values of MT/cMF and of LT/cLF were computed and their corresponding changes with time. 6 of the 9 participants underwent radiography: 2 had KL grade 1, 3 KLG 2, and 1 KLG 3.
Results: In the femorotibial joint, the root mean square coefficient of variation (RMS CV%) for cartilage volume ranged from 1.1% (FLASH at LT) to 3.5% (DESS at MT). The average RMS CV% in all femorotibial plates was 1.8% for FLASH and 3.0% for the MPR. Changes in MT between BL and Y2 were -2.3% for FLASH, -2.3% for DESS, and -0.7% for MPR. Corresponding changes were -1.6%/-3.6%/+0.6% for cMF, -3.4%/-5.4%/-2.0% for LT, and +0.4/-0.1%/+1.0% for cLF (FLASH/DESS/MPR). The average volume loss in these 4 plates was -1.7% for FLASH, -2.9% for DESS, and -0.3% for the MPR. Cartilage volume change was -2.6% in P, -0.6% in pMF, and -4.0% in pLF (DESS). Only the combined change in MT/cMF with DESS at Y2 reached statistical significance (p = 0.046).
Conclusions: FLASH and DESS displayed adequate reproducibility in a paired analysis study design with blinding to time point of acquisition. Cartilage volume change seen over 2 years was relatively little in this small sample (n = 9) with mild to moderate OA. As a trend, 0.7mm DESS showed higher sensitivity than 1.5mm FLASH, and 1.5mm FLASH higher sensitivity than 1.5mm MPR DESS, but this needs to be confirmed in larger samples.
Acknowledgment: Partially funded by NIAMS (contracts N01-AR-2-2261, N01-AR-2-2262 and N01-AR-2-2258).

P105

ANGIOGENSIS MARKERS IN OSTEONECROSIS OF THE KNEE

Y. Yamaguchi, R. Takeuchi, T. Shirai, Y. Umemoto, K. Maeda, Y. Yamazaki, R. Ito, T. Saito
Yokohama City University, Yokohama, Japan

Purpose: Spontaneous osteonecrosis (ON) of the femoral condyle has been recognized since 1968, when it was first described by Ahlbäck et al. In its early stages, ON is primarily a disease of subchondral bone and the overlying articular cartilage remains intact. When its advanced stages, the knee joint was collapsed and sift the osteoarthritis. Among several proposed causes of the disease, vascular or traumatic factors have been the main candidates. Lotke et al emphasized microfractures within osteoporotic subchondral bone as a possible etiologic mechanism.
During bone regeneration, both sufficient blood supply by stimulation of angiogenesis and well-regulated remodeling of bone matrix are prerequisites for well-organized bone formation.
We hypothesize that angiogenesis is actively developed around the necrotic lesion of patients with ON. To prove the validity we investigated variety of anigiogenic marker in the joint fluid and synovial membrane and necrotic subchondral bone of ON and OA.
Methods: From February 2003 to November 2006, synovial fluid samples which were obtained from 13 knees of 13 patients (11 women and 2 men) with ON were enrolled in this study. And all of them had ON of the medial femoral condyle and had been underwent surgical treatment.
As a control, we studied 22 knees of 18 patients (13 women and 5 men) who had been diagnosed as having OA of the medial compartment and who underwent surgical treatment.
Patients with ON were matched with OA by age, gender, height, weight and body mass index. All patients received informed consent.
The levels of angiogenin, VEGF, IL-6 and MMP-3 were measured using the ELISA technique. We confirmed that the subchondral necrotic lesion were exposed in confirmed in operation, and compared with the results of joint fluid analysis.
Synovial membrane and subchondral bone which including necrotic lesion were obtained from patient with ON at the time of operation with informed consent. VEGF and angiogenin expression in these tissue was investigated with immunohisutchemistry. Mann-Whitney U tests were done to determine if differences of each angiogenesis markers were significant between ON and OA and between exposed subchondral necrotic lesion or not. The correlation between the angiogenin and VEGF were analyzed statistically according to a simple regression correlation. A p value less than 0.05 was regarded as statistically significant.
Results: The mean $\pm$ SD levels of MMP-3 were 1397.2$\pm$513.9 ng/ml in ON and 1140.5$\pm$434.0 ng/ml in OA. The mean $\pm$ SD levels of IL-6 were 2105.7$\pm$1071.8 pg/ml in ON and 1959.1$\pm$1112.4 pg/ml in OA. The mean $\pm$ SD levels of VEGF were 957.7$\pm$692.8 pg/ml in ON and 1955.8$\pm$1256.8 pg/ml in OA. The mean $\pm$ SD levels of angiogenin were 121072$\pm$35053.3 pg/ml in ON and 100387$\pm$25934.1 pg/ml in OA. Angiogenin levels in ON were significantly higher than in OA ($p>0.030$), and VEGF levels in OA were significantly higher than in ON ($P>0.015$). Angiogenin levels correlated with VEGF levels both in ON (r=0.588) and OA (r=0.610). In ON, the mean$\pm$ SD levels of angiogenin were 84861$\pm$12855 pg/ml in the group in which subchondral lesion was not exposure and 131935 $\pm$ 32146 pg/ml in the group in which was exposure. Angiogenin levels of the exposure group were significantly higher than that of the non-exposure group.
In histchemical studies, angiogenin (green) and VEGF (co-expressing cells were detected in synovial membrane and subchondral bone. In subchondral bone, angiogenin and VEGF co expressing cells was detected deep layer of the necrotic lesion.
Conclusions: The results of the present study suggest that the angiogenesis via with angiogenin is more active in patient with ON than that with OA. And there is possibility that in the knee of patient with ON, angiogenesis via with angiogenin occur around the necrotic lesion to repair this.

