observed secondary to traumatic induction of OA by anterior cruciate ligament transection (ACLT).
Methods: Four groups of 10 female rats were subjected to either sham or ACLT surgery in both knee joints and administered twice a day for 28 days with an oral dose of salmon calcitonin (150mg/kg 5-CNAC + 2mg/kg calcitonin) or vehicle control (150mg/kg 5-CNAC). Serum samples were collected at baseline and 7, 14, 21 and 28 days and weights were recorded at regular intervals. Cartilage degradation was evaluated in serum by C-terminal telopeptide of type II collagen (CTX-II ELISA). Knee joints were collected at euthanasia and one was processed for histology and immunohistochemistry (IHC). Sections were scored on a modified Mankin score for proteoglycan content, chondrocytes cloning and cartilage erosion on a scale from 0-4, where the score 4 was most severe damage. Immunolocalization of antibodies towards CTX-II fragments, MMP-13 expression and proliferation (Ki67) was visualized by IHC.
Results: Treatment with salmon calcitonin significantly reduced serum CTX-II levels in sham+calcitonin animals on day 14 (52%, $P<0.05$) and day 28 (49%, $P<0.001$), compared to the control group. Treatment with calcitonin also reduced CTX-II levels in the ACLT+calcitonin groups on day 14 (50%, $P<0.01$) and day 28 (41%, $P<0.05$), compared to the control group. ACLT operated knees resulted in a 40% significant ($P<0.001$) increase in total Mankin score. Calcitonin restored Mankin score to below sham levels, ($P<0.05$). The most promising effect was observed on cartilage erosion. MMP-13 expression and CTX-II fragments were co-localized in the articular cartilage surface in the eroded areas. Serum CTX-I levels decreased in calcitonin treated animals compared to sham operated animals (36%, $P<0.001$).
Conclusions: Currently there are no treatments available for OA. Calcitonin has recently been proposed as a potential treatment for OA. These data are the first to demonstrate that an oral formulation of calcitonin protect against cartilage degradation in an *in vivo* model of joint trauma and increased cartilage degradation. The chondroprotective effect of salmon calcitonin may be a combination of direct effects on chondrocytes in addition to the well-established effect on bone resorption. Further clinical studies are needed to validate the herein documented effects on cartilage erosion.

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GAIT AS A SURROGATE MEASURE OF PAIN/DISABILITY IN ADDITION TO STRUCTURAL PARAMETERS OF JOINT DAMAGE AND INFLAMMATION IN TWO DIFFERENT CANINE MODELS OF OA

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Purpose: The most frequently used model for osteoarthritis (OA) is the canine joint instability, viz. ACLT, model. The ACLT model can be extended with a medial meniscectomy (i.e., ACLT-Mx model) to avoid unintentional, and with that variable, meniscal damage. More recently the canine Groove model has been developed in which OA is caused by surgically induced cartilage damage combined with temporary intermittent forced loading of the joint. Both models demonstrated comparable development of cartilage damage but they have never been compared on changes in gait as measure of pain/disability. Such a clinical measure is, in addition to structural parameters of joint damage and inflammation, of major importance in evaluation of treatment strategies of OA.
Methods: Knee osteoarthritis (OA) was induced in Labrador dogs according to the ACLT-Mx model (n=7) or Groove model (n=7). Every four weeks standardized radiographs were taken to analyze osteophyte formation. Every two weeks gait was recorded using Force Plate Analysis (FPA). Joints were macroscopic, histological, and biochemical analyzed for features of OA, 12 weeks after induction of OA.
Results: Radiographs revealed osteophyte formation in the experimental joints at the expected locations and the overall osteophyte score increased significantly ($p<0.05$) over time for both models. Cartilage integrity was damaged as reflected by an increased macroscopic (Δ 1.5 *vs.* 1), and histological score (Δ 3 *vs.* 2.5) and a decreased proteoglycan content (-29% *vs.* -18%) for the ACLT-Mx model and Groove model, respectively (all $p<0.05$). Chondrocyte activity demonstrated an increased synthesis rate (+70% *vs.* +10%) and release of proteoglycans (+200% *vs.* +60%) for the ACLT-Mx model and Groove model, respectively (both $p<0.05$). Synovial inflammation revealed the same characteristics in both models (Δ 3.5 *vs.* 1.0 and 1.2 *vs.* 0.8 for macroscopic and histological inflammation in the, ACLT-Mx *vs.* Groove model, respectively). Gait analysis revealed, a decrease in the three peak ground reaction forces of the experimental leg after OA induction ($p<0.05$), ranging from -80% in the ACLT-MX model to -40% in groove model, statistically different between both models ($p<0.05$). On average the ACLT-Mx demonstrated more pronounced changes compared to the Groove model. Interestingly, the change in gait (all three ground reaction forces) correlated significantly with the change in cartilage integrity (proteoglycan content and histological grade; r=0.445, r=0.488, and r=0.542 for peak braking, stance, and propelling force, respectively; all $p<0.003$).
Conclusions: The ACLT-Mx model demonstrates all the characteristics of OA and can be designated as a moderate to severe model of OA with clear synovial inflammatory activity. The Groove model is a less painful and significantly milder model of OA. The latter might be more suitable to study subtle changes as a result of intervention than the more robust ACLT-Mx model. Moreover, gait might be used as a surrogate measure of pain/disability. Most important, degree of cartilage damage is reflected by the extent to which the OA joint was (un)loaded.

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TIBIAL CARTILAGE SURFACE AREA, THICKNESS AND VOLUME IN VARIOUS ANIMAL SPECIES AND IN HUMANS

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Purpose: Appropriate dosage of intra-articular injections of drugs with potentially beneficial structural or symptomatic effects on articular cartilage requires information on the cartilage surface area, and potentially, on the cartilage thickness and volume. As various animal models are used to test the effect of such drugs in preclinical models, the aim of the current study was to provide quantitative, three-dimensional data on the tibial cartilage surface areas, cartilage thickness and cartilage volume in a variety of animal species and in humans.
Methods: The knees of 16 male Sprague Dawley rats (body weight 300 g) and 6 rabbits (weight 3.5 kg) were investigated with magnetic resonance imaging at 7 Tesla (T), and the knees and the knees of 3 cats (weight 4.2 kg), 18 mongrel dogs (weight 25 kg), 1 pig (weight 110 kg), 1 horse (weight 535 kg) and 1 rhinoceros (weight 1200 kg) at 1.5T. The values were compared