Sequences included sagittal, coronal and axial planes with pre-and post-Gd sequences of a single knee. Images were evaluated for semi-quantitative synovitis scores at 9 intra-articular sites (scales 0-3 or 0-1). Univariate analyses were performed to assess the degree of association between pain and MRI variables.

RESULTS: 122 patients were enrolled; mean age 63 (range 36-83), 53% women, 60% left knee, mean BMI 31.4 kg/m^2. Most patients' MRI was performed within 24 hours of clinical examination. Distribution of synovitis was extensive: 54% of patients had positive scores in all 9 sites and 84% had 6 or more positive sites; only 1% had no synovitis. The most frequent sites involved were the intercondylar notch, medial and lateral recesses and supra-patellar pouch. Neither pain VAS nor WOMAC showed a substantive or significant association with either the number of MRI-positive synovitis sites (VAS tau-b = 0.14, P=0.127 / WOMAC tau-b = 0.12, P=0.08), or the global synovitis summed semi-quantitative scores (VAS r = 0.14, P=0.129 / WOMAC r = 0.10, P=0.293). Medial aspect of knee was the commonest 'most painful' patient-reported pain location (51%). Weak but significant associations were found between painful compartment synovitis score and pain VAS score (r = 0.31, P=0.001) and WOMAC pain ((Pearson's R = 0.22, P=0.017).

CONCLUSION: Synovitis, as detected by Gd-MRI, is almost universal in painful OA knee. In the current study no association of global synovitis with global pain measures was demonstrated but the frequency of synovitis made this problematic. However there was some indication that compartmental levels of synovitis relate to site-specific pain.

SPONSOR: We are grateful to AstraZeneca for partial funding of this study
DISCLOSURE STATEMENT: Nil
CORRESPONDENCE ADDRESS: p.conaghan@leeds.ac.uk

QUANTITATIVE MRI OF PARALLEL CHANGES OF ARTICULAR CARTILAGE AND TRABECULAR BONE

*/**Lammentausta E., *Kiviranta P., ***Töyräs J., *Hyttinen M.M., ****Kiviranta I., *Jurvelin J.S., **Nieminen M.T.

* University of Kuopio, Kuopio, Finland; ** Oulu University Hospital, Oulu, Finland; *** Kuopio University Hospital, Kuopio, Finland; **** Jyväskylä Central Hospital, Jyväskylä, Finland

INTRODUCTION: Quantitative MRI parameters T_2 and dGEMRIC are able to predict the mechanical properties of cartilage, while T_2* relaxation time is related to bone mineral density (BMD) and strength. Typically, bone and cartilage are investigated separately but the interrelations of the MRI variables of bone and cartilage are rarely studied.

OBJECTIVE: To determine the relationship between quantitative MRI variables of bone and cartilage in reference to histological and mechanical properties and pQCT measurements of BMD in normal and degenerated human patellae.

METHODS: Intact patellae of human cadavers (N=14, age 55±18 years) were equilibrated overnight in 0.5mM Gd-DTPA$^{(2-)}$ solution. It has previously been shown that low contrast agent concentration has a minimal effect on T_2 relaxation time of cartilage. Six locations were defined to cover the articular surface of each patella. For MRI measurements, a clinical 1.5T scanner and a 3" receiving coil were used (GE Healthcare, Milwaukee, WI). The articular surface was oriented parallel to B_0 field to emulate clinical patient positioning. T_2 maps (multi-slice multi-echo spin echo, GE prototype sequence with improved slice profile, TR=1000ms, TE=10.3-82.4ms, ETL=8, 3-mm slice thickness, 0.31smm pixel size, room temperature) and dGEMRIC maps of cartilage (single-slice inversion recovery FSE, TR=1700ms, TE=11ms, TI=50-1600ms, ETL=6), and T_2* maps of trabecular bone (multi-slice gradient echo, TR=100ms, TE=4.7-28ms, flip angle=30^o) were calculated. dGEMRIC and T_2 values from the most superficial 1 mm of each cartilage region (width 3 mm) were averaged to characterize the superficial tissue, and bulk T_2* values of a 7x7mm region of interest (ROI), localized into the trabecular bone beneath the sites of cartilage MRI, were calculated. Stress-relaxation tests in unconfined geometry were conducted for full-thickness cartilage disks (dia.= 4 mm) to determine the Young's modulus (E_s). Blind-coded safranin-O-stained histological sections of cartilage were graded for degeneration using a modified Mankin score (MS) independently by three of the authors. Bone mineral density (BMD) was measured by using a peripheral quantitative computed tomography scanner (pQCT, 58kV, 0.175mA, pixel size 0.200mm, 0.5-mm slice thickness; XCT2000, Stratec, Birkenfeld, Germany). For mechanical testing of trabecular bone, cylindrical samples (dia.=7mm, thickness = 7mm) were isolated. Yield stress (σ_y) and ultimate strength (σ_u) were calculated from the stress-strain curve. BV/TV was calculated from unstained microscopic sections for samples too short for mechanical testing (N=24).

RESULTS: Significant differences were observed in T_2, E_s, BMD, σ_u and σ_y between the groups with MS<4 and MS≥4 ($p < 0.05$, Kruskal-Wallis test). The linear correlation coefficients were calculated for the group with MS < 4 and for all samples (Table 1). Most of the correlation coefficients were higher when the sample group with MS<4 was considered separately. The difference of the correlation coefficients was significant between dGEMRIC and BMD, E_s and T_2*, E_s and BMD and between T_2* and BV/TV ($p < 0.05$, standard Fisher Z-score test).

Table 1. The linear correlation coefficients calculated for the samples with MS < 4 and for all samples and p-values of the statistical differences in correlation coefficients between the groups.

	MS < 4	all samples	p-value
dGEMRIC vs. T_2*	0.48**	0.32**	0.38
dGEMRIC vs. BMD	-0.66**	-0.32**	0.04
dGEMRIC vs. σ_u	-0.47*	-0.23	0.34
dGEMRIC vs. σ_y	-0.46*	-0.23	0.36
dGEMRIC vs. BV/TV	-0.82*	-0.14	0.10
E_s vs. T_2*	0.70**	0.39**	0.04
E_s vs. BMD	-0.47*	-0.02	0.03
dGEMRIC vs. E_s	0.38*	0.30**	0.68
T_2 vs. E_s	-0.24	-0.54**	0.11
T_2* vs. BMD	-0.56**	-0.31**	0.15
T_2* vs. BV/TV	-0.86*	0.09	0.05
BMD vs. BV/TV	0.91*	0.58**	0.16

statistical significance for correlation coefficients:
** $p < 0.01$; * $p < 0.05$

CONCLUSION: The present results demonstrate significant relationships between the properties of articular cartilage and trabecular bone. Significant changes in these relationships are induced in the course of tissue degeneration, suggesting that the degenerative processes of bone and cartilage components advance at different rates. The degeneration of joint tissue is a complex process where several components are involved and interacting. The exact timeline of degenerative processes in joints remains open, and quantitative MRI techniques may provide powerful tools to address this process non-invasively.

SPONSOR: Academy of Finland, Finnish Cultural Foundation of Northern Savo
DICLOSURE STATEMENT: none
CORRESPONDENCE ADDRESS: eveliina.lammentausta@gmail.com

PREVALENCE OF MRI-DETECTED RELEVANT MENISCAL ABNORMALITIES AND ITS RELATION TO JOINT EFFUSION IN KNEES WITHOUT RADIOGRAPHIC OSTEOARTHRITIS

*, **Roemer F.W., **Guermazi A, ***Hunter D.J., ***Niu J., ***Zhang Y., *** Felson D.T.

* Department of Radiology, Klinikum Augsburg, Augsburg, Germany
** Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A.
*** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A.

INTRODUCTION: Meniscal damage might be a trigger of synovial activation reflected as joint effusion. This could be true especially for a subgroup of patients with early OA (KL 0-1) without other advanced features of OA that might also be causative for mechanical synovial activation.

OBJECTIVE: The analysis of the (1) prevalence of relevant meniscal pathology and (2) the correlation of meniscal status and joint effusion on MRI in knees without radiographic OA.

METHODS: In a large population-based OA study, 981 knees with no FT OA (K/L grades 0-1) were investigated with MRI. The knees were read for the amount of effusion using a semi-quantitative score of 0 to 3. The meniscal integrity or damage was assessed applying a semi-quantitative score of 0-4 in the anterior horn, body, and posterior horn of the medial and lateral menisci, respectively. Relevant meniscal damage was defined as grades ≥2 in any subregion.
A knee was defined as having joint effusion if the effusion score was 1 or more. Knees were then classified into two groups: Meniscal damage absent (meniscal scores 0 and 1 = meniscus-) and relevant meniscal pathology present (meniscal scores ≥2 = meniscus+). The meniscus+ group was further subdivided into subjects with meniscal pathology present in only one and present in both medial and lateral knee compartments. The prevalence of JE was assessed in the knees with and without meniscal damage. The odds ratios (OR) of joint effusion were estimated using a logistic regression model with meniscus- knees as reference group.

RESULTS: 981 knees were included. 100 (=10.2%) knees showed relevant meniscal pathology as defined above. Joint effusion was present in 55 (=55.0%) knees compared to 316 (=32.2%) in the meniscus-negative group. 49 (=52.7%) of the meniscus-positive knees with pathology in only one (n=93) and 6 (=85.7%) with pathology in two compartments (n=7) showed any joint effusion. The adjusted OR for having a joint effusion in a knee for the total meniscus-positive group [95% confidence interval] was 2.4 [1.6, 3.7]. The adjusted OR for the group with meniscal pathology in only one compartment was 2.2 [1.4, 3.4] and for the group with pathology in two compartments 11.4 [1.4, 100.1] compared to the group with none or only minor meniscal pathology. The results were significant. (Table 1).

Table 1: Cross-sectional association of joint effusion in a knee with meniscal damage (≥2 vs. 0-1 in any subregion) on MRI

Relevant meniscal damage	Presence of joint effusion, %	Crude OR of having joint effusion in a knee (95% CI) using logistic regression	Adjusted OR
Absence (N=881)	32.2	1.0	1.0
Presence (N=100)	55.0	2.6 (1.7, 3.9)*	2.4 (1.6, 3.7)*
In one compartment (N=93)	52.7	2.3 (1.5, 3.6)*	2.2 (1.4, 3.4)*
In both compartments (N=7)	85.7	12.6 (1.5, 105.3) †	11.9 (1.4, 100.1) †

p-value: * <0.01, †<0.05

CONCLUSION: Knees without OA but with relevant meniscal pathology on MRI exhibit joint effusion to a significantly higher degree compared to knees with no or only minor meniscal damage. The prevalence of joint effusion is increased in knees with relevant meniscal pathology in two compartments compared to knees with relevant meniscal damage in only one compartment. Knees with joint effusion and no signs of OA need to be carefully examined to exclude relevant meniscal pathology.

SPONSOR: NIH Grant No NIH AR47785
DICLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: f.w.roemer@gmx.de

THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – DEVELOPMENT OF POST TRAUMATIC BONE MARROW LESIONS, JOINT FLUID AND CARTILAGE VOLUME IN KNEES TREATED SURGICALLY OR NON-SURGICALLY

*Frobell R.B., *Roos H.P., *Roos E.M., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., *** Tamez J., * Lohmander L.S.

* Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden
** Pfizer Global Research & Development, Ann Arbour, MI, USA
*** VirtualScopics Inc ,NY, USA

INTRODUCTION: The consequences of Bone Marrow Lesions (BML) in acutely injured knees, or their association with the development of knee OA is not known. We have found no studies monitoring the first year development of post traumatic BML and cartilage volume in acutely ACL injured knees.

OBJECTIVE: To investigate the development of post traumatic BML volume and cartilage volume in patients with acute ACL injury, treated either surgically or non-surgically.

METHODS: In this longitudinal study we assessed knees with a not more than 4 weeks old ACL rupture with MRI (N=58). 34 subjects (mean age 28 (5) y) underwent ACL reconstruction within 7 (1.2) weeks from injury and 24 subjects (mean age 25 (5) y) were treated non-surgically. MRI scans were performed using a 1.5 T imager (Gyroscan, Intera, Philips) with a circular polarized surface coil. All knees were examined with a dual-echo turbo spin-echo sequence (tSEPdT2) and a T2-weighted turbo short tau inversion recovery sequence (tSTIRT2) in the coronal and sagittal views. A quantitative analysis of MRI was performed where a multi- spectral image data set was created and computer analyzed. The BML was automatically extracted by an unsupervised computer algorithm that extracted all the voxels inside the bone whose signal intensity in tSTIRT2 images was higher than that of the suppressed fat and whose T2 values were abnormal compared to behaviour of the T2 of the healthy bone marrow. Cartilage was extracted based on the T2 behaviour of cartilage. Data was collected at 4 different timepoints: baseline (BL, <4 weeks post injury), 16, 30, and 52 weeks post-injury.

RESULTS: BML volumes in K decreased more rapidly in non-surgically treated knees than in surgically treated knees, with significant differences at 3 and 6 months, fig. 1 right. VC of K, expressed as a difference from BL, significantly decreased over the first year in the surgically treated group but not in the non-surgically treated group, figure 1 left.

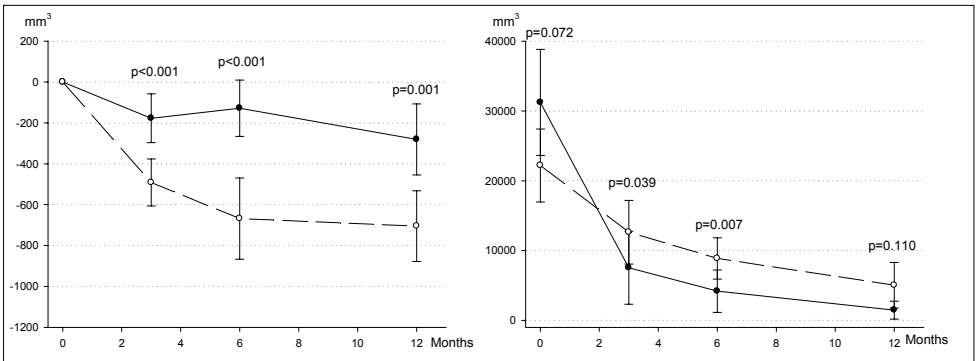

Figure 1. Differences of VC from baseline over first 12 months (left) and 1st year development of BML volume (right) in knees treated non-surgically (solid lines and filled symbols, n=24) or with ACL reconstruction (dashed lines and unfilled symbols, n=34).

CONCLUSION: The decrease in BML volume following injury was slower in the ACL reconstructed group. Additionally, VC of K decreased after surgical treatment, compared to no surgical treatment, and the differences remained throughout the 1st year. The importance of these early differences for knee function or future risk of osteoarthritis is unclear and continued long-term monitoring is needed.

DISCLOSURE STATEMENT: VirtualScopics Inc. was compensated for the image analysis

CORRESPONDENCE ADDRESS: richard.frobell@med.lu.se , Phone: +46-708-507882

QUANTITATIVE ASSESSMENT OF BONE MARROW EDEMA PATTERN AND OVERLYING CARTILAGE IN OSTEOARTHRITIC AND ACL-INJURED KNEES USING HIGH FIELD MR IMAGING AND SPECTROSCOPY

*Li X., *Bolbos R.I., **Ma C.B., *Link T.M., *Majumdar S.

* Musculo-skeletal Quantitative Imaging Research (MQIR) group, Department of Radiology, University of California, San Francisco (UCSF), San Francisco, CA, USA
** Department of Orthopaedic Surgery, UCSF, San Francisco, CA, USA

INTRODUCTION: While MR findings of bone marrow edema pattern (BMEP) are common in knee osteoarthritis (OA) and acute injuries such as anterior cruciate ligament (ACL) tear, our knowledge concerning their natural history and clinical significance is limited. In OA, BMEP has been associated with disease progression and pain in OA. In ACL tears, previous studies have proposed that the BMEP-overlying cartilage has sustained irreversible degeneration during injuries. MR $T_{1\rho}$ relaxation time has recently been proposed to probe changes in cartilage matrix during early stages of OA. Proton MR spectroscopy (MRS) provides a non-invasive method for quantifying biochemical or metabolic changes in tissues, but few studies have investigated MRS in knee bone marrow.

OBJECTIVE: 1) to quantify water and lipids changes in BMEP using 3D MR spectroscopic imaging (MRSI); 2) to assess composition changes in BMEP-overlying cartilage using $T_{1\rho}$ measurements.

METHODS: Eight healthy volunteers, 10 patients with knee OA and 14 with ACL-tears were studied. All patients had BMEP. The patients with ACL injuries were scanned within two months of the injury and prior to surgery. All images were acquired at a 3T GE MR scanner (General Electric, Milwaukee, WI). The imaging protocol included sagittal T_2-weighted fat-saturated FSE images, sagittal 3D water excitation high-resolution SPGR images and 3D $T_{1\rho}$ quantitation sequences as previously developed. 3D MRSI data were obtained using a Point REsolved Spectral Selection (PRESS) volume selection technique, with spectral box covering BMEP as much as possible, and to include some normal-appearing bone marrow as internal references. Cartilge was segmented semi-automatically in SPGR images. 3D cartilage contour was overlaid to aligned $T_{1\rho}$ maps. $T_{1\rho}$ z-scores (normalized $T_{1\rho}$ values using control data) from BMEP-overlying cartilage were calculated and compared with surrounding cartilage in the same compartment. Water, saturated-lipids and unsaturated lipids were quantified from 3D MRSI data. Volumes of significantly elevated water and unsaturated lipids were calculated for each patient. Water content, defined as water/(water+lipids), and unsaturation index, defined as unsaturated lipids/total lipids, were calculated within and outside BMEP.

RESULTS: The mean $T_{1\rho}$ z-scores of BMEP-overlying cartilage in lateral tibia of patients with ACL tears was significantly higher than that in surrounding cartilage (2.2 ± 3.1 vs. 0.3 ± 2.3, $P < 0.001$). However, no significant difference was observed in lateral femoral condyle compartment of patients with ACL tears. The mean $T_{1\rho}$ z-score in BMEP-overlying cartilage was higher than that of surrounding cartilage in patients with OA, but not significantly (1.9 ± 3.1 vs. 1.0 ± 2.1, $P = 0.37$). The volume of elevated water correlated significantly with the volume of BMEP ($R=75.5\%$, $P < 0.001$). No correlation was found between the volume of elevated unsaturated lipids and the volume of BMEP. The water content was significantly higher within BMEP than that outside BMEP (21.8 ± 9.9 % vs. 14.3 ± 5.9 %, $P = 0.002$). The unsaturation index was also higher within BMEP than that outside BMEP, but with an edge significance (3.7 ± 3.5 % vs. 2.3 ± 1.2 %, $P = 0.088$). The unsaturation index outside BMEP in patients with ACL tears was significantly higher than that outside BMEP in patients with OA (2.7 ± 1.3 % vs. 1.7 ± 0.8 % , $P = 0.04$).

CONCLUSION: 3D MRSI in bone marrow and $T_{1\rho}$ quantification in cartilage provide quantitative assessment of cartilage and bone in knee OA and knee injuries. Higher $T_{1\rho}$ in BMEP-overlying cartilage may be indicator of cartilage degeneration in these regions. Significantly elevated water and unsaturation lipids were observed in BMEP using 3D MRSI. BMEP in acute injuries (ACL-tear) may have different biochemical composition (changes in water and lipids) from those lesions in OA.

SPONSOR: The Aircast Foundation, NIH K25 AR053633 and NIH RO1 AR46905.
DICLOSURE STATEMENT: none.
CORRESPONDENCE ADDRESS: xiaojuan.li@radiology.ucsf.edu

THE ACUTELY ACL INJURED KNEE ASSESSED BY MRI – ASSOCIATED ANATOMICAL LESIONS AND BONE MARROW LESIONS SUGGEST DIFFERENCES IN TRAUMA SEVERITY.

*Frobell R.B., *Roos E.M., *Roos H.P., **Hellio Le Graverand M-P. **Buck R., ***Totterman S., ***Tamez J., * Lohmander L.S.

* Department of Orthopedics, Clinical Sciences Lund, Lund University, Sweden
** Pfizer Global Research & Development, Ann Arbor, MI, USA
*** VirtualScopics Inc ,NY, USA

INTRODUCTION: Post traumatic Bone Marrow Lesions (BML) were visualized by MRI in knees suffering from an acute ACL injury and the BML distribution was suggested to represent a footprint of the injury mechanism. In addition, traumatic compression forces to the cartilage have bee shown to result in chondrocyte death, where increased apoptosis has been related to compression forces.

OBJECTIVES: To: 1) investigate the frequency of concomitant depression fractures in the acutely ACL injured knee as visualized on MRI, 2) present location and volume (cm^3) of post traumatic BML after acute ACL injury; 3) relate BML volumes to a) the presence/absence of depression fractures, b) activity at injury.

METHODS: In this cross-sectional study we assessed a baseline sample of subjects with a not more that 4 weeks old ACL rupture to a previously un-injured knee, aged 18-35 and with an activity level of 5-9 on the Tegner scale (N=121). Mean age was 26 (5) years, 26% (n=32) were women and 78% (n=95) were injured in contact sports. MRI scans were performed using a 1.5 T imager (Gyroscan, Intera, Philips) with a circular polarized surface coil. All knees were examined with a dual-echo turbo spin-echo sequence (tSEPdT2) and a T2-weighted turbo short tau inversion recovery sequence (tSTIRT2) in the coronal and in the sagittal views. A quantitative analysis of MRI was performed where a multi-spectral image data set was created and computer analyzed. The BML was automatically extracted by an unsupervised computer algorithm that extracted all the voxels inside the bone whose signal intensity in tSTIRT2 images was higher than that of the suppressed fat and whose T2 values were abnormal compared to behaviour of the T2 of the healthy bone marrow. Clinical assessment of the MR images was performed by one of two well experienced radiologists.

RESULTS: 30% (n=36) had an associated depression fracture, mainly located in LF. All but 2 knees (n=119) had BML in K where the largest volumes were seen in T (Table 1). Contact sports were associated with increased BML volumes in T (p=.035), especially in LT (p=.022).

	BML volume (cm^3), Mean (SD)			
Location	All N=121	Depression n=36	No depression n=85	p-value
K	25.4 (19.1)	33.3 (24.6)	22.1 (15.1)	***0.025***
F	8.5 (10.7)	14.7 (15.0)	5.8 (6.8)	***<0.001***
LF	7.0 (9.3)	12.6 (13.0)	4.6 (5.9)	***<0.001***
MF	1.1 (2.6)	1.2 (2.4)	1.1 (2.7)	0.774
lTrF	0.4 (3.3)	1.0 (5.9)	0.1 (0.9)	0.610
mTrF	0.01 (0.07)	0 (0)	0.01 (0.08)	0.256
T	16.9 (12.5)	18.6 (12.5)	16.2 (12.6)	0.427
LT	11.5 (7.7)	11.8 (7.7)	11.4 (7.8)	0.959
MT	5.4 (6.7)	6.7 (7.7)	4.8 (6.2)	0.279
P	0,05 (0.3)	0 (0.01)	0.1 (0.3)	***0.048***
Compartment				
Medial	6.5 (7.6)	7.9 (8.7)	6.0 (7.0)	0.468
Lateral	18.9 (14.1)	25.4 (19.4)	16.1 (10.0)	***0.022***

CONCLUSION: We show that 30% of acutely ACL injured knees have an associated fresh cortical depression fracture. Large BML volumes were correlated with depression fractures, consistent with large post traumatic BML volumes indicating increased trauma severity, even if the ACL is similarly ruptured in all knees. On the basis of previous in vitro studies on traumatized cartilage and our own results we hypothesize that: 1) an associated fresh depression fracture; and 2) large BML volumes are risk factors for later knee OA development in the ACL injured knee.

DISCLOSURE STATEMENT: VirtualScopics Inc. was compensated for the image analysis.

CORRESPONDENCE ADDRESS: richard.frobell@med.lu.se , Phone: +46-708-507882

SUBMITTED ABSTRACTS ORAL SESSION 2: THE OAI AND OTHER MULTICENTER STUDIES

Thursday, July 12th, 2007: 11:15 to 12:55 Session Chair: Michael Nevitt

12 min presentation + 8 min discussion

11:15-11:35	*Hunter DJ, *Niu J, *Zhang YQ, **Totterman S, **Tamez J, ***Dabrowski C, ***Davies R, ****Hellio Le Graverand-Gastineau MP, *****Luchi M, ******Tymofyeyev Y, ******Beals CR for the OAI Investigators Group. *BUSM, Boston, U.S.A.,**VirtualScopics, Rochester, NY, USA.,***GSK, Collegeville, PA, USA.,****Pfizer, Ann Arbor, Michigan, USA.,*****Novartis, East Hanover, NJ, USA.,******MERCK, Rahway, NJ, USA. CHANGE IN CARTILAGE MORPHOMETRY: A SAMPLE OF THE PROGRESSION COHORT OF THE OSTEOARTHRITIS INITIATIVE (OAI)
11:35-11:55	*Maschek S., *Wirth W., **Hellio-Le Graverand M.P., **Wyman B.,*Hudelmaier M., ***Nevitt M., *Eckstein F., and the Osteoarthritis Initiative (OAI) Investigators group * Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany,** Pfizer Global Research and Development, Ann Arbor MI, USA, *** Dept. of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA CHANGE IN FEMOROTIBIAL CARTILAGE VOLUME AND SUBREGIONAL CARTILAGE THICKNESS OVER 1 YEAR, DATA FROM THE OSTEOARTHRITIS INITIATIVE PROGRESSION SUBCOHORT
11:55-12:15	*Lo G.H., *McAlindon T.E., **Niu J., **Zhang Y., ***Beals C., ****Dabrowski C., *****Graverand-Gastineau M., ******Luchi M, **Hunter DJ * Tufts-New England Medical Center, Boston, MA; ** Boston University Medical Center, Boston, MA; *** Merck Pharmaceuticals, Rahway, NJ; **** GlaxoSmithKline, Collegeville, PA; ***** Pfizer, Ann Arbor, MI; ****** Novartis, East Hanover, NH, USA STRONG ASSOCIATION OF BONE MARROW LESIONS AND EFFUSION WITH PAIN IN OSTEOARTHRITIS
12:15-12:35	*Hellio-Le Graverand M.P., *Wyman B., *Buck R., **Wirth W., *Hudelmaier M., *Eckstein F. for the A 9001140 Investigators * Pfizer Global Research and Development, Ann Arbor MI, USA,** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany TWELVE MONTH LONGITUDINAL CHANGE IN REGIONAL CARTILAGE MORPHOLOGY IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY
12:35-12:55	*Krishnan, N., **Wyman, B. **Buck, R., **Hellio, M-P, ***Tamez, J. ***Totterman S. * McKenzie, C., *Burstein, D., for the A9001140 Investigators * Beth Israel Deaconess Medical Center, Boston MA, USA,** Pfizer Global Research and Development, Groton, CT, USA,*** VirtualScopics, Rochester, NY, USA CROSS SECTIONAL ANALYSIS of dGEMRIC MEASUREMENTS IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY

CHANGE IN CARTILAGE MORPHOMETRY: A SAMPLE OF THE PROGRESSION COHORT OF THE OSTEOARTHRITIS INITIATIVE (OAI)

*Hunter DJ, *Niu J, *Zhang YQ, **Totterman S, **Tamez J, ***Dabrowski C, ***Davies R, ****Hellio Le Graverand-Gastineau MP, *****Luchi M, ******Tymofyeyev Y, ******Beals CR for the OAI Investigators Group.

*BUSM, Boston, U.S.A.
**VirtualScopics, Rochester, NY, USA.
***GSK, Collegeville, PA, USA.
****Pfizer, Ann Arbor, Michigan, USA.
*****Novartis, East Hanover, NJ, USA.
******MERCK, Rahway, NJ, USA.

INTRODUCTION: The performance characteristics of hyaline articular cartilage measurement on MRI need to be accurately delineated prior to widespread application of this technology.

OBJECTIVE: To assess the rate of natural disease progression of cartilage morphometry measures from baseline to one year in knees with OA from a subset of participants from the OAI.

METHODS: Subjects included for this exploratory analysis are a subset of the approximately 4700 participants in the OAI Study, an ongoing multi-center, longitudinal, prospective observational cohort study of knee OA. Bilateral radiographs and 3T MRI (Siemans Trio) of the knees and clinical data are obtained at baseline and annually in all participants.160 subjects from the OAI Progression subcohort (OAI public use datasets 0.1.1, 0.B.1 and 1.B.1) all of whom had both frequent symptoms and, in the same knee, radiographic OA (ROA) based on a screening reading done at the OAI clinics were eligible for this exploratory analysis. One knee from each subject was selected for analysis. 150 participants were included. Using sagittal 3D DESSwe MR images from the baseline and 12 follow-up month visit, a segmentation algorithm was applied to the cartilage plates of the index knee to compute the cartilage volume, normalized cartilage volume (Volume normalized to bone surface interface area), and percent denuded area (Total Cartilage Bone Interface area denuded of cartilage). Summary statistics of the changes (absolute and percentage) from baseline at one year and the standardized response mean (SRM), i.e. mean change divided by the standard deviation change were calculated.

RESULTS: On average the subjects were 60.9 years of age and obese with a mean BMI of 30.3 kg/m^2. The mean change and SRM for cartilage volume and normalized volume are presented in the table. The majority of participants had denuded area at baseline in the central medial femur (62%) and central medial tibia (60%). In general the SRMs were small.

location	Mean Change Cartilage Volume (mm^3) (SD)	SRM for mean change Cartilage Volume (mm^3)	Mean Change Normalized Cartilage Volume (mm (SD)	SRM for mean change Normalized Cartilage Volume (mm)	Baseline Mean Denuded Area (mm^2) (SD)	Mean Change Denuded Area (mm^2) (SD)
Femur	-38.0 (363.0)	-0.105	-0.0054 (0.058)	-0.093	176.64 (241.21)	8.97 (37.26)
Lat Tibia	-20.9 (86.2)	-0.243	-0.017 (0.063)	-0.269	6.91 (28.06)	0.96 (9.22)
Med Tibia	-4.4 (106.6)	-0.041	-0.0014 (0.079)	-0.017	44.16 (109.13)	2.06 (21.62)
Patella	-30.4 (153.5)	-0.198	-0.021 (0.11)	-0.193	97.71 (208.50)	-1.64 (30.47)
Trochlea	-1.1 (190.0)	-0.006	-0.0013 (0.073)	-0.018	99.07 (198.43)	1.14 (23.48)
Cent Lat Femur	-3.4 (58.8)	-0.057	-0.0090 (0.071)	-0.126	4.03 (18.15)	0.65 (5.48)
Cent Lat Tibia	-14.9 (68.5)	-0.217	-0.015 (0.071)	-0.215	4.57 (24.51)	0.76 (8.93)
Cent Med Femur	-37.4 (94.9)	-0.394	-0.039 (0.12)	-0.338	60.88 (128.69)	6.47 (27.08)
Cent Med Tibia	-7.9 (83.1)	-0.096	-0.0043 (0.098)	-0.044	43.28 (107.76)	1.79 (19.36)

CONCLUSION: These descriptive results of cartilage morphometry and its change at the one year timepoint from the first substantive MRI data release from the OAI Progression subcohort indicate that the annualized rates of change are small with the central medial femur showing the greatest consistent change.

SPONSOR: N01-AR-2-2262, N01-AR-2-2262, and N01-AR-2-2258
DICLOSURE STATEMENT: Affiliations listed above
ACKNOWLEDGMENT: OAI Publication Committee
CORRESPONDENCE ADDRESS: djhunter@bu.edu

CHANGE IN FEMOROTIBIAL CARTILAGE VOLUME AND SUBREGIONAL CARTILAGE THICKNESS OVER 1 YEAR, DATA FROM THE OSTEOARTHRITIS INITIATIVE PROGRESSION SUBCOHORT

*Maschek S., *Wirth W., **Hellio-Le Graverand M.P., **Wyman B.,*Hudelmaier M., ***Nevitt M., *Eckstein F., and the Osteoarthritis Initiative (OAI) Investigators group

* Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany; ** Pfizer Global Research and Development, Ann Arbor MI, USA
*** Dept. of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA

INTRODUCTION: The Osteoarthritis Initiative (OAI) is a multi-center, prospective cohort study targeted at identifying the most reliable and sensitive biomarkers for evaluating the development and progression of symptomatic knee OA. The first subset of the year 1 follow-up acquisitions in the progression subcohort have recently become publicly available, and data for the below analysis are from these OAI public-use data sets.

OBJECTIVE: To investigate 1) whether a significant change in the volume (VC) of femorotibial cartilage is observed in this cohort over 1 year, 2) whether changes are more significant when computing cartilage thickness (ThC) rather than VC and/or combining tibial and femoral measurements, and 3) whether the sensitivity of change is higher for certain anatomically defined subregions of the tibia and weight-bearing femur.

METHODS: An age and gender stratified subsample of the OAI progression subcohort (n = 156, 78 women, 78 men, age 60.9 ± 9.9 y., BMI 30.3 ± 4.7) with frequent symptoms and radiographic OA in at least one knee was studied (OAI public-use datasets 0.1.1, 0.B.1 and 1.B.1). 1.5mm coronal FLASHwe MR images of all right knees representing a mixture of OA knees (meeting inclusion criteria) and contra-lateral knees were acquired using 3T Siemens Trio scanners. A team of 7 experienced readers segmented medial/lateral tibial (MT/LT) and medial/lateral weight-bearing femoral (cMF/cLF) cartilages blinded as to order of acquisition. All segmentations were quality controlled by one reader (S.M.). Cartilage volume (VC) and mean cartilage thickness (ThC) over the entire subchondral bone (tAB), including denuded areas (ThCtAB.Me), were computed. To derive regional cartilage thickness, the tibia was divided into the central (20% of the tAB) and 4 peripheral subregions (anterior, posterior, external, internal) and the weight-bearing femur was divided into three equal (33%) subregions (central, internal, and external) using proprietary software (Chondrometrics GmbH, Ainring, Germany). The mean change, SD of change, standardized response mean (SRM = mean change / SD) and the significance of change (paired T-test, without correction for parallel testing of multiple parameters) were calculated.

