A comprehensive box-model for calcium isotopes in humans

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Calcium isotopes have been proved relevant to study peculiar physiopathological states, namely dynamic tracking of bone loss [*e.g.* 1], and the (paleo)ecology of vertebrates [*e.g.* 2]. The reasonning of all studies is based on the -0.6‰ offset of the $\delta^{44/42}$Ca values that would exist between diet and bone. However, our limited knowledge of the steady-state distribution of Ca isotopes among the main reservoirs and fluxes prevents any confident identification of the processes driving biological fractionation in vertebrate organisms.

In this study, we first compiled a set of data from literature and new isotopic measurements in tissues of human and other mammals in order to better define the relationships between reservoirs and fluxes relevant to the biological Ca cycle. This compilation mainly sheds light on the pronounced renal fractionation ($\Delta^{44/42}Ca_{urine\text{-}blood}$ = +1.2‰) as well as on the relationship between blood and bone. Contrary to former approximations, the isotope compositions of blood and bone are possibly undistinguishable and both significantly depleted in heavy isotopes when compared to diet.

In order to discuss and identify the main processes responsible for the distribution of Ca isotopes in human body, we developed a mathematical box-model. We compared the observed and calculated distributions of Ca isotopes and found as a main result that fractionation of Ca isotopes induced by kidneys accounts for a shift of -0.3‰ in blood compared to diet. We also discuss the consequences of an hypothesized fractionation at intestinal uptake, or during bone mineralization and the implications of bone loss and lactation.

[1] Morgan *et al.* (2012) *PNAS* **109** (25), 9989-94. [2] DePaolo 2004, *Rev. in Min. and Geoch.* **55**, 255-288