from 164 patients (66%, mean age [SD]: 60 [7] years, 81% female, mean BMI [SD]: 27 [5] kg/m^2). Fifety-five patients showed hand OA progression. BMI was positively correlated with leptin (Pearson's correlation coefficient, r=0.3) and resistin (r=0.2) and negatively correlated with adiponectin (r=-0.2). Leptin, adiponectin and resistin did not significantly correlate to each other. BMI was not associated with radiographic hand OA progression (β-regression coefficient -0.04 (95% confidence interval -0.08 to 0.05). The association between adipokines and progression of osteoarthritis is shown in Table 1.

Table 1. Association between adipokines and progression of hand osteoarthritis

Adiponectin	Risk Ratio (95% CI)	Risk Ratio (95% CI) after adjustment for age, sex, BMI and family effect
Leptin (ng/mL)		
<4.4	1 (reference)	1 (reference)
4.41 to 8.2	0.7 (0.3 to 1.6)	0.7 (0.3 to 1.5)
>8.2	1.1 (0.5 to 2.3)	1.2 (0.4 to 2.5)
Adiponectin (μg/mL)		
<16.6	1 (reference)	1 (reference)
16.6 to 28.4	0.3 (0.1 to 0.7)‡	0.2 (0.1 to 0.5)‡
>28.4	0.3 (0.1 to 0.6)‡	0.2 (0.1 to 0.5)‡
Resistin (ng/mL)		
<0.8	1 (reference)	1 (reference)
0.8 to 1.4	1.0 (o.4 to 2.1)	0.9 (0.4 to 1.8)
>1.4	0.8 (0.4 to 1.7)	0.7 (0.3 to 1.5)

CI: Confidence Interval.

Conclusions: We show for the first time a substantial inverse association between serum adiponectin levels and radiographic worsening of hand osteoarthritis. Further studies on the use of adiponectin as biological markers for osteoarthritis progression and studies on the biological role of adiponectin in osteoarthritis are needed.

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SERUM BIOMARKER STUDIES OF SYMPTOMATIC SUBJECTS WITH PERSISTENT KNEE PAIN, WITH AND WITHOUT OA, REVEAL SIGNIFICANT DIFFERENCES FROM ASYMPTOMATIC SUBJECTS IN SYSTEMIC MARKERS OF INFLAMMATION SUGGESTING DIFFERENCES IN INNATE IMMUNITY

J. Cibere[1], F. Baribaud[2], K. Ma[2], E.C. Sayre[1], N. Prestley[3], H. Wong[1], A. Thorne[1], J. Singer[1], A.R. Poole[4], J.A. Kopec[1], A. Guermazi[5], S. Nicolaou[1], J.M. Esdaile[1]
[1]Univ. of British Columbia, Vancouver, BC, Canada; [2]Centocor Res. and Dev. Inc, Radnor, PA; [3]Arthritis Res. Ctr. of Canada, Vancouver, BC, Canada; [4]McGill Univ., Montreal, QC, Canada; [5]Boston Univ. Med. Ctr., Boston, MA

