FLS from RA patients [3,4]. However, it remains unclear whether the response to adiponectin in terms of cytokine production is different in immune blood cells from healthy donors compared to RA patients; moreover, it is not known if FLS from healthy subjects can also produce pro-inflammatory cytokines upon adiponectin stimulation.
Objectives: The study aims to analyse if adiponectin induces pro-inflammatory cytokine production by peripheral blood mononuclear cells (PBMCs) from both early RA patients and healthy controls. We also aim to study whether adiponectin induces pro-inflammatory cytokine production by FLS from healthy subjects.
Methods: PBMCs were isolated from whole blood obtained from 5 healthy donors and 3 early untreated newly diagnosed RA patients using Ficoll-Paque PLUS. FLS were isolated from synovial tissue obtained from 3 healthy donors after knee surgery due to injury. Healthy FLS were cultured in Dulbecco's Modified Eagle Medium (DMEM GlutaMAX) supplemented with 10% FBS, 1% Penicillin-streptomycin and 0.5% Gentamycin. Harvested PBMCs and FLS were resuspended in X-VIVO 15 serum-free hematopoietic cell medium and stimulated with different doses of human recombinant adiponectin (1, 5 and 10 μg/ml), and the culture media were collected at different time points. Concentrations of IL-6, IL-8 and TNF-α were measured with ELISA.
Results: Unstimulated PBMCs from early RA patients produced higher levels of IL-6 compared to healthy subjects (P<0.001). In healthy controls, both the production of IL-6 and TNF-α was higher in PBMCs stimulated with adiponectin compared to unstimulated PBMCs (n=5, P<0.01 for IL-6 and P<0.01 for TNF-α). Likewise, the production of both IL-6 and TNF-α was higher in PBMCs from early-RA patients after stimulation with adiponectin compared with unstimulated PBMCs (n=3, P<0.01 for IL-6 and P=0.03 for TNF-α) in a dose- and time-dependent manner. After stimulation with adiponectin, levels of IL-6, but not TNF-α, were higher in PMBCs from subjects with early RA compared to healthy controls (P<0.01). Adiponectin stimulation did not induce IL-8 production from PBMCs from either healthy donors or RA patients.
Adiponectin was able to induce the production of IL-6 and IL-8 by FLS isolated from heathy donors (n=3, P=0.03 for IL-6 and P=0.02 for IL-8), but not TNF-α.
Conclusion: Our results show that adiponectin induces the production of IL-6 and TNF-α from PBMCs from both healthy subjects and patients with RA and that adiponectin is able to stimulate the production of IL-6 and IL-8 by FLS isolated from healthy subjects. Those results suggest that adiponectin may play a role in the pathogenesis of RA.

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Cartilage, synovium and bone

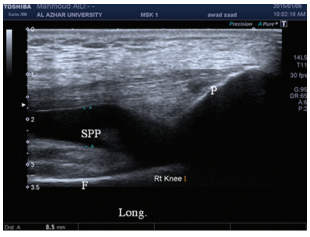
AB0084 ASSOCIATION OF SYNOVITIS VERSUS CARTILAGE LOSS WITH PAIN SEVERITY AND FUNCTIONAL LIMITATION IN PRIMARY KNEE OSTEOARTHRITIS: CLINICAL, ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING

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Background: Osteoarthritis (OA) is a common and debilitating condition associated with pain and the loss of mobility that undermines quality-of-life. Magnetic resonance imaging (MRI) has become the most important modality for assessment of pathologic changes in knee cartilage, in both clinical and research environment, also Musculoskeletal Ultrasound (MSU) is a valuable tool for imaging musculoskeletal changes in osteoarthritis. It shows early and late changes.
Objectives: The aim of the study was to detect the association of MRI and musculoskeletal ultrasound detected synovitis versus cartilage defect with knee pain severity and functional limitation in patient with primary knee osteoarthritis
Methods: This study was carried out on fifty patients of primary osteoarthritis diagnosed as primary osteoarthritis of knee joints according to American College of Rheumatology Radiologic and Clinical Criteria for Knee osteoarthritis all patients were assed clinically and knee examined for any swelling tenderness, warmth, limitation of range of motion. Pain severity and functional limitation assessed by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Musculoskeletal ultrasound and M.R.I of osteoarthritic knee joints were done.
Results: MSUS synovitis of examined joinits was (0.93 ± 0.94) and cartilage thickness(3.95 ± 1.4). MRI synovitis of examined joinits was (0.89 ± 0.93) and cartilage thickness (39.9 ± 13.26), There was Correlation between WOMAC pain score and MSU synovitis and cartilage thickness with Significant difference (p<0.01), also there was Correlation between WOMAC pain score and MRI synovitis and cartilage thickness with Significant difference (p<0.01). a positive Correlation between MSU Synovitis and MSU cartilage thickness was detected Significant difference (p<0.01) r(0.38). Also a Correlation between MRI Synovitis and MRI cartilage thickness show Significant difference (p<0.01) r (0.39).



