

#### 418 THE CLINICAL ASSOCIATIONS OF KNEE CARTILAGE DEFECTS IN AN OBESE POPULATION

A. Anandacoomarasamy<sup>1</sup>, I. Caterson<sup>2</sup>, G. Smith<sup>1</sup>, S. Leibman<sup>1</sup>, B. Giuffre<sup>1</sup>, M. Fransen<sup>3</sup>, P. Sambrook<sup>1</sup>, L. March<sup>1</sup>. <sup>1</sup>University of Sydney, Northern Clinical School, IBJR, Royal North Shore Hospital, Sydney, AUSTRALIA, <sup>2</sup>Royal Prince Alfred Hospital, Sydney, AUSTRALIA, <sup>3</sup>George Institute, Sydney, AUSTRALIA

**Purpose:** To generate hypothesis regarding the associations of knee cartilage defects in an obese population with and without OA.

**Methods:** Obese subjects (BMI >30) were recruited from laparoscopic adjustable gastric banding or exercise and diet weight loss programs. ACR clinical criteria for OA knee were determined. MRI assessment was conducted on a 3T machine (Magnetom Trio; Siemens, Erlangen, Germany) at baseline. Cartilage defects were graded according to an established protocol at medial tibial, medial femoral, lateral tibial, lateral femoral and patellar sites (grade 0–4). Composite scores for medial tibiofemoral, lateral tibiofemoral and whole compartments were obtained. All subjects completed a general health and musculoskeletal (MSK) questionnaire, WOMAC, SF-36, AQL, Moorehead-Ardelt Quality of Life Questionnaire II (developed in an obese population), and Multidimensional Assessment of Fatigue. Physical assessment was conducted by a single assessor. The MSK questionnaire assessed joint pain; activity level at work, home and leisure; medication use; previous injury and previous surgery. Physical assessment parameters included: range of knee and hip motion; crepitus; alignment; quadriceps strength; waist, hip and knee circumference. Correlations between cartilage defect scores and MSK outcomes were obtained (Stata software). Regression analysis corrected for age, gender, BMI and presence of knee OA.

**Results:** There were 111 subjects (78 women and 33 men) with mean BMI 39.9±5.8 and mean age 51±12 years. Fifty-three (48%) subjects met ACR criteria for knee OA. Knee cartilage defects were significantly associated with BMI ( $p < 0.03$ ), presence of knee OA ( $p < 0.0001$ ), knee pain ( $p < 0.05$ ), and duration of knee pain ( $p < 0.01$ ) in the medial tibiofemoral and whole compartments. There was statistically significant association with BMI and the lateral tibiofemoral compartment ( $p < 0.01$ ). Significant associations were also seen with physical function, role physical, bodily pain and general health on SF-36 ( $p < 0.05$ ); pain, stiffness and function on WOMAC ( $p < 0.0001$ ); and medication use and independence subscale ( $p < 0.02$ ) on AQL for both the medial tibiofemoral and whole compartments. The association between knee cartilage defects, and BMI ( $p < 0.04$ ) and knee OA ( $p < 0.0001$ ) remained significant in the medial tibiofemoral and whole compartments on regression analysis. ICCs for intra-observer reproducibility were >0.98 for all compartments.

**Conclusions:** Knee cartilage defects scores are significantly associated with BMI, knee OA, the presence and duration of knee pain. Cartilage defects are also significantly associated with a number of quality of life measures indicating clinical significance. They provide a time-efficient means of assessing articular cartilage which is reproducible. With the rising prevalence of obesity, it is important to assess the natural history of cartilage defects in the obese population, a group at risk for both incident and prevalent OA.

#### 419 LOCATION AND MAGNITUDE OF CARTILAGE THICKNESS LOSS IN OA PROGRESSORS

R. Buck<sup>1</sup>, F. Eckstein<sup>2</sup>, B. Wyman<sup>1</sup>, M-P. Hellio Le Graverand<sup>1</sup>. A9001140 Study Investigators. <sup>1</sup>Pfizer, Inc., New London, CT, USA, <sup>2</sup>Chondrometrics GmbH, Aining, GERMANY

**Purpose:** A 2 year study to compare change in cartilage thickness in non OA and OA subjects, also provides an opportunity to identify individuals with significant decrease in cartilage thickness, i.e., progressors. Examination of only progressors may lead to better understanding of the location and magnitude of changes in cartilage thickness over during clinical trials. The objective of this study was to identify subjects with significant medial cartilage thickness decrease over two years and assess the location and magnitude of their decrease.

