Disruption of Zn homeostasis in breast tumour patients reflected in Zn concentrations and stable isotope compositions of tumours, healthy tissue, and urine

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To study Zn dyshomeostasis associated with breast cancer, Zn concentrations and isotopic compositions ($\delta^{66}$Zn) were determined in benign and malignant tumours, healthy tissue from reduction mammoplasty, and histologically normal tissue adjacent to benign (NAT(BT)) and malignant tumours (NAT(MT)) (Sullivan et al., under review). Zinc concentrations and $\delta^{66}$Zn were also determined in urine in an effort to provide a non-invasive approach for tracing malignancy-induced Zn dyshomeostasis and evaluate whether Zn isotope signatures present are specific to breast cancer and/or observed in the benign condition (Schilling et al., under review). Benign and malignant tumours contain elevated levels of Zn compared to healthy tissue ($p = 0.0001$ and $p = 0.0002$, respectively) and NAT(MT) ($p < 0.0001$). In contrast, Zn concentrations in NAT(BT) are significantly elevated compared to HT ($p = 0.0022$) and NAT(MT) ($p = 0.0006$) and may be associated with a specific immune response to benign tumours [1]. Interestingly, the mean $\delta^{66}$Zn of both benign and malignant tumours is lower than in healthy tissue ($p = 0.04$ and $p = 0.02$, respectively) and NAT(BT) ($p = 0.03$ and $p = 0.01$, respectively), indicating a resultant $^{66}$Zn-rich reservoir may exist in patients with breast tumours. Previous work has shown that the Zn isotope signature in serum from breast cancer patients is similar to healthy controls [2]. Consistent with this, there is negligible difference in the $\delta^{66}$Zn in urine from breast cancer patients and healthy controls ($p = 0.32$). However, paradoxically, the disruption of Zn homeostasis in patients with benign tumours is reflected in slightly higher urinary Zn concentrations ($p = 0.12$) and significantly lower $\delta^{66}$Zn ($p = 0.03$) relative to healthy controls. Opposite to what was expected given the increased Zn concentrations and preferential uptake of $^{64}$Zn in benign tumours compared to NAT and healthy tissue, this represents an interesting basis for discussion. With the caveat that the analysis of additional samples is required, urine $\delta^{66}$Zn may have the potential to non-invasively indicate whether a breast lump is benign or malignant.