

## Crystals and Cartilage Degeneration in the Ankle

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Osteoarthritis is the most common form of arthritis in adults engendering large personal and societal costs. While this type of degenerative arthritis typically affects the articular cartilage of large weight bearing joints, the ankle joint is often inexplicably spared. During a careful exam of a large cohort of ankle joint cartilages (tali) from human cadavers, we noted the presence of exuberant powdery deposits in a significant portion of these samples. We set out to determine the nature of these deposits, and to correlate their presence with gross and microscopic evidence of osteoarthritis in ankle cartilage.

Adult human tali (N = 7855) from 4007 donors were harvested within 24 hours of death, through the Gift of Hope Organ and Tissue Donor Network of Illinois from April 1998 to October 2006. Each of these tali was graded for level of cartilage degeneration (see grading scale in section on “Specimen Grading” below). The presence of grossly visible crystalline deposits was documented. A subset of 63 tali displaying crystalline deposits on the trochlear articular surface was selected (in the same order in which they were received from the Gift of Hope) for photography and further examination, while a smaller subset of 12 from the subset of 63 was randomly selected for Safranin-O/Fast green staining, immunohistochemistry, and synchrotron FTIR spectroscopy for crystal analysis.

Of the pool of tali from 4007 donors 18 years of age and older, 187 or 4.7 percent demonstrated surface crystal deposits. The crystal deposits were almost always grossly associated with a cartilage lesion, either being found within, or adjacent to, a large lesion and on the surface of adjacent fibrillated lesions (Figures 2 and 4). Furthermore, the lesions appeared to be biomechanically induced, being located either at the margin of the trochlea where it rubs against the opposing articular surface of the fibula or tibia or they were “tram-track” lesions indicative of erosion caused by apposition with exostosis (osteophytes) from the anterior margin of the tibia during joint motion. Tali with crystal deposits were significantly more likely to have osteoarthritis than tali without crystal deposits. Cartilage degeneration of grade 2 or higher occurred in 54.7 % of tali with MSU crystals, and 26.0% of tali without MSU crystals ( $p < 0.05$ ). Surface zone protein was highly correlated with the presence of crystals. Synchrotron FTIR analysis revealed monosodium urate (MSU) crystals in all specimens analyzed.

We show that MSU crystals, as seen in gout, are strongly correlated with cartilage lesions in the talus, and these lesions appear to be at least partially biomechanically induced. Thus, MSU crystals may be one cause of osteoarthritis in this unusual location.