**Methods:** In the A9001140 study, 152 female subjects were imaged at 7 clinical centers using Siemens Magnetom Trio and GE Signa Excite magnets. Double oblique coronal acquisitions were obtained at baseline and 2 years, using water excitation spoiled gradient echo sequences ( $1.0 \times 0.31 \times 0.31 \text{ mm}^3$  resolution). Segmentation of femoro-tibial cartilage morphology was performed using proprietary software (Chondrometrics, Germany). Change in medial cartilage thickness (ThCTAB.aMe) over 24 months was measured for the whole compartment (cMFTC, MFTC), the femoral and tibial plates (cMF, MT), 3 subregions of the femoral plate

(ccMF, ecMF, icMF) and 5 subregions (central, exterior, interior, anterior and posterior) of the tibial plate (cMT, eMT, iMT, aMT, pMT). Kellgren and Lawrence grades (KL) were observed on standing anteroposterior (AP) and Lyon Schuss (LS) radiographs of the knee.

The 77 subjects with KL=0 scores on both AP and LS radiographs were viewed as an unambiguous healthy group and defined as non OA subjects. Of the remaining 75 subjects, 13 had KL=0 only on the AP radiographs, 4 were KL=1, 30 were KL=2, and 28 were KL=3. While some subjects had AP KL=0, for convenience this group was defined as the OA group. Progressors were defined as subjects with a larger decrease in a cartilage thickness measure than expected from examination of non OA distribution. Normalized values (z-scores) were generated for non OA and OA subjects by subtracting the mean and standard deviation of the non OA subjects. Specifically, the normalized values were translated to p values from the normal distribution and small p values were taken as indication of progression. Multiple comparisons adjustments were made using false discovery rate methods ( $\alpha = 0.1$ ) for non OA and OA groups separately. Normality plots were used to check if annualized rates of change in cartilage thickness for the non OA group were normally distributed. Summary statistics regarding frequency and magnitude of progression in different KL Groups and knee regions were computed.

**Results:** 28% of the OA group were progressors, compared to 2.6% of the non OA group. Using AP radiograph KL scores, 20% of KL2s were progressors compared to 46% of KL3s. Twelve of the 23 progressors had significant progression in a single subregion, while 4 had significant progression in 4 or more subregions. Approximately 10% of subjects had significant progression when observing compartments (cMFTC, MFTC), while 5–8% had progression when observing medial plates (cMF, eMT). The subregion with highest observed frequency of progression was MT (65% of progressors) followed by ccMF (35%). Mean percent annualized rate of change in progressors ranged from -0.6% (pMT) to -5.9% (eMT) with 4 of the subregions having annual percent decrease in thickness greater than 3%. Rate of change in non progressors ranged between -0.3 to 0.7%.

**Conclusions:** Over 2 years many subjects do have a significant decrease in cartilage thickness, but the decrease tends to be localized (1 subregion). Although two subregions, eMT and ccMF, are the most frequently observed locations for decrease in cartilage thickness, all subregions, except pMT, are observed to have important decreases in some subjects.

#### 420 DUAL ENERGY X-RAY ABSORPTIOMETRY ANALYSIS CONTRIBUTE TO PREDICT HIP OSTEOARTHRITIS PROGRESSION

M. Castano, J.C. van der Linden, J.H. Waarsing, R.M. Rozendaal, J.A. Verhaar, F. Rivadeneiro, S.M. Bierma-Zeinstra, H. Weinans. Erasmus MC, Rotterdam, NETHERLANDS

**Purpose:** To determine if parameters obtained from dual energy X-ray absorptiometry (DXA) contribute to predict progression of hip osteoarthritis (OA) and to test if the difference between affected (OA) hip and contralateral hip adds to this prediction.

**Methods:** The study group involves the “Glucosamine sulphate on osteoarthritis long term” (GOAL) cohort from which we took 189 patients that met the American College of Rheumatology clinical criteria for hip osteoarthritis and were included after their first visit to the Physician. DXA images, X-rays and pain and function scores (WOMAC) were obtained from all patients at inclusion and after 2 years follow-up.

Software was developed for DXA analysis at different regions of interest in the femoral head and proximal femur. We performed first a logistic regression analysis to test if Kellgren and Lawrence scores (KL) can predict ‘progression’ of OA, with the outcome ‘progression’ defined as 20% joint space narrowing or when patients received a total hip replacement within the two years follow-up period. In addition we tested if (1) DXA parameters contribute to the prediction of progression and (2) parameters that use the difference between the affected and contralateral hip of the patient contribute to the prediction. All the models were corrected for the variables gender, age, weight and height. We used -2log likelihood test, R square Nagelkerke and Areas Under the Receiver operator characteristic curves (ROC) to compare the models.