P106

BIOMARKERS DEMONSTRATE DEGRADATION AND INFLAMMATION AS CHARACTERISTICS OF IDIOPATHIC OSTEOARTHRITIS (OA)

R.W. Moskowitz[1], M.M. Hooper[1], D.Y. Rowland[1], P. Garnero[2], T. Saxne[3], D. Heinegard[3], J.B. Renner[4], U. Atif[5], M. Wallette[1], M. Hays[1], M.B. Sawicki[1], N.G. Singer[1]
[1]Case Western Reserve University, Beachwood, OH, [2]Inserm Research Unit 664, Lyon, France, [3]Lund University, Lund, Sweden, [4]Duke University, Durham, NC, [5]GlaxoSmithKline, Research Triangle Park, NC

Purpose: Validated biomarkers would be of value in defining OA disease severity, progression, and therapeutic response. Although identification of a single marker to assess OA natural history and severity would be ideal, a panel of biomarkers defining matrix synthesis/degradation, and inflammation may be required. Factors impacting biomarker correlations include not only stage of structural damage but also disease duration. Eleven biomarkers targeted to different responses associated with matrix synthesis and degradation, and joint inflammation were evaluated in a patient cohort from a study of Genetics of Generalized Osteoarthritis (GOGO).
Methods: Biomarker correlations were computed from data of 98 subjects, mean age 65 yrs (range 59-71), median duration 14 yrs, in all of whom x-rays of knees, and hips were available. Kellgren-Lawrence (K-L) grade (0-IV) and Joint Space Narrowing (JSN) (0-3), osteophyte severity (0-3), and sclerosis (0,1) were determined by an experienced musculoskeletal radiologist. Using standardized MRI-derived joint cartilage volumes, Total Quantitative Osteoarthritis Load (TQOL) scores were computed related to knee and hip OA. Biomarkers included serum Bone Sialoprotein

P106 – Table 1. Pearson correlation coefficients

	CTX-1I (N=55)	NTX-I (N=60)	HA (N=93)	COMP (N=91)	Epitope 846 (N=89)	CII Propeptide (N=93)
TQOL variable						
K-L 0-IV	0.298*	0.265*	0.302**	0.226*	-0.072	0.066
JSN 0-3	0.229	0.229	0.430***	0.297**	-0.131	0.032
Osteophyte 0-3	0.327*	0.243	0.277**	0.246*	0.002	0.069
Sclerosis 0-1	0.274*	-0.019	0.226*	0.195	-0.083	-0.034

*$p < 0.05$ (2-tailed test). **$p < 0.01$ level (2-tailed test). *$p < 0.001$ level (2-tailed test).

(BSP), Cartilage Oligomeric Matrix Protein (COMP), Bone Alkaline Phosphatase, Epitope 846, Hyaluronan, C-Reactive Protein (CRP), PIIANP, CII Propeptide, PINP, and urinary CTX-II and NTX-I. Bivariate Pearson correlation coefficients were calculated for each biomarker with each OA score.

Results: Significant correlations were observed with CTX-II, NTX-I, HA, and COMP, markers of collagen degradation, inflammation, and matrix turnover (Table 1). Correlations with the remainder of the biomarkers were not significant. TQOL severity averaged 35 (SD 19) for K-L grade and 7 (SD 7) for JSN. Findings contrasted with the positive correlation of biomarkers of synthetic activity observed in our prior report where individuals with hereditary OA, mean age 34 yrs, had K-L and JSN severity averaging 41 (SD 34) and 14 (SD 19) respectively.

Conclusions: The presence of OA in an older cohort demonstrated an increase in degradative/inflammatory markers, contrasting with increased PG and collagen synthesis in a younger hereditary OA population with greater disease severity. Although differences in pathophysiologic mechanisms between the groups cannot be excluded, findings suggest that biomarkers reflect disease duration as well as severity, and that biomarker responses precede changes in overt structural damage; snap-shot biomarker levels may only partially reflect disease evolution.

