Detection of Localized Tungsten Deposition and Speciation in Bone using µXRF and µXANES

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High tungsten exposure has recently been connected with several medical conditions including leukemia, stroke and epilepsy. However, despite this metal's increasing use in a variety of applications, such as in medical devices implanted in the body, there remains a significant lack of toxicological data. This has prompted the Environmental Protection Agency (EPA) to highlight tungsten as a substance for further study. Worryingly, recent investigations show that exposure to tungsten via drinking water leads to its rapid accumulation in bone tissue of mice, persisting even after the source has been removed. The toxicological consequences of this accumulation, however, are currently unclear.

To better understand the mechanism and implications of tungsten deposition in bone, its spatial distribution in mouse long bones was investigated following exposure through drinking water using synchrotron radiation micro x-ray fluorescence (SR-µXRF). Heterogeneous tungsten distribution was observed throughout the cortical and trabecular bone as well as in the bone marrow. Interestingly, tungsten localization mirrored that of zinc. This suggests that tungsten uptake is linked to bone growth and turnover as zinc is known to deposit in zones of calcification within bone. Persistence of tungsten in cortical bone was observed following removal of its source (Fig. 1), highlighting the retention of tungsten in this environment, possibly as an insoluble form.

Tungsten speciation (chemical form) is strongly dependent on its environment and can range from simple monotungstate (WO_4^{2-}) to complex homo- and heteropolytungstates. These forms have vastly different toxicological implications. Consequently, the chemical from of tungsten within the matrix of cortical and trabecular bone of tungsten-exposed mice was probed using *in situ* synchrotron radiation micro x-ray absorption near edge spectroscopy (SR-µXANES). Comparison of the spectra obtained to varying tungsten reference species indicated that tungsten in bone does not exist in the form it was administered as (monotungstate), but rather shares close similarity to the heteropolytungsate species, phosphotungstate ($PW_{12}O_{40}^{3-}$). This is concerning as this form is known to be readily redox active which may promote its interaction with a variety of normal bone functions. These observations of tungsten speciation and specific localization in bone have serious implications about how tungsten accumulation may give rise to observed toxicity.

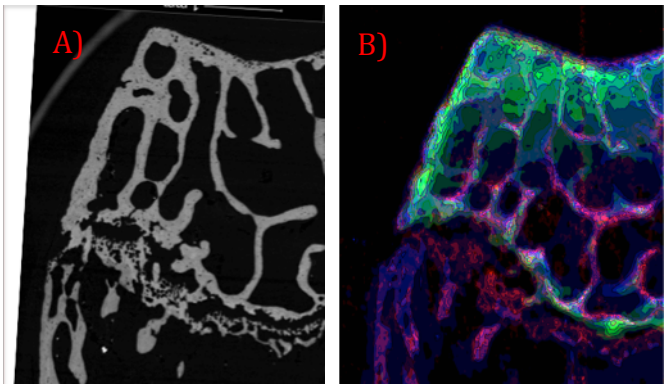

Figure 1. Longitudinal slice of mouse femoral knee. Mouse exposed to 4 weeks of 1000 ppm of tungsten followed by 8 weeks of water. A) Backscattered electron image shows the morphology of the bone surface. B) XRF overlay of tungsten (green), calcium (red) and zinc (blue). Contrary to deposition observed at 4 weeks of constant exposure, tungsten remains only outer in cortical and has been washed out of the trabecular bone tissue and bone marrow.