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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 (δ^{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 δ^{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 δ^{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 δ^{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 δ^{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 δ^{66}Zn may have the potential to non-invasively indicate whether a breast lump is benign or malignant.

[1] Comtesse, Zippel, Walle *et al.* (2005), *PNAS* **102**, 9601–6.
[2] Larner, Woodley, Shousha *et al*. (2015), *Metallomics* **7**, 112–7.