

Alterations in Subchondral Bone Composition Observed by Synchrotron Infrared Micro-Spectroscopy in a Primate Model of Osteoarthritis

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Subchondral bone sclerosis is observed by histologic and radiographic studies in osteoarthritis (OA). Mechanical impact on thickened subchondral bone has been thought to contribute to articular cartilage breakdown (1). However, the biological basis for thickened subchondral bone needs to be defined because bone changes may contribute to OA progression and influence treatment decisions (2). Low levels of CSF-1 with failure of osteoclastic resorption were considered as a basis for dense subchondral bone (3), but CSF-1 levels in OA synovial fluids did not differ from those in traumatic fluids (4). Enhanced production of IGF-1, a bone growth factor, was demonstrated in osteoblasts from OA bone (5). We have studied a model of OA in aging cynomolgus monkeys, where subchondral bone sclerosis has been shown histologically to precede cartilage breakdown (6). In the present study, samples of subchondral bone were obtained from histologically normal monkey tibias and compared with osteoarthritic tibias by means of synchrotron infrared micro-spectroscopy. This technique permits analysis of intact bone sections at 3-5 μm spatial resolution for protein and mineral content, mineral crystallinity, and collagen structure. Results can be expressed quantitatively as a function of OA severity. Our findings show increased mineralization in osteoarthritic bone with significantly higher phosphate/protein and carbonate/protein ratios ($p < 0.05$) (Figure 1). We also find altered collagen structure in OA, which may contribute to the increased mineralization. We postulate that these changes in subchondral bone may make it more brittle and lead to microfractures with increased remodeling, consistent with clinical studies (7).

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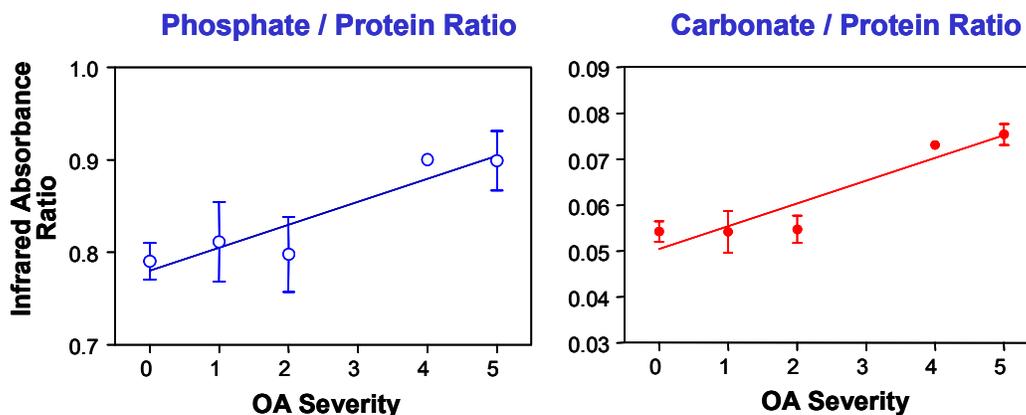


Figure 1. Phosphate / protein (left) and carbonate / protein (right) ratios as a function of disease severity. There is a significant increase ($p < 0.05$) in both the phosphate / protein ratio and the carbonate / protein ratio as a function of OA severity. OA severity in the tibial plateau was graded using a semiquantitative histological grading scheme (6) including: articular cartilage fibrillation and clefts (weighting factor 0.86), the presence of chondrocyte clones (weighting factor 0.80), severity of loss of toluidine blue staining (weighting factor 0.60), presence of osteophytes (weighting factor 0.59), average subchondral bone thickness (weighting factor 0.44), and the presence of microcracks (weighting factor 0.28).