Purpose: To contrast serum biomarker levels in population-based cohorts asymptomatic for knee pain and symptomatic for knee pain.
Methods: Subjects, 40-79 years, with knee pain (n=255) were recruited as a random population sample in a study to evaluate early knee osteoarthritis (OA) (MoDEKO study). Subjects, 40-79 years, without knee pain (n=80) were recruited as a random sample of the same population. For the symptomatic cohort, subjects were included if, in at least one knee, they had 1) pain in or around the knee on most days of the month at any time in the past; and, 2) any pain in or around the knee during the past year. In the asymptomatic cohort, subjects were included if they responded 'no' to both pain questions for both knees. OA status was assessed on magnetic resonance imaging (MRI) (1.5T) with cartilage graded from 0-4 (0=normal, 1=hyperintense signal, 2=less than 50% defect, 3=50-100% defect, 4=100% defect). Twenty-three serum biomarkers were measured in both cohorts, including matrix metalloproteinases (MMPs) 1, 3 and 9, tissue inhibitor of MMP (TIMP-1), interleukins (IL) 1a, 1b, 4, 6, 7, 8, 10, 17A, tumor necrosis factor alpha, c-telopeptide of type I collagen (CTX-I), adiponectin, resistin, eotaxin, C-reactive protein (CRP), hyaluronic acid (HA), cartilage oligomeric matrix protein (COMP) and chemokines. Means of log transformed biomarkers were compared in symptomatic vs asymptomatic cohorts using 2-sample t-tests. Analyses were adjusted for stratum sampling weights.
Results: In the symptomatic and asymptomatic cohorts, 56.3% and 56.5% were female, mean age was 56.7 and 54.6 years, mean BMI was 26.5 and 25.4, respectively. MRI abnormalities ≥ grade 1 were seen in 91% of symptomatic and 67.5% of asymptomatic subjects. No significant differences in biomarker levels in asymptomatic vs symptomatic cohorts were seen for adiponectin, CTX-I, MMP-1, MMP-3, COMP and HA (Table 1). Statistically significant differences were seen for all other biomarkers, including CRP, eotaxin, interleukins, MMP-9, TIMP-1, TNF alpha, resistin and chemokines.
Conclusions: Serum biomarkers for inflammation, especially involving pro-inflammatory and regulatory cytokines, are the key distinguishing feature between those with symptomatic knee pain and those without. This suggests that alterations in innate immunity are associated with persistent knee pain, in view of the absence of convincing evidence in the literature for adaptive immunity in OA.

Table 1. Mean (SD) of select log-transformed serum biomarkers in symptomatic and asymptomatic cohorts

Biomarker	Symptomatic cohort (n=255)	Asymptomatic cohort (n=80)	p-value
Adiponectin	3.08 (0.36)	3.01 (1.30)	0.47
CRP	1.76 (0.79)	1.31 (2.30)	0.009
CTX-I	-1.41 (0.36)	-1.23 (1.35)	0.05
IL-4	2.65 (1.58)	-3.54 (2.89)	<0.001
IL-10	1.25 (1.25)	-2.45 (2.71)	<0.001
IL-1b	0.20 (0.84)	-2.62 (1.75)	<0.001
MMP-1	2.85 (0.39)	2.72 (1.18)	0.15
MMP-3	2.59 (0.27)	2.68 (1.08)	0.21
MMP-9	5.67 (0.28)	6.00 (0.82)	<0.001
Resistin	2.23 (0.26)	3.10 (0.73)	<0.001
TIMP-1	5.13 (0.13)	5.01 (0.32)	<0.001
TNF alpha	2.54 (0.66)	-2.59 (0.69)	<0.001
COMP	7.39 (0.11)	7.36 (0.51)	0.36
HA	3.61 (0.41)	3.63 (1.27)	0.83

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THE ASSOCIATION BETWEEN SYNOVIAL FLUID LEVELS OF AGGRECAN ARGS FRAGMENTS AND RADIOGRAPHIC PROGRESSION OF KNEE OSTEOARTHRITIS

S. Larsson[1], M. Englund[1,2], A. Struglics[1], S. Lohmander[1]
[1]Lund Univ., Dept. of Orthopaedics, Clinical Sci. Lund, Lund, Sweden; [2]Boston Univ. Sch. of Med., Clinical Epidemiology Res. & Training Unit, Boston, MA