RESULTS: The change in VC was -0.4% in MT (p=0.12; SRM=-0.12) and -1.5% in cMF (p=0.008; SRM= -0.21). The change in MT.ThC was -0.5% (p=0.04; SRM=-0.16) and that in cMF.ThC -1.9% (p=0.0002; SRM= -0.30). The aggregate change in the medial compartment (MT and cMF combined) was -0.8% (p=0.007; SRM= -0.22) for VC and -1.2% (p=0.0001; SRM=-0.31) for ThC. For ThC in subregions of MT, the central (-0.9%, p= 0.013; SRM=-0.20), internal (-0.6%; p=0.046; SRM=-0.18) and external (-0.8%; p = 0.073; SRM =-0.13) areas displayed higher SRMs than the anterior (SRM=-0.05) and posterior areas (SRM=-0.06). For ThC in subregions of cMF, the central area (-2.8%; p=0.0001; SRM =-0.31) displayed a higher SRM than the internal (-1.4%; p= 0.0018; SRM=-0.25) and external (-1.6%; p=0.008; SRM=-0.22) areas. The most significant change and highest SRM was observed for aggregate ThC in combined central MT and cMF subregions (-1.7%; p=0.00005; SRM=-0.33). In the lateral compartment, only LT (but not cLF) displayed significant change (-0.5%; p=0.03; SRM=-0.17 for VC, and -0.7%; p=0.005; SRM=-0.23 for ThC). For ThC in subregions of LT, SRMs in the central (p=0.007, SRM=-0.21), external (p=0.011; SRM=-0.21) and internal (p= 0.015; SRM=-0.20) area were higher than those in the anterior (SRM=0.04) and posterior subregions (SRM=-0.16).

CONCLUSION: Measurement of changes in cartilage morphology over 1 year in >150 subjects recruited for the OAI progression subcohort revealed greater changes in the medial weight-bearing femur than in the medial tibia, and greater changes in the lateral tibia than in the lateral weight-bearing femur. Changes in cartilage thickness displayed higher significance levels and higher SRMs than changes in cartilage volume. Over all, SRMs were relatively small (<=-0.31), but it should be noted that the sample also partly included contralateral knees which may not display symptoms or signs of radiographic OA. Amongst different subregions, the central areas of the tibia and weight-bearing femoral condyle (where X-ray measurements of JSN are usually made) showed the most significant change and highest SRM values for changes in regional cartilage thickness.

SPONSOR: Pfizer GRD, Ann Arbor, MI, USA & the OAI public private partnership
DICLOSURE STATEMENT: F.E. consults for Pfizer, Glaxo Smith Kline, Merck Serono and AstraZeneca.
ACKNOWLEDGMENT: The OAI investigators, technicians & coordinating center; the NIH & private sponsors
CORRESPONDENCE ADDRESS: dr-susannemschek@web.de

STRONG ASSOCIATION OF BONE MARROW LESIONS AND EFFUSION WITH PAIN IN OSTEOARTHRITIS

*Lo G.H., *McAlindon T.E., **Niu J., **Zhang Y., ***Beals C., ****Dabrowski C., *****Graverand-Gastineau M., ******Luchi M, **Hunter DJ

* Tufts-New England Medical Center, Boston, MA; ** Boston University Medical Center, Boston, MA; *** Merck Pharmaceuticals, Rahway, NJ; **** GlaxoSmithKline, Collegeville, PA; ***** Pfizer, Ann Arbor, MI; ****** Novartis, East Hanover, NH, USA

INTRODUCTION: Radiographs are poorly predictive of symptoms, but MRIs are able to assess features not visualized on radiographs, and may allow identification of features associated with pain. Many features of OA are correlated, thus it is important to evaluate them individually and collectively.

OBJECTIVE: We hypothesized that in people with knee OA, BMLs, synovitis, and effusion would be associated with pain independently.

METHODS: This was a cross-sectional study of people with symptomatic knee OA, a convenience sample from the Osteoarthritis Initiative (OAI), a multi-center natural history study of knee OA, from public use data sets 0.1.1 and 0.B.1. One 3.0T knee MRI from each participant was scored for BMLs, synovitis, and effusion primarily using sagittal intermediate-weighted TSE, fat-suppressed images. One MRI reader used the Boston Leeds Osteoarthritis Knee Score (BLOKS) scoring system, blinded to subject data, to score size of BMLs (0-3). A different MRI reader used BLOKS to score effusion (0-3) and synovitis (0-3). The weighted kappas (intra-rater reliability) were 0.88, 0.60, and 0.64 for BMLs, effusion and synovitis. Knee pain was defined as moderate-to-extreme pain (score of 2-4) on any of the 3 WOMAC questions assessing weight-bearing pain. We performed univariate analyses using logistic regression with maximal BML, effusion, and synovitis as predictors, and knee pain as the outcome. Subsequently, all 3 factors were included in a multivariate analysis.

RESULTS: Participants (N=160) had a mean age of 61 (±9.9), mean BMI of 30.3 (±4.7) and 50% were female.

	Prevalence of mod-extreme pain	Univariate Analysis (OR of mod-extreme pain)	Multivariate Analysis (OR of mod-extreme pain)
MAX BML SCORE			
0	4/15 (26.7%)	**Referent**	**Referent**
1	20/48 (41.7%)	**2.0** (0.5 – 7.1)	**1.6** (0.4 – 6.2)
2	22/36 (61.1%)	**4.3** (1.1 – 16.3)	**3.7** (0.9 – 15.0)
3	40/61 (65.6%)	**5.2** (1.4 – 18.5)	**4.2** (1.1 – 16.1)
		p for trend = 0.001	***p for trend = 0.006***
EFFUSION SCORE			
0	7/26 (26.9%)	**Referent**	**Referent**
1	30/62 (48.8%)	**2.5** (0.9 – 6.9)	**2.3** (0.8 – 6.5)
2	35/55 (63.6%)	**4.8** (1.7 – 13.3)	**3.5** (1.2 – 10.5)
3	14/17 (82.4%)	**12.7** (2.8 – 57.8)	**11.1** (2.3 – 52.9)
		p for trend = 0.0001	***p for trend = 0.0008***
SYNOVITIS SCORE			
0	2/7 (28.6%)	**Referent**	**Referent**
1	42/79 (53.2%)	**2.8** (0.5 – 15.5)	**1.7** (0.5 – 15.5)
2	29/54 (53.7%)	**2.9** (0.5 – 16.3)	**1.8** (0.5 – 16.3)
3	13/20 (65%)	**4.6** (0.7 – 30.4)	**3.5** (0.7 – 30.4)
		p for trend = 0.20	***p for trend = 0.29***

CONCLUSION: Cross-sectionally, in a cohort of people with symptomatic knee OA, maximal BML and effusion scores are highly associated with pain. The strength of the association persists when mutually adjusting for the other features, suggesting that each feature is independently associated with pain, supporting the idea that pain in OA is multifactorial. Further, our ability to find an association between the maximal score of weight-bearing WOMAC pain questions and features on MRI as measured by BLOKS provides validation for this pain scoring method and for BLOKS.

SPONSOR: Arthritis Foundation, Arthritis Investigator Award, 2005 - 2007.
DICLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: glo@tufts-nemc.org

TWELVE MONTH LONGITUDINAL CHANGE IN REGIONAL CARTILAGE MORPHOLOGY IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY

*Hellio-Le Graverand M.P., *Wyman B., *Buck R., **Wirth W., *Hudelmaier M., *Eckstein F. for the A 9001140 Investigators

* Pfizer Global Research and Development, Ann Arbor MI, USA; ** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany

INTRODUCTION: Clinical trials for DMOAD evaluation require sensitive methods for detecting significant changes in articular structures over relatively short time periods. Recent developments in MRI hardware (3.0 T scanners) and image analysis algorithms (subregional analysis of cartilage thickness) have raised hope that change in cartilage morphology could be detected over narrower time intervals than so far possible.

OBJECTIVE: 1) To investigate whether significant change in cartilage morphology can be detected in an enriched OA population (i.e., obese women) in a multicenter, multivendor MRI study at 3.0T over a period of 12 month,; 2) to elucidate which subregions of the femorotibial cartilage plates display the highest sensitivity to change; 3) to contrast these observations with those in age and sex-matched healthy control participants.

METHODS: 1.0mm coronal FLASHwe MR images of the knee were acquired at baseline and 12 months in 158 female participants at 7 clinical centers with Siemens and GE 3.0T scanners. 96 participants had no symptoms and no evidence of radiographic OA; 62 had medial femorotibial OA on conventional standing AP radiographs (31 KLG 2 and 31 KLG 3). 7 experienced readers segmented the baseline and follow up images as pairs, with blinding to order of acquisition; all segmentations were quality controlled by one reader (F.E.). The mean cartilage thickness over the entire subchondral bone area (tAB) was computed (ThCtAB). Subregional cartilage thickness was determined for central (20% of the tAB), anterior, posterior, external and internal subregions of the medial (MT) and lateral tibia (LT), and for central (33% of the tAB), external and internal subregions and the weight-bearing medial (cMF) and lateral femur (cLF), using proprietary software (Chondrometrics). The mean change (MC%) and the standardized response mean (SRM = mean/SD of the change) were calculated.

RESULTS: At 1 year, little to no changes were observed in control subjects (KLG 0), the greatest changes being increases in the ThCtAB in the internal subregion of the MT (SRM=0.20) (Table 1). In contrast, in OA subjects, trends for reductions in the ThCtAB were observed: in KLG 2 participants, reductions in the ThCtAB in the central and external subregions of MT attained SRM values of -0.32 and 0.26 respectively; in KLG 3 participants the highest SRM throughout MT was observed in the external subregion (SRM = -0.22). Increases in ThCtAB were observed, however, in the anterior or posterior subregions of the MT in KLG 3 participants, respectively (SRM of up to +0.24) . In the cMF, a 2% reduction in the ThCtAB was observed in KLG 3 subjects (SRM = -0.28), reaching 2.4% in the external (SRM =-0.24) and 4.4% in the central (SRM =-0.40) subregions.

Table 1.

Changes at 12 months	KLG 0 (n=96) MC%	SRM	KLG 2 (n=31) MC%	SRM	KLG 3 (n=31) MC%	SRM
MT.ThCtAB	-0.03%	-0.01	-0.56%	-0.19	-0.04%	-0.01
cMT.ThCtAB	-0.16%	-0.04	-1.5%	-0.32	-0.89%	-0.14
eMT.ThCtAB	-0.59%	-0.13	-1.43%	-0.26	-2.37%	-0.22
iMT.ThCtAB	+0.87%	+0.20	-1.09%	-0.22	-0.20%	-0.05
aMT.ThCtAB	-0.33%	-0.07	+0.90%	+0.17	+1.56%	+0.24
pMT.ThCtAB	+0.10%	+0.02	+0.16%	+0.03	+0.90%	+0.22
cMF.ThCtAB	+0.15%	+0.03	+0.41%	0.09	-1.95%	-0.28
ccMF.ThCtAB	+0.11%	+0.02	+0.49%	+0.07	-4.44%	-0.40
ecMF.ThCtAB	+0.74%	+0.14	+1.10%	+0.17	-2.41%	-0.24
icMF.ThCtAB	-0.24%	-0.05	-0.12%	-0.03	+0.56%	+0.12

MC=mean change, SRM=standardized response mean; c=central, e=external, i =internal, a=anterior, p=posterior

CONCLUSION: Relatively small changes in cartilage thickness were observed at total plate level in KLG 2 and 3 patients over 1 year. Subregional analysis revealed that the sensitivity to change in cartilage thickness in the external and central subregions of MT, and in the central area of cMF was greater than at total plate level. The KLG 2 participants tended to display greater changes in MT, and the KLG 3 participants greater changes in cMF.

SPONSOR: Pfizer Global Research and Development, Ann Arbor, MI, USA.
DICLOSURE STATEMENT: F.E. consults for Pfizer, Glaxo Smith Kline, Merck Serono and AstraZeneca.
CORRESPONDENCE ADDRESS: helliomp@pfizer.com

CROSS SECTIONAL ANALYSIS of dGEMRIC MEASUREMENTS IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY

*Krishnan, N., **Wyman, B. **Buck, R., **Hellio, M-P, ***Tamez, J. ***Totterman S. * McKenzie, C., *Burstein, D., for the A9001140 Investigators

* Beth Israel Deaconess Medical Center, Boston MA, USA
** Pfizer Global Research and Development, Groton, CT, USA
*** VirtualScopics, Rochester, NY, USA

INTRODUCTION: Several prior reports have compared dGEMRIC with physiologic and radiographic data. All previous dGEMRIC studies were single-site trials and with one exception, all were at 1.5T.

OBJECTIVE: To compare dGEMRIC data from a 3.0T multicenter study with radiographic measures.

METHODS: A subset (n = 59) of the A9001140 observational MRI study data was selected for the dGEMRIC analysis. The control group (n=35), consisted of subjects with no radiographic OA (KLG 0), and an average BMI of 26±6. The OA group consisted of patients with radiographic OA, including KLG 2 (n=11) and KLG 3 (n=13) patients with an average BMI of 36±5. The 3D dGEMRIC imaging was done at 7 clinical sites with Siemens and GE scanners with standard dGEMRIC protocol. T1(Gd) were generated using custom coded software (MRIMapper, copyright 2006 BIDMC). Two ROIs were evaluated per medial / lateral compartment: the central femoral region (cMF/cLF), and the tibial plateau (MT/LT). Because of the BMI bias in the entry criteria of this clinical study, T1(Gd) were compensated for BMI dose-bias (Osteoarthritis Cartilage 2006; 14:1091-1097).

RESULTS: T1(Gd) for the different radiographic grades are given in the table, and in the figures for the central medial femur. (Only one lateral compartment had JSN Grade >0, and thus is not reported.) KLG0 was significantly higher than KLG3 in the cMF ($p<0.001$) and MT, cLF ($p<0.05$). JSN Grade 0 was significantly higher than JSN Grade 1 or 2 ($p<0.01$).

	KLG 0 (n=35)	KLG 2 (n=11)	KLG3 (n=13)	JSN 0	JSN 1	JSN 2
cMF	639±133	640±62	504±94	657±118 (n=39)	513±92 (n=13)	526±89 (n=7)
MT	605±107	551±65	548±98	596±105	568±94	534±83
cLF	681±130	658±100	613±103	663±128	----	----
LT	696±148	644±134	641±125	678±142	----	----

CONCLUSION: These results are similar to prior single-site, 1.5T studies with a lower mean dGEMRIC in higher KLG and JSN grades. 3.0T studies are preferred for cartilage studies due to the slightly better morphometric measurements. A disadvantage of 3.0T for dGEMRIC is the increased T1 at this field strength, with longer imaging times and/or lower resolution. Another potential disadvantage is the lower relaxivity of gadolinium at the higher field strengths. The relative sensitivity of dGEMRIC to disease state and progression between 1.5T and 3.0T has not yet been established. Also apparent in this, as in previous studies, is the large range of dGEMRIC within compartments graded at KLG and JSN grade of 0, indicating that this metric may provide additional information to standard radiographic metrics. Larger longitudinal studies will enable a better evaluation of whether the range of dGEMRIC in these radiographically "normal" compartments might be predictive of future disease progression, or whether they are a snap-shot of a system with progression and regression of biochemical changes.

SPONSOR: Pfizer Inc.
DICLOSURE STATEMENT: D. Burstein, C. McKenzie and VirtualScopics have received funding and consultation fees from Pfizer.
ACKNOWLEDGMENT: We gratefully thank the entire A9001140 study team for their efforts.
CORRESPONDENCE ADDRESS: Brad.Wyman@Pfizer.com

POSTER SESSION 1

Thursday, July 12th, 2007: 14:45 – 15:30 (Presenters of Posters No. 1 to 14 at posters)

1	Bouchgua M., Alexander K., Carmel E.N., Beauchamp G., Richard H, Laverty S. Faculty of Veterinary Medicine, University of Montreal, St-Hyacinthe, QC, Canada. BONE MINERAL DENSITY ASSESSED BY COMPUTED TOMOGRAPHY IN AN IN VIVO RABBIT MODEL OF OSTEOARTHRITIS
2	*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A. * Chemistry Department, New York University, New York, NY, ** Radiology Department, New York University, New York, NY. CHEMICAL EXCHANGE SATURATION TRANSFER FOR ASSESSING PROTEOGLYCANS IN CARTILAGE
3	*Gassner R., **Long P., ***Evans C., ****Deschner J., **Piesco N., ****Agarwal S. * Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria, ** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA, *** Department of Orthopedic Surgery - Brigham & Women's Hospital, Harvard Medical School, Boston, USA, **** Division of Oral Biology, Ohio State University, Columbus, OH, USA CHONDROCYTES SENSING MECHANICAL STRAIN DISPLAY ANTI-INFLAMMATORY ACTIONS IN VITRO
4	*Anandacoomarasamy A., *Giuffre B., **Stanwell P., ***Fransen M., *Sambrook P., *March L. * Royal North Shore Hospital, Sydney, Australia, ** University of Sydney, Sydney, Australia, *** The George Institute, Sydney, Australia COMPARISON OF DGEMRIC USING CORONAL AND SAGITTAL IMAGE ACQUISTION IN AN OBESE POPULATION UNDERGOING WEIGHT LOSS
5	*,**Winalski C.S., *Schneider E., **Yoshioka H., ***Shortkroff S., ****Rosen G.M. * Division of Radiology, Cleveland Clinic Foundation, Cleveland, OH, USA, ** Department of Radiology, Brigham & Women's Hospital, Boston, MA, USA, *** Orthopedic Research Laboratory, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, USA, ****Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, and NitroSci, Baltimore, MD, USA DENDRIMER-LINKED NITROXIDE MR CONTRAST AGENTS FOR CARTILAGE IMAGING: DISTRIBUTION IN CARTILAGE, PH AND CHARGE DEPENDENCE OF SOLUTE DIFFUSION
6	Fleming B.C., Bowers M.E., Tung G.A., Leventhal E.L., Trinh N., Crisco J.J., Kimia B.B. Brown Medical School, Providence, RI, USA EFFECTS OF ACL INTERFERENCE SCREWS ON FEMOROTIBIAL CARTILAGE THICKNESS MEASUREMENTS USING 1.5T AND 3T MRI
7	*Bangerter N.K., **Staroswiecki E., **Gurney P.T., *Hargreaves B.A., *Gold G.E. * Department of Radiology, Stanford University, Stanford, CA, USA, ** Department of Electrical Engineering, Stanford University, Stanford, CA, USA HIGH RESOLUTION IN VIVO SODIUM MRI OF ARTICULAR CARTILAGE AT 7T

8	*Hudelmaier M., *Wirth W., ** Charles C.H., ***Kraus V.B., ****Wyman B., ****Hellio Le Graverand-Gastineau M.-P., *Eckstein F. * Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Duke Image Analysis Laboratory, Durham NC, USA, *** Division of Rheumatology & Immunology, Duke University Medical Center, Durham NC, USA, **** Pfizer Global Research and Development, Ann Arbor MI, USA HOW DOES CHOICE OF COMPUTATIONAL ALGORITHM AND FEMORAL REGION OF INTEREST AFFECT MEASURES OF CARTILAGE MORPHOLOGY IN THE KNEE
9	Joyce M., Ryan J., Rainford L.A., Last J., Brennan P.C. University College Dublin, Dublin, Ireland IMPACT OF VARYING THE X-RAY SOURCE DETECTOR DISTANCE IN X-RAY EXAMINATION OF THE ARTHRITIC CERVICAL SPINE
10	*Wirth W., **Kunz M.,***Inglis D., ***Adachi R., ***Beattie K., **Hudelmaier M., *Eckstein F. * Chondrometrics GmbH, Ainring, Germany, ** Institute of Anatomy & Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria, *** Center for Appendicular MRI Studies, McMaster University, Hamilton, ON, Canada IMPACT ON REGION SIZE ON THE TEST-RETEST PRECISION OF REGIONAL CARTILAGE THICKNESS MEASUREMENTS IN THE FEMOROTIBIAL JOINT
11	*Marijnissen A.C.A., **Vincken K.L., *Vos P.A.J.M., ***Saris D.B.F., **Viergever M.A., *Bijlsma J.W.J., **Bartels L.W., *Lafeber F.P.J.G. *Rheumatology & Clin. Immunology, UMC Utrecht, The Netherlands, **Image Sciences Institute, UMC Utrecht, The Netherlands, ***Orthopaedics, UMC Utrecht, The Netherlands KNEE IMAGES DIGITAL ANALYSIS (KIDA): A NOVEL METHOD TO QUANTIFY INDIVIDUAL RADIOGRAPHIC FEATURES OF KNEE OSTEOARTHRITIS IN DETAIL.
12	*Kunz M., **Cahue S., **Marshall M., *Wirth W, *Hudelmaier M., **Sharma L., *Eckstein F. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA LONGITUDINAL CHANGE AND PATTERN OF PATELLAR CARTILAGE LOSS IN OA PATIENTS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT
13	*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Pettersen P., ***Christiansen C. * Department of Computer Science, University of Copenhagen, Denmark, ** Nordic Bioscience (NB), Herlev, Denmark *** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark LONGITUDINAL CHANGES IN CARTILAGE SURFACE SMOOTHNESS: A MARKER OF PROGRESSION DURING MODERATE OA?
14	*Williams T.G., ***Bowes M., *Taylor C.J., *Hutchinson C.E, **Waterton J.C., **Maciewicz R.A., **Holmes A.P. * Imaging Science and Biomedical Engineering, University of Manchester, UK. ** AstraZeneca, Macclesfield, UK. *** Imorphics, Manchester, UK. MORE SENSITITVE ANALYTICAL MEASURES CANNOT COMPENSATE FOR PATIENT HETEROGENEITY WITH RESPECT TO ANNUALISED CARTILAGE LOSS

BONE MINERAL DENSITY ASSESSED BY COMPUTED TOMOGRAPHY IN AN IN VIVO RABBIT MODEL OF OSTEOARTHRITIS

Bouchgua M., Alexander K., Carmel E.N., Beauchamp G., Richard H, Laverty S.

Faculty of Veterinary Medicine, University of Montreal, St-Hyacinthe, QC, Canada.

INTRODUCTION: As changes in the subchondral bone are an integral feature of OA development, their temporal assessment in vivo in experimental models of OA may allow detection of the disease modification in this important structural tissue of the joint. Bone mineral density (BMD), which reflects bone remodelling and its mechanical properties, has been studied ex vivo in rabbit models of OA by Dual-energy X-ray absorptiometry and μCT. However rapid in vivo non-invasive assessment of BMD using accessible equipment is desirable in this model.

OBJECTIVE: To assess, using clinical CT equipment, changes in BMD at different depths from the articular surface in an in vivo rabbit model of OA.

METHODS: Unilateral transection of the ACL was performed on a randomly assigned FT joint in skeletally mature male New Zealand White rabbits (n=10). A sham surgery was performed on the contralateral joints (n=10). Control rabbits (n=6) did not undergo surgery. Knee joints, stabilized within a plexiglass mould, were placed longitudinally on a solid dipotassium phosphate bone density calibration phantom (13002 Model 3 CT Calibration Phantom, Mindsways Software, Inc, San Francisco, California, United States) and scanned in a transverse image plane with a helical single-slice CT scanner (Hi-Speed ZXi, General Electric, Mississauga, Ontario, Canada). Density data in Hounsfield Units was obtained from oval regions of interest (ROI), placed in each phantom rod and each epiphyseal compartment (LF, MF, LT, MT). BMD was calculated using linear regression. BMD was calculated at depths of 1, 2, 3, 4, 5 and 6 mm from the articular surface in the femur and at 1, 2 and 3 mm in the tibia (to the growth plate). Baseline BMD measurements were made at 2 weeks before surgery (week -2), and then repeated at weeks 2, 4 and 8 post-surgery for all 10 ACLT rabbits, and at week 12 for 5 of the ACLT rabbits. BMD was measured at weeks -2 and 8 in the 6 control rabbits to detect any changes related to time in normal animals. The evolution of BMD over time and the differences between depths, and compartments were assessed within and between groups using a repeated-measures linear model with depth and time as within-subject factors.

RESULTS: For the control group, BMD decreased with increasing distance from the articular surface. The majority of BMD calculations at all depths in all compartments remained stable over time. In the ACLT and sham groups, of the significant changes occurring, 81% were detected in the ACLT joints and the majority were highly significant ($p < 0.001$). A reduction of BMD over time was the most frequent change observed in the ACLT joints. This significant reduction was observed by week 2 post-operatively in 3 (LF, MF and MT) out of 4 compartments in the ACLT joints, but not in the sham joints. At week 12 the significant reduction in BMD persisted in all 4 compartments but not at all depths of the ACLT joints. In the MF of ACLT joints, at weeks 4, 8 and 12 the reduction in BMD was observed to occur at greater depths into the bone (reduction measured at all 6 depths at week 8). By comparison these changes were restricted to depths of 1 and 2 mm in the LF. At week 8 in the LT and MT, reductions were measured at all 3 depths in the ACLT group, but overall they occurred more frequently in the MT. At week 12, a modest reduction was observed in the LT ($p = 0.047$) and MT ($p < 0.024$) of the sham joints.

CONCLUSION: Clinical CT equipment permitted easy and non-invasive assessment of the BMD temporally (ACLT and sham) in an in vivo OA rabbit model.

SPONSOR: Canadian Arthritis Network, Toronto, Ontario, Canada
DICLOSURE STATEMENT: None.
ACKNOWLEDGMENTS: Geneviève Rouleau, Anne-Marie Martel and Marie Lecocq are thanked for their technical assistance.
CORRESPONDENCE ADDRESS: maria.bouchgua@umontreal.ca

CHEMICAL EXCHANGE SATURATION TRANSFER FOR ASSESSING PROTEOGLYCANS IN CARTILAGE

*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A.

* Chemistry Department, New York University, New York, NY
** Radiology Department, New York University, New York, NY.

INTRODUCTION: The early onset of degeneration is generally characterized by a loss of proteoglycans (PGs). A number of MRI techniques allow one to quantify the loss of PGs and to deduce the stage of degeneration within cartilage tissue, based on ^{1}H-MRI, as well as, ^{23}Na MRI. The chemical exchange between the labile protons of low-concentration solutes and bulk water provides a novel sensitivity enhancement mechanism in MRI (Chemical Exchange dependent Saturation Transfer – CEST). Based on a 1H NMR spectroscopical study of GAG phantoms and enzymatic depleted bovine cartilage samples, we demonstrate a strong CEST effect that can be use to accurately measure the absolute glycosaminoglycan (GAG) concentration. The first images using CEST at 3T are shown.

OBJECTIVE:
1) Determine the suitable exchangeable protons that can be used for CEST imaging.
2) Determine the optimal parameters for performing CEST imaging for PG assessment.
3) Determine a correlation between CEST imaging and PG concentration.

METHODS: In 1H NMR spectroscopic analysis (HR-MAS, TOCSY, HSQC) of PG, we identified the amide proton as the strongest CEST agent, which has a one-to-one correspondence to GAG units in PG. Because of the mobility of PG in phantom/tissue, there is almost no MT effect from PG, but rather from collagen. Additional chemical exchange sites were identified as hydroxyl groups. The amide proton demonstrated the strongest CEST effect at +3.2ppm, corresponding to the single amide proton per GAG unit.
The MT effect of the method was tested by z-spectra of agarose gel at various concentrations, which leads to increased broadening of the main dip in the spectrum as the agarose concentration increases. The bovine cartilage tissue samples were evaluated before and after depletion. The GAG depletion is clearly seen, as well as some loss of the collagen matrix as evidenced by a decreased MT effect.

RESULTS: Both amide and hydroxyl-protons were identified using MR spectroscopy and z-spectra. The CEST effect was measures as a function of GAG concentration. The CEST results of intact and depleted cartilage samples were consistent with a decrease in GAG. MT effects can be ruled out sufficiently by subtracting the result of the experiment with irradiation on the other side of the water resonance. The CEST effect is almost linear with in the GAG concentration. CEST-enhanced images at 3T were obtained.

CONCLUSION: 1H MRI with CEST appears to be a powerful method for diagnosing the early degenerative changes in cartilage tissue. The PG concentration can be measured with this endogenous contrast-enhancement method based on the saturation of the exchangeable protons. We believe that this method could become an important diagnostic tool in OA.

SPONSOR: NIH 1R21ARO54002-01A1

CORRESPONDENCE ADDRESS: alexej.jerschow@nyu.edu

CHONDROCYTES SENSING MECHANICAL STRAIN DISPLAY ANTI-INFLAMMATORY ACTIONS *IN VITRO*

*Gassner R., **Long P., ***Evans C., ****Deschner J., **Piesco N., ****Agarwal S.

* Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria
** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA
*** Department of Orthopedic Surgery - Brigham & Women's Hospital, Harvard Medical School, Boston, USA
**** Division of Oral Biology, Ohio State University, Columbus, OH, USA

INTRODUCTION: Diseases disrupting the homeostasis of cartilage are coupled with progressive inflammation. In these diseases, physical therapies such as continuous passive motion (CPM) yield beneficial effects. However, the mechanisms of the beneficial actions of mechanical strain are as yet unknown.

OBJECTIVE: Since inflammatory cytokines like IL-1b play a major role in both the initiation and progression of cartilage inflammation, we hypothesized that CPM actions may involve suppression of IL-1b signal transduction via suppression of nuclear factor (NF)-kB nuclear translocation and thus inhibition of multiple proinflammatory gene induction.

METHODS: To test this hypothesis *in vitro*, primary cultures of chondrocytes from 20 rabbit knees were harvested and grown on Bioflex plates, and subjected to equibiaxial cyclic tensile strain (CTS, 6 % to 15% elongation) to mimic CPM. Presence and/or absence of recombinant human (rh)IL-1b for various time intervals was used as an inflammatory signal. The examination of the mRNA expression for multiple IL-1b-dependent proinflammatory genes was assessed by reverse transcriptase/polymerase chain reaction. Protein synthesis was assessed by Western blot analysis, and the nuclear translocation of NF-kB was examined by immunofluorescence. One-way ANOVA was applied to compare differences in IL-1b response in CTS alone, IL-1b, CTS and IL-1b groups, and controls.

RESULTS: Low magnitude CTS (6%) inhibited IL-1b-dependent induction of mRNA and proteins involved in catabolic actions of IL-1b, such as inducible nitric oxide synthase, cyclooxygenase, and collagenase (MMP-1). Whereas, higher magnitudes of CTS (10 to 15%) did not suppress IL-1b actions. CTS (6%) also abrogated IL-1b-induced inhibition of tissue inhibitor of metallo-protease-II and collagen type I induction. Furthermore, examination of the signal transduction pathways of IL-1b showed that CTS inhibited IL-1b-induced NF-kB nuclear translocation. Interestingly, CTS did not downregulate IL-1 receptors (IL-1R) on chondrocytes suggesting that IL-1R down regulation may not be the mechanism of CTS action. In particular, immunofluorescence staining of cells for presence of NF-kB within the nucleus or within the cytoplasm revealed statistically significant differences ($p < 0.05$) regarding responses to IL-1b dependent chondrocyte activation when chondrocytes were exposed to IL-1b alone in comparison to CTS and IL-1b.

CONCLUSION: Since, CTS exerts its effects at concentrations of IL-1b similar to those present in inflamed knees, these findings indicate the clinical relevance of continuous passive motion for postoperative and posttraumatic therapy. Present observations show that low magnitude tensile strain is a potent antagonist of IL-1b actions in chondrocytes, and that it acts upstream of mRNA induction via inhibition of NF-kB nuclear translocation in the IL-1b signal transduction cascade.

SPONSOR: National Institutes of Health Grants NIH 1R15DE13799-01, NIH 1R15DE12976-01, AT00646-01, and AAOMS Foundation.
DISCLOSURE STATEMENT: none.
CORRESPONDENCE ADDRESS: Robert.Gassner@uki.at

COMPARISON OF dGEMRIC USING CORONAL AND SAGITTAL IMAGE ACQUISTION IN AN OBESE POPULATION UNDERGOING WEIGHT LOSS

*Anandacoomarasamy A., *Giuffre B., **Stanwell P., ***Fransen M., *Sambrook P., *March L.

* Royal North Shore Hospital, Sydney, Australia
** University of Sydney, Sydney, Australia
*** The George Institute, Sydney, Australia

INTRODUCTION: dGEMRIC of the knee has been used to assess the relative distribution of GAG in cartilage. To date, few studies have utilized a 3T MRI scanner. The acquisition of these images is time consuming and it is not clear if coronal or sagittal images alone would suffice. There are no studies assessing dGEMRIC index (T1Gd) values in a purely obese population.

OBJECTIVE: 1) To describe the range of T1Gd values in an obese population with and without knee OA. 2) To assess the correlation between T1Gd values obtained in the coronal plane compared to the sagittal plane.

METHODS: Fifty obese subjects (body mass index, BMI >30) undergoing weight loss through surgical and non-surgical means underwent MRI with a dGEMRIC protocol at 3T (Magnetom Trio; Siemens, Erlangen, Germany). Double dose (0.2 mM/kg) $GdDTPA^{2-}$ was administered 90 minutes prior to imaging. Patients were required to walk for 15 minutes after injection. Two-dimensional single-slice dGEMRIC images in the mid-coronal, medial sagittal and lateral sagittal planes were obtained with a FSE inversion recovery sequence with 5 inversion delays ranging from 50 to 2080msec (TR 2200 msec; TE 14 msec). Slices were 3 mm thick with an in-plane resolution of 275μm. T1Gd maps were generated with a pixel-by-pixel 3-parameter T1 fit using Matlab software (The MathWorks, Natick, MA). dGEMRIC indices were calculated for each region (8 in total), and also as an average of T1Gd values in a given region of interest (ROI). In the sagittal plane, this was the weight-bearing femoral cartilage and all of the tibial cartilage. In the coronal image, this was all of the cartilage in the view. Patients also underwent quantitative cartilage imaging of the index knee. All subjects completed a general health and musculoskeletal questionnaire, WOMAC and SF-36 questionnaires. They also underwent a physical assessment, and blood and urine testing for evaluation of serum and urine biomarkers. Cross-sectional analysis was performed, and dGEMRIC indices were compared between coronal and sagittal values using correlations (Stata software).

RESULTS: There were 33 females and 17 males. Mean age was 51 ± 13.5 years (range 24-75 years). BMI range was 29.8-50.6 kg/m^2 (mean 39.5 ± 5.2 kg/m^2). Sixteen patients (32%) met clinical criteria for knee OA. Fourteen patients underwent laparoscopic gastric banding for weight loss and the others were engaged in a combination of dietary modification and exercise. The average T1Gd values for whole coronal, medial sagittal and lateral compartments were 527 ± 56 msec (range 423 - 660 msec), 542 ± 86 msec (range 240-790 msec) and 546 ± 83 msec (range 237-680 msec) respectively. There was a significant but modest correlation between coronal and sagittal T1Gd values of the MT, MF and LF ($p< 0.005$). There was poor correlation between coronal and sagittal T1Gd values of the LT. Intra-rater reliability for each of the 8 individual ROIs revealed ICCs >0.91.

CONCLUSION: There is a wide range of T1Gd values in the obese population with and without clinical OA. There is a statistically significant correlation between coronal and sagittal images at the MT, MF and LF. This may obviate the need to obtain images in both planes. However, there is a wide range of variability in this population and correlation with other clinical and MRI parameters is required. Recruitment is still underway and follow-up at 1 year will provide a measure of change with weight loss.

