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Developing matrix-matched standards for LA-MC-ICPMS analysis of Cu isotopes in biological material

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Stable metal isotopes receive increasing attention as medical biomarkers due to their potential to detect changes of the metal metabolism related to disease. Among them, Cu stable isotopes have proven to be a particularly powerful tool to identify differences in isotope composition between tumors and healthy tissue suggesting application in cancer diagnosis [1, 2]. Potential mechanisms causing isotope fractionation include biological processes that involve redox- or bond-forming reactions and interaction of metals during transmembrane import and export. In order to advance our understanding of the underlying processes responsible for isotope fractionation between normal and diseased cells, we need *in situ*, spatially resolved methods. Despite its frequent use, laser ablation - multi-collector - inductively coupled plasma mass spectrometry (LA-MC-ICPMS) analysis of biological material is severely limited by the scarcity of matrix-matched standards. Such matrix-matched standards are necessary to correct for instrumental sources of isotope fractionation such as particle size distribution, ablation physics and differential ionization, which currently restrict the application of LA-MC-ICPMS in isotope metallomics [3]. In addition, these matrix-matched standards will also enable traceable and thus comparable isotope ratio values.

Gelatin properties partially resemble properties of protein-rich cellular material and their composition can be adjusted to the needed application by admixing specific elements. Due to its ability to mimic biological matrices, gelatin was successfully used as calibration standard for bioimaging by LA-ICPMS [4]. Here we present a novel approach to overcome existing instrumental correction limits of LA-MC-ICPMS by producing gelatin-based micro-droplet standards spiked with known amounts of Cu stable isotopes of a known Cu isotope composition. The Cu isotope compositions of the gelatin standards are validated by routine solution-nebulized MC-ICPMS analysis. Matrix-matched Cu isotope enriched gelatin will be used as bracketing standard and the strategy will be tested on tumorous and healthy tissue.

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