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Benchmarking the isotopes of diseases: Fingernail composition as a proxy of the blood baseline

REBECCA RYAN, YUNHAN FANG, THEO TACAIL, ESTHER LAHOUD AND FRANÇOIS L.H. TISSOT

California Institute of Technology

Calcium isotopes have been shown as a promising tracer for bone mineral balance and systemic Ca balance in the body [1-3]. To date, most studies have focused on the isotopic composition of blood, serum, or urine - matrices that offer only instantaneous snapshots and are highly sensitive to short-term physiological fluctuations [4]. The resulting intra-individual short-term variability undermines the potential of isotope ratios as cross-sectional disease markers, limiting their medical applicability and diagnostic sensitivity. One way to overcome these limitations is to use a self-referencing approach, provided the average blood isotopic composition of the individual can be established. Fingernails could transform this landscape by providing a stable, integrative record of systemic isotope composition, creating a metabolically relevant baseline archive. Due to the growth rate of nails, a ~1 mm clipping provides approximately a 3-week average of blood values from 3–5 months prior to sample collection. This would not only set the foundations for self-referencing isotopic monitoring of disease progression and treatment response but also address a key limitation of current cross-sectional approaches.

To test the potential of nails as a baseline archive, we collected paired urine and fingernail samples from two participants over a 1 to 3-year period, tracking changes in the $\delta^{44/42}$Ca ratio through time. We found a significant reduction in the variability of $\delta^{44/42}$Ca ratios in fingernail samples compared with urine, even for samples collected more than one year apart. Additionally, the offset between the urine and nails was comparable to that between blood and urine. Our results show that nails are a promising, non-invasive, self-referencing tool for tracking systemic Ca balance and changes in bone formation and absorption. Based on concentration data, fingernails also show promise as a baseline archive for other isotopic systems (e.g., Fe, Zn), allowing their broader biomedical applications.

References

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