SPONSOR: National Health and Medical Research Council Medical Postgraduate Research Scholarship (ID number 402901)
DISCLOSURE STATEMENT: none
ACKNOWLEDGEMENT: Charles Chen for statistical advice, Rob Preston for technical assistance
CORRESPONDENCE ADDRESS: anaananda@med.usyd.edu.au

DENDRIMER-LINKED NITROXIDE MR CONTRAST AGENTS FOR CARTILAGE IMAGING: DISTRIBUTION IN CARTILAGE, pH AND CHARGE DEPENDENCE OF SOLUTE DIFFUSION

*,***Winalski C.S., *Schneider E., **Yoshioka H., ***Shortkroff S., ****Rosen G.M.

* Division of Radiology, Cleveland Clinic Foundation, Cleveland, OH, USA
** Department of Radiology, Brigham & Women's Hospital, Boston, MA, USA
*** Orthopedic Research Laboratory, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, USA
****Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, and NitroSci, Baltimore, MD, USA

INTRODUCTION: Polypropylenimide (DAB) dendrimer-linked nitroxide (DLN) MR contrast agents are positively charged at physiologic pH and, thus, targeted to glycosaminoglycans [1]. DLNs are available in a range of molecular sizes and charges, potentially demonstrating differential affinities and abilities to permeate articular cartilage [1]. Since DLNs have a pKa value around 9, molecular charge can be altered by varying pH (maximum charge occurs at lower pH and no charge at high pH). Measurements of DLN diffusivity at various pH values may help elucidate the influence of molecular charge on solute diffusion into cartilage.

OBJECTIVE: Determine: 1) the ability of DLNs to enhance cartilage; and 2) the effect of molecular charge, as altered by variation of pH, on the solute diffusivity of DLNs into cartilage.

METHODS: Part 1) Enhancement of cartilage. 10 calf patellae were cut into 5mm thick cartilage-bone samples. Cartilage T1 was measured at 1.5T by MR imaging in saline. Samples were then immersed for 5 days in a saline solution of either nitroxide monomer (3.2mM, n=4), DLN-4 (0.8 mM, n=4), DLN-8 (0.4 mM, n=4), DLN-16 (0.2 mM, n=3), DLN-32 (0.1 mM, n=3), or Gd-DTPA (0.1mM, n=9), or saline control (n=3). Cartilage T1 maps were calculated from FSE inversion recovery acquisitions with 10 TIs between 50ms and 4000ms and TR = 6.6s. "Relaxivity per dose", R1dose, (change in cartilage 1/T1 divided by agent concentration) were calculated.
Part 2) pH dependence of diffusion. 3mm diameter cylindrical plugs of calf bovine cartilage were sequentially imaged at 8.5T within a device that allowed only radial diffusion. Cartilage T1 was measured before and following immersion of the plugs using saturation recovery sequences. The solute diffusivity, D, was calculated (3 plugs each) for 1mM solutions of DLN-4 at pH values of 4, 7, 8.4, 10, and 12, and 1mM solutions of Gd-DTPA at pH values of 4, 7, and 10 using the method of Gillis [2]. Values were compared using 2-tailed Students t-Test.

RESULTS: Part 1) Enhancement of cartilage. Cartilage immersed in Gd-DTPA and DLNs had significantly decreased T1 values. Cartilage soaked in DLN-32 did not reach equilibrium. DLNs had a greater cartilage R1dose than monomer nitroxide, and, for each increase in size and magnitude of positive charge of the DLN, there was an increase in R1dose. DLN-8, -16, and -32 had cartilage R1dose between 3.5 and 68 times greater than Gd-DTPA.
Part 2) pH dependence of diffusion. For DLN-4 solutions, diffusivity was faster at pH 10 (no charge) than pH 7 (+2 charge). D progressively increased from 1.9×10^{-7} at pH 7 to 6.0×10^{-7} at pH 10 ($p<0.002$). Values at the extremes of pH (4 and 12) showed intermediate D values. Gd-DTPA had significantly more rapid diffusion than DLN-4 with D for Gd-DTPA at pH 7 = 13.0×10^{-7} ($p<0.002$). For Gd-DTPA, there was no significant difference in D between pH 7 and pH 10.

CONCLUSION: Dendrimer-linked nitroxides strongly enhance normal cartilage and are potentially useful as articular cartilage-specific MR contrast agents as well as for investigation of factors that influence diffusion into cartilage. Positive charge appears to slow molecular diffusion into cartilage.

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SPONSOR: National Institutes of Health grants AR-46320 and AG-20445
DICLOSURE STATEMENT: Dr. Gerald Rosen has a minority financial interest in NitroSci.
CORRESPONDENCE ADDRESS: winalsc@ccf.org

EFFECTS OF ACL INTERFERENCE SCREWS ON FEMOROTIBIAL CARTILAGE THICKNESS MEASUREMENTS USING 1.5T AND 3T MRI

Fleming B.C., Bowers M.E., Tung G.A., Leventhal E.L., Trinh N., Crisco J.J., Kimia B.B.

Brown Medical School, Providence, RI, USA

INTRODUCTION: ACL injury places patients at risk for OA. qMRI can be used to track changes in FT ThC, and could provide insight into OA progression after ACL reconstructive surgery. Titanium interference screws are frequently used to fix ACL grafts. However, metallic implants can produce magnetic susceptibility artifacts with MRI. These artifacts may be greater on a 3T scanner.

OBJECTIVE: To assess the effects of titanium screws and magnetic field strength on FT ThC values.

METHODS: 5 intact right human knees (mean age = 56, range 51-59) were imaged on 1.5T and 3T scanners (Siemens Symphony and Trio, Erlangen, Germany) using a knee coil. The T1-weighted WE-3D FLASH sequence (0.3x0.3x1.5mm) was used on the 3T scanner, and a similar sequence was programmed for the 1.5T magnet (0.3x0.3x2mm). Each knee was imaged with and without two 9x20mm titanium interference screws implanted (Arthrex, Inc; Naples, FL). The FT cartilage plates were manually segmented in the sagittal plane and reconstructed using commercial software (Mimics 9.11). 3-D voxel models were generated and wrapped with a triangular mesh to create virtual models of the LF, MF, LT and MT cartilage plates. 3 regions of interest were identified in the weightbearing aspects of both the LF and MF. A cylinder was fit to the bone-cartilage interface of pLF and pMF. A line from the cylinder axis to the junction between the FT and FP joints defined the 0^o reference. The LF and the MF were then divided at 40^o, 70^o, 100^o, and 130^o posteriorly to bound the cartilage patches; the width of each patch was set at 20% of the overall width of the FT cartilage and centered about the midline of each condyle. A region of interest was identified in the weight bearing regions of the MT and LT by calculating the respective centroids for each compartment (MATLAB). The inertial axes of the MT were used to define the orientation of the tibial coordinate system. The patches were defined as the area comprising ±20% of the overall depth (anteroposterior) and ±15% of the overall width (mediolateral) about each centroid. The mean ThC values for each patch were calculated by the closest point algorithm. Repeated measures analyses of variance were used to compare the ThC of each patch in response to screw condition and magnetic field strength. Pair-wise comparisons were made with the Holm-Sidak test.

RESULTS: There were no significant differences in the average MF or LF ThC thickness values due to field strength or screw condition for any ROI examined (Table 1). There were no significant differences in tibial articular cartilage thickness values at different field strengths. There was no significant difference in the mean MT ThC values with different screw conditions. However, there was a significant difference in the LT ThC values at different field strengths (3T>1.5T, p=0.04). The difference was independent of screw condition; however, there was a trend for an interaction between magnetic field strength and screw condition (p=0.06).

Magnet	3T		1.5T	
Screw	Yes	No	Yes	No
MF	1.97(.06)	1.96(.06)	1.89(.06)	1.92(.06)
LT	3.86(.05)	4.04(.05)	3.69(.05)	3.59(.05)
MT	2.29(.07)	2.62(.07)	2.21(.07)	2.48(.07)
LT	3.86(.05)	4.04(.05)	3.69(.05)	3.59(.05)

Table 1: Mean (±SE) ThC in millimeters. MF and LF values are pooled.

CONCLUSION: Our data demonstrate that measurements of ThC in the FT joint are not affected by the presence of titanium interference screws for the ACL-reconstructed knee when using the T1-weighted WE-3D FLASH sequence at 1.5T. The lack of screw effect, however, was not independent of magnetic field strength. While the difference in ThC in the lateral compartment of the tibia between screw conditions was not statistically significant, there was a trend for an interaction between these parameters. Thus, caution should be used when interpreting the mean ThC values in the LT condyle at 3T when titanium interference screws are present.

SPONSOR: National Institutes of Health (RO1-AR047910S1)
DICLOSURE STATEMENT: Arthrex, Inc. donated the intereference screws for this study.
CORRESPONDENCE ADDRESS: Braden_Fleming@brown.edu

HIGH RESOLUTION IN VIVO SODIUM MRI OF ARTICULAR CARTILAGE AT 7T

*Bangerter N.K., **Staroswiecki E., **Gurney P.T., *Hargreaves B.A., *Gold G.E.

* Department of Radiology, Stanford University, Stanford, CA, USA
** Department of Electrical Engineering, Stanford University, Stanford, CA, USA

INTRODUCTION: Early degenerative changes in cartilage leading to osteoarthritis are accompanied by PG depletion in the cartilage matrix. Sodium MRI has been shown to correlate with PG concentration [1-3], and may be useful in detecting and tracking early PG depletion. Despite the challenges associated with sodium MR, improved MR hardware coupled with higher fields and efficient pulse sequences may enable diagnostic-quality sodium MRI in vivo in reasonable scan times.

Short-TE gradient-spoiled sequences with efficient k-space trajectories are often employed to maximize sodium signal and minimize blurring from signal decay [4]. In this work, we present a novel, relatively fast, high-resolution, high-SNR 3D sodium imaging sequence for rapid in vivo imaging of human articular cartilage at 7T.

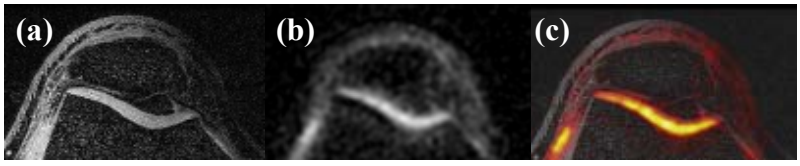
OBJECTIVE: The objectives of this study were to (1) validate the new technique in normal volunteers at 7T, and (2) perform measurements of sodium T2* in articular cartilage for sequence optimization.

METHODS: A fast gradient-spoiled sequence using a 3D cones k-space trajectory [5] and rapid RF excitation was developed for sodium image acquisition. The centric 3D cones trajectory allows for extremely short echo times and very high SNR efficiency. It is similar to the twisted projection trajectories often used for sodium MRI [4], but makes more efficient use of scanner gradient resources.

The sodium sequence was implemented on a 7T GE Excite whole body scanner with HFD gradients. The patellar cartilage of several normal volunteers was scanned to assess the performance of our technique. Sodium imaging parameters were: TR/TE = 50/0.6 ms, FOV = 16x16x12.8 cm, resolution = 1x1x2 mm, readout time = 16 ms, and 16 averages for a total scan time of 26 min.

The patellofemoral cartilage was then scanned at a lower resolution in five normal knees to perform sodium T2* measurements. Acquisitions were performed at eight echo times, and a 3D cartilage ROI for signal measurement was defined by manually segmenting patellar and femoral cartilage from other tissue in each knee series. SNR was measured across each ROI at each echo time, and a T2* exponential decay curve was fit to the resulting data.

RESULTS: Our high-resolution (1x1x2 mm) sodium MR protocol at 7T achieved excellent SNR (sodium cartilage SNR > 20) with full 3D coverage of the patellofemoral cartilage in approximately 26 minutes. The figure shows (a) an anatomical proton reference image, (b) a high-resolution sodium image, and (c) a sodium color overlay on the anatomical reference image.



Measured T2* values were consistent across all subjects, with T2* = 13 +/- 1.4 ms. These values are consistent with other previously published results (both in vitro and in vivo) at different field strengths.

CONCLUSION: We have demonstrated the feasibility of using a fast 3D cones trajectory for the acquisition of high resolution sodium images of articular cartilage achieving excellent SNR in reasonable total scan times. We further performed measurements of sodium T2* in articular cartilage at 7T to enable sequence optimizations. The technique shows great promise for providing a method to accurately quantitate proteoglycan concentrations in articular cartilage.

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SPONSOR: GlaxoSmithKline and NIH grants 1R01-EB002524 and 1R01-EB005790.
DICLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: nealb@stanford.edu

HOW DOES CHOICE OF COMPUTATIONAL ALGORITHM AND FEMORAL REGION OF INTEREST AFFECT MEASURES OF CARTILAGE MORPHOLOGY IN THE KNEE

*Hudelmaier M., *Wirth W., ** Charles C.H., ***Kraus V.B., ****Wyman B., ****Hellio Le Graverand-Gastineau M.-P., *Eckstein F.

* Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany
** Duke Image Analysis Laboratory, Durham NC, USA
*** Division of Rheumatology & Immunology, Duke University Medical Center, Durham NC, USA
**** Pfizer Global Research and Development, Ann Arbor MI, USA

INTRODUCTION: Quantitative MRI of knee articular cartilage morphology initially focused on cartilage volume, but more sophisticated parameters (e.g. cartilage thickness) have become available. Thickness can be computed from the cartilage surface to the bone interface or vice versa, and larger cartilage plates, such as the femur, require division into various regions of interest (ROIs).

OBJECTIVE: To investigate the following questions: 1) Which computation of cartilage thickness is more reproducible: minimal distance from the **c**artilage surface (AC) to the bone interface (tAB) [**c** implementation], minimal distance from the **b**one interface (tAB) to the AC [**b** implementation], or the **a**verage of both [**a** implementation]? 2) How do computations compare for shorter and longer ROIs of the weight-bearing femoral condyle based on different anatomical landmarks?

METHODS: Test-retest. 1.5 mm coronal FLASHwe MR images of the knee were acquired in 30 female participants (15 with and 15 without OA) using a Siemens Magnetom 1.5 T scanner. The medial and lateral tibial (MT/LT) and weight-bearing femoral (cMF/cLF) cartilages (tAB and AC) were segmented using proprietary software. The ROI on the femoral condyle was defined as either 1) the area between the intercondylar notch anteriorly and the intercondylar bone bridge posteriorly (short ROI), or 2) the area between the intercondylar notch and 60% of the distance to the posterior end of the femoral condyle (long ROI). Cartilage thickness was computed as minimal distance from AC to tAB and vice versa, and values were determined for tibial, short and long femoral ROIs.

RESULTS: The short femoral ROI comprised 10 ± 2 slices, and the long ROI 13 ± 1 slices. The tAB of "cMF long" was 25% larger than that of the "cMF short" (5.5 ± 0.6 mm² versus 4.1 ± 0.8 mm²), and that of "cLF long" 26% larger than that of "cLF short" (6.0 ± 0.6 mm² versus 4.4 ± 0.8 mm²). The inter-subject variability for long ROIs was 25% smaller compared with that of the short ROIs. Computation of the mean thickness (ThCtAB.Me) was more reproducible than that of cartilage volume (VC), but no obvious difference was observed between a,b and c implementations for thickness. Thickness computations in "cMF long" displayed slightly higher reproducibility than in "cMF short", but laterally precision errors for thickness were similar for the short and long ROI (Table 1).

Table 1: Root mean square (RMS) coefficient of variation (CV%) for cartilage morphology computations with different algorithms for various anatomical regions of interest (ROIs) in the knee.

	MT	LT	cMF short	cMF long	cLF short	cLF long
VC	2.7 %	2.3%	2.8%	2.5%	3.6%	3.4%
ThCtAB.aMe	1.9%	1.8%	2.8%	2.5%	2.7%	2.6%
ThCtAB.bMe	2.0%	1.7%	2.8%	2.5%	2.8%	2.7%
ThCtAB.cMe	1.9%	1.9%	2.7%	2.4%	2.6%	2.6%

VC = cartilage volume; ThCtAB.xMe = mean cartilage thickness; a,b,c = various implementations

CONCLUSION: The computation of cartilage thickness is more reproducible than that of cartilage volume, regardless whether minimal distance is computed from AC to tAB or vice versa. The choice of a larger ROI representing the weight-bearing femoral condyle tends to provide lower inter-subject variability of the ROI size and lower precision errors for cartilage thickness.

SPONSOR: Pfizer Global Research and Development, Ann Arbor MI USA.
DICLOSURE STATEMENT: M.H. and W.W. have part time employments with Chondrometrics GmbH. F.E. is CEO of Chondrometrics GmbH and provides consulting services to Pfizer Inc., Glaxo Smith Kline Inc. and Merck Serono Inc.
CORRESPONDENCE ADDRESS: martin.hudelmaier@pmu.ac.at

IMPACT OF VARYING THE X-RAY SOURCE DETECTOR DISTANCE IN X-RAY EXAMINATION OF THE ARTHRITIC CERVICAL SPINE

Joyce M., Ryan J., Rainford L.A., Last J., Brennan P.C.

University College Dublin, Dublin, Ireland

INTRODUCTION: Radiography is the gold standard in assessment of joint damage in patients with established arthritis. It is essential that X-ray images required for diagnosis and evaluation of treatment regimens are of high quality to demonstrate early arthritic changes. One of the limitations associated with examination of the cervical spine is the unavoidable distance between the neck and the image receptor which presents measurable levels of geometric unsharpness. This reduces image quality and can hinder arthritic scoring.

OBJECTIVE: To establish the impact on important arthritic indicators by increasing the distance between the X-ray source and image detector (SID) from the commonly employed levels.

METHODS: A human cadaver with evidence of osteoarthritic change was chosen for this study. Multiple lateral cervical spine exposures were acquired without the limitation of excessive patient irradiation. The cadaver was placed in a supine position and the central ray was directed midway between the upper and lower skin surfaces of the neck at the level of the cricothyroid cartilage. A GE MAXI-Ray 100 tube assembly was employed to take the exposures using automatic exposure control and 65kVp. The images were acquired with a direct digital, amorphous silicon flat-panel design image receptor, rotated horizontally. A variety of SID distances from 150 to 210cm were considered, producing 5 images at each distance. An evaluation panel of four experienced clinicians assessed the images by means of visual grading analysis, using objective criteria based on normal anatomic features and arthritic indicators. A radiographic reference image was employed and image viewing conditions remained constant throughout the investigation. The radiation dose for each exposure was monitored using a dose area product meter (DAP). The non-parametric Mann-Whitney U-test and an ANOVA was used for analysis of the image quality and dose data respectively and a significance of $p<0.05$ was utilised.

RESULTS: A statistically significant improvement in image quality was observed with images acquired at 210cm compared with those acquired at 150cm and 180cm ($p<0.05$). Out of a maximum achievable score of 72, the overall mean image quality scores obtained for 150cm, 180cm and 210cm were 56.0 (SE=1.105), 50.85 (SE=1.415) and 65.35 (SE=0.737) respectively. All images with a SID of 210cm scored higher for visually sharp reproduction of the spinous processes, facet joints, intervertebral disc spaces and trabecular bone pattern compared with both 180cm and 150cm.

CONCLUSION: The results indicate that total image quality and visualisation of specific anatomical features is enhanced in cervical spine radiographs for arthritic patients when traditionally employed SID distances are increased. Further research into this cost-effective radiographic technique will investigate the effects of increasing the SID for other areas of the body susceptible to arthritis.

SPONSOR: University College Dublin, Ad Astra Scholarship
DISCLOSURE STATEMENT: None
ACKNOWLEDGEMENT: School of Medicine & Medical Science, University College Dublin
CORRESPONDANCE ADDRESS: maria.joyce.1@ucdconnect.ie

IMPACT ON REGION SIZE ON THE TEST-RETEST PRECISION OF REGIONAL CARTILAGE THICKNESS MEASUREMENTS IN THE FEMOROTIBIAL JOINT

*Wirth W., **Kunz M.,***Inglis D., ***Adachi R., ***Beattie K., **Hudelmaier M., *Eckstein F.

* Chondrometrics GmbH, Ainring, Germany
** Institute of Anatomy & Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria
*** Center for Appendicular MRI Studies, McMaster University, Hamilton, ON, Canada

INTRODUCTION: MR imaging is a powerful tool for monitoring changes in cartilage morphology in epidemiological, clinical and drug development studies. Changes in cartilage volume, however, occur at a very slow rate. Quantitative analysis of cartilage thickness in anatomically defined subregions may provide a more sensitive tool for detecting morphologic changes than analysis of entire cartilage plates.

OBJECTIVE: To determine the impact of subregion size on precision errors of regional analysis of cartilage thickness in the weight-bearing femoro-tibial joint.

METHODS: An algorithm was developed for the subdivision of the medial (MT) and lateral tibial (LT) cartilage in one central and 4 peripheral (anterior, posterior, internal, external) subregions, based on the center of gravity of the total subchondral bone area (tAB) and the orientation to the tAB of the other compartment. The medial (cMF) and lateral (cLF) weight-bearing femur was divided into central, internal, and external subregions. The impact of region size on the test-retest reproducibility of regional cartilage thickness measurements was investigated by varying the central region between 10 and 50 % of the tAB in the tibia, and between 25 and 75 % of the tAB in the femur. The size of the peripheral subregions changed accordingly. The algorithm was applied to test-retest datasets of 12 subjects (6 healthy, 6 with mild radiographic OA) acquired with a 1.5T scanner and coronal FLASHwe sequence. The test-retest precision was expressed as the root mean square (RMS) coefficient of variation (CV%).

RESULTS: Test-retest precision was relatively high with CV% values of <= 5% for all subregions. Medially (MT and cMF), precision errors for the central subregions became lower with increasing their size (Tables 1 and 2), whereas in LT and cLF precision errors were not affected by region size.

Table 1: RMS CV% for cartilage thickness in the medial (MT) and lateral tibial (LT) subregions

ctAB	cMT	cLT	eMT	eLT	iMT	iLT	aMT	aLT	pMT	pLT
10%	2.6	1.7	1.4	1.9	2.3	3.5	2.9	2.8	1.6	3.9
20%	2.4	1.9	1.5	2.0	2.3	3.7	3.0	2.8	1.7	4.7
30%	2.1	1.7	1.6	2.1	2.3	3.8	3.0	2.9	2.0	5.1
40%	2.0	1.8	1.6	2.4	2.2	3.7	3.1	3.3	2.4	5.1
50%	1.8	1.9	1.8	2.7	2.3	3.7	3.6	3.7	2.8	5.0

Table 2: RMS CV% for cartilage thickness in the medial (cMF) and lateral femoral (cLF) subregions

ctAB	ccMF	ccLF	ecMF	ecLF	icMF	icLF
25%	3.4	2.6	3.2	3.9	2.5	3.1
33%	3.3	2.4	3.5	4.2	2.6	3.1
50%	2.9	2.3	3.7	4.8	2.6	3.0
66%	2.7	2.4	4.3	5.3	2.7	2.9
75%	2.5	2.3	4.9	5.4	2.6	3.3

c = central, e = external, i = internal, a = anterior, p = posterior subregions

CONCLUSION: Low precision errors can be achieved for regional cartilage thickness measurement under test-retest conditions. Smaller precision errors are observed with larger central regions in the medial, but not in the lateral femorotibial compartment. This technology will be applied to longitudinal data to identify which of the regions has the highest sensitivity to change in OA progression studies.

SPONSOR: None.
DICLOSURE STATEMENT: F.E. provides consulting services for Pfizer, Glaxo Smith Kline, Merck Serono and AstraZeneca
CORRESPONDENCE ADDRESS: wirth@chondrometrics.de

KNEE IMAGES DIGITAL ANALYSIS (KIDA): A NOVEL METHOD TO QUANTIFY INDIVIDUAL RADIOGRAPHIC FEATURES OF KNEE OSTEOARTHRITIS IN DETAIL.

*Marijnissen A.C.A., **Vincken K.L., *Vos P.A.J.M., ***Saris D.B.F., **Viergever M.A., *Bijlsma J.W.J., **Bartels L.W., *Lafeber F.P.J.G.

*Rheumatology & Clin. Immunology, UMC Utrecht, The Netherlands
**Image Sciences Institute, UMC Utrecht, The Netherlands
***Orthopaedics, UMC Utrecht, The Netherlands

INTRODUCTION: Conventional radiography is still the gold standard for imaging of osteoarthritic (OA) features, e.g. joint space narrowing, subchondral sclerosis, and osteophyte formation. Objective evaluation, however, remains difficult.

OBJECTIVE: The objective of the present study was to develop and evaluate a solid, reliable, and simply to use digital method to analyze plain radiographs of knees.

METHODS: Standardized radiographs of 20 healthy and 55 OA (according to ACR criteria) knees were taken according to the semi-flexed method of Buckland-Wright. Radiographs were taken with an aluminium step wedge alongside in order to quantify bone density and correct for magnification of the radiograph. JSW, osteophyte area, subchondral sclerosis, joint angle deviation, and eminentia height were measured using the newly developed interactive Knee Images Digital Analysis (KIDA) on a standard PC.
KIDA consists of several interactive steps that provide multiple measures for JSW (e.g. minimum, lateral, medial, mean), for subchondral bone density, height of the eminentia, joint angle, and osteophyte areas, all as continuous variables. The entire procedure including data storage takes less than 10 minutes. *Evaluation* Two observers evaluated the radiographs on two different occasions with an interval of at least one week. The observers were blinded to the source of the radiographs and to previous measurements. Statistical analysis to compare measurements within and between observers was performed according to Bland and Altman (Lancet; 307-310, 1986). Additionally, KLG was determined and compared to individual KIDA parameters and differences in KIDA data between healthy and OA knees were evaluated.

RESULTS: Intra- and interobserver variations for JSW, subchondral bone density, osteophytes, eminentia and joint angle were small. Observer A, e.g., found a minimum JSW of 2.8 ±1.7 mm with a mean difference between two observations of -0.02 mm. Subchondral bone density was 28.6 ±4.6 mm Alu Eq. with a mean difference of 0.0. Osteophyte area was 9.9 ±6.8 mm^2 with a mean difference of –0.31. Several of the individual KIDA parameters correlated with the overall KLG (E.g. R= -0.57, 0.57, and 0.27 for minimum JSW, osteophytes, and subchondral bone density, respectively; $p<0.05$). But within one KLG still a large variation exists in individual KIDA parameters. Significant differences were found between healthy and OA knees (e.g. minimum JSW of 4.3 ±0.6 vs. 2.2 ±1.6 mm, subchondral bone density of 23.5 ±5.9 vs. 32.0 ±3.7 mm Alu Eq., osteophyte area of 4.1 ±2.3 vs. 12.0 ±6.7 mm^2 all $p<0.001$).

CONCLUSION: In addition to JSW measurement, objective evaluation of osteophyte formation and subchondral sclerosis (as a continuous variable) is possible on standard radiographs. On the basis of measured differences between OA and healthy individuals KIDA seems to be sensitive to detect OA changes in time, however follow-up studies to study sensitivity to change will be performed.

SPONSOR: The study is financially supported by the Dutch Arthritis Association
DISCLOSURE STATEMENT: none
ACKNOWLEDGEMENT: we acknowledge Marja Lafeber for her work as observer A
CORRESPONDENCE ADDRESS: a.c.a.marijnissen@umcutrecht.nl

LONGITUDINAL CHANGE AND PATTERN OF PATELLAR CARTILAGE LOSS IN OA PATIENTS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT

*Kunz M., **Cahue S., **Marshall M., *Wirth W, *Hudelmaier M., **Sharma L., *Eckstein F.
* Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany
** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA

INTRODUCTION: Quantitative MR imaging of cartilage morphology now permits the investigation of cartilage loss in individual cartilage plates and compartments throughout the knee. Previous work has established that varus and valgus malalignment have a strong impact on cartilage loss in the medial and lateral femorotibial compartment, respectively, but little work has been done on the relationship between malalignment of the knee and cartilage loss in the patella.

OBJECTIVE: 1) To determine the magnitude of patellar cartilage loss (change in cartilage volume) in a community-recruited cohort of participants with mild to moderate OA; 2) to determine whether change in cartilage volume is driven by a reduction of cartilage thickness over the cartilaginous area, by an increase in denuded bone areas (=reduction of cartilaginous areas) or both, and 3) to determine whether valgus and varus malalignment influence the magnitude of cartilage loss in the patella

METHODS: A community-recruited cohort (n = 84) with radiographic (KLG 2-3) knee OA (age 72 ± 9 years [mean ± SD], BMI 29.9 ± 5.5, 72% women) had alignment measurement taken using a full limb x-ray. 38 participants had neutral alignment (-2° to +2° deviation from the biomechanical knee axis); 26 had varus (> +2°), and 20 valgus malalignment (< -2°). An axial FLASHwe sequence (1.5 x 0.31 x 0.31 mm^3 resolution) was acquired at baseline and approximately 26.7 ± 2.6 months later using 1.5T (Siemens) and 3.0T (GE) scanners. Segmentation was performed by tracing the total subchondral bone (tAB) and cartilage surface area (AC) of the patella. Where denuded areas were observed, the cartilaginous subchondral bone area (cAB) and denuded area (dAB) were separated. Baseline and follow up scans were processed in parallel pairs blinded as to acquisition order. Cartilage volume (VC), tAB, cAB, dAB, and the average cartilage thickness throughout the cAB (ThCcAB) were quantified, using proprietary software (Chondrometrics GmbH, Ainring, Germany).

RESULTS: Across the cohort, the annual patellar cartilage volume loss was 1.8 ± 3.8% ($p < 0.001$). The reduction in cartilage thickness over the cAB, and the decrease in cartilaginous area (= increase in denuded area) made approximately equal contributions (-1.0% versus 1.2% per year) to cartilage volume loss (Table 1). Participants with varus and valgus malignment did not show a higher rate of cartilage loss than those with a neutral knee axis (Table 1).

Table 1: Magnitude, standard deviation and significance of cartilage change, normalized to annual (12 month) values for all participants and persons with neutral, varus and valgus alignment.

	All (n = 84)	Neutral (n = 38)	Varus (n = 26)	Valgus (n = 20)
VC	-1.8 ± 3.8%***	-2.2 ± 3.8%**	-1.6 ± 3.0%***	-1.4 ± 4.9% n.s.
ThCcAB	-1.0 ± 2.9%**	-0.7 ± 2.5%**	-1.3 ± 2.9%*	-1.0 ± 3.4% n.s.
cAB	-1.2 ± 4.0%**	-1.9 ± 4.2%*	-0.3 ± 2.1% n.s.	-1.2 ± 5.5% n.s

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; n.s = not statistically significant (paired student's t-test)

CONCLUSION: The results show that 1) significant cartilage volume loss occurs in the patella at a magnitude of about 2% per annum in subjects with mild to moderate OA, that 2) a reduction of cartilage thickness over the cartilage-covered area and a reduction in the cartilage-covered area (increase in denuded area) make similar contributions to the amount of cartilage volume loss, and that 3) valgus and varus malalignment do not appear to influence the magnitude of longitudinal patellar cartilage change. Further steps to take include confirming these results in a larger sample and separately analyzing patellar cartilage change in the medial and lateral patellar facets, since valgus and varus malalignment may selectively impact cartilage loss in these regions of interest.

SPONSOR: National Institute of Health.
DICLOSURE STATEMENT: M.K., M.H. and W.W. have part time employments with Chondrometrics GmbH. F.E. is CEO of Chondrometrics GmbH and provides consulting services to Pfizer Inc., Glaxo Smith Kline Inc., Merck Serono Inc. and Astrazeneca Ltd.
CORRESPONDENCE ADDRESS: manuela.kunz@pmu.ac.at

LONGITUDINAL CHANGES IN CARTILAGE SURFACE SMOOTHNESS: A MARKER OF PROGRESSION DURING MODERATE OA?

*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Christiansen C.

* Department of Computer Science, University of Copenhagen, Denmark
** Nordic Bioscience (NB), Herlev, Denmark
*** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark

INTRODUCTION: Local changes on the cartilage surface are related to the smoothness of the surface and are related to e.g., focal lesions and fibrillations which are established effects beginning at the moderate stages of OA, at Kellgren-Lawrence index (KL) 1-2.

OBJECTIVE: To evaluate the articular cartilage surface smoothness determined from MRI data cross-sectionally and longitudinally, in relation to radiographic signs of OA.

METHODS: Knee MR scans were acquired sagittally using a low-field 0.18T scanner (40 degrees flip angle, TR 50 ms, TE 16 ms), resolution 0.7x0.7x0.8mm^3, along with posterior-anterior x-rays for KL and tibial plateau width. Of the knees with KL 0 at baseline, 18% had a higher KL after 21 months. The baseline study consisted of 313 scans, 25 for training and 288 for testing (population 56±16 years, 44% females, baseline KL distribution [145,88,30,24,1] for KL 0-4). Follow-up scans were acquired of 243 knees 21 months and 31 knees a week after baseline. From the MR scans, the cartilage was first segmented automatically in 3D, then the cartilage surface smoothness for the medial tibial compartment were estimated automatically using fine scale curvature analysis since it is related to high curvature values locally on the surface. Measures were normalized with tibial plateau width for inter-subject comparisons.

RESULTS: At baseline, the surface smoothness was lower in the OA population (KL > 0) compared to the healthy (KL 0), with a p-value of 1.7*10^-4. The area under the ROC curve was 0.77 for separating KL <=1 from KL > 1 populations at baseline. For the 31 test-retest pairs, the mean coefficient of variation was 4.1%. For the longitudinal study, there was a significant decrease in smoothness for baseline healthy and borderline OA populations (p = 0.0029 and p = 0.0018 respectively, Fig. 1 right).

CONCLUSION: Smoothness deterioration was present for moderate and severe OA at baseline and longitudinal changes were predominant for knees that were healthy and early OA at baseline, which is consistent with the loss of cartilage surface integrity during moderate stages of OA. Thereby, cartilage smoothness has potential as a marker for OA progression during moderate OA where the disease may still be reversible.

DISCLOSURE STATEMENT: Dam and Karsdal are employees of NB. Folkesson is funded by a grant partly sponsored by NB. Christensen is a shareholder of both CCBR and NB.
CORRESPONDENCE ADDRESS: jenny@diku.dk

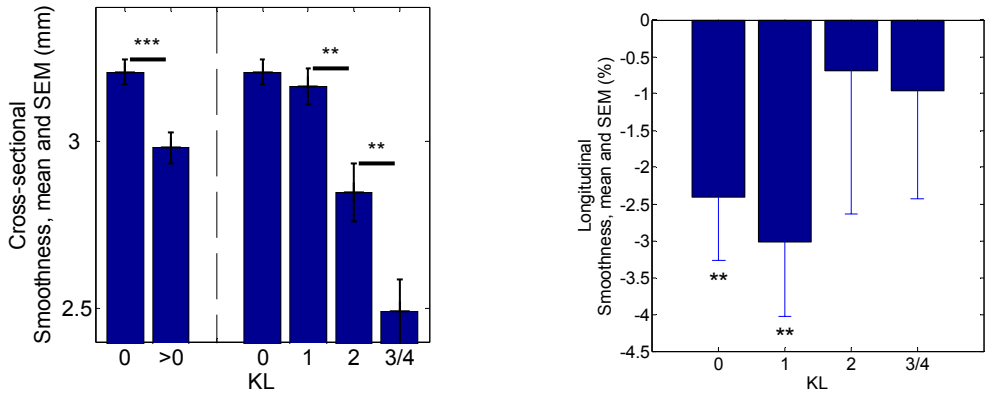


Figure 1. Cross-sectional distribution (left) and longitudinal changes (right) in KL populations at baseline.

