The current study aimed to investigate whether hyperactivation of the RAS influences OA using forced-running mice models.

**Methods:** C57/BL6 mice and Tsukuba hypertensive mice (THM) were forced to run (25m/min, 30 min/day, 5 days/week) (n=10). OA histopathology was analyzed using the OARSI score at 0, 2, 4, 6, and 8 weeks. Expression of type II collagen, type X collagen, MMP-13, ADAM-T5S and some RAS components were also analyzed.

**Results:** The OARSI scores of the lateral femoral condyles were significantly higher in the THM than in the C57/BL6 mice at 4, 6 and 8 weeks. However, in medial femoral condyles, there were not significant differences between C57/BL6 mice and THM. At 8 weeks, type II collagen was stained in a lower number of chondrocytes in the THM than C57/BL6 mice. The expression of type X collagen, MMP-13 and ADAM-T5S was confirmed in the THM, but not in the C57/BL6 mice. In the THM, we compared the expression of angiostatin II type 1 receptor (AT1R) and AT2R at each week. At 0 weeks, we could not confirm the expression of AT1R and AT2R. However, we confirmed the expression of AT1R and AT2R at 2, 4, 6, 8 weeks.

**Conclusions:** We confirmed that the hyper activation of RAS induces OA changes in the lateral knee components of the mice under the load of forced running.

**OA: Clinical Aspects**

### 510 PRESENCE OF INTERLEUKIN-17 IN OSTEOARTHRITIS: DOES IT INDICATE A DIFFERENT OSTEOARTHRITIS PHENOTYPE


**Purpose:** Interleukin-17 (IL-17) is an important factor in the pathogenesis of autoimmune diseases and allergy, and IL-17 antagonists are currently evaluated in randomized trials with encouraging results. In OA IL-17 contributes to cartilage breakdown and synovial infiltration by inducing the release of chemokines by chondrocytes and synovial fibroblasts independent of the IL-1 and TNF-α pathway. It also affects cartilage matrix turnover, induces angiogenesis in articular tissue, and amplifies joint inflammation. However, IL-17 is only infrequently detected in OA and clinical studies are sparse.

We aimed at evaluating the relation between absence or presence of IL-17 in synovial fluid (SF) of patients with end stage OA and OA clinical aspects.

**Methods:** Cross-sectional study including patients prior to total hip (THA) and knee arthroplasty (TKA) operated upon for primary OA at a large tertiary hospital between January and December 2010. The morning of surgery concentrations of IL-17, IL-6, leptin, visfatin, adiponectin, resistin, MCP-1, MCP-3 and NGF were sampled from synovial fluid and assessed using ELISA kits. Baseline characteristics recorded preoperatively included age, sex, BMI, co-morbidities, pain and function (WOMAC), and radiographic analyses (OA features, K&L grade, minimal JSW).

**Results:** 152 patients were included, 68 prior to THA and 84 to TKA. Mean age was 73 (±9) years, 64% were women. In 14 patients (9.2%) IL-17 was present in the SF (median concentration 7.9 pg/mL, IQR 1.6; 20.6). These patients had significantly higher median SF concentrations of IL-6, leptin, resistin, MCP-3 and β-NGF, and a tendency to be female, younger, and obese class II, as compared to those without IL-17. Radiographic analyses revealed a significantly reduced minJSW together with a lower proportion of sclerosis and osteophytes in the presence of IL-17 in SF. No differences were found with respect to pain, function, and comorbidities. There was a moderate correlation between IL-17 concentrations in SF and serum (r=0.482).

**Conclusions:** The presence of IL-17 in SF of patients with primary end stage OA was associated with high levels of several other proinflammatory adipokines, cytokines and chemokines, and with a different radiographic OA feature pattern. Moreover, patients tended to be younger, more often women and obese class II. Our results may indicate a different OA phenotype with a potential for a new treatment option.

