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## Rapidly assessing changes in bone mineral balance using natural stable calcium isotopes

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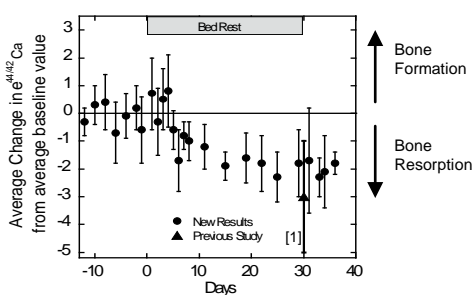
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We demonstrate that variations in the Ca isotope ratios in urine rapidly and quantitatively reflect changes in bone mineral balance. This variation occurs because bone formation depletes soft tissue of light Ca isotopes, while bone resorption releases that isotopically light Ca back into soft tissue.

In a study of 12 individuals confined to bed rest, a condition known to induce bone resorption, we show that Ca isotope ratios shift in a direction consistent with net bone loss after just 7 days, long before detectable changes in bone density occur. Consistent with this interpretation, the Ca isotope variations track changes observed in N-teleopeptide, a bone resorption biomarker, while bone-specific alkaline phosphatase, a bone formation biomarker, is unchanged. Ca isotopes can in principle be used to quantify net changes in bone mass. Ca isotopes indicate an average loss of  $0.62 \pm 0.16$  % in bone mass over the course of this 30-day study. The Ca isotope technique should accelerate the pace of discovery of new treatments for bone disease and provide novel insights into the dynamics of bone metabolism.



**Figure 1:** Change in Ca isotope ratios of urine as a result of bed rest.

[1] Skulan *et al.* (2007) *Clinical Chem.* **53**, 1155-1158