Purpose: Aggrecanase cleavage at the Glu-Ala bond in the interglobular domain of aggrecan, releasing N-terminal ARGS fragments, is an early key event in arthritis and joint injuries. We have previously shown that synovial fluid levels of ARGS (SF ARGS) are elevated early after knee injury and in arthritis. Here we investigate whether SF ARGS levels distinguish subjects with progressive radiographic knee osteoarthritis (ROA) from those with stable or no ROA.
Methods: We studied 141 subjects whom at examination A had undergone meniscectomy some 18 years earlier. Seventeen un-operated individuals without injury to the meniscus or ligaments were used as references. At examinations A and B, with a mean follow up time of 7.5 years, we obtained SF and standing tibiofemoral and skyline patellofemoral radiographs. SF ARGS was measured by a sandwich immunosorbent electrochemiluminescence assay using an anti-aggrecan antibody (AHP0022; Invitrogen) for capture, and a monoclonal anti-ARGS (OA-1) for detection. Radiographs were graded according to the OARSI atlas. The association between levels of SF ARGS at examination A and progression of radiographic features of knee OA between examinations A and B were assessed using logistic regression with or without adjustments for age, gender, BMI, and time between examinations A and B.
Results: The levels of SF ARGS 18 years after meniscectomy ranged from 0.15 to 15.07 pmol/ml (mean 6.95 pmol/ml), were no different from levels in un-operated individuals, and were unrelated to radiographic status at examination A. A weak negative association was found between levels of SF ARGS and loss of joint space: The likelihood of progression of radiographic

Table 1. Association of SF ARGS at examination A and progression of radiographic features of OA from examination A to examination B 7.5 years later. Odds ratios (95% CI) adjusted for age, gender, BMI and time between examinations A and B

Radiographic feature	Total sample, n=141	Stratified for absence or presence of ROA at examination A	
		No ROA, n=63	ROA, n=78
JSN	0.89 (0.79-0.996)*	0.77 (0.62-0.95)*	0.96 (0.81-1.13)
Osteophyte	0.97 (0.87-1.09)	0.92 (0.76-1.11)	0.99 (0.86-1.15)
ROA (JSN and/or Osteophyte)	0.89 (0.78-1.02)	0.87 (0.72-1.04)	0.91 (0.73-1.13)

*P<0.05.

joint space narrowing (JSN) decreased 0.89 times per pmol/ml increase in SF ARGS; without ROA at examination A the decrease in risk was 0.77, and with ROA at examination A the association was not significant (Table 1). No association was found between SF ARGS and progression of osteophytes or progression of ROA defined as progression in either or both JSN and osteophytes. Analysis without adjustments by univariate logistic regression did not change these results.
Conclusions: In this longitudinal study of a cohort with previous knee meniscectomy, higher SF ARGS levels were weakly associated with less progression of radiographic knee OA.

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SYSTEMIC INFLAMMATION AND ANTIBODIES TO CITRULLINATED PEPTIDES IN HAND OSTEOARTHRITIS

E. Assirelli[1], P. Dolzani[1], L. Pulsatelli[1], O. Addimanda[1], L. Mancarella[1], G. Peri[2], A. Mantovani[2,3], A. Facchini[1,4], **R. Meliconi**[1,4]
[1]Istituto Ortopedico Rizzoli, Bologna, Italy; [2]Istituto Clinico Humanitas, Rozzano (MI), Italy; [3]Università di Milano, Milano, Italy; [4]Università di Bologna, Bologna, Italy