MORE SENSITITVE ANALYTICAL MEASURES CANNOT COMPENSATE FOR PATIENT HETEROGENEITY WITH RESPECT TO ANNUALISED CARTILAGE LOSS

*Williams T.G., ***Bowes M., *Taylor C.J., *Hutchinson C.E, **Waterton J.C., **Maciewicz R.A., **Holmes A.P.

* Imaging Science and Biomedical Engineering, University of Manchester, UK. ** AstraZeneca, Macclesfield, UK. *** Imorphics, Manchester, UK.

INTRODUCTION: A previously published analysis of 11 OA patients showed "No loss of cartilage volume over three years in patients with knee osteoarthritis as assessed by magnetic resonance imaging" [Gandy *et al.*,. OA&C 10(p929) 2002], a result which appears inconsistent with other published studies [Eckstein *et al.*, MRI of Articular Cartilage in Knee OA: Morphological Assessment. OA&C 14 (Sup1,p46) 2006]. Mean thickness in central anatomically corresponded sub regions of the knee has been shown to be more sensitive to longitudinal change than compartmental volume measures [Williams et al., Cartilage Loss in Osteoarthritis Detected by Statistical Shape Analysis of Magnetic Resonance Images. OARSI 2005. Boston]. We asked whether this more sensitive method would provided a similar low rate of annualized cartilage loss.

OBJECTIVES: 1) Compare the published changes in total knee cartilage volume with thickness changes using central anatomically corresponded segmentation and analysis techniques. 2) Investigate changes in thickness in anatomical sub regions of the Tibio-Femoral (TF) joint that exclude the periphery of the cartilage sheets.

METHODS: The original study imaged 11 patient volunteers at baseline and 37±2 months using 1T MRI (3D spoiled gradient-echo with fat-suppression image: slice thickness 1.56mm, in-plane 0.55mm and T2-wieghted image: slice thickness 3mm, in-plane 0.55mm). One subject's data could not be recovered. For this analysis, images were re-segmented. Bone-reference cartilage thickness maps were produced using the method described in [Williams 2005]. Statistical shape models were used to automatically segment and propagate a set of anatomically corresponding landmark points on each bone surface. This failed for one image, leaving 9 of the original 11 patients available for re-analysis (6F, 3M, baseline K-L grades 1–3). Anatomical regions of interest defined on a single bone surface were propagated to each individual bone surface using the landmarks yielding anatomically equivalent regions of interest within which the mean thickness of (manually segmented) cartilage was calculated. Point estimates and 95% confidence intervals for annualised percentage change were calculated using a standard t-test for the log of the ratio, and back transforming (Figure 1).

RESULTS: Total knee cartilage volume (K.VC) decreased by 0.54% per year for the 9 subjects analysed (95% CI -1.99%,0.93%), confirming the 0.53% reported by Gandy *et al.* for all 11. Using current best available analysis methods, we identified ncMF (the nuclear/central cMF) as the region with the strongest signal for change. Evidence that the progression is most likely in the medial aspect of the TF is consistent with previous findings [Williams 2005] and other literature [Eckstein 2006].

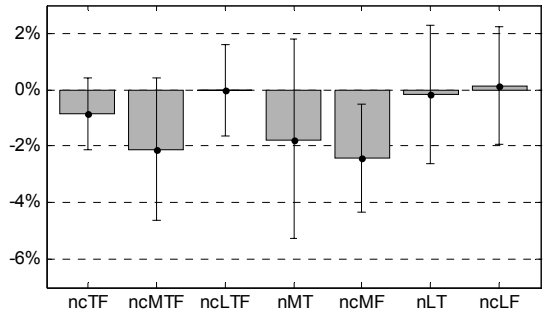


Figure 1. Annualized percentage change in

CONCLUSION: The measured changes were small and non-significant (after correction for multiple comparisons), confirming the published results of previous analysis. The lack of clear significant signal is attributed to the small size and heterogeneous disease characteristics of the cohort.

SPONSOR: AstraZeneca.
DICLOSURE STATEMENT: As affiliations.
ACKNOWLEDGMENTS: S.J Gandy, P.A. Dieppe, I. Watt.
CORRESPONDENCE ADDRESSES: tomos.williams@manchester.ac.uk, andrew.holmes@astrazeneca.com, mike@imorphics.com.

POSTER SESSION 2

Thursday, July 12th, 2007: 15:30 – 16:15 (Presenters of Posters No. 15 to 27 at posters)

15	*Tamez-Pena J., * Barbu-McInnis M., * Totterman S. *VirtualScopics, Rochester, NY, USA MRI BASED METHDOLOGY FOR THE QUANTITATIVE EVALUATION OF SUBCHONDRIAL BONE PLATE SURFACE CHANGES
16	*Fischer K.J., *Thoomakuntla B.R., *Waller A.A., **Bilgen M., **McIff T.E., **Toby E.B. * University of Kansas, Lawrence, KS, USA, ** University of Kansas Medical Center, Kansas City, KS, USA MRI-BASED MODELING OF RADIOCARPAL JOINT CONTACT PRESSURE DISTRIBUTIONS DURING FUNCTIONAL LOADING: CURRENT VALIDATION DATA
17	Bouchgua M., Alexander K., d'Anjou M.A., Girard C., Beauchamp G., Richard H., Laverty S. Faculty of Veterinary Medicine, University of Montreal, St Hyacinthe, QC, Canada. MULTIMODALITY IMAGING OF TEMPORAL CHANGES IN KNEE OSTEOARTHRITIS LESIONS IN AN IN VIVO RABBIT MODEL
18	*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A. * Chemistry Department, New York University, New York, NY, ** Radiology Department, New York University, New York, NY. NA-MRI: AN EARLY MARKER FOR CARTILAGE DEGENERATION
19	*Stok K.S., **Pelled G., **Zilberman Y., **Kallai I., **Gazit D., *Müller R. * Institute for Biomedical Engineering, University and ETH Zürich, Zürich, Switzerland , ** Skeletal Biotech Lab, Hebrew University, Jerusalem, Israel OSTEOARTHRITIS IMAGING USING CONFOCAL MICROSCOPY AND MICRO-COMPUTED TOMOGRAPHY – A MURINE STUDY
20	*Sochor, M.A., *,**Witschey II, W.R.T., *,**Borthakur, A., *,**Reddy, R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA USA ** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA OSTEOARTHRITIS PACKAGE: AN MRI PROTOCOL FOR DETECTION OF EARLY OA.
21	*Wlk MV, *Chochole M, **Landsiedl F * Herz-Jesu Hospital Vienna, Orthopedic Dep., Austria, ** Orthopedic Hosp. Speising Vienna, 1. Dep., Austria PATHOLOGY OF THE DISCUS TRIANGULARIS OF THE WRIST IN MRI AND ARTHROSCOPY: A COMPARISON
22	*Haslam J., *Lacey T., *Brett A., **Tengowski M.W. * Optasia Medical Ltd, Manchester, UK, ** Pfizer Global Research & Development, 2800 Plymouth Rd., Ann Arbor, MI, USA REPRODUCIBILITY OF AUTOMATED RADIOGRAPHIC JOINT SPACE WIDTH AND FRACTAL SIGNATURE ANALYSIS MEASUREMENTS IN THE MEDIAL TIBIOFEMORAL COMPARTMENT OF THE KNEE

23	*Sasho T., *Nakagawa K., *Ochiai N., *Ogino S., *Nagashima R., *Matsuki K., ** Wada Y., **Watanabe A., *Moriya H. * Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University. Japan, ** Department of Orthopaedic Surgery, Teikyo University Chiba Medical Center, Japan SEMI-AUTOMATIC EVALUATION OF DISEASE SEVERITY OF OSTEOARTHTITIS OF THE KNEE FROM MRI USING NEWLY DEVELOPED SOFTWARE
24	*Qazi A.A., **Karsdal M.A., ***Christiansen C., **Dam E.B. * Image Group, Department of Computer Science, University of Copenhagen, Denmark, ** Nordic Bioscience (NB), Herlev, Denmark, *** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark SEPARATION OF HEALTHY AND EARLY OA BY QUANTIFICATION OF CARTILAGE HOMOGENEITY FROM MRI: A LONGITUDINAL STUDY
25	*Wyman, B. *Buck, R.,*Hellio, M-P, **Krishnan, N.,** McKenzie, C., ***Totterman S. ****Charles, C. **Burstein, D, ***Tamez, J., for the A9001140 Investigators * Pfizer Global Research and Development, Groton, CT, USA, ** Beth Israel Deaconess Medical Center, Boston MA, USA *** VirtualScopics, Rochester, NY, USA, ****Duke Image Analysis Laboratory, Durham, NC, USA SIX MONTH LONGITUDINAL CHANGE IN DGEMRIC MEASUREMENTS IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY
26	*,**Witschey II W.R.T., *,**Borthakur A., *,** Elliott M.A., *Sochor M.A., *,**Reddy R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA, ** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA SLIPS: AN MRI PULSE SEQUENCE FOR RAPID AND QUANTITATIVE 3D T1 MRI OF CARTILAGE IN A CLINICAL SETTING.
27	*Waarsing JH, **Rozendaal RM, **Bierma-Zeinstra SM, *Weinans, H. * Dept. of orthopedics, Erasmus Medical Center, Rotterdam, The Netherlands, ** Dept. of General Practice, Erasmus Medical Center, Rotterdam, The Netherlands STATISTICAL APPEARANCE MODELS OF THE PROXIMAL FEMUR IN DXA SCANS ASSOCIATE WITH STATE AND PROGRESSION OF CLINICAL OA.

MRI BASED METHDOLOGY FOR THE QUANTITATIVE EVALUATION OF SUBCHONDRIAL BONE PLATE SURFACE CHANGES

*Tamez-Pena J., * Barbu-McInnis M., * Totterman S.

*VirtualScopics, Rochester, NY, USA

INTRODUCTION: The analysis of bone changes in the development of OA has been primarily concentrated to the analysis of osteophytes and bone lesions. This work presents a method for the analysis of small changes in the surface of the subchondrial bone plates of the knee joint.

OBJECTIVE: To study the reproducibility of advanced image analysis methods for the evaluation of changes in knee subchondrial bone plates curvatures and the shifts in the location of subchondrial bone plates surfaces form MRI.

METHODS: A pair of two timepoints (baseline and one year) of nine healthy volunteers between 31 and 71 years old (mean age of 44), five female and four male, with no clinical evidence of OA were MRI scanned using standard T1 weighted SPGR subsequences and GRE T2* weighted images. The MRI images were fused and independently segmented using VirtualScopics' proprietary software for the extraction of bone tissue and cartilage tissue. After than, the baseline segmentations and the one year segmentations were analyzed by a computer algorithm that aligned the 3D reconstructions of bone-cartilage interface and computed the shifts in the location of the subchondrial bone plate and the changes in the curvature of the subchondrial bone plate at the bone-cartilage interface. The shift in the bone plates was computed by averaging the distance between surfaces while the change in curvature was computed after computing the median value of the differences in surface patch to surface patch curvature values. Mean changes, standard deviations of the differences (SDD) and their corresponding 95% confidence intervals of the mean change (95% CI) were computed.

RESULTS: The data showed that the MRI method is able to locate the subchondrial bone plate surface with an accuracy of 30 □m. The curvature was able to be computed with accuracy in the order of 0.003 mm^{-1}. The change in curvature was also associated with local displacement in the surfaces location (r=0.6)

Plate	Curvature(mm^{-1})		Average Displacement (mm)	
	Change (SDD)	95% CI	Change (SDD)	95% CI
cMT	0.000 (0.003)	-0.003 to 0.002	-0.001 (0.025)	-0.020 to 0.018
cLT	-0.001 (0.005)	-0.005 to 0.003	0.020 (0.048)	-0.017 to 0.057
P	-0.003 (0.008)	-0.009 to 0.004	-0.022 (0.034)	-0.048 to 0.005
TfF	-0.005* (0.003)	-0.006 to -0.003	0.000 (0.026)	-0.020 to 0.020
cMF	0.001 (0.005)	-0.003 to 0.004	0.008 (0.033)	-0.018 to 0.034
cLF	-0.003 (0.004)	-0.006 to 0.001	-0.009 (0.033)	-0.034 to 0.016
Entire Femur	-0.004* (0.003)	-0.006 to -0.002	-0.034 (0.069)	-0.086 to 0.019

* $p<0.05$

CONCLUSION: The small pilot study proved that the bone-cartilage interface of the subchondrial bone plates can be precisely measured using MRI. The level of precision allowed detecting statistical significant average annual curvature changes at the entire femur and the trochlea (TrF) form the nine subjects enrolled in the study. Furthermore, the changes in curvature were correlated to changes in the location of the subchondrial bone surfaces. These findings are preliminary; therefore, larger studies will be required to understand the significance of the changes in subchondrial bone plate surface topography in the development of OA.

SPONSOR: VirtualScopics, Inc.
DICLOSURE STATEMENT: J. Tamez-Pena and S. Totterman hold VirtualScopics stocks.
ACKNOWLEDGMENT: We gratefully thank the entire VirtualScopics, team for their efforts.
CORRESPONDENCE ADDRESS: tamez@virtualscopics.com

MRI-BASED MODELING OF RADIOCARPAL JOINT CONTACT PRESSURE DISTRIBUTIONS DURING FUNCTIONAL LOADING: CURRENT VALIDATION DATA

*Fischer K.J., *Thoomakuntla B.R., *Waller A.A., **Bilgen M., **McIff T.E., **Toby E.B.

* University of Kansas, Lawrence, KS, USA
** University of Kansas Medical Center, Kansas City, KS, USA

INTRODUCTION: Arthritis is strongly associated with abnormally high joint contact pressures and abnormal kinematics. The ability to measure joint contact pressures in vivo would provide a means for characterizing the relationship between joint contact pressures and the degeneration of cartilageThe overall goal of our research is to develop and apply MRI-based joint contact models to measure in vivo joint contact pressures during functional loading activities—currently focused on radiocarpal joints.

OBJECTIVE: To validate the use of MRI-based computer models for the evaluation of joint contact pressures during functional loading.

METHODS: This study included a combination of experimental measurements compared with MRI-based model data. For the experiments, the pressures in the radiocarpal joints of each of five (5) cadaver forearm specimens was measured during simulated grasp using pressure sensitive film and a Tekscan electronic sensor. Idealized accuracy tests were also performed for both experimental measures. The experimental apparatus was plastic, to allow the same test conditions in a 9.4T MRI scanner (Unity INOVA, Varian Inc., Palo Alto, CA). Each image set was obtained with slight variations of a gradient echo sequence (TR=800ms, TE=min, FOV= 60x60 mm, data array=1024x512, slice thickness=1 mm, resulting in an in-plane resolution of 0.114 mm. Images were obtained with and without simulated grasp loading. The image set obtained without loading was manually segmented, and the resulting contours were used to generate the 3D geometric surface model of the radius, scaphoid and lunate. Both image sets were used with 3D voxel registration to determine the kinematic transformation of the unloaded bones to their loaded position and orientation. Geometric models and carpal kinematics were implemented in the Joint_Model program (developed at Columbia University) to determine the contact pressure distributions, contact area and contact force at each joint. Cartilage thickness was assumed uniform at 1.0 mm on each bone with an effective compressive modulus of 4 Mpa, and the pressure was proportional to the overlap of the model surfaces in the loaded state. The model data was then compared to that from the experimental sensor systems and to contact area measured directly from the MR images.

RESULTS: Qualitatively, relative size, shape and location of radioscaphoid and radiolunate contact areas are consistent between methods (Figure 1). Idealized experiments demonstrated errors of about 10% for both experimental measures, partially explaining substantial discrepancies between the pressure film and Tekscan data (Table 1). Generally, the model tended to produce values for all measures between the Tekscan data and the pressurex film data. The most encouraging result is the correspondence of the contact area from the models and that measured directly from MRI (for specimens 1-3, currently).

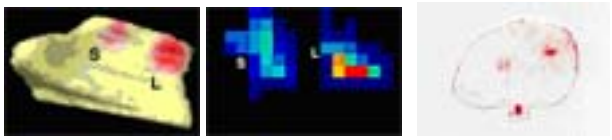


Figure 1. Specimen 5 pressures from the MRI-based Model (left), the Tekscan sensor (middle) and Pressurex.

CONCLUSION: MRI-based modeling of contact during functional loading is at least as accurate as, and likely more accurate than, current ex vivo experimental measures.

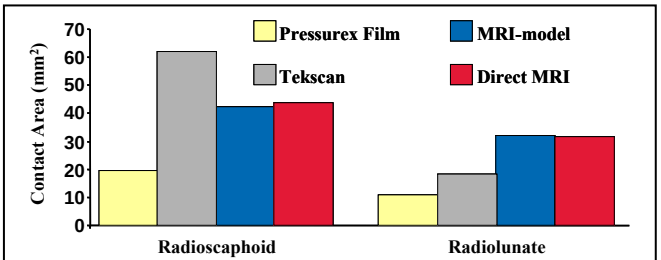


Figure 2. Specimen 1 contact areas from all measures.

SPONSOR: The American Society for Surgery of the Hand
DICLOSURE STATEMENT: none.
ACKNOWLEDGMENT: We thank Gerard Ateshian for access to Joint_Model and related assistance.
CORRESPONDENCE ADDRESS: fischer@ku.edu, +1 (785) 864-2994, USA

MULTIMODALITY IMAGING OF TEMPORAL CHANGES IN KNEE OSTEOARTHRITIS LESIONS IN AN IN VIVO RABBIT MODEL

Bouchgua M., Alexander K., d'Anjou M.A., Girard C., Beauchamp G., Richard H., Laverty S.

Faculty of Veterinary Medicine, University of Montreal, St Hyacinthe, QC, Canada.

INTRODUCTION: Rapid, easy, repeatable and non-invasive in vivo assessment of osteoarthritic changes in animal models of osteoarthritis is necessary to measure the magnitude of disease-related changes and the response to novel therapeutic interventions. Validation of clinical 1.5 Tesla MRI and CT and combined in vivo use of these widely-available imaging modalities for the assessment of OA changes in animal models should provide comprehensive assessment of joint structure.

OBJECTIVE: To describe the evolution over time of knee lesions in an in vivo rabbit model of OA using clinically-available imaging modalities: computed radiography (CR), CT and 1.5 T MRI.

METHODS: Unilateral transection of the ACL was performed on a randomly assigned FT joint in skeletally mature male New Zealand White rabbits (n=10). A sham surgery was performed on the contralateral joints (n=10). Control rabbits (n=6) did not undergo surgery. CR, CT and MRI were performed 2 weeks before surgery (week -2), and then repeated at weeks 2, 4 and 8 post-surgery for all 10 ACLT and sham joints, and at week 12 for 5 of the ACLT rabbits. Images were acquired at weeks -2 and 8 in the 6 control rabbits to detect changes related to time in normal animals. The controls and 5 ACLTs were euthanized at week 8 and the other 5 ACLTs at week 12, and macroscopic and histologic evaluation of the joints was made. The following parameters were assessed with one or more of the 3 modalities (modality and view or section in parentheses): osteophytosis (CR caudocranial (CC) and mediolateral (ML) views; CT dorsal and transverse sections (DS and TS); MRI sagittal 3D SPGR-fat saturation sections (SS 3D SPGR-FS), DS dual proton density/T2-fat saturation (DS PD/T2-FS)), subchondral bone sclerosis (CR CC; CT DS), BM lesions (MRI DS PD/T2FS), JSW measurement (CR CC; CT DS; MRI SS 3D SPGR-FS and DS PD/T2), femoropatellar effusion (CR ML; CT TS; MRI SS 3D SPGR-FS), cartilage thickness (mm) and defects (mm) (MRI SS 3D SPGR-FS and DS PD/T2). The sensitivity (Se) and specificity (Sp) of the 3 imaging modalities to detect osteophytes, and of MRI to detect cartilage defects, were calculated using the corresponding macroscopic and histologic evaluation, respectively. Agreement between quantitative modality measures was assessed using a repeated-measures linear model. The differences between joint groups and the evolution of lesions over time were assessed with a linear repeated-measures model with time and groups as within-subject factors, and with a Cochran-Mantel-Haenszel test for semi-quantitative parameters.

RESULTS: CT had the highest Se (90%) and Sp (91%) to detect osteophytes. A significant increase in total joint osteophyte score was detected with CT as early as 2 weeks post-surgery ($p = 0.04$) and persisted until week 12 ($p = 0.03$). The osteophytes were observed most commonly in the medial femoral epicondyle. Subchondral bone sclerosis was not reliably assessed with CR and CT. BM lesions occurred most commonly in the LF of the ACLT joints and were most severe at week 4 post-surgery. BM lesions were not detected in the tibia in any group. With MRI, minimal JSW in the lateral compartment increased significantly at weeks 4 ($p=0.0007$), 8 ($p=0.02$) and 12 ($p=0.006$) in the ACLT joints. A significant increase in synovial effusion was measured on MRI at week 2 ($p=0.01$), peaked at week 4 ($p=0.002$) and remained elevated until week 8 ($p=0.03$) in the ACLT joints. 1.5 Tesla MRI under our laboratory conditions had a low Se and Sp to detect articular cartilage defects.

CONCLUSION: Combined clinically-available CT and 1.5 T MRI allowed assessment of most of the characteristics of OA over time in an in vivo ACLT rabbit model, including osteophytosis, bone marrow lesions, minimal joint space width and femoropatellar effusion. However 1.5 Tesla MRI in this rabbit OA model and under our laboratory conditions was not able to detect cartilage lesions.

SPONSOR: Canadian Arthritis Network, Toronto, Ontario, Canada
DICLOSURE STATEMENT: None
ACKNOWLEDGMENTS: Eric Norman Carmel, Geneviève Rouleau, Anne-Marie Martel, Suzie Lachance and Marie Lecocq are thanked for their technical assistance.
CORRESPONDENCE ADDRESS: maria.bouchgua@umontreal.ca

Na-MRI: AN EARLY MARKER FOR CARTILAGE DEGENERATION

*Ling W., **Regatte R. R., **Schweitzer M. E., *Jerschow A.

* Chemistry Department, New York University, New York, NY
** Radiology Department, New York University, New York, NY.

INTRODUCTION: The high abundance of ^{23}Na in tissue, especially in cartilage, offers promising prospect for ^{23}Na-MRI as a powerful diagnostic method for early detection of cartilage degeneration. While both free and ordered (bound) sodium are prevalent throughout the body, monitoring the levels of the latter is of particular interest due to the anticipated strong correlation between changes in ordered sodium concentration and the early symptoms for most musculoskeletal disorders. The double-quantum filtered (DQF) experiment, the Jeener-Broekaert sequences and experiments with shift reagents were previously used to selectively probe sodium signals in different environments. The purpose of the work is to introduce novel pulse sequences based on frequency-swept pulses and nutation effects that can be used for probing cartilage degeneration at early stages via ^{23}Na-MRI, and to investigate the correlation between the quadrupolar interactions in cartilage samples as a function of proteoglycan (PG) and collagen depletion.

OBJECTIVE:
1) Determine the correlation between the ^{23}Na parameters (concentration, quadrupolar coupling, ratio free/bound) and PG and collagen depletion.
2) Develop practical methods for separating the signals between free and bound sodium.
3) Demonstrate ^{23}Na-MRI assessment in intact and PG and collagen-depleted tissue samples.

METHODS: We use two techniques for the separation between free and bound sodium: (1) a method based on frequency-swept pulses and (2) a method based on the altered nutation frequencies of quadrupolar nuclei by a residual quadrupolar interaction (quadrupolar filter by nutation). These sequences are tested on several liquid-crystalline model systems, as well as intact and enzymatically-depleted cartilage samples. Sequential PG and collagen depletion studies were performed using trypsin and collagenase respectively (n=5 samples). We correlate the variation of quadrupolar coupling constants - QCCs with PG and collagen depletion levels.

RESULTS: The residual quadrupolar interaction is shown to increase by 50% through the course of both PG and collagen depletion. The developed pulse sequences are shown to cleanly select the bound over the free sodium. The quadrupolar nutation technique is being implemented on an MRI scanner.

CONCLUSION: We clearly show that monitoring the bound sodium pool is a good indicator for cartilage degeneration, and correlates well with both PG and collagen depletion levels. Since the quadrupolar interaction is intimately related to the degree of anisotropy and motion, we feel that characterizing the bound sodium pool in vivo will provide a good assessment of cartilage integriety. The developed pulse sequences were shown to be fit for the implementation on MRI scanners.

SPONSOR: NIH 1R21ARO54002-01A1, NSF CHE0554400

CORRESPONDENCE ADDRESS: alexej.jerschow@nyu.edu

OSTEOARTHRITIS IMAGING USING CONFOCAL MICROSCOPY AND MICRO-COMPUTED TOMOGRAPHY – A MURINE STUDY

*Stok K.S., **Pelled G., **Zilberman Y., **Kallai I., **Gazit D., *Müller R.

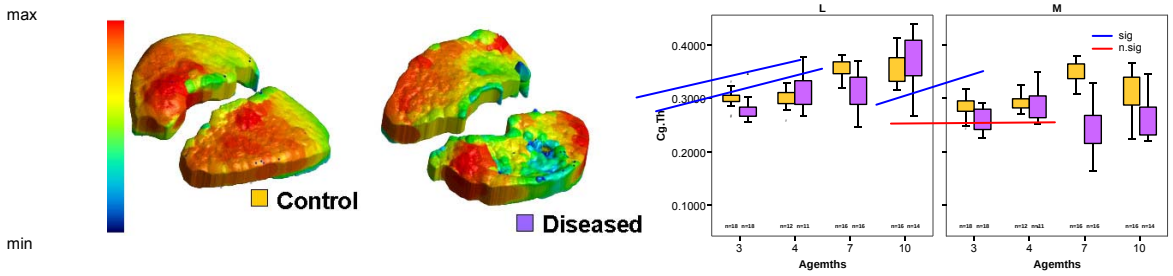
* Institute for Biomedical Engineering, University and ETH Zürich, Zürich, Switzerland
** Skeletal Biotech Lab, Hebrew University, Jerusalem, Israel

INTRODUCTION: Experimental induction of OA in animals makes it possible to influence the onset and course of the disease for the purpose of investigating therapeutic effects. The highest incidence of naturally-occurring OA in mice is reported in the STR/1N strain; where STR/ort mice are derived from this parent strain and develop histopathological lesions in the medial tibia similar to the human disease.

OBJECTIVE: The aim is to provide tools for imaging which are specific to murine articular cartilage and subchondral bone, for assessment of new OA therapies in mouse models. Novel techniques multiplexing confocal laser scanning microscopy (CLSM) with micro-computed tomography (µCT) are developed for volumetric and topographical imaging of articulating joints.

METHODS: 30 male STR/ort mice were used as the OA model, ranging in age from 3 to 10 months. Equal numbers of the CBA strain were used as age-matched controls. The mice were sacrificed and the knees dissected free of surrounding tissue. The joints were imaged with µCT (µCT 40, Scanco Medical, Bassersdorf, CH) at an isotropic voxel size of 12 µm, providing data of the subchondral bone. The cartilage was then scanned through its depth using a CLS microscope (SP2, Leica Microsystems, CH) with an isotropic voxel size of 6 µm, a 5x objective and a UV-laser source ($\lambda = 430$ nm).
Images from both systems were processed using µCT evaluation tools. Cartilage tissue thickness (Cg.Th) and volume (Cg.V), bone volume density (BV/TV), trabecular thickness (Tb.Th), spacing (Tb.Sp) and number (Tb.N) in the metaphyseal and epiphyseal bone, and cortical thickness (Ct.Th) and porosity (Ct.Po) in the subchondral bone were measured. A univariate analysis of variance was conducted for each parameter of interest, looking for significant effects of age, treatment, and any age/treatment interaction. A priori power analysis set the level for significance at 0.05.

RESULTS: Age-related changes and strain-related differences in the joint compartments, as well as important interactions that occur with age and the onset of disease were found. In the medial cartilage diseased specimens did not display the steadily increasing age-related Cg.Th behaviour of their control counterparts, whereas the lateral side showed no strain-related differences (see figure). Ct.Po differences were due primarily to differences between strains, except at 7 and 10 months when interaction between age and disease were observed in diverging measures. Significant Ct.Th, epiphyseal Tb.Th and metaphyseal Tb.Th changes were due to age, except at 7 and 10 months when interaction was again observed in diverging trends. Epiphyseal BV/TV increased in the controls while stagnating in the diseased, while metaphyseal BV/TV was consistent in the controls, while decreasing in the diseased. The results indicate that specific architectural alterations occur with OA, others may simply be age-related, and still others occur with an interaction between the onset of disease and age.



CONCLUSION: Using a novel multimodal imaging approach combining CLSM and µCT, architectural changes to knee-joint subchondral bone and cartilage due to disease and age have been shown in mice. This technique offers a unique potential for gene therapy assessment in murine models.

SPONSOR: European Union Project, QLRT-2001-02039
DICLOSURE STATEMENT: none
ACKNOWLEDGMENT: Thanks to AG. Bitterman and M. Höchli, EMZ, University of Zürich, for advice on CLSM imaging.
CORRESPONDENCE ADDRESS: kas@ethz.ch

OSTEOARTHRITIS PACKAGE: AN MRI PROTOCOL FOR DETECTION OF EARLY OA.

*Sochor, M.A., *,**Witschey II, W.R.T., *,**Borthakur, A., *,**Reddy, R.

* Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA USA ** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA

INTRODUCTION: Early OA is characterized by a significant decrease in the proteoglycan (PG) content of the cartilage extracellular space (1). It has been shown by MRI that T1rho relaxation can quantitatively measure changes in PG content (2) and that ^{23}Na MRI can be used to measure the fixed charge density (FCD) of cartilage (3) which is directly related to PG content. These two techniques naturally complement each other in tracking early OA.

OBJECTIVE: To develop a noninvasive MRI protocol to detect early OA by T1rho mapping and ^{23}Na concentration mapping for FCD without patient repositioning in a clinically reasonable time span

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METHODS: The right leg of a healthy, asymptomatic volunteer (age=22, sex=male) was scanned on a 3T Siemens Trio scanner. Five sodium phantoms were placed anterior to the knee for ^{23}Na concentration (4) and FCD (3) measurements as previously described. A double tuned ^{23}Na/^{1}H, double quadrature, transmit/receive birdcage knee coil (Stark Contrast) was interfaced to a three channel ^{1}H, ^{17}O, ^{23}Na Tx/Rx box (Stark Contrast). The scanning protocol is outlined in the table below. Post-processing of images was performed in the IDL programming environment (ITT VIS) and in Matlab (Mathworks).

Sequence	Nuclei	Orientation	Approximate Time	Purpose
3-plane localizer	1H		0:30	
3D-MPRAGE	1H	Sagittal	5:00	Future slice planning
T1-W GRE	1H	Axial	3:00	Anatomical overlays
5 T1ρ-W TRUFI	1H	Axial	11:00	PG assesment
3D-FLASH	23Na	Axial	30:00	FCD measurement

RESULTS**:** Mean and standard deviation of T1rho, ^{23}Na concentration, and FCD were measured in the 4 compartments of the cartilage in the table below. Values are displayed ± 1 standard devation ^{23}Na concentration maps (Figure 1) and T1rho maps (Figure 2) were overlayed anatomical images.

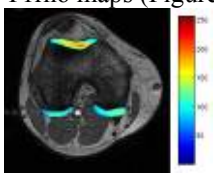


Fig. 1: [Na] overlayed T1-W GRE. Slice thickness = 6mm.

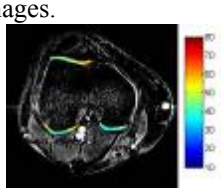


Fig. 1: T1rho map over layed T1rho-W image. Slice thickness = 4mm.

n=1	**Lateral femoral**	**Medial Femoral**	**Lateral Patellar**	**Medial Patellar**
[Na] mM	181 ± 16	177 ± 18	202 ± 15	182 ± 20
FCD mM	-72 ± 24	-66 ± 29	-105 ± 21	-75 ± 30
T1rho ms	47.0 ± 3.9	45 ± 2.7	48.1 ± 2.0	45.0 ±2.5

CONCLUSION: Measured T1rho values agree with previous findings. Measured FCD was lower than expected, possibly caused by partial voluming of cartilage. Further research will consist of sequence optimization to achieve identical T1rho and ^{23}Na slices, slice planning using MPRAGE, and an increase in the patient pool to achieve statistically significant data for both healthy and OA populations.

SPONSOR: NCRR-funded Research Resource (RR02305); NIH grant R01-AR045242.
ACKNOWLEDGMENT: Raj Sarkar, Chenyang Wang, Daniel Wallman, Mark Elliott.
CORRESPONDENCE ADDRESS: matthew.sochor@gmail.com
REFERENCES: (1) LeRoux MA, et al. J. Orthop. Res. 18: 383-392 (2000) (2) Wheaton AJ, et al. Magn. Reson. Med. 54: 1087-1093 (2005) (3) Shapiro EM, et al. Magn. Reson. in Med. 47: 284-291 (2002) (4) Shapiro EM, et al. J. Magn. Reson. 142: 24-31 (2000)

PATHOLOGY OF THE DISCUS TRIANGULARIS OF THE WRIST IN MRI AND ARTHROSCOPY: A COMPARISON

*Wlk MV, *Chochole M, **Landsiedl F

* Herz-Jesu Hospital Vienna, Orthopedic Dep., Austria
** Orthopedic Hosp. Speising Vienna, 1. Dep., Austria

INTRODUCTION: Lesions of the discus triangularis (TFCC) and associated problems are responsible for ulnar sided wrist pain. MRI findings are import for the indication of an arthroscopy. MRI studies report high sensitivity and specificity for TFCC lesions. Our retrospective study compared Arthro-MRI findings of ulnar sided wrist pain, evaluated by non specialized radiologists, with arthroscopic findings.

OBJECTIVE: This study investigates the effect of observer experience on MRI diagnosis of TFCC-lesions by non specialized radiologists in comparison to arthroscopy.

METHODS: Between 2000 and 2005 102 arthroscopic procedures of the wrist were performed as either isolated or in combination with open surgery at out department. 86 cases with Arthro-MRI and arthroscopic findings were available for our study. The mean age of the patients were 38a (+/- 24a). The Mayo classification for TFCC lesions was used: intact, degeneration Type I, Type II-IV, traumatic I radial, II central, III ulnar, IV palmar (ulnovolar).

