

Coherent normalization for *in vivo* bone lanthanum XRF measurements

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Lanthanum carbonate (LaC) is an orally administered phosphate binding drug that is routinely prescribed to patients with end-stage renal disease to reduce serum phosphate concentrations. The low bioavailability of LaC is a characteristic that makes it more preferential over aluminum-based phosphate binders, as it is minimally absorbed in the gastrointestinal tract. Although a large fraction of the lanthanum-phosphate complex is eliminated via biliary and faecal excretion, previous studies have shown deposition of lanthanum (La) in trace quantities in bone, which raises questions as to whether LaC has adverse long-term effects. In addition, La-based agents have recently been proposed as therapeutic agents for bone resorption disorders. Current techniques used to quantify bone La concentrations are achieved through invasive bone biopsies, which motivates the use of a non-invasive X-ray fluorescence (XRF) technique to achieve the same results.

We previously evaluated the feasibility to measure *in vivo* bone lanthanum in a 90° geometry using a K X-ray fluorescence (K-XRF) system that includes a 1.09 GBq Am-241 (59.5 keV, 36%) excitation source. In this work, bone La measurements and simulations in hydroxyapatite phantoms were conducted to investigate the ability to correct for overlying tissue thickness at the measurement site. As with any human measurement, the presence of overlying soft tissue can cause signal attenuation. When certain criteria are fulfilled this can be corrected through coherent normalization, where the measured K X-ray peak area is normalized to the coherent peak area of the excitation source, which was developed for the Pb K-XRF system and has recently shown to be successful for another rare earth element, gadolinium (Gd). One such criteria that must be satisfied for coherent normalization to be valid is that the X-ray signal and coherent signal are attenuated in the same manner. This is not the case for systems in which the excitation source is significantly larger than the K-edge of the target element. Since the 59.5 keV gamma rays emitted from the source are 20.6 keV above the 38.9 keV K-edge of La, the La X-rays are excited from scattered and non-scattered photons that correspond to the secondary and primary component of the photon fluence, respectively. Thus, the relative contribution of each component to the La K XRF signal was investigated. Monte Carlo methods were used to calculate coherent normalization for a range of overlying soft tissue thickness between 0 and 12 mm, and to decouple the fluence components contributing to the fluorescence of La. Experimental work was shown to be in reasonable agreement with the simulation results. The secondary fluence component provides an additional fluorescence signal which compensates for the differential attenuation of X-ray and coherent signal leading to an insignificant slope of normalized signal against overlying tissue thickness. It was also found that although the primary component is the dominant contributor to fluorescence for an excitation energy of 59.5 keV, the secondary component increases with overlying thickness and becomes the dominating component for larger excitation energies as was observed for the Gd system. This work suggests that the bone-La system is robust and able to quantify La in patients of varying body type by applying coherent normalization.