Developing a clinically useful calcium isotope biomarker

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Near-real-time monitoring of bone metabolism in metabolic bone diseases such as osteoporosis and multiple myeloma (MM) would help clinicians detect disease onset earlier than is currently possible. A biomarker detecting asymptomatic bone destruction would also help evaluate the efficacy of bone-specific therapies. We are developing naturally occurring Ca isotope ratios ($\delta^{44/42}$Ca) in serum and urine as such a biomarker.

We previously reported that natural changes in $\delta^{44/42}$Ca of urine provide quantitative information on short-term changes in net bone mineral balance, information unavailable from conventional biochemical measures of bone metabolism. The basis of this biomarker is that blood and urine are enriched or depleted in light Ca isotopes as a consequence of net bone gain or loss, respectively. In our studies of bed-rest induced bone loss, a net bone mineral loss rate of about <4%/year is detectable, consistent with results of X-Ray densitometry.

Here, we report data in clinically relevant populations. Bed-rest induces bone loss due to unloading, and so is used to model the effects of space flight on bone metabolism. Hence, we examined Ca isotopes in urine samples from 30 astronauts on International Space Station missions. We find a systematic shift toward preferential excretion of lighter Ca isotopes during flight, correlated with increased Ca excretion. The results are consistent with expectations from bed-rest.

Extending into populations with active bone disease, we examined Ca isotopes in serum collected from 71 adult patients diagnosed with either MM or asymptomatic precursor diseases. Samples of patients with active disease had statistically significant lower mean $\delta^{44/42}$Ca than those with non-active disease, regardless of diagnosis. The significant relationship between $\delta^{44/42}$Ca and myeloma activity is likely due to a myeloma-induced increased level of bone resorption.