RESULTS: We found conformity of MRI and arthroscopy in 70% of cases in our non selective patient cohort. Whereas 33 were true positive and 25 true negative. 30% of the cases were discordant with 13 false positive and 15 false negative. In 15% surgical intervention was performed (6 refixations, 6 resections). In this group we found 4 false negative MRI and 9 true positive. The general sensitivity of all TFCC-lesions was 69% and the specificity 34%. These results are inconsistent to the literature, which states, according to study design, sensitivity from 72 to 100% and specificity from 70 to 96%. Blazar et al. claim that the published accuracy rates for prediction of TFCC lesion may be reproducible only in very specialized centers.

CONCLUSION: According to our own results and the literature we validate MRI findings of TFCC lesions by non specialized radiologists with care. Therefore we would emphasize a close cooperation between radiologists and hand specialists.

CORRESPONDENCE ADDRESS: matthias.wlk@aon.at

REPRODUCIBILITY OF AUTOMATED RADIOGRAPHIC JOINT SPACE WIDTH AND FRACTAL SIGNATURE ANALYSIS MEASUREMENTS IN THE MEDIAL TIBIOFEMORAL COMPARTMENT OF THE KNEE

*Haslam J., *Lacey T., *Brett A., **Tengowski M.W.

* Optasia Medical Ltd, Manchester, UK
** Pfizer Global Research & Development, 2800 Plymouth Rd., Ann Arbor, MI, USA

INTRODUCTION: Radiographic minimum Joint Space Width (minJSW) is the primary structural endpoint used as an indirect measure of articular cartilage thickness in clinical trials of knee osteoarthritis (OA). Standardized radiographic protocols are used to minimize variation in acquiring the radiographic images, and computerized methods of measurement are used to improve the reproducibility of minJSW. Fractal Signature Analysis (FSA), which assesses texture and can be used to quantify trabecular bone structure in proximal tibia radiographs, may have utility for monitoring OA.

OBJECTIVE: To determine the intra-observer reproducibility of a semi-automatic software application to measure radiographic minJSW and FSA.

METHODS: PA knee radiographs were acquired from 21 subjects representative of a target population for clinical trials (OA and controls) at 7 study centres using the modified Lyon-Schuss method (all subjects) and fixed flexion (10 subjects) at baseline and 1 year. Digital images had resolutions ranging from 0.385-0.038 mm/pixel. All images were acquired with a SynaFlexer™ positioning frame and phantom within the image for calibration. Test/re-test data were simulated by duplicating images and giving them new identifiers, resulting in a total of 51 image pairs. KneeAnalyzer software (Optasia Medical, Manchester, UK) was used by an operator with no clinical expertise to make measurements from the radiographs. Images were presented to the operator in random order. The software employs a proprietary statistical model-based image analysis technique, which uses a crude manual 6-point initialisation to then automatically segment the femoral and tibial margins of the knee joint space. Measurements of the minJSW and FSA (for images digitized at <0.2 mm/pixel) were calculated automatically for the medial compartment. Time elapsed between the start of the user interaction (including image load) and the presentation of the measurement results by the software was measured. Intra-observer reproducibility for minJSW was calculated as the root of the mean squares (rms) of the standard deviations (SD) of all pairs of duplicate images from the same patient. Reproducibility for FSA was calculated as mean SD over the range of scales 0.5-1.2mm normalized by mean response.

RESULTS: Analysis took 36s per image averaged over all images. The result from the small set of pairs for fixed flexion at <0.2 mm/pixel are dominated by two outlying data points of 0.62 and 0.61 mm. The table below presents results for the two imaging protocols and groups of image resolution:

			minJSW	**FSA @ 0.5-1.2mm**
imaging protocol	resolution	# of pairs	rms SD [mm]	norm. mean SD
fixed flexion	all pairs	20	0.18	-
	<0.2 mm/pixel	10	0.23	0.6%
modified L-S	all pairs	31	0.12	-
	<0.2 mm/pixel	19	0.14	0.3%

CONCLUSION: We found intra-observer reproducibility for minJSW that compares favorably to other manual and automated methods described in the literature. In addition, for images with a pixel size of <0.2mm, we were able to reproducibly measure FSA with fully automatic region placement. The short user interaction and processing time makes this tool suited for the processing of large data sets. Automated segmentation and measurement appeared more precise using the modified Lyon-Schuss positioning than for fixed flexion. However, this was caused by two outliers and may not reflect the inherent reproducibility of the positioning technique. Further testing is needed to document inter-observer reproducibility and sensitivity to disease progression.

SPONSOR: Pfizer Global Research & Development, Ann Arbor, MI, USA
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: tony.lacey@optasiamedical.com

SEMI-AUTOMATIC EVALUATION OF DISEASE SEVERITY OF OSTEOARTHTITIS OF THE KNEE FROM MRI USING NEWLY DEVELOPED SOFTWARE

*Sasho T., *Nakagawa K., *Ochiai N., *Ogino S., *Nagashima R., *Matsuki K., ** Wada Y., **Watanabe A., *Moriya H.

* Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University. Japan
** Department of Orthopaedic Surgery, Teikyo University Chiba Medical Center, Japan

INTRODUCTION: Objective assessment of disease severity of OA is essential for evaluating efficacy of interventions as well as establishing treatment system. But up until now, no objective assessment is reliable enough for this purpose. We direct our attention to contour of femoral condyle on MRI that shows irregular changes as disease progresses. To evaluate irregularity, new computer software was developed.

OBJECTIVE: In the present study, 1) correlation between two parameters (tentatively named RULL and SDWC) that represent irregularity of contour of media femoral condyle (MFC) and knee functional score was examined. 2) Specimens retrieved at total knee arthroplasty (TKA) were histologically studied and number of cystic lesions formed at subchondral area of MFC and its correlation to RULL and SDWC was examined.

METHODS: Fifty-five medial-type OA knees were involved. Their age, gender, and knee functional score employing Lysholm score were recorded. For the assessement of irregularity of contour, MR images with sagittal proton density weighed sequence were utilized (Signa 1.5-T, GE medical system, TR 2000ms, TE 16ms, FOV 14-16cm, matrix 512X512, slice thickness 4mm, 0mm gap). Following are procedures to evaluate irregularity of contour using newly developed software: Firstly, three slices that represented the center of medial compartment were selected and they were converted into black and white images. Secondly upper surface of the contour and lower surface of the contour were extracted. Thirdly, ratio of length of upper surface and lower surface was calculated (RULL) and width of the contour were calculated at each pixel and standard deviation of them was calculated (SDWC). Average of three slices was counted as parameters expressing irregularity of the contour. Statistical analysis was done with Pearson's correlation coefficient where p less than 0.01 were considered as significant.
For histological analysis, bone samples cut at TKA were decalcified and 6-micrometer sagittal sections were made. They were stained with hematoxyline and eosin (HE). Cystic lesions were counted manually and expressed as number of cysts per 10-mm length along cartilage surface.

RESULTS: Average age of the patients was 72.8 years old. Forty-two knees were female and thirteen were male. RULL and SDWC were significantly correlated with Lysholm score with r=-0.448 and -0.501 respectively. Seven knees received TKA afterwards and correlation coefficient between number of cysts and RULL and SDWC were 0.645 and 0.775.

CONCLUSION: Evaluating irregularity of contour of femoral condyle appeared to be good indicator of disease severity of OA. Due to semi-automatic system, this system has minimum inter-observer discrepancy and good reproducibility.

ACKNOWLEDGMENT: This study was supported by a research grant for rheumatoid arthritis from the Minstry of Health, Labour and Welfare of Japan..
CORRESPONDENCE ADDRESS: sasho@faculty.chiba-u.jp

SEPARATION OF HEALTHY AND EARLY OA BY QUANTIFICATION OF CARTILAGE HOMOGENEITY FROM MRI: A LONGITUDINAL STUDY

*Qazi A.A., **Karsdal M.A., ***Christiansen C., **Dam E.B.

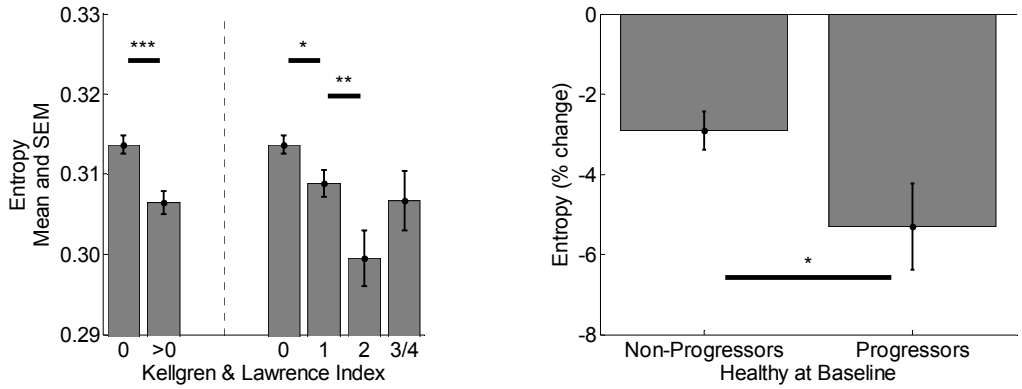
* Image Group, Department of Computer Science, University of Copenhagen, Denmark
** Nordic Bioscience (NB), Herlev, Denmark
*** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark

INTRODUCTION: Future DMOADs should ideally target early OA where it may still be reversible. Therefore, biomarkers that can separate healthy from early OA cross-sectionally as well as longitudinally are required. Cartilage Homogeneity is related to knee cartilage water distribution and altered proteoglycan distribution/integrity and may therefore be a suitable biomarker for very early OA.

OBJECTIVE: The aim of this study was to evaluate the performance of the homogeneity measure in detecting the early changes in the knee cartilage over time and comparing it to volume quantification.

METHODS: A population was scanned at baseline and after 21 months using a Turbo 3D T1 sequence (flip angle 40°, TR 50 ms, TE 16 ms, scan time 10 minutes, resolution 0.7mm*0.7mm*0.8mm) on a 0.18T MRI Esaote scanner. At baseline there were 313 knees of which 25 were used for training of computer-based methods. The validation set had 288 right and left knees at baseline (subject aged: 21-81, females: 44%, BMI: 26.7 ± 4.3) and 243 at follow-up The knees were examined by radiography and categorized by the Kellgren and Lawrence (KL) Index (with distribution [145,88,30,24,1] for KL 0-4). The medial compartments of the tibial and femoral cartilage sheets were segmented using a fully automatic voxel classification scheme and the total cartilage volume and homogeneity were quantified. Homogeneity was quantified by measuring entropy from the MRI signal intensities – this quantifies cartilages with fewer, more dominant intensities as being more homogeneous. For precision evaluation, 31 knees were re-scanned a week after baseline. The healthy subjects at baseline were divided in two groups: 1) 101 subjects that remained healthy at follow-up and 2) 25 subjects that progressed to early OA (KL 1). For each group and both volume and homogeneity changes over the 21 months were computed and the statistical significances based on an un-paired t-test were calculated.

RESULTS: The scan-rescan precision (mean CV) of volume and homogeneity were 3.6% and 2.7%. The left figure shows that homogeneity succeded in separating healthy from early OA ($p<0.05$). The right figure shows that homogeneity succeeded in seperating the progressors from non-progressors ($p<0.05$). The decrease for the early progressors was 3.4% for volume and 5.3% for entropy.



CONCLUSION: The results demonstrated that cartilage homogeneity measured by entropy was able to quantify early OA both cross-sectionally and longitudinally. The decrease in entropy for progressors over the 21 months is twice the measurement precision (for volume it is only equal to the precision). The decrease in entropy for the non-progressors might be attributed to aging effects. Thus the use of cartilage homogeneity may prove valuable for the detection and quantification of early OA progression.

DISCLOSURE STATEMENT: Dam and Karsdal are employees of NB. Qazi is funded by a grant partly sponsored by NB. Christensen is a shareholder of both CCBR and NB.
CORRESPONDENCE ADDRESS: erikdam@nordicbioscience.com

SIX MONTH LONGITUDINAL CHANGE IN dGEMRIC MEASUREMENTS IN A MULTICENTER, MULTIVENDOR MRI STUDY AT 3.0 T- THE A9001140 STUDY

*Wyman, B. *Buck, R.,*Hellio, M-P, **Krishnan, N.,** McKenzie, C., ***Totterman S. ****Charles, C. **Burstein, D, ***Tamez, J., for the A9001140 Investigators

* Pfizer Global Research and Development, Groton, CT, USA
** Beth Israel Deaconess Medical Center, Boston MA, USA
*** VirtualScopics, Rochester, NY, USA
****Duke Image Analysis Laboratory, Durham, NC, USA

INTRODUCTION: To implement delayed gadolinium enhanced magnetic resonance imaging of cartilage (dGEMRIC) for the study of disease modifying OA drugs it is important to both implement this technique in multi-center studies and to characterize longitudinal changes in the study population.

OBJECTIVE: 1) To investigate the utility of dGEMRIC in a multicenter, multivendor study to measure change over 6 months in a cohort of OA and control subjects. 2) To compare the changes in the OA group to the control group over the same period.

METHODS: A subset of paired visits at baseline (BL) and 6 months (n = 53, female) of the A9001140 observational MRI study was selected for the dGEMRIC analysis and further subdivided by KLG score. The control group (n=31), consisted of subjects with no radiographic OA [Kellgren and Lawrence Grade (KLG 0)], and had an average body mass index (BMI) of 26 ± 6.3. The OA group consisted of patients with radiographic OA, including KLG 2 (n=10) and KLG 3 (n=12) with an average BMI of 36 ± 4.7. The 3D dGEMRIC imaging was done at 7 clinical sites with Siemens and GE 3.0T scanners. Subjects were injected with a double dose of Gd-$DTPA^{2-}$ (Magnevist) and asked to walk for 10 minutes. After 59-110 minutes post injection thirty-two 3.0 mm sagittal slices were acquired using an inversion recovery spoiled gradient recalled echo (IR-SPGR) with 5 inversion times (TI=2100, 800, 400, 200 and 130 ms), TR=6.5ms (GE) or nominal (Siemens), TE = 2.7 ms, flip angle=15 degrees, field of view = 16 cm, matrix = 256x256, bandwidth=62.5 kHz.

Cartilage masks for the medial and lateral weight-bearing femur (cMF, cLF) and medial and lateral tibia (MT, LT) were generated using proprietary software (VirtualScopics) from the IR-SPGR series. The 5 dGEMRIC T1 weighted image sets were coregistered using a targeted articulated algorithm (VirtualScopics). T1 values were calculated for each cartilage voxel using Levenberg-Marquardt fitting. Summary statistics for each cartilage region were computed for the central weight-bearing regions. Voxels outside the range (200ms <T1<1300ms) and those with a fitting error 2.5 times larger than signal noise were excluded. No correction was done for BMI dose-bias. Statistical comparison was done using a paired comparison t test.

RESULTS: Mean dGEMRIC values at baseline (BL) and change at 6 months (± standard deviation).

	KLG 0		KLG 2		KLG 3	
	BL	**Δ 6M**	**BL**	**Δ 6M**	**BL**	**Δ 6M**
cMF	571	37 (±83)*	532	39(±35)**	454	21 (±87)
MT	582	59 (±106)**	529	31 (±107)	466	53 (±109)
cLF	615	33 (±83)*	541	15 (±66)	514	21 (±98)
LT	620	58 (±79)**	542	30 (±66)	528	22 (±69)

*P < .05, ** P<.01.

CONCLUSION: A global increase between baseline and 6 months occurred for the mean dGEMRIC Index which was significant for all compartments in the KLG 0 group and the cMF in the KLG 2. The reason for this shift is not understood. Further analysis of the remaining subjects and timepoints are still pending. Also, further studies will be required to determine the range of change in dGEMRIC that might be induced by interventional trials, compared with the increases observed in this non-interventional study.

SPONSOR: Pfizer Inc.
DICLOSURE STATEMENT: D. Burstein, C. McKenzie, C. Charles, and VirtualScopics have received funding and consultation fees from Pfizer.
ACKNOWLEDGMENT: We gratefully thank the entire A9001140 study team for their efforts.
CORRESPONDENCE ADDRESS: Brad.Wyman@Pfizer.com

SLIPS: AN MRI PULSE SEQUENCE FOR RAPID AND QUANTITATIVE 3D T1ρ MRI OF CARTILAGE IN A CLINICAL SETTING.

*,**Witschey II W.R.T., *,**Borthakur A., *,** Elliott M.A., *Sochor M.A., *,**Reddy R.
* Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA
** Graduate Group in Biochemistry & Molecular Biophysics, University of Pennsylvania, Philadelphia, PA, USA

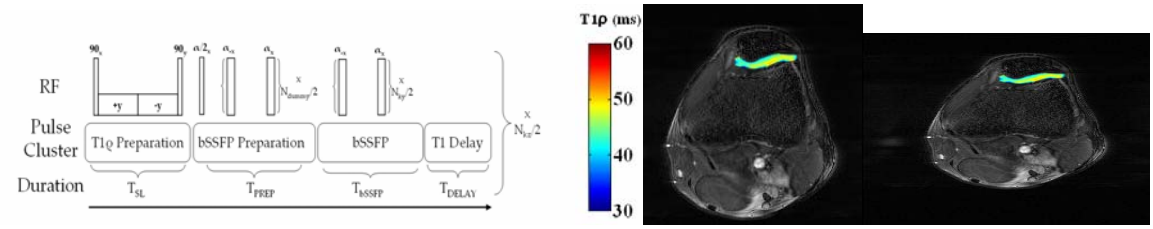
INTRODUCTION: T1ρ MRI is an unconventional MRI contrast mechanism and is used to quantitatively assess biochemical changes such as proteoglycan loss in human cartilage (1). In practice, T1ρ relaxation times are significantly different among patients with early OA (2) compared to normal controls and have detected trauma-induced cartilage changes not seen with conventional MRI (3). Unfortunately, unreasonably long scan durations (> 30 min) prohibit full 3D coverage of the knee joint with current T1ρ pulse sequences and the technique is not amenable to clinical scanning.

OBJECTIVE: To design and implement an MRI pulse sequence (SLIPS) for rapid 3D T1ρ MRI of the knee in a clinical setting and validate the technique in asymptomatic controls (N = 8).

METHODS: The pulse sequence for rapid 3D T1ρ MRI consists of an inversion recovery (TI = 1700) preparatory period designed to null joint space fluid, a spectrally selective fat saturation cluster, T1ρ preparation, N_{dummy} pulses and magnetization readout with a centrically encoded balanced steady-state free precession (b-SSFP) pulse train (N_{pulses} = 256), followed by a recovery delay (Figure 1). The pulse sequence is repeated for each slice encode (N_{slice} = 20) for a total scan duration of 2 min. Images were obtained with an 8-channel transmit/receive parallel RF coil (*InVivo*) on a 1.5 T Siemens Sonata with the following imaging parameters: TE/TR/FLIP = 3.7/7.4 ms/70 deg, matrix = 256x256x20, Resolution = 0.7x0.7x4 mm^3, T_{DELAY} = 6 s, BW = 500 Hz/pixel. 5 scans with varying T1ρ-preparation periods (T_{SL} = 2, 10, 20, 30 and 40 ms) were used to obtain a T1ρ relaxation map. Intra- (N = 4) and intersubject (N = 8) reproducibility was determined (mean, standard deviation and coefficient of variation) among asymptomatic control subjects ages 20-48. Statistical analysis was performed by two factor ANOVA (factors: cartilage location and age). Phantom imaging was performed on a two compartment phantom (different T1, T2 and T1ρ) using a similar protocol.

RESULTS: Mean, standard deviation and coefficient of variation were determined intra- and intersubject among 4 compartments of the knee cartilage. No significant difference in T1ρ was detected by either cartilage location ($p < 0.3$) or age ($p < 0.16$). T1ρ relaxation maps were obtained for two views (axial and coronal) in 1/3 the total acquisition time (20 minutes) of a similar FOV 3D T1ρ GRE acquisition (> 60 minutes).

CONCLUSION: Rapid 3D T1ρ MRI was achieved using a T1ρ-prepared b-SSFP sequence and T1ρ relaxation times were reproducible (COV < 9%) among 8 asymptomatic sybjects. Significant reduction in scan time (1/3) with enhanced SNR was achieved compared to conventional 3D T1ρ GRE acquisition.



INTRASUBJECT	Lateral Femoral	Medial Femoral	Lateral Patellar	Medial Patellar
x ± s (ms)	47.4 ± 2.7	48.7 ± 1.4	48.5 ± 1.2	42.3 ± 2.0
COV (= 100*s/x)	5.8	2.9	2.5	4.8
INTERSUBJECT	Lateral Femoral	Medial Femoral	Lateral Patellar	Medial Patellar
x ± s (ms)	46.6 ± 4.6	48.4 ± 2.6	44.4 ± 5.2	45.2 ± 4.0
COV (= 100*s/x)	9.8	5.3	11.7	8.7

SPONSOR: NCRR-funded Research Resource (RR02305); NIH grant R01-AR045242
ACKNOWLEDGMENTS: Chenyang Wang, Daniel Wallman, Raj Sarkar.
CORRESPONDENCE ADDRESS: witschey@mail.med.upenn.edu

STATISTICAL APPEARANCE MODELS OF THE PROXIMAL FEMUR IN DXA SCANS ASSOCIATE WITH STATE AND PROGRESSION OF CLINICAL OA.

*Waarsing JH, **Rozendaal RM, **Bierma-Zeinstra SM, *Weinans, H.

* Dept. of orthopedics, Erasmus Medical Center, Rotterdam, The Netherlands
** Dept. of General Practice, Erasmus Medical Center, Rotterdam, The Netherlands

INTRODUCTION: One of the problems that OA research is faced with is the poor predictability of development and progression of the disease. Exemplary is the distinction between clinical OA and radiological OA. The pain and loss of function as experienced by the patient is poorly related to Kellgren & Lawrence Scores as derived from x-ray images. Still assessment of radiological OA is standard diagnostic practice. Although radiological OA does not relate to clinical OA, still many studies have shown that changes in bone shape and density are related to progression of the disease, suggesting that current radiological scoring methods may not be specific or sensitive enough.

OBJECTIVE: In this study we aim to find shape and density characteristics of the hip that relate to clinical OA and can be used as predictors of progression of OA using Statistical Appearance Models of the proximal femur.

METHODS: Statistical Appearance Models (SAM) were created of the proximal femur in DXA images of the hips. The resulting independent modes together quantitatively describe the total shape and density, while each mode separately describes a specific characteristic of the shape or density.
The DXA images formed part of the GOAL cohort. In GOAL, 200 patients were included on their first visit to the physician with complaints on the hip. DXA images and x-rays were made at baseline and at three year follow-up. At both time points WOMAC questionnaires were taken to obtain clinical information on pain, stiffness and function. The WOMAC scores on pain, stiffness and function at baseline and follow-up were combined into two independent variables using Principle Component Analysis. The first component represented general 'well-being', while the second component represented a change in 'well-being' from baseline to follow-up. Multivariate Stepwise regression was used to relate the various shape and density modes to patient *well-being* and *change in well-being*. The data presented in this abstract entails a partial analysis of 100 subjects.

RESULTS: The 4^{th} shape mode and the 6^{th} and 13^{th} density mode related significantly to patient *well-being*, after correction for age, BMI and gender. The total model explained 30% of the variance in *well-being*. Of the SAM, the 4^{th} shape mode gave the strongest contribution to the regression model. This mode represents differences in the transition from head to neck. A gradual transition was associated with less *well-being*.
A *change in well-being* did not associate to shape, but only to density (28^{th} and 30^{th} mode). The significant regression model explained 12% of the variance, after correction for age, gender and BMI. Interpretation of the density changes corresponding to these modes is hard, since changes are subtle. However, the changes were limited to density inside the femoral head (fig. 1).
None of the classical measures of radiological OA (Kellgren&Lawrence or Joint Space Width) showed any significant relation with *well-being* or *change in well-being*.

CONCLUSION: The data of this study demonstrate that pain and function as is experienced by the OA patient is indeed related to bone shape and density, even though this is not detected by traditional measures of radiological OA. We did not only see a relation with general well-being (state of OA), but also with changes in well-being during the follow-up period (progression of OA). The finding that a gradual transition from neck to head is associated with status of OA was found previously, in an independent dataset (Gregory et al, Arthritis&Rheum, in press). It is not known whether the observed changes in density and shape of the head represents changes caused by OA or are bone characteristics that relate to susceptibility for OA. Analysis of the follow-up DXA scans might clarify this question.

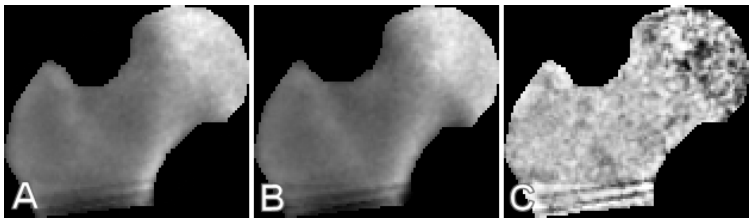


fig.1: Visualisation of density described by the 30^{th} mode. A) -3SD: increase in well-being; B) +3SD: decrease in well-being; C) difference between A and B, note how density changes mainly in the femoral head.

SPONSOR: Dutch Arthritis Association
CORRESPONDENCE ADDRESS:
e.waarsing@erasmusmc.nl

POSTER SESSION 3 – LATE BREAKING

Thursday, July 12th, 2007: 16:15 – 17:00 (Presenters of Posters No. 28 to 39 at posters)

28	*Bolbos R.I., *Zuo J., *Banerjee S., *Cheng J., *Link T.M., **Ma B.C., *Li X., *Majumdar S. *Musculoskeletal and Quantitative Imaging Research Group, Department of Radiology, University of California San Francisco, CA, USA, **Department of Orthopaedic Surgery, University of California San Francisco, CA, USA INTERRELATIONSHIP BETWEEN TRABECULAR BONE AND ARTICULAR CARTILAGE OF THE KNEE JOINT IN EARLY OA USING PARALLEL MRI AT 3T
29	*Carballido-Gamio J., *Link T.M., *Majumdar S. * University of California, San Francisco, San Francisco, CA, USA NEW TECHNIQUES FOR CARTILAGE MRI RELAXATION TIME ANALYSIS
30	*Eckstein F., *Stein V., *Lengfelder V., *Hudelmaier M., *Wirth W, **Cahue S., **Marshall M., **Sharma L. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany, ** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA REGIONAL CARTILAGE LOSS IN PATIENTS WITH FEMOROTIBIAL OSTEOARTHRITIS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT
31	*Wong A.K.O., **Inglis D. Ph.D., ***Beattie K.A. Ph.D., ***Adachi J.D. M.D. FRCP(C) * Department of Biology, McMaster University, Hamilton, ON, Canada, ** Department of Civil Engineering, McMaster University, Hamilton, ON, Canada, *** Department of Medicine, McMaster University, Hamilton, ON, Canada REPRODUCIBILITY OF COMPUTER-ASSISTED JOINT ALIGNMENT MEASUREMENT IN KNEE RADIOGRAPHS
32	*Kennan R.P., **Rasa C., **Loewrigkeit C., **Lowitz K., *Liu H., **Ronan, J. ,**Wickham L. A, **Visco D. * Merck & Co Inc, *Imaging, ** Laboratory of Animal Resources, Rahway, NJ, USA IN VIVO HIGH FIELD T2 MAPPING OF CARTILAGE DEGRADATION IN A RAT MODEL OF OSTEOARTHRITIS INDUCED BY PARTIAL MENISCAL TRANSECTION.
33	*Koo S., **Hargreaves B.A., **Bangerter N.K., *,***Andriacchi T.P., **Gold G.E. * Department of Mechanical Engineering, Stanford University, Stanford, California, USA, ** Department of Radiology, Stanford University, Stanford, California, USA, *** Department of Orthopaedic Surgery, Stanford University, Stanford, California, USA AUTOMATIC SEGMENTATION OF KNEE ARTICULAR CARTILAGE FROM MRI: A MULTI-CONTRAST AND MULTI-DIMENSIONAL APPROACH
34	*Losina E., **Emrani P.S., **Kessler C.L., **Reichmann W.M., **Wright E.A., ***McAlindon T.E., **Katz J.N. * Brigham and Women's Hospital & Boston University School of Public Health, Boston, MA, USA, ** Brigham and Women's Hospital, Boston, MA, USA, *** Tufts-New England Medical Center, Boston, MA, USA. INFLUENCE OF RADIOGRAPHIC VIEW AND FOLLOW-UP TIME ON THE ANNUAL RISK OF PROGRESSION OF AT LEAST ONE K-L GRADE IN KNEE OSTEOARTHRITIS (OA): AN ANALYTIC LITERATURE SYNTHESIS
35	*Losina E., **Meredith D.S., ***Neumann G., ***Yoshioka H., ***Lang P., ***Katz J.N. *Brigham and Women's Hospital, Boston, MA & Boston University School of Public Health, Boston, MA, USA, **Harvard Medical School, Boston, MA, USA, ***Brigham and Women's Hospital, Boston, MA, USA. USING MRI FOR EMPIRICAL EVALUATION OF THE WHOLE JOINT HYPOTHESIS FOR THE PATHOGENESIS OF KNEE OSTEOARTHRITIS

36	*Hunter DJ, *Niu J, **Totterman S, **Tamez J, ***Hellio Le Graverand-Gastineau MP, ****Beals C, *****Maschek S, ***** Hudelmaier M, ***** Eckstein F. *BUSM, Boston, U.S.A, **VirtualScopics, Rochester, NY, USA, ***Pfizer, Ann Arbor, Michigan, USA. ****MERCK, Rahway, NJ, USA, ***** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany COMPARISON OF TWO MRI-BASED TECHNIQUES FOR MEASURING CHANGE IN CARTILAGE MORPHOLOGY OVER ONE YEAR IN THE OAI PROGRESSION SUBCOHORT
37	*Sonka M., **Zhang X., ***Millington S. * The University of Iowa. Iowa City IA, USA, ** Medical Imaging Applications, LLC, Coralville IA, USA, *** Royal London Hospital, Whitechapel, London, UK THREE-DIMENSIONAL SEGMENTATION AND ANALYSIS OF ARTICULAR CARTILAGE
38	*Stahl R., *Li, X., *Majumdar, S., **Luke, A., *Link, T.M. * Department of Radiology, University of California, San Francisco, CA, U.S.A., ** Department of Orthopedic Surgery, University of California, San Francisco, CA, U.S.A. T1RHO, T2 AND FOCAL CARTILAGE PATHOLOGY IN PHYSICALLY ACTIVE AND SEDENTARY HEALTHY SUBJECTS VERSUS EARLY OA PATIENTS
39	*Wiener E., *Settles M., *Weirich G., *Rummeny E.J. *Klinikum rechts der Isar, Technische Universität München, München, Germany THE QUANTIFICATION OF RELAXATION EFFECTS, DYNAMICS AND SPATIAL DISTRIBUTIONS OF IONIC AND NON-IONIC CONTRAST AGENTS IN ARTICULAR CARTILAGE AT 1.5 T

INTERRELATIONSHIP BETWEEN TRABECULAR BONE AND ARTICULAR CARTILAGE OF THE KNEE JOINT IN EARLY OA USING PARALLEL MRI AT 3T

*Bolbos R.I., *Zuo J., *Banerjee S., *Cheng J., *Link T.M., **Ma B.C., *Li X., *Majumdar S.

*Musculoskeletal and Quantitative Imaging Research Group, Department of Radiology, University of California San Francisco, CA, USA
**Department of Orthopaedic Surgery, University of California San Francisco, CA, USA

INTRODUCTION: It has been suggested that early OA changes are seen in the adjoining subchondral and trabecular bone in relationship with cartilage degeneration in OA patients.

OBJECTIVE: The aim of this study was to use high-resolution MRI to evaluate the relationship between trabecular bone changes and articular cartilage degeneration in the distal femur and the proximal tibia of the OA knee at 3T strength field.

METHODS: Ten healthy controls (without any clinical symptoms of OA or other knee injuries) and ten patients with mild OA (KLG of 1 or 2) were studied using 3T GE MR scanner and 8 channel phased-array knee coil. To quantify the trabecular bone structure, axial 3D GRAPPA-based Fiesta-c images were acquired with parameters: accelerator factor = 2, TR/TE = 11/4.2 ms, acquisition matrix = 512×384, flip angle (FA) = 60^{o}, FOV = 10cm, 90 slices, slice thickness = 1mm, scanning time 10 minutes. Six different compartments were defined for bone analysis: F, LF, MF, T, LT, and MT. Trabecular structure was evaluated by computing parameters such as: app. BV/TV, app. Tb.N [1/mm], app. Tb.Sp [mm] and app. Tb.Th [mm]. For cartilage analysis, sagittal images with FOV of 14-16cm were acquired: a 3D SPGR sequence (matrix 512×512, locations per slab (LPS) = 100, slice thickness = 1mm, FA=18°), a 3D T1rho mapping (matrix 256×128, LPS = 36, slice thickness = 3mm, time of spin lock (TSL) = 0/10/40/80 ms, spin lock frequency = 500Hz, views per segment = 48, FA =12°), and a 3D T2 mapping (matrix 256×128, LPS=36, slice thickness = 3mm, 4 different images acquired with TE = 4.1/14.5/25/45.9 ms). Four compartments were defined for cartilage analysis: MF, LF, MT, and LT. High resolution SPGR images were segmented to calculate cartilage thickness and volume. For T1rho/T2 maps, ROIs were defined by the SPGR segmentation that was mapped by the registration with the T1rho/T2 images.
The coefficients of variation (CV) characterizing the reproducibility of trabecular bone parameters measurements were assessed in 4 control subjects based on 2 repeated scans. T-tests were applied in order to compare OA group with the control group in terms of cartilage and bone parameters. Spearman's rank correlations were performed between cartilage and bone parameters.

RESULTS: The computed CVs showed good measurement precision, specifically ranging from 1.8% for app. Tb.N to 5.5% for app. Tb.Sp. Overall, the bone parameters for the OA group at this early stage showed a trend to lower values compared to the control group. Significant differences between both groups were mainly found on the lateral side of the knee: for LF – BV/TV (P=0.021), Tb.N (P=0.003) and for LT – BV/TV (P=0.008), Tb.N (P=0.04). Increased values in cartilage matrix parameters (T1rho and T2) were demonstrated in mild OA subjects compared with controls, but significant differences were only found at the femur: LF ($P<0.05$) and MF (P=0.05). T1rho and T2 were both negatively correlated ($P<0.05$) with app. BV/TV and app. Tb.N only at the MF compartment in mild OA subjects. For control subjects, both T1rho and T2 values were also negatively correlated ($P<0.05$) with all trabecular bone parameters, but only in the LT compartment.