### 511 ASSOCIATIONS BETWEEN KNEE PAIN SEVERITY AND PROGRESSION VERSUS MRI FEATURES: THE VANCOUVER LONGITUDINAL STUDY OF EARLY KNEE OA


**Purpose:** To determine the associations between knee pain severity and progression versus MRI features, including cartilage, osteophytes, bone marrow lesions (BML), subchondral cysts, subchondral cysts and effusion, in a population-based cohort with knee pain.

**Methods:** Baseline, mean 3.3- and mean 7.5-year follow-up MRI assessments of the study (painful) knee were performed for 122 subjects with baseline knee pain, age 40-79 at baseline, sample-weighted for population (with knee pain) representativeness in Vancouver, BC (the Vancouver Longitudinal Study of Early Knee OA). MRIs were acquired on a 1.5T magnet at a single centre using a transmitter-receiver extremity knee coil, and 3 planes double-echo weighted sequences with and without fat suppression were obtained. MRIs were scored by a single experienced reader for cartilage (0-normal to 4-full thickness defect: 0/1 collapsed to 1-only signal change), BML (0-absent to 3-severe), subchondral sclerosis (0-absent to 3-severe) and subchondral cyst (0-absent to 3-severe) in 6 regions: lateral and medial femur, lateral and medial tibia, patella and trochlear groove. Meniscus (0-normal to 3-maceration/resection) was also scored in 6 regions: lateral anterior, lateral body, lateral posterior, medial anterior, medial body and posterior. Osteophytes (0-absent to 3-large) were scored in 8 regions: lateral and medial femur, lateral and medial tibia, and lateral, medial, superior and inferior patella. For each feature, region scores were added up and the sum divided by the number of regions. Effusion (0-absent to 3-severe) was scored for the overall knee and included as an indicator for >2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) knee pain scale (normalized 0-100; higher numbers worse) was administered at each time point.

Cross-sectional models of pain were fit on 3 time points simultaneously (N=366), using generalized estimating equations (GEE) to account for correlated data. Longitudinal (change) models of delta pain, and indicators for 10+ points increase in pain, and 20+ points increase in pain were fit on both 2-cycle changes simultaneously (cycles 1-2 and 2-3; N=244), using GEE for binary or linear regression. Models for each feature were adjusted for age, sex and BMI (and follow-up time for longitudinal models).

**Results:** 55.7% of the weighted sample was female. At baseline, mean BMI was 26.1 and mean age was 55.5. Mean divided score sums at baseline were 1.74 for cartilage, 0.93 for osteophytes, 0.27 for BML, 0.08 for subchondral sclerosis, 0.48 for meniscus and 0.06 for subchondral cysts. Average normalized WOMAC pain at baseline was 19.1. 29.6% had baseline effusion >=2. Spearman rank correlations among the seven MRI features were all significantly >0, ranging from 0.21 (meniscus vs. subchondral cyst) to 0.68 (osteoophyte vs. cartilage).

In cross-sectional regression models, osteophytes were significantly associated with pain (coefficient=7.17; 95% CI=3.19, 11.15), as was subchondral sclerosis (11.03; 0.68, 21.39). In longitudinal linear models of delta pain score, cartilage and osteophytes were significantly associated with pain change, respectively 4.51 (0.67, 7.95) and 4.51 (0.53, 8.49). In longitudinal binary models of delta pain score >=10, osteophytes (OR=3.20; 1.36, 7.55), subchondral sclerosis (OR=5.69; 1.06, 24.89), and subchondral cysts (OR=3.19; 0.68, 16.51) were significantly associated with pain increase. Finally, in binary models of delta pain score >=20, cartilage and osteophytes were significantly associated with pain increase, respectively OR=2.42 (1.24, 4.74) and 3.79 (1.41, 10.20). No associations were observed between pain severity or pain progression and BML or subchondral cysts, after adjusting for age, sex and BMI.

**Conclusions:** In this population-based cohort with 7-year follow-up we found a positive association between knee pain severity and both...