

Summary – Osteoarthritis Session: Interaction of subchondral bone and cartilage in OA

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Changes in subchondral bone and calcified cartilage are well-recognized features of the joint failure process termed osteoarthrosis (also, osteoarthritis, OA). How these changes contribute to joint breakdown remains an issue of contention, despite more than four decades of research in this area. In the overview talk, **Dr. M. B. Schaffler** (Mount Sinai School of Medicine) reviewed the concept of OA as an organ-level failure, involving cartilage, bone and capsule. He then provided a historical overview of the idea that mineralized tissue changes are involved in the pathogenesis of OA, beginning with the observations of Ogston in the 1870s and following up with the recent studies by Radin and Sokoloff. He also pointed out that the factors that initiate joint injury are not the same factors that cause it to progress to OA. **Dr. A. Bendele** (University of Colorado) then presented a comprehensive overview of small animal models for studying the pathogenesis of OA, emphasizing both naturally occurring OA in C57Bl6 mice and Dunkin-Hartley strain guinea pigs. She also showed how cartilage degradation in these models could be dramatically accelerated using surgical meniscal injury, leading to cartilage loss in a matter of weeks rather than months. Data were presented which suggest that matrix metalloproteinase (MMP) inhibitors can ameliorate cartilage changes in these models. Subchondral bone changes appear to be present, but the contribution of these changes to OA in these accelerated models remains unknown. Lastly, data from a meniscal injury model in skeletally mature dogs show the reverse situation to that in rodents. Dogs show very pronounced early changes in subchondral bone, with only minor

changes in the overlying cartilage; in this model, cartilage changes were refractory to treatment with MMP inhibitors.

Many of the previous studies of the subchondral mineralized tissue in OA have focused on mechanical effects, i.e. bony end-plate thickening leads to subchondral stiffening and tidemark advance leads to thinning of cartilage. The remaining speakers in this session demonstrated that there are significant changes in the biology of the bone cells and bone matrix in OA patients, changes that may play an important role in the progression of the disease. **Dr. D. Lajeunesse** (Université de Montréal) presented data showing that osteoblasts from more advanced (“high”) OA differ fundamentally from osteoblasts obtained from mild (“low”) OA patients, with regard to the suite of cytokines they express. **Dr. A. Bailey** (University of Bristol) demonstrated that the composition of collagen in the subchondral bone in OA differs from that in normal bone. OA bone shows less cross-linking, consistent with less mature collagen resulting from high bone turnover. Collagen composition also differed, with OA bone showing a collagen I homotrimer (3 alpha-1 chains), rather than the heterotrimer found in normal bone. In the final talk, **Dr. C. Westacott** (University of Bristol) showed that osteoblasts from OA patients can directly cause matrix breakdown of normal articular cartilage. Her studies revealed that when normal articular cartilage is cultured with OA-derived osteoblasts, there is a 3-fold increase in proteoglycan release from the cartilage. This effect appears to be a direct result of factors secreted by the osteoblast, and is not mediated through the chondrocytes.

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