

Using natural stable calcium isotopes to rapidly assess changes in bone mineral balance using a bed rest model to induce bone loss

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Metabolic bone diseases like osteoporosis result from the disruption of normal bone mineral balance (BMB) resulting in bone loss. During spaceflight astronauts lose substantial bone. Bed rest provides an analog to simulate some of the effects of spaceflight; including bone and calcium loss and provides the opportunity to evaluate new methods to monitor BMB in healthy individuals undergoing environmentally induced-bone loss. Previous research showed that natural variations in the Ca isotope ratio occur because bone formation depletes soft tissue of light Ca isotopes while bone resorption releases that isotopically light Ca back into soft tissue (Skulan et al, 2007). Using a bed rest model, we demonstrate that the Ca isotope ratio of urine shifts in a direction consistent with bone loss after just 7 days of bed rest, long before detectable changes in bone mineral density (BMD) occur. The Ca isotope variations tracks changes observed in urinary N-telopeptide, a bone resorption biomarker. Bone specific alkaline phosphatase, a bone formation biomarker, is unchanged. The established relationship between Ca isotopes and BMB can be used to quantitatively translate the changes in the Ca isotope ratio to changes in BMD using a simple mathematical model. This model predicts that subjects lost $0.25 \pm 0.07\%$ (\pm SD) of their bone mass from day 7 to day 30 of bed rest. Given the rapid signal observed using Ca isotope measurements and the potential to quantitatively assess bone loss; this technique is well suited to study the short-term dynamics of bone metabolism.