

## **Evaluating spaceflight-induced bone loss in astronauts using Ca isotopes**

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Spaceflight-induced bone loss remains a major challenge for extended duration human space missions. Bone loss not only increases the potential risk of fracture, but also leads to elevated urine calcium (Ca) excretion which increases the risk for renal stones. To date, the most promising countermeasures for spaceflight-induced bone loss include diet, resistive exercise, and/or antiresorptive medications (e.g., alendronate). However, the longterm effectiveness and side effects of these countermeasures remains unclear because we lack an adequate understanding of the time course of net bone resorption in crewmembers utilizing current bone loss countermeasures.

To overcome these limitations, we have developed a new quantitative bone biomarker based on mass-dependent isotopic fractionation of Ca isotopes in urine samples collected during spaceflight and returned for analysis. Here, we report results from 30 International Space Station (ISS) crewmembers who participated in nominal 180 day missions aboard the ISS. Crewmembers who utilized dietary and resistive exercise alone showed significantly lower Ca isotope values during space flight, corresponding to enhanced net bone resorption. In contrast, crew members who received 70 mg/week of the bisphosphonate alendronate showed no evidence for a shift in Ca isotopes or enhanced bone resorption. When examining variations in Ca isotope patterns between individual crewmembers, our results suggest exercise and diet alone may counteract bone loss in some, but not all, crewmembers, while bisphosphonates appear to be more uniformly effective in preventing bone loss.

This work, in combination with upcoming Ca isotope experiments to measure changes in bone mineral balance during year-long missions aboard the ISS, has important implications for planning longterm human spaceflight missions to the Moon and Mars, and suggests that Ca isotopes will prove to be an important new bone biomarker in ground-based clinical medicine.