CONCLUSION: Trabecular bone parameters were assessed with good reproducibility using parallel imaging at 3T. At this early stage, the mild OA group indicated a decreasing trend compared to control group in terms of bone parameters and increased cartilage thickness compared to healthy controls. Significant correlations were found between trabecular bone and cartilage parameters suggesting that the loss of the trabecular bone structure is directly proportional to the increasing values of T1rho and T2.

SPONSOR: NIH R01 AR46905.
DICLOSURE STATEMENT: none
CORRESPONDENCE ADDRESS: radu.bolbos@radiology.ucsf.edu

NEW TECHNIQUES FOR CARTILAGE MRI RELAXATION TIME ANALYSIS

*Carballido-Gamio J., *Link T.M., *Majumdar S.

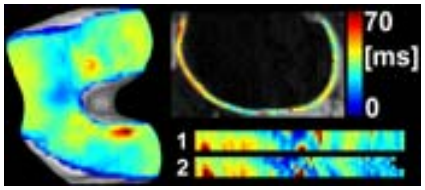
* University of California, San Francisco, San Francisco, CA, USA

INTRODUCTION: Increase in MRI T1rho and T2 relaxation times has been reported in subjects developing knee OA. In addition to this global change, there is an increasing interest in performing a more localized analysis of the cartilage morphometric, molecular, and biochemical integrity, as well as in extracting textural information embedded in anatomic images or relaxation time maps.

OBJECTIVE: 1) To develop a technique for localized intra and inter-subject comparisons of MRI cartilage relaxation times. 2) To develop a technique to flatten cartilage relaxation time maps for texture analysis parallel and perpendicular to the cartilage layers. 3) To test the feasibility of generating a mean femoral MRI cartilage relaxation time map. 4) To quantify the reproducibility of 1) and 2).

METHODS: MRI: Sagittal anatomic (0.312x0.312x1mm) and relaxometry scans (0.546x0.546x3mm) for T1rho measurements (TSL=0, 10, 40, 80ms) of the knee joint (n=5) were obtained at 3 Tesla using SENSE 3D fat suppressed SPGR and segmented elliptic-centric SPGR sequences, respectively. Image post-processing: T1rho maps were calculated by fitting a mono-exponential decay for each pixel. Femoral cartilage and bones were semi-automatically segmented from the anatomic images and mapped to the T1rho maps. For each cartilage point in the bone-cartilage interface, a normal vector ending in the articular surface was computed. All normal vectors were then sampled at equally spaced points, and by using cubic interpolation T1rho values at each sampled point were stored as feature vectors. Essentially, each feature vector represented T1rho values at different cartilage layers. T1rho localized comparisons: Cartilage and bone segmentations were shape-interpolated to represent them with isotropic voxels. T1rho vectors of the shape-interpolated cartilage were computed using linear interpolation and the previously obtained T1rho vectors. The bone-cartilage interfaces of the isotropic bones were replaced with those of the isotropic cartilages. Shape matching of the isotropic bones to be compared was implemented to identify corresponding anatomic points. This set of points was used to calculate an affine transformation, or an affine transformation followed by warping for intra- and inter-subject registration, respectively, to perform point to point or regional comparisons of T1rho vectors. By using established techniques to build statistical shape models, a mean femoral shape and T1rho map were generated. Cartilage flattening of slices for texture analysis: The non-interpolated T1rho vectors were put together into a single matrix to generate an image (# cartilage layers by # points in the bone-cartilage interface). A second approach consisted in connecting with a spline, points at corresponding cartilage layers given by the sampled normal vectors, and sampling T1rho values along the splines to generate an image (# cartilage layers by # points in the layers). Texture analysis was performed with second order texture measures using co-occurrence matrices (GLCM). Reproducibility: It was assessed using 2 scans obtained at different sessions and reported in % as a coefficient of variation (CV_{SD}).

RESULTS: The global T1rho CV_{SD} was 5.9%, and for intra-subject point comparisons of vector means was 18.8%. Figures below show the mean T1rho map on the mean shape and a flattening example.



1, 2nd

N GLCM H	2.1	3.6	1 GLCM E	3.9	4.9
N GLCM A	20.5	21.9	1 GLCM C	1.9	4.1
N GLCM E	10.3	11.3	2 GLCM H	2.0	2.0
N GLCM C	3.9	6.4	2 GLCM A	14.3	13.9
1 GLCM H	0.3	1.7	2 GLCM E	5.3	5.0
1 GLCM A	10.9	13.9	2 GLCM C	0.9	3.2

2=1st,

flattening method. For GLCM CV_{SD} values: N=Not flattened; H=Homogeneity; A=ASM; E=Entropy; C=Correlation; 1st, 2nd column=horizontal, vertical direction; 1 pixel offset.

CONCLUSION: Successful localized intra- and inter-subject T1rho comparisons were obtained, with an intra-subject CV_{SD} similar to those reported in the literature for regional T2. A twofold improvement of the CV_{SD} of GLCM features was obtained by flattening the T1rho maps. These techniques are currently under evaluation with healthy controls, OA patients, and subjects of the OA initiative cohort.

SPONSOR: This work was supported by NIH grants R01 AR 46905 and UO1 AR-06-006.
DISCLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: Julio.Carballido@radiology.ucsf.edu

REGIONAL CARTILAGE LOSS IN PATIENTS WITH FEMOROTIBIAL OSTEOARTHRITIS WITH NEUTRAL, VALGUS, AND VARUS KNEE ALIGNMENT

*Eckstein F., *Stein V., *Lengfelder V., *Hudelmaier M., *Wirth W, **Cahue S., **Marshall M., **Sharma L.
* Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany
** Feinberg School of Medicine, Northwestern University, Chicago, MI, USA

INTRODUCTION: Malalignment is known to alter the load distribution between the medial and lateral femorotibial knee compartment, and there is increasing evidence that malalignment of the knee impacts the magnitude and distribution of cartilage loss in knee OA. However, because radiography does not allow one to assess regional cartilage loss throughout femorotibial cartilage plates,, little is known about the spatial distribution of cartilage loss in varus- and valgus deformity.

OBJECTIVE: To determine the rate and regional pattern of femorotibial cartilage loss in a community-recruited cohort of participants with mild to moderate OA, including persons with neutral alignment, varus and valgus malalignment.

METHODS: A community-recruited cohort with radiographic (KLG 2-3) knee OA (n = 174; age 66 ± 11 y.; BMI 30.2 ± 6.1, 76% women) had alignment measurement by full limb x-ray: 74 had neutral alignment (-2° to +2° deviation from the biomechanical knee axis), 57 had varus (> +2°), and 43 valgus malalignment (< -2°). A coronal FLASHwe sequence (1.5 x 0.31 x 0.31 mm^3 resolution) was acquired at baseline and 26.6 ± 5.4 months later using 1.5 and 3.0T scanners. Segmentation was performed by tracing the total subchondral bone (tAB) and cartilage surface area (AC) of the medial and lateral tibia (MT/LT) and the media and lateral weight-.bearing central femur (cMF/cLF). Baseline and follow up scans were processed in parallel with blinding to acquisition order. All segmentations were quality controlled by another expert reader. Cartilage volume (VC), tAB, cartilaginous area (cAB), denuded area (dAB), and the mean cartilage thickness throughout the cAB (ThCcAB) were quantified, using proprietary software (Chondrometrics GmbH, Ainring, Germany).

RESULTS: Annualized changes were small in OA participants with neutral alignment , but were larger in the mechanically stressed compartment in participants with varus and valgus malalignment, respectively (Table 1), with SRMs up to 0.71. Averaging changes over both cartilage plates in each compartment, the rate of cartilage loss was 1.4:1 (medial vs. lateral) in participants with neutral alignment, 3.9:1 in participants with varus, and 1: 5.3 in participants with valgus malalignment. Regional changes were greatest in the central and external subregion in MT, in the central subregion of cMF, in the central and internal subregions of LT, and in the external subregion of cLF, respectively.

Table 1: Annual mean change (MC) of ThCtAB in %, level of significance (p) and standardized response mean (SRM = MC divided by SD of change) normalized to 12 months.

	Neutral (n = 74)			Varus (n = 57)			Valgus (n = 43)		
	MC	p	SRM	MC	p	SRM	MC	p	SRM
MT	-1.1%	***	-0.50	-2.6%	***	-0.52	-0.2%	n.s.	-0.06
cMF	-1.7%	**	-0.37	-2.6%	***	-0.49	-0.7%	n.s.	-0.22
LT	-0.9%	**	-0.32	-1.2%	***	-0.54	-3.0%	***	-0.71
cLF	-1.0%	**	-0.36	-0.2%	n.s.	-0.1	-1.9%	**	-0.42

** $p < 0.01$; *** $p < 0.001$; n.s = not statistically significant (paired Student's t-test)

CONCLUSION: The results show that the rate of cartilage loss and sensitivity to change in knee OA are strongly affected by alignment. In addition, subregional analysis can reveal different patterns of cartilage loss in the medial and lateral compartment, respectively. When recruiting participants for clinical studies investigating the effect of DMOADs, determining knee alignment may be used to select "fast progressors", with higher rates of change compared with participants with neutral alignment.

SPONSOR: National Institute of Health.
DICLOSURE STATEMENT: F.E., M.H. and W.W. have part time employments with Chondrometrics GmbH. F.E. is CEO of Chondrometrics GmbH and provides consulting services to Pfizer Inc., Glaxo Smith Kline Inc., Merck Serono Inc. and Astrazeneca Ltd.
CORRESPONDENCE ADDRESS: felix.eckstein@pmu.ac.at

REPRODUCIBILITY OF COMPUTER-ASSISTED JOINT ALIGNMENT MEASUREMENT IN KNEE RADIOGRAPHS

*Wong A.K.O., **Inglis D. Ph.D., ***Beattie K.A. Ph.D., ***Adachi J.D. M.D. FRCP(C)

* Department of Biology, McMaster University, Hamilton, ON, Canada
** Department of Civil Engineering, McMaster University, Hamilton, ON, Canada
*** Department of Medicine, McMaster University, Hamilton, ON, Canada

INTRODUCTION: Previous studies have demonstrated that knee malalignment is a result rather than a cause of OA. As such, measurement of knee alignment angle may provide information on site-specific OA progression.

OBJECTIVES: 1) To determine the reproducibility of custom designed software in assessing knee alignment angle of subjects with or without OA from digitized radiographs and 2) to determine the optimal placement of radiographic landmarks for knee alignment angle measurement.

METHODS: From 46 volunteers comprised of 16 healthy subjects (14F, 2M; 41±12 yrs; BMI=24±4 $kg \cdot m^{-2}$) and 30 TKA patient volunteers (17F, 13M; 66±9 yrs; BMI=31±6 $kg \cdot m^{-2}$), knee alignment angle was determined in 70 knees with (n=38) and without (n=32) radiographic evidence of OA. Posteroanterior (PA) radiographs of the knee were acquired in the fixed-flexion position.

Three measurement-guiding rules were interactively placed on each digitized radiograph by mouse control. The end points of the first rule were placed on the tips of the tibial spines. The remaining two rules were placed on the femur and tibia such that their distance measured to the tibial spine rule (from midpoint to midpoint) was no more than 10.0 ± 0.5 cm. Tibial and femoral rules were aligned according to the following choices of radiographic landmarks: i) endpoints of both rules placed at inner or outer cortical edges with ii) midpoint to midpoint distance from tibial spine rule varied between 5.0 and 10.0 cm and iii) femoral rule aligned parallel to femoral condyles or tibial plateau. The angle subtended by lines connecting the midpoints of the femoral and tibial rules to the tibial spine rule was measured as the anatomical angle, $\grave{e}_A$, and converted to a mechanical angle, $\grave{e}_M$, according to Kraus et al (Arthritis Rheum 2005 52**:**1730-1735):

$$\grave{e}_M = (0.69 \times \grave{e}_A) + 53.69°$$

Angles were measured by three readers to assess interobserver reproducibility. Analyses were performed on two separate days by the same reader to determine intraobserver reproducibility. Test-retest reproducibility was evaluated with duplicate radiographs from the healthy cohort, also analysed on separate days. Reproducibility was evaluated using root-mean square coefficient of variation (RMSCV%). A repeated-measures ANOVA was performed on data obtained from varying radiographic landmarks with CI=95%.

RESULTS: Reproducibility analyses revealed a high degree of intraobserver (RMSCV=0.29%) and interobserver (RMSCV=0.33%) reproducibility for the single acquisition radiographs (n=38). In test-retest experiments, overall interacquisition variance was higher than both intra- and interobserver variances but still well under 1% (n=32, RMSCV=0.86%). The higher variance observed with reacquisition may be explained by subtle differences in knee positioning in X-rays in addition to intraobserver error. Varying the orientation of tibial and femoral rules according to radiographic landmarks did not make a significant difference in the measurement of knee alignment angle (n=38, P=0.70, F=0.48, CI=95%).

CONCLUSIONS: Our custom designed software provides a robust method for measuring knee alignment angles in digitized PA radiographs of healthy subjects and OA patients. Although test-retest analyses were performed only in the healthy cohort, we anticipate a similar degree of reproducibility in an osteoarthritic sample allowing assessment of knee OA progression to be performed in the clinical research setting.

SPONSOR: none.
DICLOSURE STATEMENT: none.
ACKNOWLEDGMENT: Joyce Obeid is to be thanked for her participation as a reader.
CORRESPONDENCE ADDRESS: dean.inglis@camris.ca

IN VIVO HIGH FIELD T2 MAPPING OF CARTILAGE DEGRADATION IN A RAT MODEL OF OSTEOARTHRITIS INDUCED BY PARTIAL MENISCAL TRANSECTION.

*Kennan R.P., **Rasa C., **Loewrigkeit C., **Lowitz K., *Liu H., **Ronan, J. ,**Wickham L. A, **Visco D.
* Merck & Co Inc, *Imaging, ** Laboratory of Animal Resources, Rahway, NJ, USA

INTRODUCTION: Rodent models of biomechanically induced OA provide a useful means to study the pathogenesis of OA. In order to evaluate treatment protocols, there is a need to develop accurate biomarkers for staging such models. MRI has been used to monitor biomechanically induced cartilage degradation in ex-vivo rat models but has had limited applications to date for similar in-vivo studies.

OBJECTIVE: The objective of this study was to determine an efficient means for characterization of cartilage damage in a surgically induced model of osteoarthritis in the rat using high field (9.4Tesla) MR microimaging. High resolution T_1w and T_2w MR images were used to evaluate cartilage morphology and structure at 3, 6 and 12 weeks post surgery. We hypothesize that high field spin echo imaging can detect changes in rodent cartilage structure through quantitative changes in T_2. These protocols can be used for efficient throughput in small animal imaging studies.

METHODS**:** Age-matched adult (N=6, 20-21 week old) male Lewis rats (Charles Rivers Laboratories, Portage, MI) weighing approximately 450–520 grams, received pre-surgical MRI evaluation of the knee joints. Selected rats (N=4) then underwent aseptic unilateral arthrotomy with partial medial meniscectomy (PMM) of the right knee to induce OA. MR imaging of rat knee joints was conducted at 3, 6 and 12 weeks post surgery and post mortem at 16 weeks. The remaining unoperated control rats (N=2) were imaged at week 12 and post mortem. Imaging was performed on a 9.4 Tesla horizontal bore MR imaging systems (Bruker, Karlsruhe Germany). The knees were imaged using a 2.5cm diameter single turn solenoid coil in which the knee was stretched perpendicularly to the body of the rat. The imaging protocol included high resolution 3D T_1-w gradient echo imaging to visualize articular cartilage (res = 256x192x32, FOV= 15x15x8mm, TR=100msec, TE=3msec, flip angle ~30 degrees, NA=2), and multi-slice 2D multi-echo spin echo imaging (res = 256x192, FOV = 22x22mm, slice thickness =0.7mm, 11 slices, TR=3.5sec, 8 echoes , echo spacing = 9msec, NA=2) for T_2 characterization. Typical imaging times were 20 minutes for the 3D sequences and 20 minutes for the spin echo images. T_2 data analysis was performed on the medial and lateral compartments of the tibial plateau. Group comparisons were evaluated via Students t-statistic. For qualitative comparison stifle joints were collected, processed, embedded in paraffin, serially sectioned at a thickness of 8 µm in the sagittal plane and were stained with hematoxylin and eosin or toluidine blue.

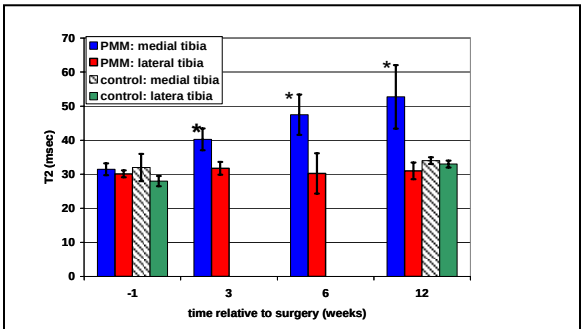


*Figure 1: T2 values in medial and lateral compartments of the right tibia. * denotes p<0.006.*

RESULTS: Figure 1 shows the mean T_2 values for cartilage in the medial and lateral condyles of right tibia for each timepoint (ranging from 1 week prior to surgery to 12 weeks post surgery). There is a significant increase in T_2 in the medial compartment of the PMM animals relative to control animals ($p<0.003$, 0.002, and 0.004 at weeks 3, 6 and 12 respectively). The T_2 increase was also significant compared to the lateral compartment of the tibia in the same animals ($p<0.004$, 0.006, and 0.004 at weeks 3 6, and 12). No significant T_2 differences were observed in control animals or in the lateral tibial condyle. Ex-vivo MRI and histology confirmed late stage cartilage loss in the medial tibial condyle.

CONCLUSION: This study shows that high field T_2 mapping can be used to quantify cartilage degradation in a mechanically induced model of OA in the rat. The ability to perform longitudinal quantification in such models can be applied to preclinical treatment studies to gauge compound efficacy to alter the progression of OA.

SPONSOR: Merck & Co Inc.

CORRESPONDENCE ADDRESS: richard_kennan@merck.com

AUTOMATIC SEGMENTATION OF KNEE ARTICULAR CARTILAGE FROM MRI: A MULTI-CONTRAST AND MULTI-DIMENSIONAL APPROACH

*Koo S., **Hargreaves B.A., **Bangerter N.K., *·***Andriacchi T.P., **Gold G.E.

* Department of Mechanical Engineering, Stanford University, Stanford, California, USA
** Department of Radiology, Stanford University, Stanford, California, USA
*** Department of Orthopaedic Surgery, Stanford University, Stanford, California, USA

INTRODUCTION: An analysis of articular cartilage regional morphology (thickness or volume) is frequently used for evaluating the initiation and progression of OA. MRI can provide a non-invasive method to assess the morphology of articular cartilage. Quantifying regional cartilage thickness or volume requires MR image segmentation and three-dimensional reconstruction. Previously, numerous computational methods have attempted to segment articular cartilage from MR images taken with a single sequence. Yet, fully automatic segmentation seems to be a difficult goal to achieve. There exist many different MR sequences that utilize tissue properties such as T1 and T2 relaxation times to increase the contrast between cartilage and its surrounding soft tissues in joints. Multiple sets of MR images taken with different sequences provide different contrast mechanisms between tissues and help separate different tissues. We adapted a machine learning algorithm to achieve automatic segmentation of knee articular cartilage from multiple sets of MR images taken with different pulse sequences.

OBJECTIVE: To segment knee articular cartilage automatically from multiple sets of MR images using a support vector machine method, a kernel-based machine learning algorithm.

METHODS: Three sets of knee MR images were taken for a healthy subject using a 3.0T scanner (GE Healthcare, Waukesha, WI) with fat-suppressed SPGR, 3D Spin Echo, and FIESTA (SSFP) pulse sequences. Spatial alignment between the three sets of MR images was confirmed for the slices used in this study. One slice was selected from each set of MR images at the same location in the knee to generate training data for a support vector machine. Articular cartilage in the slice was manually segmented. Thus, the training data consisted of pixels of the slice with three signal intensities from the three sequences and a binary value determining whether it was a cartilage or non-cartilage pixel. Conceptually speaking, each pixel was mapped to a three-dimensional space and marked as either black or white. The color was determined by whether the pixel represented cartilage or not in the slice. The support vector machine calculated an optimal hyperplane that separated the pixels of articular cartilage from the pixels of surrounding tissues. For the calculation, we used the Spider machine learning package for MATLAB. Another slice was selected from the same sets of MR images of the subject to generate testing data for the support vector machine. Testing data consisted of pixels of the test slice with three signal intensities from the three sequences. The pixels were divided into cartilage and non-cartilage pixels using the hyperplane of the support vector machine. To assess the performance of the support vector machine, the cartilage in the test slice was manually segmented as a gold standard, and the sensitivity and specificity of the classification results were calculated.

RESULTS: The sensitivity and specificity of the support vector machine were 78 % and 97 %, respectively, when tested on its own training data. The sensitivity and specificity measured on a new slice was 84 % and 96 %, respectively.

DISCUSSION: This study could achieve a sensitivity of about 80% in classifying cartilage pixels based on the signal intensities from three sequences using a support vector machine method. It is expected that the classification performance could be improved with an increase in the number of sequences that serve as features for the support vector machine. We are investigating other candidate sequences for this classification method, and the best combination of the sequences should increase the sensitivity and reduce the scan time. The specificity can also be improved in the post processing steps by using the spatial geometry of the pixels. Next steps include improving the spatial alignment between sequences, normalizing the signal intensities between subjects and accounting for coil sensitivity profiles to apply this method to the whole knee and for different subjects.

SPONSOR: 1R01-EB002524, 1R01-EB005790
DICLOSURE STATEMENT: For the support vector machine method, we used the Spider machine learning package for MATLAB available at http://www.kyb.tuebingen.mpg.de/bs/people/spider/
CORRESPONDENCE ADDRESS: skoo@stanford.edu

INFLUENCE OF RADIOGRAPHIC VIEW AND FOLLOW-UP TIME ON THE ANNUAL RISK OF PROGRESSION OF AT LEAST ONE K-L GRADE IN KNEE OSTEOARTHRITIS (OA): AN ANALYTIC LITERATURE SYNTHESIS

*Losina E., **Emrani P.S., **Kessler C.L., **Reichmann W.M., **Wright E.A., ***McAlindon T.E., **Katz J.N.

* Brigham and Women's Hospital & Boston University School of Public Health, Boston, MA, USA.
** Brigham and Women's Hospital, Boston, MA, USA.
*** Tufts-New England Medical Center, Boston, MA, USA.

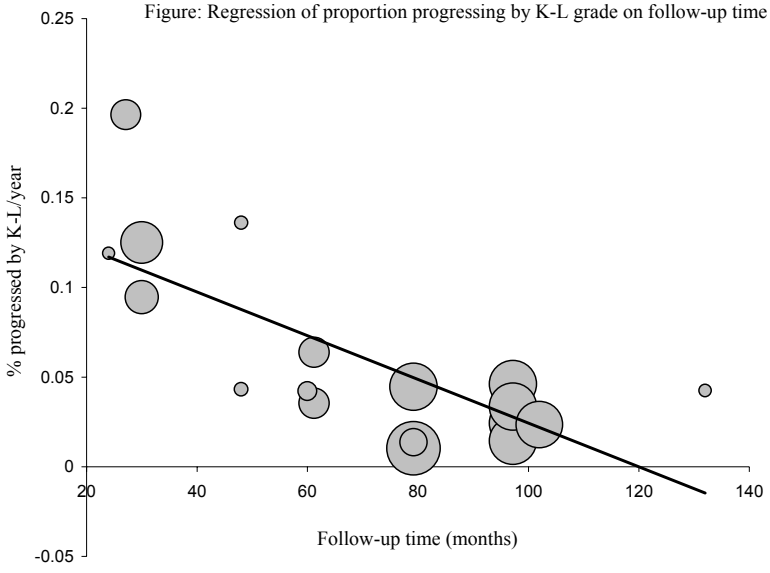
INTRODUCTION: Knee OA is highly prevalent and disabling. While it is recognized that the disease progresses insidiously over time, published results with respect to the rate of radiographic disease progression differ across studies.

OBJECTIVE: We aim to summarize the data on annual progression using the Kellgren-Lawrence (K-L) scale as a measure of OA severity, and to examine whether specific study features such as length of follow-up and radiographic view influence reported OA progression.

METHODS: We used PubMed to search literature published between 1985 and 2006 for studies that analyzed knee OA progression. We included studies that assessed radiographic progression based on the K-L scale. We excluded literature reviews and studies not published in English. We extracted estimates of the proportion of the study sample that progressed at least one K-L grade over the study follow-up time, in addition to specific study features, including study sample demographic characteristics, study design, follow-up time, and type of radiographic view. We noted whether studies included or cited inter- and intra-reader reliability analyses. We analyzed the associations of these features with annual progression estimates. We performed a meta-regression to identify factors explaining variability of K-L progression.

RESULTS: Of 239 studies identified by the search, 13 met the inclusion criteria. These studies presented 21 distinct K-L progression estimates. Eleven of the 13 studies were observational in design, and 2 were RCTs. Follow-up times ranged from 24 to 132 months. 23% (3/13) used semi-flexed radiographic view and 77% used full extension view. 85% (11/13) of studies included measures of reader reliability. The annual estimates of progression by at least one K-L grade ranged from 1.0% to 19.6%, with the overall mean risk of progression of 6.2%. Annual progression estimates were associated with radiographic view and length of follow-up. On average, studies using semi-flexed view reported a risk of K-L progression of 2.7% compared to 7.0% for studies using full-extension view. Longer studies reported lower progression estimates (Figure). We did not find an association between K-L progression and study design, age and gender distribution.

Figure: Regression of proportion progressing by K-L grade on follow-up time



CONCLUSION: Estimates of progression using change in K-L grade depend on the type of radiographic view and length of follow-up time. There is a pressing need for consensus on a standardized method to evaluate change in K-L grade as a measure of structural progression.

SPONSOR: National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, USA. Grant no. RO1 AR 053112
DISCLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: elosina@partners.org

USING MRI FOR EMPIRICAL EVALUATION OF THE WHOLE JOINT HYPOTHESIS FOR THE PATHOGENESIS OF KNEE OSTEOARTHIRIS

*Losina E., **Meredith D.S., ***Neumann G., ***Yoshioka H., ***Lang P., ***Katz J.N.

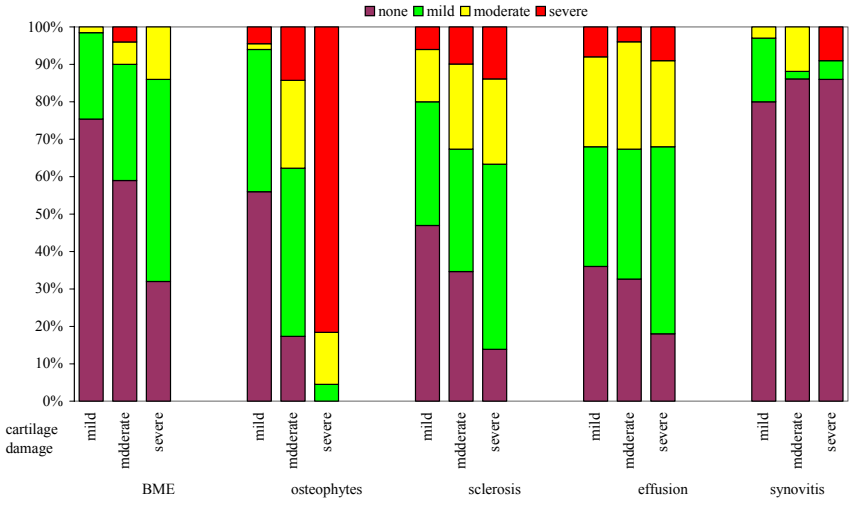
*Brigham and Women's Hospital, Boston, MA & Boston University School of Public Health, Boston, MA, USA.
**Harvard Medical School, Boston, MA, USA.
***Brigham and Women's Hospital, Boston, MA, USA.

INTRODUCTION: The pathogenesis of osteoarthritis (OA) has traditionally been thought to be a consequence of aging characterized by cartilage degeneration and bony remodeling in the affected joint. However, recent research suggests that OA involves pathologic processes occurring in multiple joint structures including bone, cartilage, meniscus, and synovium. In this cross-sectional study, we use 1.5T MRI to examine the association between cartilage damage and the presence and severity of pathology in other joint structures in a cohort of patients with widely varying degrees of OA evaluated prior to arthroscopic partial meniscectomy.

METHODS: Knee MRI scans from patients over 45 years-old without evidence of anterior cruciate ligament instability or inflammatory arthritis were assessed using a semi-quantitative knee MRI assessment form. We evaluated the pathology of six distinct articular elements: cartilage, osteophytes, subchondral sclerosis, bone marrow edema, joint effusion and synovitis. Each type of pathology was graded using an ordinal scale with a value of zero indicating no pathology and higher values indicating increasingly severe levels of pathology. We calculated an overall cartilage disease score (CDS) as the sum of cartilage pathology, defined by both grade and size, across all joint compartments. The severity of each component pathology was further categorized as none, mild, moderate or severe. The chi-square test of independence was used to determine the association between specific component severity and CDS severity.

RESULTS: MRI studies from 140 patients were available for this study. The cohort had a mean age of 60 years and was 61% female. The cohort included a wide spectrum of OA severity.
This analysis revealed a statistically significant trend towards a greater number of involved articular elements as CDS worsened. Also, as shown in the Figure, more severe pathology was associated with worse CDS for several structures including osteophytes, bone marrow edema, and subchondral sclerosis, but not for joint effusion or synovitis.

Figure: Association of cartilage degeneration severity with pathology for osteophytes, bone marrow edema (BME), subchondral sclerosis, joint effusion and synovitis



CONCLUSION: Our results support the whole joint hypothesis of OA pathogenesis in that an association was observed between worsening cartilage disease and both the number of articular elements showing pathological changes as well as the severity of the changes for each element. These findings should serve as a basis for future prospective studies of OA pathogenesis in humans using MRI and correlation of these findings to clinically relevant outcomes such as pain and function.

SPONSOR: Novartis.
DISCLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: elosina@partners.org

COMPARISON OF TWO MRI-BASED TECHNIQUES FOR MEASURING CHANGE IN CARTILAGE MORPHOLOGY OVER ONE YEAR IN THE OAI PROGRESSION SUBCOHORT

*Hunter DJ, *Niu J, **Totterman S, **Tamez J, ***Hellio Le Graverand-Gastineau MP, ****Beals C, *****Maschek S, ***** Hudelmaier M, ***** Eckstein F.

*BUSM, Boston, U.S.A.
**VirtualScopics, Rochester, NY, USA.
***Pfizer, Ann Arbor, Michigan, USA.
****MERCK, Rahway, NJ, USA.
***** Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany

INTRODUCTION: Rapid advances have been made in pulse sequences and image segmentation development for measuring cartilage morphology using MRI. These advances may lead to improvements in the ability to quantify tissue loss over short time intervals.

OBJECTIVE: To directly compare the rate of disease progression (thinning of cartilage) using two pulse sequence and image analysis approaches in knees with OA from a subset of participants from the OAI.

METHODS: Subjects included for this exploratory analysis represent a subset of the approximately 1400 participants from the OAI Progression subcohort and are from OAI public use datasets 0.1.1, 0.B.1 and 1.B.1. All participants had both frequent symptoms and radiographic OA (ROA) in the same knee, based on a screening reading done at the OAI clinics. The right knees of 75 participants were studied, in which two MRI sequences (DESSwe and FLASHwe at 3 Tesla) were obtained at baseline and at 12 months follow up in the same knee. One analysis center (Virtualscopics) applied a semiautomated segmentation algorithm to the sagittal DESSwe (0.7 mm slice thickness-every other slice was used); at the other center (Chondrometrics) the cartilages were segmented on coronal FLASHwe images (1.5 mm slice thickness) by a team of 7 experienced readers and all segmentations quality controlled by one reader (S.M.). As an outcome measure, Virtualscopics provided cartilage volume normalized to the subchondral bone area (VCtAB) and Chondrometrics cartilage thickness over the entire tAB (ThCtAB) for the entire medial and lateral tibia (MT/LT), the central medial and lateral tibia (cMT/cLT), and the central weight-bearing medial and lateral femur (cMF / cLF). Summary statistics of the changes (absolute mean change (MC) and percentage change (%Δ)) from baseline at one year and the standardized response mean (SRM), i.e. mean change divided by the standard deviation change were calculated. Paired T-test was used to test the hypothesis that the mean change of MRI feature is 0.

RESULTS: On average the 75 subjects were 59.8 years of age and obese with a mean BMI of 30.2 kg/m^2. The mean change and SRM for cartilage volume and normalized volume/thickness are presented in Table 1. In general the SRMs were small and similar between both techniques.

Table 1: Change in knee cartilage thickness over 1 year in the femoro-tibial cartilage plates for DESSwe and FLASHwe

	Cartilage thickness (ThCtAB or VCtAB)									
	DESS (VS)					**FLASH (CHM)**				
	MC	SD	SRM	%Δ	p value	MC	SD	SRM	%Δ	p value
MT	-0.001	0.09	-0.01	-0.11	0.92	-0.009	0.06	-0.15	-0.55	0.19
LT	-0.016	0.09	-0.18	-0.60	0.13	-0.016	0.07	-0.24	-0.79	**0.04**
cMF	-0.045	0.12	-0.37	-2.26	**0.002**	-0.042	0.12	-0.36	-2.47	**0.003**
cLF	-0.014	0.08	-0.17	-0.17	0.14	-0.003	0.07	-0.05	-0.18	0.72
cMT	-0.004	0.1	-0.04	-0.31	0.72	-0.030	0.11	-0.28	-1.28	**0.02**
cLT	-0.012	0.09	-0.13	-0.47	0.28	-0.037	0.16	-0.23	-1.18	**0.04**

CONCLUSION: These descriptive results of changes in cartilage morphology at the one year timepoint from the first substantive MRI data release from the OAI Progression subcohort indicate that the annualized rates of change are relatively small, irrespective of the pulse sequence (sagittal DESSwe or coronal FLASHwe) used. With both imaging sequences and analysis approaches, the central medial femur showed the greatest detectable change.

SPONSOR: N01-AR-2-2262, N01-AR-2-2262, and N01-AR-2-2258
DICLOSURE STATEMENT: Affiliations listed above
ACKNOWLEDGMENT: OAI
CORRESPONDENCE ADDRESS: djhunter@bu.edu

THREE-DIMENSIONAL SEGMENTATION AND ANALYSIS OF ARTICULAR CARTILAGE

*Sonka M., **Zhang X., ***Millington S.