Purpose: To investigate systemic inflammation and autoimmune response to citrullinated peptides in patients with erosive and non erosive "lone" hand osteoarthritis (HOA) with no hip/knee involvement and their relationship with radiographic structural damage.
Methods: Sera were obtained from a total of 99 patients (3 males and 96 females, age range 50-88 years, mean 65 years) with HOA (52 patients with erosive HOA and 47 patients with non erosive HOA) and from 50 controls subjects (NC) (2 males, 48 females, age range 51-86 years, mean 65 years). Hand OA diagnosis was made according to the American College of Rheumatology Clinical Criteria for Hand OA. Plain hand radiographs were obtained from all patients. All radiographs were scored for joint damage following the Kellgren-Lawrence and the Kallman scores. Patients were included in erosive HOA subsets according to the presence of well defined typical erosive changes (gull-wing and saw-tooth appearance) in two or more digits. Serum levels of high sensitive CRP (hsCRP), IL-6, anti-CCP and anti-Modified Citrullinated Vimentin (MCV) antibodies were evaluated by commercial sandwich enzyme immunoassay (ELISA) kits. PTX3 was detected by a sandwich ELISA based on a monoclonal antibody (mAb) MNB4 (ascites diluted 1:5000 in coating buffer) and rabbit antiserum as previously described. Non-parametric data analysis was performed by Kruskal-Wallis test with Dunn's multiple comparison post-hoc test. Spearman's correlation analysis was used to assess relationships between variables. Statistical Analysis was carried out using the GraphPad Prism for Windows (CA, USA).
Results: Circulating levels of inflammatory biomarkers hsPCR, IL-6 and PTX3 were not significantly different in two groups of patients with erosive and non erosive HOA compared to NC and no significant difference was seen between non erosive and erosive HOA. Anti-CCP positivity were detected respectively in 1/47 (2.1%) patient with non erosive HOA and in 1/52 (1.9%) erosive HOA patient. Anti-MCV antibodies were present in 4/47 (8.5%) patients with non erosive HOA, and 4/52 (7.7%) erosive HOA patients. In the control group, one subject (2%) was positive for anti-CCP and 2 subjects (4%) had anti MCV antibodies. Significant correlation was obtained only between body mass index and hsCRP concentration (r = 0.2569; p = 0.0115) No correlation between inflammation markers/autoantibodies and disease duration and radiological scores was found.
Conclusions: These results confirm the association between BMI and CRP and underline the lack of systemic inflammation in "lone" HOA. A small minority of HOA patients circulate anti MCV antibodies.

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AUTOMATED MRI ATLAS-BASED STANDARDIZED QUANTIFICATION OF SUBCHONDRAL BONE PLATE CURVATURE: DATA FROM THE OSTEOARTHRITIS INITIATIVE

J.G. Tamez-Peña[1,2], P.C. González[2,3], E.H. Schreyer[3], J.M. Farber[3], S.M. Totterman[3]
[1]Escuela de Med., ITESM, Monterrey, Mexico; [2]IMITEK S.C., Monterrey, Mexico; [3]Qmetrics, Rochester, NY

Introduction: Bone remodeling in osteoarthritis (OA) changes the shape of articulating bone surfaces. This phenomenon has been demonstrated in plain films and more recently in MRI studies, where novel measurements such as subchondral bone plate curvature have been introduced. There are, however, very few attempts to establish their association to traditional plain radiographic measurements.
Objective: To assess the association of an automated MRI-Atlas-based standardized quantification of bone curvature to traditional X-Ray based measurements.
Methods: The baseline, 12 month and 24 month DESS sagittal MRI knee images of 133 subjects from the OAI progression cohort releases: 0.C.2, 1.C2, 3.C.1 were automatically segmented to extract the cartilage plates and bones using an automated atlas segmentation algorithm. Once segmented, all the segmentations were evaluated for quality; 4 subjects had to be removed due to large segmentations errors. Using the atlas deformations 3D map, the subchondral bone curvatures were mapped back to the anatomic atlas space and were compared point by point to the atlas subchondral bone curvatures. Differences in the atlas and the subject curvatures' values were statistically described by mean, variance and percentiles of curvature values for cMF, cLF, MT, LT, F, T, medial WB, lateral WB, and the entire tibia femoral joint (TF). A linear regression model adjusted for subject height was used to compare the paired KL scores, the JSN OARSI scores, and the average joint space width to the curvature measurements of the 133 subjects. The radiological data was provided by the OAI site (http://www.oai.ucsf.edu).
Results: Table 1 shows the results of the quantitative analysis.

