612 EARLY SUBCHONDRAL BONE CHANGES IN AN OSTEOARTHRITIS MODEL IN WILD TYPE AND TGF-ALPHA KNOCKOUT MICE

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Purpose: To examine early subchondral bone changes in the DMM (destabilization of medial meniscus) model of injury-induced osteoarthritis (OA) in wild type (WT) as well as in TGFalpha knockout (KO) mice.

Methods: C57/B16 Wt and TGFalpha KO mice were subjected to DMM or SHAM surgery at 12-weeks of age and harvested at 2-, 5- and 10-weeks post-surgery. Catwalk gait analyses, Micro-Computed Tomography (μCT), Toluidine Blue (TB), Picrosirius Red (PR) and Tartrate-Resistant Acidic Phosphatase (TRAP) staining of paraffin-embedded sections were used to investigate gait patterns, 3D joint morphology, bone mineral density (BMD) of subchondral bone, histology, collagen organization and activity of osteoclasts.

Results: In WT mice, OA severity progressed from mild or moderate (5-week post-surgery) to severe (10-week post-surgery) according to OARSI histopathology scoring. Gait disparity occurred only at 10-week post-surgery in DMM mice but not at earlier time-points. Osteophyte formation around the surgical joint was noticed as early as 2-week post-surgery in DMM mice but not at earlier time-points. Osteophyte formation was more severe and progressed to severe (10-week post-surgery) according to histology, collagen organization and activity of osteoclasts.

Conclusions: BMD of subchondral bone increased at the early stages of OA and reverted to baseline at latter stages. Gait disparity in mice only occurred at later stages of OA. Osteoclast activity increased during OA progression. TGFalpha KO might be protective for articular cartilage but detrimental for bone.

613 CORRELATION OF SUBCHONDRAL BONE MORPHOMETRY AND OARSI GRADE IN OSTEOARTHRITIC HUMAN KNEE SAMPLES

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Purpose: Osteoarthritis (OA) is a disease of a whole joint and there is increasing evidence that the subchondral bone contributes or coincides significantly to the pathogenesis of OA. Yet most of the diagnostic methods are focused mainly on cartilage degeneration and erosion. Consequently, there is a lack of data about relationship between bone morphometric and densitometric parameters of human trabecular bone and subchondral plate in relation to the actual histological degeneration of the overlaying cartilage. The aim of this study was to characterize morphological changes in human tibial trabecular bone and subchondral plate as a function of histological progression of OA.

Methods: 25 osteochondral samples were prepared from 13 OA patients treated with total knee arthroplasty at Oulu University Hospital. Samples were prepared from tibial plateaus which are always taken during replacement surgery of the damaged tibial plateau. Samples were visually classified into three categories in terms of degeneration of the articular cartilage: 1) most inviolable (or intact) cartilage, 2) moderate cartilage degeneration, and 3) partly or fully exposed subchondral bone. Cylindrical osteochondral samples with a diameter of 6.0 mm were prepared from all macroscopic visual grades. Samples were stored in phosphate-buffered saline (PBS) for μCT imaging. Osteochondral cylinders were scanned with μCT device at isotropic 27.8 μm voxel size (Skyscan 1172, Bruker microCT, Kontich, Belgium). Images were reconstructed and analyzed with software package provided by the manufacturer. Finally a novel 3D local binary pattern (LBP) analysis was performed for volumetric dataset with a custom made Matlab program. After the μCT imaging, cylinders were formalin-fixed, parafin embedded and sectioned. Sections of 5 μm were stained with Safranin-O. Histological sections were graded by three independent evaluators according to the standardized OARSI grading system. Final OARSI grade was defined as an average from three evaluators, which was then correlated with bone architectural and densitometric properties (Figures 1 and 2).

Results: All knees had large internal variation in OARSI grades depending on the site. Most of the analyzed morphological parameters showed significant increase with increasing OARSI grade in both trabecular bone compartment as well as in subchondral bone plate. Trabecular bone volume fraction, number and thickness increased 273%, 123% and 54%, respectively, between OARSI grades 1 and 6. At the same time trabecular separation and structure model index decreased by 46% and 70%, respectively. Subchondral plate thickness increased from 250 μm to 810 μm and bone specific surface decreased from 8.1% to 3.1%, between OARSI grades 1 and 6. Furthermore, local binary pattern analysis showed that there was a significant increase of different local patterns in trabecular bone, whereas in subchondral bone plate there was a significant decrease of different local binary patterns when normalized to number of analyzed voxels. Interestingly, we did not observe any changes in tissue mineral density (excluding pores) or porosity of subchondral bone plate when OARSI grade was increased.

Conclusions: This study further highlights the importance of subchondral bone changes in OA and demonstrates feasibility of using tissue material which is discarded during endoprosthetisation and which appears to contain a representative variety of samples with different OA grades. Increased sclerosis of subchondral bone had strong association with the OARSI grade similarly to the trabecular volume fraction. This was not only due to an increase in trabecular number but the trabeculae became also thicker and more closely packed leading to more plate-like shape. The LBP analysis of trabecular bone indicated more complex patterns for higher OARSI grades. Conventional morphometric analysis of subchondral bone plate showed significant thickening of subchondral bone plate, while reduced bone specific surface with constant porosity indicates of reduced surface roughness that could be also detected in 3D models (figure 1). Similar conclusion was also supported by LBP analysis. This study highlights the features of bone architecture changes in the progression of OA.