Sagittal an proton density–weighted magnetic resonance imaging shows focal cartilage loss in the lateral tibiofemoral joint
Conclusion: The severity of cartilage loss and severity of the synovitis/effusion are the most significant determinants of pain and functional disability. Synovitis has role on increasing cartilage los MRI and MSU are a non-invasive method which allows comprehensive assessment and detection of early structural changes in osteoarthritic joints



Longitudinal scan show first grade of synovitis of right knee

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AB0085 ULTRASONOGRAPHIC EVALUATION OF THE METACARPAL CARTILAGE THICKNESS IN WEIGHTLIFTERS AND VOLLEYBALL PLAYERS

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Background: Articular cartilage is inevitably exposed to impact and loading in different sports play. Despite the fact that it is quite prone to different forms of overloading, the metacarpal cartilage has not been looked into in the pertinent literature. Accordingly, in this comparative study, we have assessed the metacarpal cartilage in volleyball players and weightlifters whereby different forms of stress is naturally prevalent in the athletes' hands.

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Objectives: To evaluate the possible effects of impact and loading on the metacarpal cartilage and hand functions in young athletes.
Methods: A total of 42 male athletes (19 weight-lifters and 23 volleyball players) and 46 healthy control subjects were enrolled. Demographic and clinical characteristics (age, height, weight, smoking habit, duration/type of sport, dominant hand) were recorded. The 2nd to 5th finger metacarpal head cartilage thicknesses were measured bilaterally using ultrasonography. Handgrip strength was measured with Jamar dynamometer; pinch strengths (lateral, tip to tip and three jaw chuck pinch) were measured using a pinchmeter. Michigan Hand Outcomes Questionnaire was also completed for each and every participant.
Results: Metacarpal cartilage thicknesses of the athletes (more predominant in weightlifters) were found to be thicker than those of the healthy controls (all $p<0.001$). There were no differences between the dominant and non-dominant hands (all $p>0.05$). Athletes' handgrip and pinch strengths were higher than those of the controls. In the weightlifting group, Michigan Hand Outcome Questionnaire work performance and pain scores were worse than the other groups.
Conclusion: The presence of increased cartilage thickness measurements in the athletes suggests that sports activities might affect the metacarpal articular cartilage. Highest pain scores and lowest work performance scores in the weightlifters with highest metacarpal cartilage thickness might suggest that impact and loading during their sports play could lead to cartilage edema.

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AB0086 BCP AND CPPD CRYSTALS INFLUENCE THE CHONDROCYTE PHENOTYPE IN DIFFERENT WAYS