**Results:** The model that included the DXA variables was significantly better in predicting hip OA progression than the model with KL score of the affected side alone ( $p < 0.01$ ). The addition of DXA differences within hips slightly added to the prediction of progression ( $p < 0.05$ ).

The difference in bone mineral density (BMD) and bone mineral content (BMC) in the superior and medial part of the femoral head between the

affected and contralateral hip are the most important predictors of hip osteoarthritis progression ( $p < 0.01$ ). (Figure 1, area a and b). Similarly, there are size differences between progressors and non-progressors in the superior part of the femoral head and trochanter major. However the KL score of the affected side was still the most relevant variable in the prediction of OA progression.

**Conclusions:** DXA parameters can significantly contribute to predict future progression of joint space narrowing or total hip replacement in patients with (beginning) hip osteoarthritis. The analysis of the DXA differences between two hips of the patient represents a small but significant contribution to this prediction. These analyses show the importance of bone density changes in the etiology of OA. Accurate measurements of bone density and bone shape can help to diagnose OA and predict its chances of fast progression.

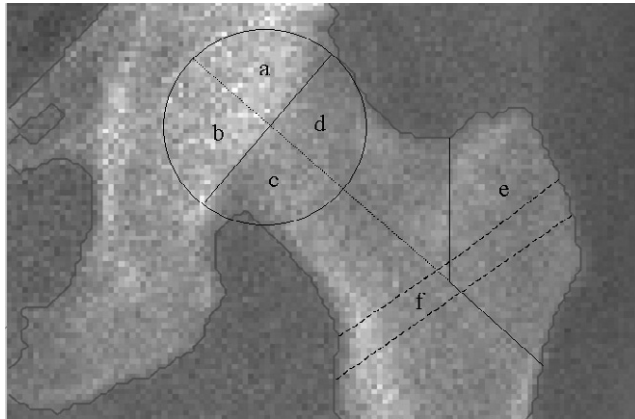


Figure 1. Important areas of division of the hip using DXA analysis. These areas show differences with respect to its contralateral side in those OA patients where the disease will progress. (a) superior, (b) medial, (c) inferior, (d) lateral parts of the femoral head, (e) black lines demarking trochanter major area, (f) broken lines limit the intertrochanteric area.

**421 SIDE-DIFFERENCES OF FEMOROTIBIAL CARTILAGE LOSS IN KNEE OA**

**M. Kunz<sup>1</sup>, S. Cahue<sup>2</sup>, M. Marshall<sup>2</sup>, M. Hudelmaier<sup>1</sup>, L. Sharma<sup>2</sup>, F. Eckstein<sup>1</sup>.** <sup>1</sup>Paracelsus Medical University, Salzburg, AUSTRIA, <sup>2</sup>Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

**Purpose:** Osteoarthritis of the knee is often considered to be a bilateral disease, in which one knee (i.e. the functionally dominant one) may be more advanced than the contralateral knee. Also, in studies testing intra-articular DMOADs, the question arises to what extent the contralateral (untreated) knee can be used as a control. It is, however, currently unclear to what extent cartilage loss correlates in left and right knee, and whether cartilage loss in the dominant knee precedes or is greater than that in the non-dominant knee. Here we study the correlation of femoro-tibial cartilage loss in bilateral knees of community-recruited persons with knee OA using quantitative MR imaging, and we test the hypothesis that cartilage loss in the dominant knee is greater than in the non-dominant knee due to the higher mechanical loading encountered by dominant knees.

**Methods:** We studied the left and right knees of 124 participants (age  $72 \pm 9$  years [mean $\pm$ SD], BMI  $29.9 \pm 5.5$ , 72% women), with mild to moderate symptomatic OA in at least one knee. Double oblique coronal FLASHwe MRI sequences were acquired bilaterally at baseline and  $26.6 \pm 5.4$  months later. Segmentation of the cartilage was performed by tracing the total subchondral bone area (tAB) and the cartilage surface (AC) throughout the weight-bearing femorotibial cartilage plates with baseline and follow up scans being processed in parallel (readers blinded to acquisition order). All segmentations were quality controlled by one observer. The cartilage thickness (ThCtAB) was determined using proprietary software (Chondrometrics, Ainring, Germany). Progression was expressed as change in ThCtAB per annum in the medial (MT) and lateral tibia (LT), in the medial (cMF) and lateral weight-bearing femur (cLF) and for aggregate values in the medial and lateral femoro-tibial compartment (MFTC/LFTC).

