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Temporal changes in subchondral bone and cartilage in a post-traumatic osteoarthritis rabbit model

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Anterior cruciate ligament (ACL) rupture increases the risk for osteoarthritis (OA). This study aims to clarify temporal alterations in subchondral bone (SCB) and articular cartilage in a rabbit model with surgical ACL transection (ACLT).

Operated (ACLT) and contralateral (C-L) knees were harvested two (n=8) and eight (n=6) weeks after ACLT, surgery together with collection of age-matched control (CNTRL, n=8) knees. Each knee was divided into lateral and medial condyles and plateaus, groove and patella. Bone morphology was quantified using micro-computed tomography. Thickness and fixed charged density (FCD) of the cartilage were measured with optical coherence tomography and digital densitometry, respectively.

Trabeculae in ACLT knees were thinner compared to C-L in the lateral plateau (-6.7%;$p=0.007$) and groove (-10.9%;$p=0.015$) two weeks after surgery. At eight weeks, thinner trabeculae compared to C-L were observed at all locations. Trabecular bone volume fraction was decreased in ACLT compared to CNTRL at all locations except for the patella. Subchondral plate was thinner than C-L in the lateral plateau (-26.2%;$p=0.022$), groove (-19.8%;$p=0.005$) and patella (-19.5%; $p=0.001$).

Two weeks after surgery, FCD was reduced at the lateral plateau, the medial condyles, the groove, and the patella in ACLT compared to CNTRL. FCD was lower in the ACLT compared to C-L at all locations except for the lateral plateau. Interestingly, eight weeks after surgery, the FCD was increased in the medial plateau of C-L compared to CNTRL group knees. FCD loss in ACLT was progressive in the condyles, but the initial FCD loss was compensated for in the groove and patella. Also, the cartilage was thicker (50.5%;$p=0.007$) in the lateral plateau of ACLT knees eight weeks after surgery compared to CNTRL.

Summarizing, bone loss and cartilage degeneration occurred in a tissue- and site-specific manner in post-ACLT knees and bone loss spread progressively while some compositional changes of cartilage were recovered.

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Measurements of bone microarchitecture by histology, microCT and HRpQCT in CKD patients

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Introduction: Current available tools such as bone mineral density and biomarkers are insufficient to predict bone fragility in CKD patients. As chronic kidney disease (CKD) patients with fractures have impaired cortical bone, the characterization of bone is therefore crucial to identify patients at high risk.

Objective: we aimed to investigate the cortical and trabecular bone measurements assessing the microarchitecture in bone biopsies comparing histology and microcomputed tomography (μCT) and at the tibia using high resolution peripheral quantitative computed tomography (HRpQCT).

Methods: Nine patients were referred for vertebral or hip fracture (4 with one fracture, 5 with >2). The mean age was 70.3±7.2 years and the mean duration in dialysis therapy of 7.2 years (1-19). Bone microarchitecture was analyzed in transiliac biopsy using histology and in vitro μCT (μCT). Microarchitecture was assessed at the tibia by HR-pQCT. Correlations were performed by Pearson tests.

Results: BV/TV was similar in histology and μCT (0.12±0.03 vs 0.14±0.03%, p NS), while lower in HRpQCT (0.08±0.04%, p< 0.05), but no correlation between histology and μCT (r=0.58, p=0.10). Tb.Th was higher in histology than in μCT or HRpQCT (0.80±0.02, 0.11±0.02, 0.05±0.01 mm respectively, p< 0.01). Conversely, Tb.Sp was not significantly different in histology than in μCT or HRpQCT (0.58±0.12, 0.67±0.11, 0.73±0.43 mm respectively). There was no correlation in Tb.N, Tb.Th and Tb.Sp quantified by histology and μCT, neither with μCT and HRpQCT. However, the mean cortical thickness (Ct.Th) was closed in the 3 methods (0.63±0.25 vs 0.60±0.18 vs 0.59±0.23 mm respectively). Histology Ct.Th was positively correlated to μCT Ct.Th (r=0.75, p< 0.05), but no correlation were found between μCT and HRpQCT Ct.Th (p=0.21).

Conclusions: Neither trabecular or cortical indices measured in bone biopsies correlates with HRpQCT measurement at the tibia. However, cortical thickness is similar throughout the 3 techniques, suggesting an accurate way to measure bone fragility

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Real-time impedance-based monitoring of the growth and inhibition of osteomyelitis pathogen *Staphylococcus aureus* biofilms treated with novel bisphosphonate-fluoroquinolone antimicrobial conjugates