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Background: Calcification of cartilage with BCP crystals is a common finding during osteoarthritis (OA) and is directly linked to the severity of the disease and hypertrophic differentiation of chondrocytes. In some OA cartilage samples calcium pyrophosphate dihydrate (CPPD) crystals can be found. The mechanism underlying the formation of the CPPD crystals and their effects on the chondrocytes are not completely understood.
Objectives: The aim of this study was to evaluate the effect of CPPD compared to BCP crystals on the chondrocyte phenotype in OA cartilage.
Methods: Cartilage samples of patients with chondrocalcinosis were used and compared with samples of severe OA patients without chondrocalcinosis and healthy cartilage samples served as control. Radiological presence of chondrocalcinosis was evaluated using standard X-ray pictures, as well as macroscopically inspection. The cartilage samples were stained using von Kossa/Safranin-orange staining. These stainings were used for OA severity scoring using the Chambers-Score. Chondrocyte differentiation markers were evaluated using Collagen 2 and X, as well as Sox9 and aggrecan as markers for chondrocyte hypertrophic differentiation in immunohistochemistry and qRT-PCR. TUNEL staining was performed to investigate cell death. In vivo results were validated using qRT-PCR for the expression of the respective genes after stimulation of C28 chondrocytes with CPPD and BCP crystals.
Results: Radiologically detectable cartilage calcifications were evident in chondrocalcinosis patients, but absent in OA patients without chondrocalcinosis. Chondrocalcinosis cartilage exhibited an increased collagen 10 expression compared to healthy cartilage, as well as to severe OA cartilage containing BCP calcification. Interestingly, aggrecan and collagen 2 were not reduced in chondrocalcinosis cartilage, but markedly reduced in OA cartilage. TUNEL positive cells were significantly increased in CPPD cartilage compared to OA cartilage, although the histological OA severity was lower. qRT-PCR indicated no relevant influence of CPPD crystals on hypertrophic marker genes, whereas BCP crystals significantly induced hypertrophic differentiation.
Conclusion: BCP and CPPD crystals seem to trigger differential effects on the chondrocyte phenotype. BCP crystals induce hypertrophic differentiation, which is not induced by CPPD crystals.
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AB0087 DLX5 AND DLX6 PROMOTES THE COMMITMENT OF MSC TO OSTEOBLASTIC LINEAGE AND CORTICAL BONE FORMATION

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Background: Osteoporosis which affects 200 million women worldwide is the consequence of an imbalance of low anabolism to high catabolism, causing a risk of fracture. Impaired anabolism involved reduced osteoblast differentiation. The osteoblast differentiation is mediated by transcription factors, including Dlx5 and Dlx6. Dlx5 is known to have a role in osteoblast/osteoclast couple and as a promotor of osteoblast lineage commitment [1, 2]. Thus, Dlx5 is a transcriptional actor of Runx2 [3], a key element of osteoblastic differentiation.
Objectives: The goal of this project is to expand our knowledge about bone formation and cellular precursors of osteoblasts, focusing on Dlx5 and Dlx6.
Methods: We analyze the kinetic expression of Dlx5, Dlx6 and osteoblastic markers during the osteoblastic differentiation from murine osteoblastic progenitor derived from calvaria and bone marrow. Same analysis was carried out in osteoblastic precursors from control cells, Dlx5/Dlx6 cells with *ex vivo* recombination or from KO mice in parallel to human bone marrow cells. We analyzed the bone phenotype of mutated mice in the absence of expression of Dlx5 and Dlx6 under Osx promoter.
Results: Dlx5 and Dlx6 increases at D7 during osteoblastic differentiation in the murine bone marrow and then was stable to D21. The absence of Dlx5/6 in cells derived from calvaria and bone marrow resulted in decreased levels of osteocalcin and alkaline phosphatase. *Dlx5/6 $^{fl/fl}$ Osx-Cre* mice were lethal. Dlx5/6 $^{fl/+}$ Osx Cre mice does not affect cortical and trabecular parameters at 6 weeks but had a significant lower cortical thickness and also lower Tb. BV/TV and Tb. Th along with a lower BMD at 3 months in both sexes. Moreover, periosteal volume was also lower in mutated mice. The skulls revealed a lack of sutures closures and dental abnormalities at 6 weeks and 3 months in both sexes.
Conclusion: The deletion of these transcription factors under the action of the Osterix promoter generates lethality, in favor of an essential role in bone development. Heterozygous mutation show impaired bone acquisition during growth. To obtain a total deletion of Dlx5 and Dlx6 in osteoblastic precursor cells, a new murine model of conditional induced deletion is generated. Dlx5 and Dlx6 promote osteoblastic differentiation with an effect on late bone markers, in favor of a role in terminal differentiation. Analysis *in vitro* of Dlx5 and Dlx6 will be confirmed by ongoing *in vivo* experimentation.

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