**Results:** The correlation for cartilage thickness loss between left and right knees was  $r = 0.23$  in the medial and  $r = 0.32$  in the lateral femoro-tibial

compartment. Medial cartilage loss was 0.8% annually in non-dominant and 1.1% in dominant knees ( $r = 0.23$ ); with the rate of change not being significantly different (Table 1).

Table 1: Rate of annual cartilage loss and correlation between dominant and non-dominant knees

	Dominant Knee	Non-dominant Knee	p value (dom. vs. non-dom.)	Correlation
MT	-1.1%	-0.9%	0.61	0.34
cMF	-1.2%	-0.7%	0.29	0.17
LT	-1.1%	-1.4%	0.37	0.31
cLF	-0.7%	-1.0%	0.43	0.401

In the lateral femorotibial compartment, the rate of change was 1.2% in non-dominant and 0.9% in dominant knees ( $r = 0.46$ ), again the rate of change not being significantly different (Tab. 1).

**Conclusions:** It is known that cartilage morphology (thickness, volume) in healthy persons is highly symmetric between dominant and non-dominant knees (no significant difference) and displays a high correlation. However, bilateral cartilage loss in OA has not been studied systematically using quantitative MR imaging. In this study of participants with symptomatic and radiographic OA of at least one knee, we do not find significant differences in cartilage loss between dominant and non-dominant or between left and right knees. The correlation of cartilage loss between dominant/non-dominant or left/right knees was only modest. These data provide no evidence that cartilage loss in functionally dominant knees is greater than in contralateral (non-dominant) knees and that the mechanical loading associated with limb dominance is a risk factor for OA progression.

**422 STATISTICAL SHAPE MODELLING REVEALS FOCAL PATTERN OF CARTILAGE LOSS IN OAI PROGRESSION COHORT**

**M.A. Bowes<sup>1</sup>, T.G. Williams<sup>2</sup>, C.J. Taylor<sup>2</sup>, C.E. Hutchinson<sup>2</sup>, R.A. Maciewicz<sup>3</sup>, J.C. Waterton<sup>3</sup>, A.P. Holmes<sup>3</sup>, G.R. Vincent<sup>1</sup>.** <sup>1</sup>Imorphics Ltd, Manchester, UNITED KINGDOM, <sup>2</sup>Imaging Science and Biomedical Engineering, University of Manchester, Manchester, UNITED KINGDOM, <sup>3</sup>AstraZeneca, Macclesfield, UNITED KINGDOM

**Purpose:** MRI offers the opportunity to assess the integrity of articular cartilage directly. However, in order for this information to be of most value, it is important to understand the pattern of change as the disease progresses.

The objective is to determine (1) the change in cartilage thickness and (2) the distribution of any such change in a 12-month progression group of individuals with knee OA, comparing the pattern in men and women.

**Methods:** A convenience group of 50 individuals (29 male) was identified from the OAI progression group 0.B.1 and 1.B.1. The subjects chosen had K-L scores of 2 or 3; medial JSN greater than lateral JSN, evidence of medial osteophytes and knee alignment of  $\geq 1^\circ$  of varus mal-alignment measured using the anatomic axis. BMI and varus (average) were for females ( $32.7, -3.1^\circ$ ) and males ( $31.3, -3.9^\circ$ ).

Pairs of images were manually segmented using EndPoint software (Imorphics, Manchester, UK), by trained segmenters blinded as to time point, but not to subject. A dense set of anatomically corresponded points was automatically identified on the femur ( $n = 6000$ ) and tibia ( $n = 5000$ ) bone surface of each image, allowing mapping of cartilage change both within and across subjects. Average thickness (ThCtAB) of the cartilage for each major compartment of the femur and tibia was calculated and loss between the baseline and 12m follow-up assessed using paired t-tests with results expressed as a percentage of the baseline mean. At each point at which the thickness of cartilage was measured, the standardized response mean at each point across the population were calculated.

**Results:** The percentage change in average thickness for males and females by compartment, and by sex of subject is shown in Table1. Distribution of SRM values plotted on mean bone shapes for males and females is shown in Figure 1.

Table 1: % Change in average thickness by compartment, and by sex of subject

	ALL (n=50)			Females (n=21)			Males (n=29)		
	%	SRM	p	%	SRM	p	%	SRM	p
MF	-4.69	-0.723	0.00001	-4.38	-0.74	0.003	-4.89	-0.719	0.001
MT	-2.64	-0.279	0.05440	-2.42	-0.169	0.448	-2.78	-0.489	0.014
LF	0.64	0.145	0.31142	1.73	0.422	0.068	-0.05	-0.011	0.952
LT	-1.37	-0.354	0.01558	-0.93	-0.185	0.406	-1.63	-0.513	0.010