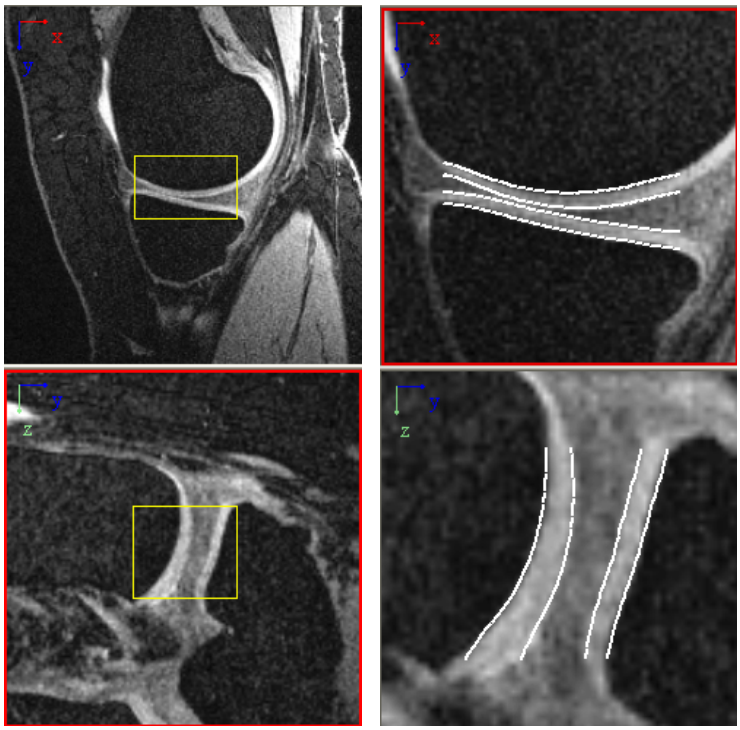
* The University of Iowa. Iowa City IA, USA
** Medical Imaging Applications, LLC, Coralville IA, USA
*** Royal London Hospital, Whitechapel, London, UK

INTRODUCTION: Manual analysis of MR images of articular cartilage is tedious and suffers from inter- and intra-observer variability. We report a novel inherently three-dimensional multi-surface detection method for assessment of local cartilage thickness in the entire bone contact area.

OBJECTIVE: Our objectives are to 1) develop 4-surface segmentation approach for simultaneous detection of cartilage and bone surfaces in the joint contact area and 2) provide its initial validation.

METHODS: We report a fully 3D surface detection method capable of accurate, robust, and efficient segmentation of globally optimal bone and cartilage surfaces (bone/cartilage, cartilage/synovial fluid, synovial fluid/cartilage, cartilage/bone) in volumetric datasets. In our approach, multiple interacting surfaces are detected simultaneously and the optimality is controlled by surface-specific cost functions and by geometric constraints defining the surface smoothness and interrelations. The method solves the surface segmentation problem by transforming it into computing a minimum *s-t* cut in a derived arc-weighted directed graph. The proposed algorithm has a low-order polynomial time complexity and is computationally efficient. The 4 surfaces are identified fully automatically in an interactively determined 3-dimensional region of interest. The cartilage assessment accuracy was determined in 10 MR T1-weighted 3D image data sets (5 ankles, 5 knees with almost isometric voxel sizes ranging from 0.31×0.31×0.30 to 0.39×0.39×0.40mm). The 4 bone and cartilage borders traced by expert orthopedist in 10 randomly selected image slices from each of 10 MR datasets served as independent standard. Local cartilage thickness is calculated from the four detected surfaces. Cartilage surface distances allow determination of the joint-contact area size. Histograms of cartilage thickness can be easily generated.

RESULTS: The automated cartilage segmentation method yielded average signed surface positioning error of 0.12±0.38mm for ankles (talus, tibia) and 0.09±0.47mm for knees (femur, tibia, patella). The borders resulting from the analysis were not manually edited and no borders were excluded. Absolute errors of local cartilage thickness were 0.26±0.22mm for ankles and 0.40±0.31mm for knees. A typical analysis time was 5-20 seconds using a standard Windows computer. Figure shows interactively defined 3D region of interest (left) in which 4 bone and cartilage surfaces are automatically determined (right).



CONCLUSION: In a preliminary validation study involving 5 ankles and 5 knees, the reported method for detection of cartilage and bone surfaces offered sub-voxel segmentation accuracy in the joint contact area and yielded accurate morphological measurements of local and global cartilage thickness.

SPONSOR: NIH - National Institute of Arthritis and Musculoskeletal and Skin Diseases, AR052983.
DICLOSURE STATEMENT: M. Sonka is co-founder of Medical Imaging Applications, LLC.
CORRESPONDENCE ADDRESS: milan-sonka@uiowa.edu

T1rho, T2 AND FOCAL CARTILAGE PATHOLOGY IN PHYSICALLY ACTIVE AND SEDENTARY HEALTHY SUBJECTS VERSUS EARLY OA PATIENTS

*Stahl R., *Li, X., *Majumdar, S., **Luke, A., *Link, T.M.

* Department of Radiology, University of California, San Francisco, CA, U.S.A.
** Department of Orthopedic Surgery, University of California, San Francisco, CA, U.S.A.

INTRODUCTION: The potential of MRI based T2– and T1rho- mapping techniques as non-invasive early biomarkers of cartilage matrix breakdown is currently under investigation. Early studies have shown promising results in the diagnosis of early OA. It is well known that subjects engaged in certain professional sports have an accelerated course of osteoarthritis. Yet it is less known how recreational activity affects cartilage matrix and initiates early degeneration.

OBJECTIVE: (I) To determine T1rho- and T2 values in physically active and sedentary healthy subjects as well as patients with early OA. (II) To assess prevalence and degree of focal cartilage pathology in these groups and (III) to relate these findings with MR-based cartilage matrix measurements.

METHODS: Thirteen asymptomatic physically active subjects (32.69 ± 9.02 years, 6 male, 7 female, performing recreational sports like long-distance running, biking, skiing, hiking, Tegner Score 4-6), seven asymptomatic sedentary subjects (35.43 ± 10.66 years, 4 male 3 female, Tegner Score 1-3), and 17 patients with mild OA (54.00 ± 9.98 years, radiographic KL-score 1-2, 9 female, 8 male) underwent 3.0 Tesla MRI of the knee joint using cartilage matrix and high resolution morphological MR sequences. T1rho and T2 values, cartilage volume and thickness as well as the WORMS scores were obtained in six compartments (medial/lateral femur, medial/lateral tibia, trochlea, patella). ANOVA and t-tests were used for intergroup comparison. Correlations between the parameters were examined with Spearman's rho. ANCOVA with age as covariate was used.

RESULTS: Significant differences ($p<0.05$) in T2 and T1rho were found between healthy subjects and early OA patients with T1rho measurements being superior to T2 in differentiating the two groups (Table). Differences between active and sedentary healthy subjects were not significant. A high prevalence of focal cartilage pathology was found in physically active healthy subjects (9/13 in active versus 2/7 in sedentary subjects). T1rho and T2 values in active subjects with and without focal cartilage pathology were significantly different ($p<0.05$). Differences were found at all compartments, not only these affected by focal pathology. A significant correlation between age and T1rho was found for the healthy active subjects ($r=0.78$ for tibial cartilage T1rho, $p<0.05$).

Compartment	MRI Parameter	Sedentary	Active	Early OA
Trochlea	T1rho	40.09 ± 4.42	40.49 ± 2.63	43.30 ± 2.56 (*)
Patella	T1rho	38.33 ± 3.30	36.90 ± 6.98	42.46 ± 3.39 (*)
Femur condyles	T1rho	39.12 ± 2.29	39.93 ±2.04	42.19 ± 3.09 (*)
Whole Knee	T1rho	38.46 ± 2.20	39.02 ± 2.73	41.17 ± 2.47 (*)
Medial femur condyle	T2	30.56 ± 2.63	30.91 ±1.29	33.33 ± 2.49 (*)
Whole Knee	T2	30.13 ± 0.96	30.29 ± 0.30	31.68 ± 0.62

Table: Average T1rho/T2 values ± STD in ms. (*): These values are significantly higher ($p<0.05$) in early OA patients compared to those in sedentary and active healthy subjects

CONCLUSION: The results of this study show that (i) T1rho is well suited to differentiate healthy subjects and early OA patients, (ii) physically active subjects show a high prevalence of focal cartilage pathology and (iii) active subjects with and without focal cartilage pathology have different T1rho composition of cartilage. Thus T1rho may be a parameter suited to identify active healthy subjects at higher risk for developing cartilage degeneration and, long-term, osteoarthritis.

SPONSOR: Research Evaluation and Allocation Committee (REAC) of the University of California, San Francisco, CA, U.S.A. (Clough G Memorial Endowment Fund), Glaxo Smith Kline (GSK) Inc., Research and Development, London, U.K., National Institute of Health (NIH) grant No R01 AR 46905.
DICLOSURE STATEMENT: S. Majumdar and T.M. Link receive research funding from Merck & Co, One Merck Drive P.O. Box 100 Whitehouse Station, NJ, U.S.A.; Pfizer Global Research and Development, 2800 Plymouth Road, Ann Arbor, MI, 48105, U.S.A.; and GSK.
CORRESPONDENCE ADDRESS: Thomas.Link@radiology.ucsf.edu, 1-415-353-2450

THE QUANTIFICATION OF RELAXATION EFFECTS, DYNAMICS AND SPATIAL DISTRIBUTIONS OF IONIC AND NON-IONIC CONTRAST AGENTS IN ARTICULAR CARTILAGE AT 1.5 T

*Wiener E., *Settles M., *Weirich G., *Rummeny E.J.

*Klinikum rechts der Isar, Technische Universität München, München, Germany

INTRODUCTION: The tissue contrast agent concentration within cartilage can be deduced from either the difference in longitudinal ΔR_1 or transversal ΔR_2 relaxation rates following application of the contrast agent, according to $\Delta R_{1,2} = (R_{1,2}-R_{1,2}^0) = (1/T_{1,2}-1/T_{1,2}^0) \sim$ [contrast agent]. Usually, T1 measurements after Gd-DTPA application are used to quantify cartilage degradation assuming T_1^0 of unenhanced cartilage is constant. In a few studies positively charged manganese ions or the non-ionic Gd-HP-DO3A were used as well as enhancing agents. Furthermore it is well known that even small concentrations of paramagnetic ions decrease both T_1 and T_2.

OBJECTIVE: To compare systematically the T_1 and T_2 relaxation effects, dynamics and spatial distributions of ionic and non-ionic contrast agents in articular cartilage at 1.5T.

METHODS: Dynamic MR-studies over 11 hours were performed in fifteen bovine patella specimens.
For each of the contrast agents Gd-DTPA, Gd-BOPTA, Gd-HP-DO3A and Mn-DPDP three patellae were placed in 2.5 mmol/L contrast solution. Simultaneous measurements of T_1 and T_2 were performed every 30 minutes using a high-spatial-resolution MIX-sequence. This sequence consists of an inversion recovery sequence interleaved with a spin echo sequence. A 180°-90° pulse pair, separated by the inversion delay T_I (100ms), is followed by a 90° SE excitation pulse after the SE repetition time TR_{SE} (650ms). These three pulses are continuously repeated after the IR repetition time TR_{IR} (2000ms). After every 90° excitation pulse ten 180° refocusing pulses generate ten spin echos (echo spacing 10ms). To consider the depth dependent variation of MR relaxation parameters across cartilage thickness an interactive subroutine was programmed to generate profiles across cartilage depth for each time point of the dynamic study in any of the parameter maps. T_1, T_2 and ΔR_1, ΔR_2 profile plots across cartilage thickness were calculated to demonstrate the spatial and temporal distributions of the contrast agents.

RESULTS: Unenhanced cartilage shows a depth dependent variation with a maximal T_1^0 of 600 ms and a small peak at the surface and a value of about 350 ms at the subchondral bone interface. T_2^0 shows a parallel variation with a decrease from 140 ms to 70 ms from the surface to the subchondral bone. The immersion resulted in a continuous decrease of the T_1 relaxation time over time for all contrast agents, most pronounced in superficial cartilage. After 11 hours a maximum decrease throughout cartilage was achieved for all contrast agents. At a depth of 1 mm the non-ionic contrast agent Gd-HP-DO3A shows the strongest decrease from $T_1 \approx 430$ ms of unenhanced cartilage to 60 ms. The negatively charged Gd-BOPTA, Gd-DTPA and Mn-DPDP show a decrease to $T_1 \approx 70$ ms, $T_1 \approx 100$ ms and $T_1 \approx 140$ ms respectively. Apart from the well known decrease of T_1 in the presence of contrast agents, the T_2 curves obtained from the same measurement show qualitatively the same courses as the T_1 profiles with a considerable decrease post contrast. At a depth of 1 mm the strongest decrease as compared to unenhanced cartilage was observed for the non-ionic Gd-HP-DO3A $T_2 \approx 40$ ms followed by the negatively charged Gd-BOPTA $T_2 \approx 45$ ms, Gd-DTPA $T_2 \approx 55$ ms and Mn-DPDP $T_2 \approx 57$ ms respectively. To demonstrate the contrast agent distribution across cartilage thickness, profile plots of the relaxation rate changes ΔR_1 and ΔR_2 were calculated in addition. The absolute ΔR_2-effect in cartilage is at least as large as the ΔR_1-effect for all contrast agents. Maximum changes were 5-12 s^{-1} for ΔR_1 and 8-15 s^{-1} for ΔR_2.

CONCLUSION: All contrast agents have significant T_2-effects within cartilage at 1.5 T. ΔR_1 and ΔR_2 show a non-uniform distribution across cartilage thickness for both ionic and non-ionic contrast agents. This implies that the charge of the contrast agent controls the amount diffusing into cartilage, but not the spatial distribution. The absolute ΔR_2-effect in cartilage is of the same magnitude as the ΔR_1-effect for all contrast agents. Therefore, the measurement of T_2 before and after contrast application to deduce contrast agent concentrations within articular cartilage is an interesting alternative since the quantification of T_2 affords a single multi echo sequence, while a multiple inversion time T_1 measurement requires at least two measurements that are more time consuming to measure.

CORRESPONDENCE ADDRESS: edzard.wiener@balgrist.ch

SUBMITTED ABSTRACTS ORAL SESSION 3: MRI TECHNIQUES AND ANIMAL MODELS

Friday, July 13th, 2007: 9:00 to 10:30 Session Chair: Erika Schneider

(10 min presentation + 5 min discussion)

9:00-9:15	*Li W, *Scheidegger R, *Wu Y, **Vu AT, and *Prasad PV *Department of Radiology, Evanston Northwestern Healthcare, Evanston, IL, USA.,**GE Healthcare, Waukesha, WI, USA. VALIDATION OF 3D LOOK-LOCKER TECHNIQUE FOR DGEMRIC
9:15-9:30	*Nishii T., **Kuroda K., **Matsuoka Y., *Yoshikawa H. * Osaka University Medical School, Suita, Osaka, Japan, ** Institute of Biomedical Research and Innovation, Kobe, Hyogo, Japan ASSESSMENT OF KNEE CARTILAGE T2 IN RESPONSE TO MECHANICAL LOADING AT 3.0 T MR IMAGING
9:30-9:45	*/**Lammentausta E., *Kiviranta P., ***Töyräs J., ****Kiviranta I., */***Jurvelin J.S. , **Nieminen M.T. * University of Kuopio, Kuopio, Finland,** Oulu University Hospital, Oulu, Finland,*** Kuopio University Hospital, Kuopio, Finland,**** Jyväskylä Central Hospital, Jyväskylä, Finland DEGENERATION-INDUCED DEPTH-WISE VARIATION IN T2 OF HUMAN PATELLAR CARTILAGE
9:45-10:00	*,**Wang C., *Borthakur A., *Witschey W.R.T., *Reddy R. * Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA ** Depts. Of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA T1RHO RELAXATION EVALUATION OF KNEE OA IN A GUINEA PIG MODEL
10:00-10:15	Piscaer T.M., Waarsing J.H.., Kops N., Pavljasevic P., Verhaar J.A.N., van Osch G.J.V.M., Weinans H. Erasmus University Medical Center, the Netherlands IN-VIVO IMAGING OF CARTILAGE DEGENERATION IN SMALL ANIMAL MODELS USING MICRO-CT-ARTHROGRAPHY.
10:15-10:30	*Gassner R., ** Ferretti M., **Deschner J., **Srinivasan A., **Wang Z., **Perera P., Sowa G., ***Piesco N., ****Salter R., **Agarwal S. * Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria,** Division of Oral Biology, Ohio State University, Columbus, OH, USA ,*** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA,**** Department of Orthopaedic Surgery, Hospital for Sick Children, Toronto, Ontario, Canada BIOMECHANICAL SIGNALS SUPPRESS PRO-INFLAMMATORY RESPONSES IN ARTICULAR CARTILAGE IN VIVO

VALIDATION OF 3D LOOK-LOCKER TECHNIQUE FOR DGEMRIC

*Li W, *Scheidegger R, *Wu Y, **Vu AT, and *Prasad PV

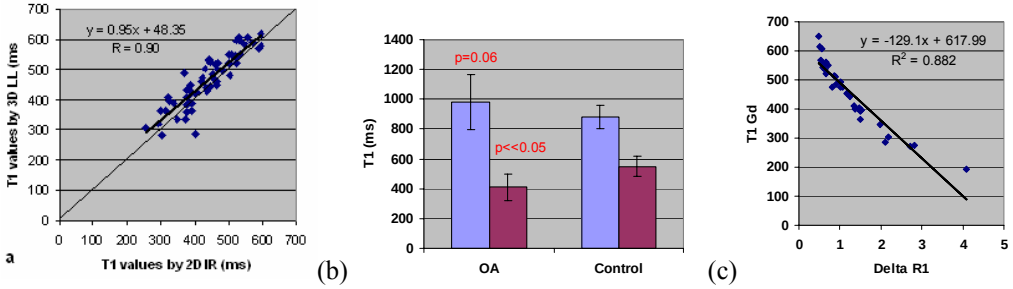
*Department of Radiology, Evanston Northwestern Healthcare, Evanston, IL, USA.
**GE Healthcare, Waukesha, WI, USA.

INTRODUCTION: Delayed Gadolinium Enhanced MRI of cartilage (dGEMRIC) has been demonstrated as a technique for molecular imaging of proteoglycan in cartilage [*AJR* 2004;182:167]. The technique requires quantitative T1 mapping to determine glycosoaminoglycan (GAG) level with joint cartilage. Recently, feasibility of a 3D Look-Locker (3D LL) sequence was demonstrated [Invest Radio. 2006; 41:198] for fast T1 mapping for dGEMRIC.

OBJECTIVE: (1) To validate the T1 measurements by 3D LL technique against 2D IR-FSE in subjects with OA and healthy controls. (2) To evaluate the need for pre-contrast T1 measurements.

METHODS: Thirty-one subjects, including 17 with self reported osteoarthritis (OA, 5 men and 12 women, average age of 60.0 years (range 40-86)) and 14 volunteers without OA symptoms (Controls, 5 men and 9 women, average age of 29.2 years (range 18 – 40)) were involved in this study.
Data were acquired on 1.5T GE Signa short bore Twin speed system (GE Healthcare, Milwaukee, WI) using a commercial transmit/receive extremity coil. dGEMRIC data was acquired typically after 90 min following administration of 0.2 mmol/kg Magnevist. A 2D IR-FSE sequence [*AJR* 2004;182:167] was used first as the reference with five inversion times, TI=1.68, 0.65, 0.35, 0.15, 0.05 s, followed by 3DLL imaging [*Invest Radio*. 2006; 41:198]. Pre-contrast T1 data was acquired with either the 2D IR-FSE sequence (n=21), or the 3DLL sequence (n=10).
T1 mapping was performed with a custom software analysis routine written in MATLAB (The Mathworks; Natick, MA) using a 3-parameter curve-fitting. Regions of interest defined in the central femoral cartilage and tibial plateau. Because the body mass indices (BMI) of the controls (24.7±3.2) and OA (30.2±5.8) was significantly different, post-contrast T1 was corrected for BMI: *T1(corrected) = T1(measured) +3(BMI – 20)* [OsteoAthritis and Cartilage. 2006; 14:1091]. T1 estimates were compared at matched slice locations. Regression analysis was used for comparison.

RESULTS:



(a) Note the good agreement between the two techniques with R values of 0.90, slope ~ 1.0 and intercept that is not statistically different from zero ($p>0.05$). (b) shows that in OA the mean pre-contrast T1 (blue) in central medial femoral cartilage is slightly higher compared to controls probably implying increased hydration and/or reduced macromolecules while post-contrast T1 is lower (purple). (c) shows that the post-contrast T1 is highly correlated with the difference in pre- and post-R1.

CONCLUSION: 3D LL can provide accurate and comparable T1 estimates compared to a single slice 2D IR-FSE method, while providing full joint coverage in a comparable acquisition time. The higher pre-contrast T1 and lower post-contrast T1 in OA suggest that ΔR1 would be a preferred metric. However, the high correlation between T1(Gd) and ΔR1 suggests that either measures would be useful in monitoring changes. Measurement of pre-contrast T1 involves additional time and effort to acquire data and implement spatial registration. These need to be considered when planning multi-center trials.

SPONSOR: Work supported in part by a grant from Berlex Inc.
DICLOSURE STATEMENT: None
ACKNOWLEDGMENT: We thank Ms. S. Chapman and E. Gliwa for their efforts in recruiting subjects for this study and Drs. A. Williams and D. Burstein for many discussions.
CORRESPONDENCE ADDRESS: pprasad@enh.org

ASSESSMENT OF KNEE CARTILAGE T2 IN RESPONSE TO MECHANICAL LOADING AT 3.0 T MR IMAGING

*Nishii T., **Kuroda K., **Matsuoka Y., *Yoshikawa H.

* Osaka University Medical School, Suita, Osaka, Japan
** Institute of Biomedical Research and Innovation, Kobe, Hyogo, Japan

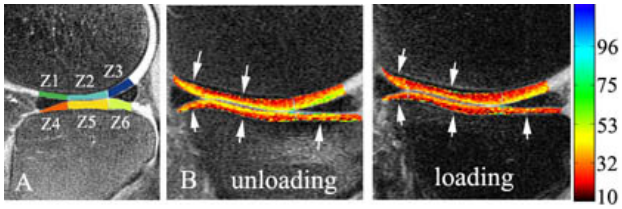
INTRODUCTION: The articular cartilage in the knee joint provides a load-bearing function in conjunction with the interposed meniscus, and failure to respond to normal load-bearing may occur due to disorder of articular cartilage or meniscus. There have been few studies of evaluation of the load-bearing function of the knee cartilage using *in vivo* MR imaging.

OBJECTIVE: We have developed a loading apparatus that applies an axial load to the knee joint during MR imaging, in order to simulate the physiological load-bearing conditions of standing. The purpose of the present study was to prospectively examine the clinical feasibility of MR imaging using mechanical loading system, to assess changes in T2 in the femoral and tibial cartilage of the normal knee joints.

METHODS: Twenty-two volunteers (9 men and 13 women) with no history of knee pain or stiffness were enrolled. Their mean age and body mass index were 25 years (21 to 43) and 21.4 (18.0 to 29.7). All participants provided informed consent to participate in the study, which was approved by the Institutional Review Board. A unilateral knee joint was imaged under unloading and loading conditions, using a 3.0 T MR imaging scanner (GE Healthcare, WI) and a home-built 14-cm transmit-receive birdcage coil. The volunteer was 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 cranially via the foot plate, on loading condition. On unloading and loading conditions, one sagittal T2 map at each medial and lateral FT joint was obtained from multi-echo spin echo sequence with fat-suppression (TR=1500 ms, 8 TEs between 15-120 ms, 3-mm section thickness, NEX=2, FOV=12 cm, Matrix=512 × 256 interpolated to 512×512). Three regions of interest (ROIs) in the femoral cartilage (Z1,Z2,Z3) and tibial cartilages (Z4,Z5,Z6) at the weight-bearing portion were manually defined using the anterior and posterior meniscus as an anatomical landmark (Fig A). T2 values on unloading and loading conditions in each ROI were compared using a paired t-test. The relationship between change of T2 values by loading and gender, age or BMI of volunteers were evaluated using the Spearman correlation coefficient.

RESULTS: The cartilage thickness of femoral and tibial cartilage in the lateral joint was significantly greater under unloading conditions (1.5 mm ± 0.4 and 2.7 mm ± 0.5) than under loading conditions (1.4 mm ± 0.3 and 2.5 mm ± 0.6) ($p<0.05$). By loading, there was a significant decrease in T2 at Z2, Z4, Z5 and Z6 ($p<0.005$) in the medial joint, and at Z2 and Z4 ($p<0.05$) in the lateral joint (Fig B). Under loading conditions, the mean decrease in T2 ranged from 0.2% to 4.1% in the femoral cartilage, and 0.6% to 6.2% in the tibial cartilage. There was no significant relationship between changes in T2 under loading conditions and the gender, age or BMI of volunteers.

CONCLUSION: The present findings indicated clinical feasibility of MR imaging on loading, with respect to yielding significant changes of T2 on the weight-bearing portion of FT cartilages. From responsiveness of loading, T2 evaluation under loading will be expected to allow detection of early degenerative changes of the cartilage and meniscus before morphological changes appear, and to provide biomechanical assessment of ill-condition with respect to localized stress concentration in the cartilage.



SPONSOR: None
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: nishii@rf7.so-net.ne.jp

DEGENERATION-INDUCED DEPTH-WISE VARIATION IN T2 OF HUMAN PATELLAR CARTILAGE

*/**Lammentausta E., *Kiviranta P., ***Töyräs J., ****Kiviranta I., */***Jurvelin J.S. , **Nieminen M.T.

* University of Kuopio, Kuopio, Finland
** Oulu University Hospital, Oulu, Finland
*** Kuopio University Hospital, Kuopio, Finland
**** Jyväskylä Central Hospital, Jyväskylä, Finland

INTRODUCTION: The role of T_2 relaxation time mapping as a surrogate marker for cartilage degeneration has previously been investigated in several studies. In vivo studies with human subjects have revealed that T_2 increases in osteoarthritis and with age. Experimental studies have revealed both an increase and a decrease in T_2 after enzymatic degradation. Experimental models with specific enzymatic treatments and animal cartilage, however, may not mimic actual changes taking place in disease.

OBJECTIVE: To characterize in vitro the depth-wise changes in T_2 relaxation time of human cartilage with different levels of histologically confirmed degeneration at a clinically applicable field strength.

METHODS: Patellae of human cadavers (N=14, age 55±18 years) were equilibrated overnight in 0.5mM Gd-DTPA(2-) solution. It has been previously shown that, at low contrast agent concentrations, the effect on T_2 relaxation time of cartilage is minimal. For MRI measurements, a clinical 1.5T scanner and a 3" receiving coil were used (GE Signa 1.5T, GE Healthcare, Milwaukee, WI). Articular surface of intact patellae was oriented parallel to B_0 to emulate clinical patient positioning. Six locations of interest were defined to cover the articular surface of each patella. T_2 maps were calculated from multi-slice multi-echo spin echo experiments (GE prototype sequence with improved slice profile, TR=1000ms, 8 TE's between 10.3-82.4ms, ETL=8, 3-mm slice thickness, 0.31 mm in-plane resolution). Depth-wise T_2 profiles were calculated by averaging ten pixels along the cartilage surface to match the slice thickness. The length of the profiles was normalized to unity and the profiles were resampled for further comparison. Cylindrical disks (dia.=4mm) were detached from measurement sites for histological analyses. Blind-coded safranin-O-stained histological sections from the samples were graded for degeneration using a modified Mankin score independently by three of the authors. Depth-wise profiles of main collagen orientation calculated from polarized light microscopic images were used to exclude samples without a visible superficial collagenous zone, leaving 42 samples for further analysis. The samples were divided into three groups according to their Mankin score (I ($0<MS<3.3$, n= 12), II ($3.3<MS<6.7$, n=20) and III ($6.7<MS<9$, n=10)), and averaged profiles were calculated for each group. The significance of the difference in T_2 values of different groups was assessed using Kruskal-Wallis test.

RESULTS: The samples studied represented relatively early stages of cartilage degeneration. As compared to the group of least degeneration (group I), group II showed a trend toward prolonged T_2 values to approximately 10% of tissue thickness. Group III showed a remarkable increase of T_2 to approximately 50% of tissue thickness as compared to groups I and II. For the remaining 50% the depth-wise profiles for the three groups showed similar T_2 values. The most superficial layer of articular cartilage was not visible in the T_2 profiles because its thickness is typically beyond the resolution of clinical MRI devices. Due to large deviations, there were no significant differences between the groups at any point along depth-wise profile; however the p-values were considerably smaller near the surface.

CONCLUSION: T_2 relaxation time seems to increase with degeneration. It is noteworthy that the histological scoring system used here assesses tissue properties other than those of the collagen network, and consequently probes different aspects of the tissue than T_2. Polarized light microscopy confirmed that the articular surface was present and therefore the material represents the very early stages of degeneration. The present results suggest that tissue with an intact surface and characteristic orientation of collagen fibrils may have undergone degenerative changes that are reflected by an elevation of T_2 relaxation time. While decreasing T_2 relaxation has previously been reported in an enzymatic model of degeneration, we were unable to reproduce this finding with degenerated native human tissue. In the clinical setting, the angular dependence of the dipolar interaction at different joint surfaces has to be considered. The cartilage zone with collagen fibrils oriented parallel to the B_0 field will experience weaker dipolar interaction, and therefore T_2 in different areas may show variations in sensitivity to degenerative changes.

SPONSOR: Academy of Finland, Finnish Cultural Foundation of Northern Savo
DICLOSURE STATEMENT: none
CORRESPONDENCE ADDRESS: eveliina.lammentausta@gmail.com

T1RHO RELAXATION EVALUATION OF KNEE OA IN A GUINEA PIG MODEL

*,**Wang C., *Borthakur A., *Witschey W.R.T., *Reddy R.

* Metabolic Magnetic Resonance Research & Computing Center, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA
** Depts. Of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA

INTRODUCTION: T1rho-weighted imaging has shown promise as a diagnostic measure of early OA(1). The T1rho relaxation time during a spin-locking pulse has enhanced sensitivity to the interaction between bulk water molecules and extracellular matrix macromolecules such as the proteoglycans in the articular cartilage. In this study, we evaluated the efficacy of T1rho MRI in determining the OA changes in an animal model (Dunkin-Hartley guinea pig) of spontaneous OA. Guinea pigs of young and old age groups (2.5 month and 9 month-old accordingly) are imaged with a T1rho MRI pulse sequence (2), and their cartilage T1rho values were measured at the femoral-tibial joint.

OBJECTIVE: Determine T1rho relaxation times in an animal model of spontaneous OA.

METHODS: All animal-related experiments were reviewed and approved by our institute's animal use committee (IACUC). MRI was performed on the left knee joint of three 2.5-month-old and three 9-month-old guinea pigs on a Varian 9.4T horizontal-bore MRI scanner with a custom-built 2.5 cm diameter knee coil. A series of T1rho images were obtained in the coronal plane using a spin-lock prepared gradient-echo pulse sequence (2) with the following parameters: TE/TR=8.04/1500ms, TSL (duration of spin-lock pulse)= 1, 10, 20, 30 and 40 ms, spin-lock frequency=1500Hz, slice thickness=1mm, FOV=3x3cm, Matrix=512x256. This protocol yields an in-plane resolution of 59x117 microns, with the highest resolution across the femoral-tibial cartilage. Cartilage was manually segmented from each image by simple thresholding of pixel intensities, and the cartilage signal was fitted to an exponentially decaying function (1) in order to obtain T1rho values on a pixel-by-pixel basis (Figure 1).

RESULTS:

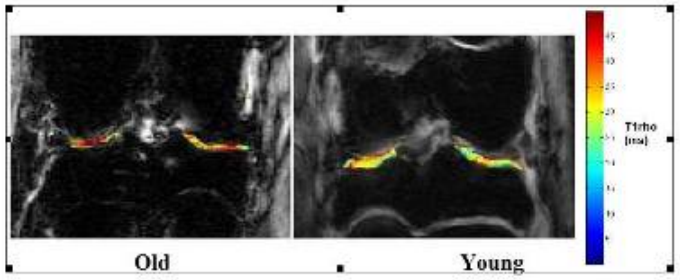


Figure 1. T1rho maps (in color) of articular cartilage overlaid on T1rho-weighted images (grayscale) of two representative guinea pig knees obtained *in vivo* with a pixel size of 59x117 microns in-plane resolution.

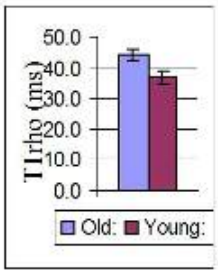


Figure 2. Average T1rho values and standard deviation bar.

Figure 1 shows that the femoral-tibial cartilage from the old animal is thinner than that of the young animal and has elevated T1rho values. Indeed, the average T1rho is significantly greater ($p<0.025$) in the cartilage in all three 9-month animals compared to the three younger animals (Figure 2), suggesting that T1rho is directly related to the degree of cartilage degeneration in this model of spontaneous OA.

CONCLUSION: T1rho is shown to be sensitive to knee OA in this animal model. The protocol is sensitive to OA cartilage degradation. In the future, we will use a 3D T1rho imaging protocol to image animals of multiple age groups. Although this result is preliminary, it nevertheless shows the feasibility of using T1rho MRI in conjunction with guinea pig model in evaluating potential therapies in longitudinal studies.

SPONSOR: This work was performed with grant support from R01-AR051041 and NCRR (RR02305).
ACKNOWLEDGEMENT: Steve Pickup, Weixia Liu, Matt Sochor
CORRESPONDENCE ADDRESS: wangch@seas.upenn.edu

IN-VIVO IMAGING OF CARTILAGE DEGENERATION IN SMALL ANIMAL MODELS USING MICRO-CT-ARTHROGRAPHY.

Piscaer T.M., Waarsing J.H.., Kops N., Pavljasevic P., Verhaar J.A.N., van Osch G.J.V.M., Weinans H.
Erasmus University Medical Center, the Netherlands

INTRODUCTION: Cartilage of experimental osteoarthritis (OA) small animal models is nowadays normally assessed by destructive histological or biochemical techniques. These methods allow no follow-up measurements and are time consuming. In-vivo imaging of cartilage in these animal models would considerably contribute in OA etiology research and finding new therapies. Micro-CT(µCT) is already well known for its detailed quantitative assesment of bone structure, though cartilage cannot be imaged directly by µCT. Negatively charged radiopaque dyes distribute inversely to the glycosaminoglycan distribution in cartilage [1], this would enable in-vivo µCT-imaging of cartilage quality in small animal models.

OBJECTIVE: In-vivo imaging of cartilage degeneration using µCT in combination with a negatively charged radiopaque dye.

