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Magnitude and timescales of Ca isotope variability in human urine

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As bones in vertebrates have significantly lighter isotope composition than soft tissues [1], Ca isotopes ($\delta^{44/42}$Ca) in blood/urine have been proposed as potentially powerful tracers of bone mass balance in the human body. Relative to a healthy control, a subject experiencing net bone mass loss would exhibit a shift in blood/urine composition towards low, bone-like $\delta^{44/42}$Ca values. Since then, pioneering studies have started to lay down the foundation of this novel biomedical application of stable isotopes, exploring Ca homeostasis in animal models [2, 3], and the human body, with a particular focus on bed rest experiments [4-6], and metabolic bone diseases such as osteoporosis [7-11].

While Ca isotopes could become *bona fide* clinical diagnostic tools, important questions remain that hinder the realization of this potential. Importantly, little is known about the range of natural Ca isotope variations in healthy subjects over time, or how demographics and/or lifestyle affect an individual's baseline Ca isotope composition and its temporal variability.

To gain insights into these questions, we measured the Ca isotope composition of urine from 28 healthy participants (evenly split between males and females, age 19 to 60) over timescales ranging from days to months. The data reveals large inter-individual variability in $\delta^{44/42}$Ca (up to 2.5 ‰) but encouraging intra-individual stability (within ~ ±0.2-0.3 ‰). The details of the dataset will be presented, and the implications for Ca isotopes as tracer of bone mass balance discussed.

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