Alterations of mineralized matrix in the cultured bone model caused by Pb exposure

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This work investigated mineralization process when the bone is subjected to lead (Pb) exposure using an *in vitro* bone model. Pb, a known toxic substance, has been evidenced to accumulate in bone tissue, and its strong correlation with osteoporosis and osteoarthritis. However, there are very few studies investigated the effects of Pb on bone mineralization at sub cellular and nanoscale levels. The bone like cultures (from MC3T3) were treated with Pb at varied concentrations from 0.2 -50 M. The Pb with concentrations of 50 M and lower did not reduce cell growth and mineralization of the culture, but they changed expressions levels of several bone proteins including type I collagen, osteopontin, osteocalcin, osteoprotegerin, and also divalent metal transporter-1 (DMT1). Exposure to 0.2, 0.4, 2, 10 and 50 M Pb directly resulted in Pb accumulation in the cultured bone nodules with 0.0965±0.0049, 0.210±0.0035, 0.8604±0.064, 2.5168±0.068, 12.2306±0.639 mg/g dry weight of the bone nodules, respectively. Pb was present in the culture as Pb complex with bone apatite and oxide forms (PbO and PbO_2). The ultrastructure analysis confirmed the co-localization of Pb and calcium phosphate in only bone mineral, but not in the organic matrix. Pb was also found in the intracellular calcified vesicles which play a role in cell regulated mineralization mechanism. This could suggest one of pathways on how Pb incorporates into bone tissue. Pb was observed in both globular and needle shape minerals (early and mature mineralization stages) with different degree of Pb in their structures (globular > needle). This change in mineral chemistry may also affect on interaction between mineral and collagen fibrils (basic build block of bone), and might lead to pathological conditions and changes in the bone mechanical properties.