P107

INCREASED EXPRESSION OF CELL DEATH-ASSOCIATED C-JUN KINASE IN OSTEOARTHRITIC CARTILAGE

H. Hulejová[1], V. Barešová[2], M. Polanská[1], Z. Klézl[3], M. Adam[1], L. Šenolt[1]

[1]Institute of Rheumatology, Prague 2, Czech Republic, [2]Institute of Inherited Metabolic Disorders, Prague 2, Czech Republic, [3]Orthopaedic Clinic of the Central Military Hospital, Prague 6, Czech Republic

Purpose: The aim of this study was to compare the expression of active cell-death associated c-jun protein and major pro-inflammatory cytokines IL-1 and TNF-α in synovial membrane and cartilage explants with that in control tissues.

Methods: Synovial membrane and cartilage explants from patients with OA and healthy controls were used for this experiment. Levels of cytokines IL-1α and TNFα in tissue extracts were measured by Immulite system and ELISA, respectively. Markers of apoptosis active caspase-3 and c-jun kinase were analyzed in paraffin embedded cartilage and synovial membrane samples by immunohistochemistry.

Results: The expression of phospho-c-jun was observed only in OA cartilage, but not in other examined tissues. Caspase-3 activity was higher in OA than in control cartilage (10% vs. $<$5% of positive cells), although there was no difference between OA and healthy synovial membranes. Furthermore, significantly higher expression of TNF-α was demonstrated in both OA synovial membrane and cartilage compared with counterpart control tissues. On the other side, IL-1α expression was significantly higher only in OA cartilage.

Conclusions: These data stress the role of pro-inflammatory cytokines and apoptosis of chondrocytes in the pathogenesis of osteoarthritis.

Acknowledgments: This work was supported by MH, CZ, grant No. NR/7907-3

P108

TQOL-LITE: A SIMPLIFIED ASSESSMENT TOOL FOR TOTAL QUANTITATIVE OSTEOARTHRITIS (OA) LOAD

R.W. Moskowitz[1], M.M. Hooper[1], D.Y. Rowland[1], P. Garnero[2], T. Saxne[3], D. Heinegard[3], J.B. Renner[4], U. Atif[5], M. Wallette[1], M. Hays[1], M.B. Sawicki[1], N.G. Singer[1]

[1]Case Western Reserve University, Beachwood, OH, [2]Inserm Research Unit 664, Lyon, France, [3]Lund University, Lund, Sweden, [4]Duke University, Durham, NC, [5]GlaxoSmithKline, Research Triangle Park, NC

Purpose: Current consensus suggests that biomarker correlations be based on total body burden of OA. In prior studies, we demonstrated positive correlations with proteoglycan and collagen synthetic activity in subjects with familial precocious hereditary OA utilizing a new assessment tool, Total Quantitative Osteoarthritis Load (TQOL). TQOL methodology defined OA cartilage involvement computed by joint disease severity multiplied by standardized MRI-derived joint cartilage volume at risk. Subsequent studies in a population of older subjects with idiopathic OA revealed significant correlations between TQOL scores and biomarkers CTX-II, NTX-I, HA, and COMP, markers of collagen degradation/inflammation and matrix turnover. To further validate a simplified TQOL instrument (TQOL-LITE), scores were calculated for this new instrument based on similar cartilage volumes for knee weight-bearing area (7 ml) and hip (9 ml), and compared to the previously obtained correlations utilizing the comprehensive classic TQOL measure.

Methods: Biomarker correlations were computed from data of 98 subjects, mean age 65 yrs (range 59-71), median duration 14 yrs, in all of whom x-rays of knees and hips were available. Kellgren-Lawrence (K-L) grade (0-IV) and Joint Space Narrowing (JSN) (0-3), were determined by an experienced musculoskeletal radiologist. Using standardized MRI-derived joint cartilage volumes, Total Quantitative Osteoarthritis Load (TQOL) scores were computed related to knee and hip OA. Biomarkers included serum Bone Sialoprotein (BSP), Cartilage Oligomeric Matrix Protein (COMP), Bone Alkaline Phosphatase, Epitope 846, Hyaluronan, C-Reactive Protein (CRP), PIIANP, CII Propeptide, PINP, and urinary CTX-II and NTX-I. Bivariate Pearson correlation coefficients were calculated for each biomarker with each classic TQOL OA score. Similar correlation coefficients were derived for TQOL-Lite using the Sum of Severity K-L scores and the Sum of Severity JSN scores.

Results: Significant correlations were observed for NTX-I, CTX-II, HA, and COMP, when using the Sum Severity scores (Table 1); correlations were most consistent with KL grade. No consistent significant correlations were seen with other biomarkers. Correlations were similar to results utilizing the classic TQOL assessment tool.

Conclusions: A simplified TQOL assessment tool based on