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Osteomyelitis is a limb- and life-threatening orthopedic infection predominantly caused by *Staphylococcus aureus* biofilms. Bone infections are extremely challenging to treat clinically. Therefore, we have been designing, synthesizing, and testing novel antibiotic conjugates to target bone infections. This class of conjugates comprises bone-binding bisphosphonates as biochemical vectors for the delivery of antibiotic agents to hydroxyapatite. In the present study, we utilized a real-time impedance based assay to study the growth of *Staphylococcus aureus* biofilms over time, and to test the antimicrobial efficacy of our novel conjugates on biofilm growth and inhibition in the presence and absence of hydroxyapatite. We tested early and newer generation fluoroquinolone compounds (ciprofloxacin, moxifloxacin, sitafloxacin, and nemonoxacin),

and bisphosphonate-conjugated versions of these antibiotics (bisphosphonate-carbamate-sitafloxacin, bisphosphonate-carbamate-nemonoxacin, etidronate-carbamate-ciprofloxacin, and etidronate-carbamate-moxifloxacin), and found that they were able to inhibit *Staphylococcus aureus* biofilms in a dose-dependent manner. Among the conjugates, the greatest antimicrobial efficacy was observed with bisphosphonate-carbamate-nemonoxacin with an MIC of 1.48 μg/mL. Conjugates demonstrated varying antimicrobial activity depending on the specific antibiotic used for conjugation, the type of bisphosphonate moiety, the chemical conjugation scheme, and the presence or absence of hydroxyapatite. The conjugates designed and tested in this study retained the bone binding properties of the parent bisphosphonate moiety as confirmed by high-performance liquid chromatography. They also retained the antimicrobial activity of the parent antibiotic in the presence or absence of hydroxyapatite, albeit at lower levels due to the nature of their chemical modification. These findings will aid in optimization and testing of this novel class of drugs for future applications to pharmacotherapy in osteomyelitis.

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Risk factors for avascular bone necrosis in patients with lupus nephritis

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Objectives: The aim of this study was to investigate the risk factors for symptomatic avascular necrosis of bone (SAVN) in lupus nephritis (LN) patients.

Material and methods: The records of 374 patients (43 males, 331 females) with kidney biopsy-proven LN were reviewed retrospectively. The patients with LN who did not have SAVN were evaluated as a control group. The demographic, clinical, laboratory and management characteristics of two groups of patients were compared and analyzed by logistic regression.

Results: SAVN was present in 17 patients (4 males, 13 females, mean age of 27,4±6,7 years). Among the 17 patients, 28 joints presented SAVN. 12 occurred in hips (2 bilateral), 6-in ankles, 4-in knees, 3-in shoulders and 1- in lumbar spine. In 9 patients SAVN involved 2 or more joints. 14 patients were on steroids at the time of presentation of SAVN. 2 patients were not on steroids and 1 patient did not has documentation of steroid use. Meta-analysis demonstrates a significant increased risk of SAVN in patients with high disease activity and class IV LN ($p< 0,005$). LN patients with SAVN showed an earlier onset age ($p< 0,05$) and received significantly higher total cumulative corticosteroid dose. SAVN was not significantly associated with use of immunosuppressive agents. Serositis, coagulation disorders, vasculitis, cigarette smoking were higher incidence in male with LN and SAVN. Raynaud´s phenomenon, autoimmune thyroiditis, arthritis, Sjögren´s syndrome, antiphospholipid syndrome were higher incidence in female with LN and SAVN.

Conclusion: Many risk factors have been involved in the development of AVN in LN patients. SAVN is prevalent in class IV LN and in younger patients.. Corticosteroids are the principal risk factor, although some cases of SAVN occur in relatively steroid naïve patients. Early detection of AVN is important because the prognosis depends of the stage and location of the lesion.

Keywords: lupus nephritis, avascular bone necrosis

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Effect of 12-months of isoflavone intake on menopausal symptoms, bone metabolism and risk factors of cardiovascular disease

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Background: Isoflavones are structurally similar to 17-beta estradiol and has “estrogen-like” effect in vivo. The purpose of this study was to investigate the effects of 12 months of isoflavone intake on climacteric symptoms, bone metabolism and risk factors of cardiovascular disease in postmenopausal women.

Methods: Postmenopausal women who were not taking drugs that may affect their estrogen metabolism were randomly recruited. The participants were divided into the isoflavone (18% isoflavone concentration in a 200-ml can; one can per day) and control groups and were studied for 12 months. 51 participants were randomized into each group (isoflavone n=26 versus control n=25).

Results: Climacteric symptoms in the isoflavone group improved significantly by the 12-month follow-up point compared to the baseline levels(, P=0.010), however this improvement did not significantly differ between the two groups

There were no significant differences in the changes in body composition, blood pressure, serum glucose, lipid concentration, c-reactive protein and bone mineral density (lumbar spine, femur neck and total hip) after 12-months between the isoflavone and control groups

Conclusion: In this study, isoflavone supplementation had no significant effect on menopausal symptoms, bone metabolism and cardiovascular risk factors compared to the placebo group after 12 months. Additional large-scale follow-up studies that could verify the effects of isoflavone on postmenopausal women are needed.

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Bone mass density variability in activity vs remission of the disease in young patients with inflammatory bowel disease: Case series

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Introduction: Bone mass density in inflammatory bowel disease is influenced by several factors, including malabsorption, malnutrition, glucocorticoid treatment, endocrine disfunctions. Disease activity is another parameter than can influence it, but there are no studies upon how fast these changes can appear. The aim of the