METHODS: To induce cartilage degeneration, 1 mg mono-iodoacetate (MIA) was injected in the right knees of 14 rats. The left knees served as control condition and were injected with an equal volume of saline. 2 Days (N=2), 14 Days (N=5) and 44 Days (N=5) after induction of cartilage degeneration, µCT-arthrography was performed on the rats knee joints. To obtain a µCT-arthrogram, 100 µL full strength Hexabrix320: a negatively charged iodine dimer was injected into the knee joint prior to scanning. Epinephrine was mixed with the Hexabrix320 to obtain vasoconstriction in the synovial membrane and by this minimize leakage of the contrast agent out of the joint cavity. A micro-CT scan (Skyscan 1076, resolution: 35 micrometer, aquisition-time:15 minutes) was obtained immediately after injection. µCT data were analyzed using Skyscan software, images were segmented and the cartilage selected. Thickness, volume and attenuation of the 3D patellar cartilage were determined.

RESULTS: Cartilage in the healthy knee was visible as a well defined band, the cartilage in the degenerated knees however was not clearly distinct from its surrounding contrast fluid in the joint cavity, indicating contrast dye diffusion into the GAG-depleted cartilage matrix. Mean attenuation values of the cartilage were increased within four days, indicating fast GAG-depletion of the cartilage (fig.2A). Cartilage thickness and volume decreased till 44 days after MIA injection, following the entire degenerating process (fig 2B,C.).

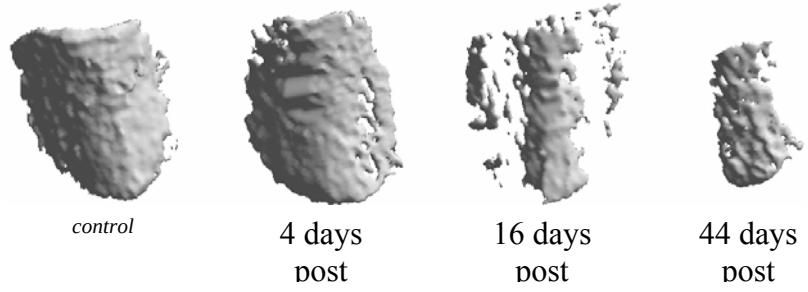


Fig 1. a time-sequence of the 3- dimensional reconstructions of the patellar cartilage layer,

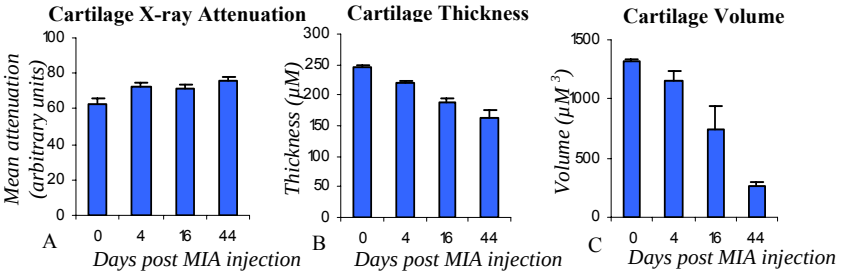


Fig. 2. 3-dimensional quantifications of the patellar cartilage layers

CONCLUSION: µCT-arthrography makes quantitative in-vivo monitoring of cartilage degeneration possible at high resolution. As we know this is the first time cartilage attenuation, thickness and volume is assessed in a rat small animal model. Though it seemed that the contrast dye diffused into the cartilage, indicating imaging of the GAG-containing cartilage matrix, it is not yet possible to image the entire cartilage matrix,e.g. GAG containg and GAG depleted, though the use of a combination of contrast dyes can make this possible in the future. CT-arthrography will accelerate evaluation of therapeuticall interventions and etiology research of OA.

REFERENCES:1.Palmer, A.W. et al.; Proc Natl Acad Sci U S A, 2006. **103**(51): p. 19255-60.
ACKNOWLEDGMENT: We thank the The Dutch Arthritis Foundation for their contribution in this research.
CORRESPONDENCE ADDRESS: h.weinans@erasmusmc.nl

BIOMECHANICAL SIGNALS SUPPRESS PRO-INFLAMMATORY RESPONSES IN ARTICULAR CARTILAGE *IN VIVO*

*Gassner R., ** Ferretti M., **Deschner J., **Srinivasan A., **Wang Z., **Perera P., Sowa G., ***Piesco N., ****Salter R., **Agarwal S.

* Department of Oral & Maxillofacial Surgery, Medical University of Innsbruck, Innsbruck, Austria
** Division of Oral Biology, Ohio State University, Columbus, OH, USA
*** Department of Oral Medicine & Pathology, University of Pittsburgh, Pittsburgh, PA, USA
**** Department of Orthopaedic Surgery, Hospital for Sick Children, Toronto, Ontario, Canada

INTRODUCTION: Although biomechanical signals generated during joint mobilization are vital in maintaining integrity of inflamed cartilage, the molecular mechanism of their actions are little understood. Moreover, motion-based therapies have been applied to promote healing of arthritic joints.

OBJECTIVE: The goal of the current study was to determine the early molecular events that are responsible for the beneficial actions of motion-based therapies on articular cartilage using histochemical and immunofluorescence analyses.

METHODS: Rabbit knees with Antigen-Induced-Arthritis (AIA) were exposed to continuous passive motion (CPM) for 24, 48, 96 hours or 12h per day for 2 weeks and compared to immobilized knees. Following senzitation subcutaneously first and then intra-articular injection with 0.5 mg of BSA, the right knee of the rabbits (n=5/group/timepoint) was immediately placed on CPM device (Orthomotion Inc, Pickering, Ontario, Canada). The angle of flexion of the joint was 70° with movement between 40° and 110° at a rate of 45 seconds per cycle. In the immobilized group (n=5/group/timepoint), right knee immediately after intraarticular injection was wrapped with bandages to immobilize the knee. In all groups, the left limbs of the rabbits (a total of 40) were not subjected to any treatment. All protocols were approved by the Institutional Animal Care Committee at the University of Pittsburgh and University of Toronto. The femoral condyles of knees were harvested and glycosaminoglycans (GAG), interleukin 1b (IL1b), matrix metalloproteinase-1 (MMP-1), cyclooxygenase-2 (COX-2), and interleukin-10 (IL-10) were determined by histochemical and immunofluorescence analysis. One-way ANOVA and the posthoc multiple comparison Tukey test were applied to compare induction of proinflammatory molecules in rabbits exposed to IMM and CPM.

RESULTS: Within 24 hours, immobilized knees exhibited marked GAG degradation. The expression of proinflammatory mediators MMP-1, COX-2, and IL-1b was notably increased within 24 hours and continued to increase during the next 24 hours in immobilized knees, which was also prolonged at the time points at 96 hrs and 2 weeks. Knees subjected to CPM revealed a rapid and sustained decrease in GAG degradation and the expression of all proinflammatory mediators during the entire period of CPM treatment. More importantly, CPM induced synthesis of the anti-inflammatory cytokine IL-10. In all analyzed sections from all animals at each time point statistically significant differences exist for mean fluorescence density measurements between CPM and IMM treated knees ($p < 0.05$).

CONCLUSION: The results demonstrate that mechanical signals generated by CPM exert potent anti-inflammatory signals on articular cartilage. Furthermore, these studies explain the molecular basis of the beneficial effects of CPM observed on articular cartilage and suggest that CPM suppresses the inflammatory process of arthritis more efficiently than immobilization.

SPONSOR: National Institutes of Health Grants HD40939 (National Institute of Child Health and Human Development), AR48781 (National Institute of Arthritis and Musculoskeletal and Skin Diseases), AT0006646 (National Center for Complementary and Alternative Medicine).
DISCLOSURE STATEMENT: none.
CORRESPONDENCE ADDRESS: Robert.Gassner@uki.at

SUBMITTED ABSTRACTS ORAL SESSION 4: CLINICAL STUDIES

Friday, July 13th, 2007: 11:00 to 13:00 Session Chair: Thomas Link

(12 min presentation + 8 min discussion)

11:00-11:20	***Mamisch, T.C., *Welsch G.Z., * Szomolanyi P, **Marlovits S, *Trattnig S * AKH Vienna, Department of Radiology, Vienna, Austria,** AKH Vienna, Department of Trauma Surgery, Vienna, Austria *** University Bern, Department of Orthopedic Surgery, Bern, Switzerland BIOCHEMICAL IMAGING OF CARTILAGE REPAIR: COMPARISON OF NON-CONTRAST AND CONTRAST TECHNIQUES FOR ASSESSMENT OF CARTILAGE REPAIR TISSUE COMPOSITION AND MATURATION OVER TIME.
11:20-11:40	*Hunter DJ, *Niu J, *Zhang YQ, *McLennan C, *LaValley M, **Hudelmaier M, **Eckstein F, *Felson DT. *BUSM, Boston, MA,**Institute of Anatomy & Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria. MEASURES OF CARTILAGE MORPHOMETRY BY RADIOGRAPHIC OA STATUS; THE FRAMINGHAM STUDY
11:40-12:00	*Kim, Y.-J., *Jessel, R., *Dudda, M., **Mamisch, T.C., *Millis, M.B. * Children's Hospital-Boston, Harvard Medical School, Boston, MA, USA,** University of Bern, Bern, Switzerland APPLICATION OF DGEMRIC IN ASSESSING CARTILAGE DAMAGE IN HIP DYSPLASIA AND FEMOROACETABULAR IMPINGEMENT
12:00-12:20	*Guermazi A, *, **Roemer F.W., ***Hunter D.J., *** Neogi T., ***Niu J., *** Felson D.T. * Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A.,** Department of Radiology, Klinikum Augsburg, Augsburg, Germany,*** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A. OSTEOPHYTOSIS AND RADIOGRAPHIC OSTEOARTHRITIS IN KNEES WITH MODERATE TO ADVANCED CHONDROPATHY ASSESSED BY MRI
12:20-12:40	*Oka H., *Yoshimura N., *Muraki S., *Mabuchi A., **Nakamura K., **Kawaguchi H *22nd Century Medical Center, and **Sensory & Motor System Medicine, The University of Tokyo, Tokyo, Japan FULL-AUTOMATIC MEASUREMENT OF KNEE OSTEOARTHRITIS PARAMETERS BY A NOVEL COMPUTER-ASSISTED SYSTEM ON STANDARD RADIOGRAPHS
12:40-13:00	*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Pettersen P., ***Christiansen C. * Department of Computer Science, University of Copenhagen, Denmark,** Nordic Bioscience (NB), Herlev, Denmark *** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark LONGITUDINAL CHANGES IN CARTILAGE SURFACE INCONGRUITY: A MARKER OF PREDISPOSITION FOR OA?

BIOCHEMICAL IMAGING OF CARTILAGE REPAIR: COMPARISON OF NON-CONTRAST AND CONTRAST TECHNIQUES FOR ASSESSMENT OF CARTILAGE REPAIR TISSUE COMPOSITION AND MATURATION OVER TIME.

***Mamisch, T.C., *Welsch G.Z., * Szomolanyi P, **Marlovits S, *Trattnig S

* AKH Vienna, Department of Radiology, Vienna, Austria; ** AKH Vienna, Department of Trauma Surgery, Vienna, Austria; *** University Bern, Department of Orthopedic Surgery, Bern, Switzerland

INTRODUCTION: For MR imaging of cartilage repair morphologic scores, allow visualizing filling of the defect by repair tissue, the structure and surface of the implant and the integrity to the adjacent native cartilage and bone but do not define the course of cartilage matrix remodelling. Various parametric mapping sequences as T_1 mapping with delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC), T_2 mapping calculated from multiple spin-echoes or Diffusion Weighted Imaging (DWI) proved to be potential tool to reflects biochemical structure and composition of the cartilage tissue.

OBJECTIVE: In this cross-sectional and follow-up study after MACT(matrix-associated autologous chondrocyte transplantation), each patient received MR imaging at specific time points and in a 1 year follow up after initial scan. The latest follow-up was at 5 years post surgery. The change of signal intensities, diffusion parameters, T2 - and pre and post-contrast T1-relaxation times were used to evaluate the time course of cartilage repair maturation and the prospect of complete restitution compared to normal hyaline cartilage.

METHODS: 30 femoral condyles in 15 patients with MACT of the knee joint underwent initially MR scanning at a 3T at different time points after therapy and in a 1 year follow up. Based on the postoperative interval the patients were divided into two groups: group 1 up to 18 month (n = 14) and 2 more then 18 month (n = 16). The imaging protocol included a 2D SE-MC sequence for T2 relaxation times, SS - gradient echo pulse sequence with diffusion weighting (3D-DW PSIF) and a 3D VIBE sequence with two different flip angles for assessment of T1 relaxation times. For changes in T1 the 3D VIBE with two different flip angles was performed before and after i.v.administration of anionic gadolinium DTPA (Magnevist®). For the evaluation 3 region of interest (ROI) from deep to superficial layer within the cartilage repair tissue representing the zonal variation and 3 ROI of healthy appearing cartilage within the same knee joint were assessed and compared. For evaluation of the morphological score within the cartilage repair tissue a 3D DESS sequences was performed.

RESULTS: All three biochemical imaging techniques showed significant differences for the cartilage repair tissue and the reference cartilage in both groups.For T2 mapping we observed a significant decrease of the T2 values from group1 to group2 (79.41 to 51.31), and the zonal variation was significantly different in group1 compared to healthy cartilage, and similar in group 2. For the diffusion behaviour the diffusity decreased from group 1 to group 2 (1.61 to 1.43) and the zonal variation showed a decrease of diffusity from the deep to the surperficial in repair tissue in reference cartilage and no changes in the 1 year follow up in group 2. For T1 mapping the mean $\Delta R1$ values for the repair cartilage dropped significantly from 2.35 to 1.69 in the 1 year follow up period, with a $\Delta R1$ of 1.23 to 1.26 for the reference cartilage. For the zonal variation there was an increase of values from deep to superficial layer in the reference cartilage ($\Delta R1$ 0.93 for deep up to 1.54 for superficial), with the same variation but significantly higher values for the transplant cartilage ($\Delta R1$ 2.14 deep up to 2.60 for the superficial layer). In the 1 year follow up this values drop significantly with the highest rate of changes in the superficial layer ($\Delta R1$ 2.60 to 1.47). The morphological score could not differentiate within the two groups and showed most of the changes within the first year of follow up.

CONCLUSION: T1 dGEMRIC, T2 mapping and DWIall monitor changes in cartilage maturation after MACT more sensitive then standard morphological imaging. Based on the zonal variation different results were observed, which could reflect assessment of different macromolecular components of cartilage. By comparisons of the techniques dGEMRIC and DWI showed similar behaviour and wider range of changes in long term follow up of MACT therapy, whereas T2 was more constant. The differences within zonal variation of repair tissue and surrounding tissue showed significant differences between the different methods, which could reflect the different assessment of macromolecular structure within the repair tissue.

SPONSOR: Founding for this study was provided by Austrian Science Found (FWF) FWG-TRP-Project: L 243-B15
DICLOSURE STATEMENT: none
ACKNOWLEDGMENT: We thank the support of Luisa Brandi.
CORRESPONDENCE ADDRESS: mamisch@bwh.harvard.edu

MEASURES OF CARTILAGE MORPHOMETRY BY RADIOGRAPHIC OA STATUS: THE FRAMINGHAM STUDY

*Hunter DJ, *Niu J, *Zhang YQ, *McLennan C, *LaValley M, **Hudelmaier M, **Eckstein F, *Felson DT.
*BUSM, Boston, MA
**Institute of Anatomy & Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria.

INTRODUCTION: In OA diagnosis is based on pain and radiographic features. While cartilage can now be quantified using MRI, different measures can be derived, and it is unclear which of these parameters is most valid.

OBJECTIVE: To determine how well do different measures of cartilage morphology discriminate between subjects with and without evidence of radiographic osteoarthritis?

METHODS: 968 participants from the Framingham OA Study Cohort, a population based study of elderly subjects recruited from the community, had MRIs of the knee performed (2002 – 2004). The cartilage volumes of the patella, medial femur, lateral femur, medial tibia and the lateral tibia were quantified, using coronal and axial 3D FLASH-water excitation sequences (resolution 1.5 mm x 0.3 mm x 0.3 mm) and digital image analysis, involving three-dimensional reconstruction. All participants had lateral and fully extended weight bearing knee radiographs that were read for individual radiographic features and K&L grade. Medial TF OA was defined as K&L≥ 2 excluding knees with lateral JSN≥ 1, whilst lateral TF OA defined as K&L≥ 2 excluding knees with medial JSN≥ 1. PF ROA was defined as JSN≥ 1 or any of 3 osteophytes≥ 1 in the PF joint. We conducted gender specific analyses to explore the mean and SD of total cartilage volume (VC), total cartilage volume normalized to total bone interface area (VCtAB = denuded + cartilaginous interface), and percentage of total bone interface covered with cartilage (cABp=cartilaginous areas/total BI*100).

RESULTS: The mean age of the 968 study participants was 63.4± 8.8 years, 67% were women. 18% of participants had a K&L Grade ≥ 2. In analysis of the cartilage morphometry parameters by compartment affected on their radiograph clear discrimination and delineation between those affected by OA and those who were not was seen for percentage of total bone interface covered with cartilage (see Table below). For the majority of plates total cartilage volume normalized to total bone interface area also provided clear delineation between those with and without OA with the exception of lateral TF OA where the sample with lateral TF ROA was small. In contrast cartilage volume did not provide a consistent clear delineation between those with and those without compartment specific ROA.

	Men				Women			
	n	VC (mm^3)	VCtAB (mm^3/mm^2)	cAB (%)	n	VC (mm^3)	VCtAB (mm^3/mm^2)	cAB (%)
Medial tibia								
Medial TF ROA	50	2362 (661)	1.65 (0.41)	90.9 (15.4)	78	1761 (461)	1.54 (0.34)	94.0 (12.8)
No Medial TF ROA	316	2570 (482)	1.87 (0.21)	99.9 (0.36)	382	1728 (310)	1.63 (0.18)	100 (0.18)
p value		0.008	<0.0001	<0.0001		0.44	0.0008	<0.0001
Patella								
PF ROA	93	2961 (914)	2.17 (0.61)	94.1 (13.5)	108	1921 (634)	1.75 (0.49)	91.6 (12.2)
No PF ROA	288	3488 (694)	2.56 (0.37)	99.7 (1.8)	382	2278 (522)	2.09 (0.39)	99.2 (2.9)
p value		<0.0001	<0.0001	<0.0001		<0.0001	<0.0001	<0.0001

CONCLUSION: We show that both cAB and VCtAB have good construct validity through their ability to distinguish participants with and without compartment specific radiographic knee OA. The large intersubject variability of bone size (and thus VC) and the age-related metaphyseal expansion may increase the apparent VC at the expense of cartilage thickness, and thus we would discourage use of total VC as a stand-alone variable unless this is normalized to subchondral bone area.

SPONSOR: NIH AG18393 and by NIH AR47785
DICLOSURE STATEMENT: No relevant disclosure
ACKNOWLEDGMENT: The participants and staff of the Framingham Osteoarthritis Study.
CORRESPONDENCE ADDRESS: djhunter@bu.edu

APPLICATION OF DGEMRIC IN ASSESSING CARTILAGE DAMAGE IN HIP DYSPLASIA AND FEMOROACETABULAR IMPINGEMENT

*Kim, Y.-J., *Jessel, R., *Dudda, M., **Mamisch, T.C., *Millis, M.B.

* Children's Hospital-Boston, Harvard Medical School, Boston, MA, USA;** University of Bern, Bern, Switzerland

INTRODUCTION: Hip deformity is an important cause of premature OA in hips. Joint preserving surgeries such as periacetabular osteotomy for hip dysplasia and femoral head-neck junction osteoplasty for impingement improve patient symptoms but it is not clear if the natural history of OA progression is altered. Furthermore, the long term results of such surgeries are a function of the amount of pre-existing joint damage at time of operation. Delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) is a functional MRI technique for detecting loss of charge density in articular cartilage, which occurs early in cartilage degeneration.

OBJECTIVE: We have applied dGEMRIC to detect early OA in these hips and to better understand patient and radiographic factors associated with early OA.

METHODS: Two cross section studies involving one-hundred-three hips in seventy-seven patients with acetabular dysplasia (Study DDH) and femoroacetabular impingement (Study FAI) were performed. Patients were recruited from our clinic population referred for evaluation of hip pain. Patient and radiographic factors associated with early OA as measured using dGEMRIC were noted. Study DDH: Ninety-six hips in seventy-four patients were assessed with standard radiographs and a dGEMRIC scan. On standing AP radiograph the following were measured: lateral center-edge angle of Wiberg (LCE), acetabular index of Tönnis (TILT), and break in Shenton's line. Anterior under coverage was measured on Lequense's false profile view using the anterior-center edge angle (ACE). Using dGEMRIC, significant OA was defined as a value below 390 msec. Labral tear was present when contrast enhancement was seen through the entire thickness of the labrum. Multiple stepwise logistic regression analysis was performed to identify factors associated with significant OA in dysplastic hips. Study FAI: Thirty seven hips in 30 patients who had a dGEMRIC scan and radiographic evidence of FAI were identified. Clinical symptoms were assessed using the WOMAC. Radiographic measurements were performed to determine acetabular and femoral morphology: LCE, TILT, and femoral head ratio of Murray (FHR). Acetabular version was assessed by the presence or absence of the cross-over and the posterior wall signs. The type of impingement, Cam, Pincer, or Mixed was assessed on the anteroposterior view and the cross-table lateral view. The severity of radiograph OA was determined using Tönnis grade and minimum joint space width (JSW). On MRI, the alpha angle was measured on the sagittal oblique cuts and the presence of a labral tear was noted. Along with patient age, correlations between dGEMRIC index, patient symptoms, morphologic measurements, and radiographic findings were determined.

RESULTS: Study DDH: The mean dGEMRIC index for this cohort (473 ± 104 msec) was significantly lower than a morphologically normal hip (570 ± 90 msec). ACE, JSW, and presence of labral tears were all univariate predictors of significant osteoarthritis. Multivariate analysis identified age, ACE, and presence of a labral tear as independent predictors of significant OA. A second model was fitted omitting ACE as LCE and ACE are highly correlated. Model II identified age, LCE, and presence of a labral tear as significant independent predictors. Study FAI: Significant correlations were observed between dGEMRIC index, pain ($p<0.05$), and alpha angle ($p<0.05$). The negative correlation of dGEMRIC and alpha angle implies that hips with more femoral deformity show signs of early OA.

CONCLUSION: In hip dysplasia, significant OA onset is associated with increasing age and severity of dysplasia, measured using both LCE and ACE. Additionally, labral tear is associated with more OA. In FAI, similar to our previous finding in dysplasia dGEMRIC does correlate with patient symptoms. Additionally, dGEMRIC does correlate with more femoral deformity but the correlation is weak. Therefore dGEMRIC is a measure of early OA in the hip joint, which is the best predictor of outcome after joint preserving surgery for dysplasia. Based on these studies we feel staging of cartilage lesions based on dGEMRIC is clinically useful. We propose that dGEMRIC is a useful technique for staging and monitoring cartilage lesions for other disease modifying therapies for OA, as well.

SPONSOR: Orthopaedic Research and Education Foundation Research Grant.
DICLOSURE STATEMENT: none
ACKNOWLEDGMENT: We thank the support of Drs. Deborah Burstein and Martha Gray.
CORRESPONDENCE ADDRESS: young-jo.kim@childrens.harvard.edu

OSTEOPHYTOSIS AND RADIOGRAPHIC OSTEOARTHRITIS IN KNEES WITH MODERATE TO ADVANCED CHONDROPATHY ASSESSED BY MRI

*Guermazi A, *,**Roemer F.W., ***Hunter D.J., *** Neogi T., ***Niu J., *** Felson D.T.

* Department of Radiology, Boston Medical Center, Boston University, Boston, MA, U.S.A.
** Department of Radiology, Klinikum Augsburg, Augsburg, Germany
*** Clinical Epidemiology Research and Training Unit, Boston University, Boston, MA, U.S.A.

INTRODUCTION: Since the implementation of MRI in OA research, it has been observed that in moderate to advanced stages of cartilage deterioration osteophytosis is commonly observed as has been shown from studies applying conventional radiography. It is not known why a subgroup of patients with relevant cartilage damage exhibits marked osteophytosis and a minor subgroup with comparable cartilage alterations does not develop osteophytosis to the same extent.

OBJECTIVE: The aim of the present study was the analysis of 1) the prevalence of osteophytosis and 2) radiographic OA in a population with moderate to advanced cartilage deterioration defined by a semi-quantitative scoring method on MRI.

METHODS: In a large population-based osteoarthritis study MRI was performed on a 1.5 T system using triplanar proton-density weighted fat suppressed sequences and a sagittal T1 weighted sequence. Cartilage was assessed in ten tibio-femoral subregions (central/posterior femur, anterior/central/posterior tibia in medial/lateral compartments respectively) using a semi-quantitative score from 0-6. Knees with a cartilage score of $\geq$3 in at least one of the subregions were included for analysis. A maximal score of 3 or 4 in at least one subregion was considered moderate cartilage damage, a score of 5 or 6 advanced cartilage damage. Osteophytosis was scored from 0 to 3. The prevalence of osteophytosis was calculated for each of the two cartilage damage groups. Prevalence of radiographic tibiofemoral OA was described for each of the subgroups.

RESULTS: 517 knees were included. Demographics for the two subgroups did not differ significantly concerning age, body mass index and sex (Table 1). Among the 333 knees with moderate cartilage damage a maximal osteophyte score of 0 in any subregion was observed in 13 (3.9%), a score of 1 in 200 (60.1%), a score of 2 in 115 (34.5%) and a score of 3 in 5 (1.5%) knees. Among the 184 knees with advanced cartilage damage, a maximal osteophyte score of 0 was observed in 1 (1.5%), a score of 1 in 32 (17.4%), a score of 2 in 104 (56.6%) and a score of 3 in 47 (25.6%) knees. Radiographic tibiofemoral OA was observed in 93 (29.1%) subjects with moderate chondropathy and in 163 (90.1%) subjects with advanced damage.

Table 1: Demographic characteristics and prevalence data by cartilage damage group

	Moderate cartilage damage (N=333)	Advanced cartilage damage (N=184)
Age, mean $\pm$ SD	65.7 $\pm$ 8.8	69.1 $\pm$ 8.3
BMI, kg/m^2, mean $\pm$ SD	29.1 $\pm$ 5.7	30.8 $\pm$ 6.0
Female, N (%)	190 (57.1)	98 (53.3)
FT TF OA on X-ray, N (%)	93 (29.1)	163 (90.1)
Maximal osteophyte score		
0	13 (3.9)	1 (0.5)
1	200 (60.1)	32 (17.4)
2	115 (34.5)	104 (56.5)
3	5 (1.5)	47 (25.6)

CONCLUSION: There is substantial heterogeneity in osteophytosis in knees with moderate and advanced tibio-femoral cartilage damage suggesting that these pathophysiologic processes may have different risk factors or rates of change in disease. Surprisingly, the majority of knees with moderate cartilage damage do not exhibit radiographic OA

SPONSOR: NIH Grant No NIH AR47785
DICLOSURE STATEMENT: None.
CORRESPONDENCE ADDRESS: ali.guermazi@bmc.org

FULL-AUTOMATIC MEASUREMENT OF KNEE OSTEOARTHRITIS PARAMETERS BY A NOVEL COMPUTER-ASSISTED SYSTEM ON STANDARD RADIOGRAPHS

*Oka H., *Yoshimura N., *Muraki S., *Mabuchi A., **Nakamura K., **Kawaguchi H

*22nd Century Medical Center, and **Sensory & Motor System Medicine, The University of Tokyo, Tokyo, Japan

INTRODUCTION: Although knee OA is characterized by joint space narrowing, osteophyte formation, and joint angulation, quantitative method to evaluate these changes has not yet been well established. Despite a rapid progress of MRI with high resolution, standard radiography is still considered the golden standard to evaluate the OA severity in general clinical settings. However, inter-observer variation is unavoidable in the most frequently used KLG. While several semi-automatic methods for measurement of JSW or femorotibial angle (FTA) using computer-assisted systems have recently been developed, there still remains observer variations since initial operations should be manually performed. Here we report a novel computer program named KOACAD (knee OA computer-aided diagnosis) which realized a full-automatic measurement of major six parameters of knee OA: medial & lateral minimum JSW (mJSW), medial & lateral joint space area (JSA), osteophyte area (OPA), and FTA, at once on standard radiographs.

OBJECTIVE: 1) To examine the reliability and reproducibility of KOACAD. 2) To investigate the association of KOACAD parameters with knee pain using a large-scale database.

METHODS: Anteroposterior X-rays of bilateral knees with standing on both legs were obtained as a DICOM file from database of the entire 3,040 participants in the ROAD (research on osteoarthritis against disability) study. The KOACAD program includes the following automatic operations. After noise reduction by filtering three times, medial and lateral sides were judged based on the difference of calculated widths of tibia and fibula. The joint space was determined as the area surrounded by the medial and lateral lines between the ends of femoral condyle and tibial plateau, and the outlines of femoral condyle and tibial plateau. The medial and lateral JSAs were then calculated, and interbone distance at the narrowest point within the areas was measured as medial and lateral JSWs. OPA and FTA were also calculated from the medial and lateral outlines of femur and tibia. Variation of intra- or inter-observer was evaluated by ICC of KOACAD, semi-automatic measurement, or KLG on randomly selected 50 radiographs. Correlations of sex, age, and the six KOACAD parameters with knee pain were examined on 1,979 radiographs in the database of the urban cohort in the ROAD study by a Student's t test. Odds ratio (OR) and 95% confidence intervals (95%CI) were calculated by logistic regression analysis.

RESULTS: The KOACAD system could automatically measure the six parameters within one second without any manual operation. ICCs of inter- and intra-observer of semi-automatic measurement were rather low: 0.53-0.56 and 0.62-0.65 for medial & lateral mJSW, JSA, and OPA; 0.72 and 0.75 for FTA; and those of KLG were 0.76 and 0.84, respectively. However, there was no variation of inter- or intra-observer measurement in KOACAD (all ICC=1.0). Among the parameters, medial mJSA and FTA were strongly correlated with KLG (r=-0.41 and +0.31, respectively, by Spearman's correlation test). In the 1,979 knees, 594 had pain and 1,385 did not. Step-wise logistic regression analysis after adjustment for age revealed that low medial mJSW (OR=1.46, 95%CI=1.16-1.90 in men; OR=1.41, 95%CI=1.22-1.63 in women) and high FTA (OR=1.07, 95%CI=1.01-1.13 in men; OR=1.07, 95%CI=1.03-1.10 in women) were positively associated with pain, while neither lateral mJSW nor OPA was.

CONCLUSION: We have established a full-automatic computer-assisted program KOACAD to quantify the knee OA severity on standard radiographs, and confirmed the high reliability and reproducibility. Unlike the conventional KLG, this system could evaluate distinct parameters, so that medial JSN and varus deformity of knee joints, but not lateral JSN or osteophyte formation, was shown to be risk factors for symptomatic knee pain. This system will not only be a useful tool in objective evaluation of knee OA patients in daily clinical settings, but also make a proper outcome measure for the development of epochal structure-modifying drugs for OA.

STUDY SPONSOR: None
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: hoka@k3.dion.ne.jp

LONGITUDINAL CHANGES IN CARTILAGE SURFACE INCONGRUITY: A MARKER OF PREDISPOSITION FOR OA?

*Folkesson J., **Dam E.B., *Olsen O.F., **Karsdal M.A., ***Pettersen P., ***Christiansen C.

* Department of Computer Science, University of Copenhagen, Denmark
** Nordic Bioscience (NB), Herlev, Denmark
*** Center for Clinical and Basic Research (CCBR), Ballerup, Denmark

INTRODUCTION: Joint congruity is determined by the global surface shape, and describes the extent of which contacting joint surfaces match each other. Joint incongruity is related to biomechanical factors and could be related to the initiation and progression of degenerative processes of articular cartilage.

OBJECTIVE: To evaluate the articular cartilage surface incongruity determined from MRI data cross-sectionally and longitudinally, in relation to radiographic signs of OA.

METHODS: Knee MR scans were acquired sagittally using a low-field 0.18T scanner (40 degrees flip angle, TR 50 ms, TE 16 ms), resolution 0.7x0.7x0.8 mm^3, along with posterior-anterior x-rays for Kellgren-Lawrence index (KL) and tibial plateau width. The baseline study consisted of 313 scans, 25 for training and 288 for testing (population: 56±16 years old, 44% females, baseline KL distribution [145,88,30,24,1] for KL 0-4), follow-up scans were acquired of 243 knees 21 months and 31 scans were acquired a week after baseline.
From the MR scans, the cartilage was first segmented automatically in 3D, then the cartilage surface incongruity for the medial tibial compartment was estimated automatically using curvature analysis globally on the surface, since a varying curvature on the overall surface may lead to mismatching of the surfaces as the joint bends. Measures were normalized with tibial plateau width.

RESULTS: At baseline, the surface incongruity was significantly higher in the OA population (KL > 0) than the healthy ($p = 2.5*10^{-11}$, Fig 1 left). The incongruity also enabled separation early OA (KL 1) from the healthy population ($p = 6.4*10^{-6}$, Fig 1 left). The incongruity only had a limited linear correlation with age. For the 31 test-retest pairs, the mean CV was 7.8%. Longitudinally, there was a significant increase in incongruity only for the KL >= 3 population ($p=0.04$, Fig 1 right).

CONCLUSION: The results at baseline suggested that incongruity detects predisposition of OA. There were no significant longitudinal changes until the KL 3 population, which could be related to the collapse of the joint in severe OA. Incongruity could be useful in treatment development targeting early stages of OA.

DISCLOSURE STATEMENT: Dam and Karsdal are employees of NB. Folkesson is funded by a grant partly sponsored by NB. Christensen is a shareholder of both CCBR and NB.
CORRESPONDENCE ADDRESS: jenny@diku.dk

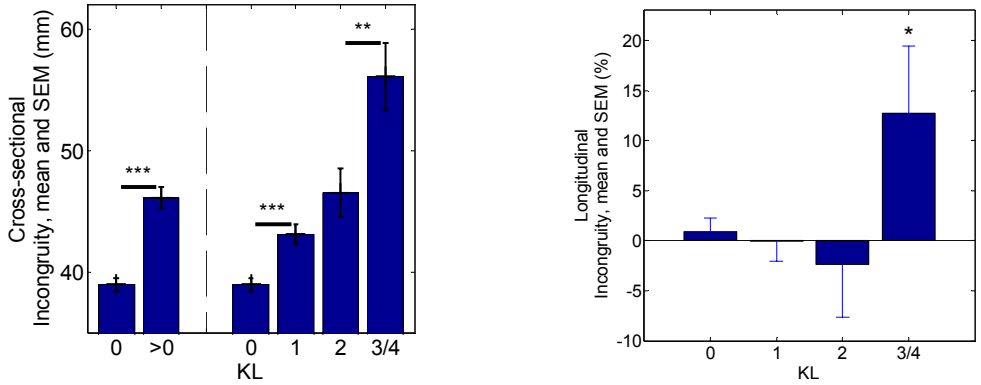


Figure 1. Cross-sectional distribution (left) and longitudinal changes (right) in KL populations at baseline.

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