Table 1. The average value, the standard deviation and the average curvature of the values higher than the 95% percentile were compared to the paired KL scores, the medal JSN OARSI score and the average medial joint space width (JSW)

Measurement		Population Stats	cMF	cLF	MT	LT	F	T	MWB	LWB	TF
Plate Curvature Average	Descriptive statistics	Average (mm)	0.02	0.01	0.04	0.05	0.02	0.04	0.03	0.03	0.06
		STD (mm)	0.01	0.01	0.02	0.02	0.00	0.02	0.02	0.01	0.02
	Model Correlation	KL	0.49*	0.15	0.22*	0.05	0.40*	0.22*	0.39*	0.04	0.29*
		Medial JSN Score	0.25*	0.15	0.14	0.08	0.15	0.10	0.07	0.08	0.09
		Average JSW	0.26*	0.08	0.21*	0.05	0.11	0.13	0.30*	0.07	0.15
Plate Curvature Standard Deviation	Descriptive statistics	Average (mm)	0.08	0.08	0.09	0.09	0.12	0.06	0.09	0.09	0.18
		STD (mm)	0.02	0.01	0.02	0.02	0.02	0.03	0.02	0.01	0.03
	Model Correlation	KL	0.48*	0.08	0.37*	0.07	0.12	0.06	0.44*	0.11	0.10
		Medial JSN Score	0.20*	0.07	0.13	0.12	0.11	0.11	0.18	0.10	0.13
		Average JSW	0.35*	0.10	0.27*	0.08	0.12	0.10	0.34*	0.09	0.12
Average of top 95% Percentile of the plate curvature values	Descriptive statistics	Average (mm)	0.13	0.12	0.23	0.26	0.13	0.26	-0.07	-0.07	-0.15
		STD (mm)	0.06	0.02	0.07	0.08	0.03	0.06	0.01	0.01	0.02
	Model Correlation	KL	0.48*	0.13	0.24*	0.07	0.36*	0.22*	0.40*	0.05	0.28*
		Medial JSN Score	0.29*	0.18	0.10	0.08	0.15	0.11	0.15	0.02	0.08
		Average JSW	0.30*	0.10	0.20*	0.05	0.23*	0.06	0.34*	0.04	0.16

*Indicates adjusted correlations coeffcients statistically different from zero ($p<0.05$).

Conclusions: The Atlas-based curvature measurements generated at least 6 MRI-Atlas-based metrics that associate moderately to the radiological severity of OA ($0.49 \geq r > 0.40$) as measured by KL scores and correlate weakly to the medial JSN OARSI scores and to the JSW ($r<0.34$). This result provides supporting evidence that subchondral bone curvature is a potential marker to stage the severity of OA.

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DETECTION OF EARLY CHANGES IN SUBCHONDRAL BONE PLATE CURVATURE IN OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE

J.G. Tamez-Peña[1,2], P.C. González[2,3], E.H. Schreyer[3], J.M. Farber[3], S.M. Totterman[3]
[1]Escuela de Med., ITESM, Monterrey, Mexico; [2]IMITEK S.C., Monterrey, Mexico; [3]Qmetrics, Rochester, NY

Introduction: Osteoarthritis (OA) is characterized by changes in all structures in an involved joint, including articular cartilage, menisci, subchondral bone, and subchondral bone plate, (SCBP). Understanding the evolution and interplay of these changes would provide an understanding of the pathophysiology of OA and help establish the efficacy of therapies aimed at preventing, halting or reversing structural damage. Although most research into OA has focused on the articular cartilage, there is increasing evidence of the significant role of SCBP changes in the disease progression.
Objective: To evaluate the rate of change and the sensitivity of atlas-based standardized measures of SCBP's curvature in subjects with OA symptoms but no plain radiographic evidence of OA.
Methods: The baseline, 12 month and 24 month sagittal 3D DESS WE MRI knee images of 133 subjects from the OAI progression cohort releases: 0.C.2, 1.C2, 3.C.1 were segmented into bone and cartilage using a fully automated atlas-based segmentation algorithm. Once segmented, all the segmentations were evaluated for quality and four subjects were removed due to large segmentations errors. Using the atlas deformations 3D map,