Nuclear Inst, and Methods in Physics Research B 433 (2018) 1–9

Contents lists available at ScienceDirect

Nuclear Inst. and Methods in Physics Research B

journal homepage: www.elsevier.com/locate/nimb

Feasibility of chromium measurement in skin using a portable hand-held XRF system

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ARTICLE INFO

Keywords:
X-ray Fluorescence
Chromium
Radiation Detection

ABSTRACT

Chromium (III) is a trace mineral that plays an important role in glucose and lipid metabolism in the body, in addition to being used in clinical formulations for the treatment of hypoglycemia. Chromium (Cr) deficiency in humans is known to cause insulin resistance and diabetes, however, effects of over exposure are not well studied or understood. This study aims to determine the feasibility of measuring Cr in skin using a portable InnovX XRF system at 40 kVp and 100 μA with a mean beam energy of 20 keV. Calibration lines were developed for K_α and K_β X-ray peaks using fiberglass resin phantoms with 1000 mg/L Cr(III) atomic standard solution, assuming a homogeneous distribution of Cr in skin. This assumption was validated through previously acquired XRF data from tissue cross-sections. Analysis of these data not only showed the presence of Cr in tissue samples, but also that Cr was distributed evenly across the tissue cross-section. Phantom concentrations were validated using delayed neutron activation analysis of fragments of each phantom via the neutron capture reaction ^{50}Cr(n,γ)^{51}Cr. Minimum detection limit (MDL) of the XRF system was determined using these calibration lines to be 5 ± 1 μg/g. This system was used to acquire data from the skin surface of five different parts of the body on four cadavers through a 300 s acquisition at each location. Cr was measurable at the 95% confidence level in 90% of the cadaver skin sites. The effective dose was determined to be 0.013 μSv which is small compared to a dental X-ray. However, the beam was very narrow so the skin dose delivered at the central axis of the beam was 201 mSv. Although the Cr levels did not vary significantly between the cadavers, the different parts of the body showed statistically significant differences in Cr levels. The XRF system used for this study shows promise as an effective monitoring tool for quantifying Cr levels in skin, although adjustments to produce a less collimated beam, and interrogate a larger area of skin, will be preferable so that the central dose is not as intense.

1. Introduction

Chromium(III) is an essential mineral that plays a key role in normal glucose metabolism in the form of a molecular complex known as glucose tolerance factor [1]. Chromium supplementation has been shown significantly to improve glycemia among certain patients with diabetes [2] and chromium chloride, chromium nicotinate, and chromium picolinate are commonly used formulations of Cr(III) used in suggested diabetes therapies. Chromium picolinate has been shown to be a significantly superior form of supplement in terms of improving absorption of Cr into the body as well as its efficacy [3].

Severe chromium deficiency is known to cause reversible insulin resistance and diabetes [4–6]. Although Cr supplementation has not been shown to have any significant impact on individuals that were not severely deficient, it has been demonstrated that it not only improves glycosylated haemoglobin levels, but also improves fasting glucose levels [2]. The observation of lowered levels of Cr may therefore signify an increased risk of diabetes that is treatable through the ingestion of Cr based supplements.

Recently, the Ontario government and the Ministry of Northern Development and Mines unveiled plans for chromite mining and smelting in the region of Northern Ontario known as the 'Ring of Fire'

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https://doi.org/10.1016/j.nimb.2018.07.012
Received 15 June 2016; Received in revised form 28 June 2018; Accepted 12 July 2018

[7]. Among the environmental concerns that have arisen with the unveiling of these plans, is the possibility of Cr(III) contamination of the ground water and subsequently the exposure of plant and animal life. This uptake of chromium could, of course, ultimately enter the food chain and lead to exposure of the population. Although the effects of exposure to Cr(VI) are well studied, there is a lack of literature on effects of over exposure to Cr (III). A 'safe' or normal exposure level is not necessarily well known or understood.

Another major source of potential Cr(III) exposure to the population is from metal-on-metal hip implants [8–10]. Often times these Chromium-Cobalt implants have mismatched sizing between the ball and socket of the joint, leading to friction between the two metallic components which results in the leakage of both Co and Cr into the surrounding tissue, and potentially into the bloodstream [8]. Although elevated Co levels have already been observed and their toxic symptoms manifested in many affected patients [9], similar studies for Cr exposure are lacking. The ability to detect and quantify Cr levels swiftly and non-invasively would lend itself to monitoring Cr levels in such cases.

Portable X-ray fluorescence techniques have recently been utilized in for the detection and quantification of trace elements in skin, and have provided minimum detection limits with comparable to competing XRF techniques, while delivering similar doses [11,12]. They provide unique advantages such as the ability to be used in the field with shorter measurement times with the trade-off being a lack of complete control over experimental conditions [13]. While benchtop XRF relies on excitation from a single, unfiltered incident energy, portable XRF devices are able to provide a continuum of photon energies, enabling preferentially higher excitations of analytes due to higher photoelectric absorption cross-sections [13]. Portable XRF has been used for measurements of Arsenic [14,15], Selenium [16], and Plutonium [17] in skin, as well as the measurement of Chromium[18] in nail and nail clippings. In addition to applications with superficial tissues like skin and nails, portable XRF has also shown promise in the *in vivo* measurements of lead in bone [19,20]. These studies establish the feasibility of portable XRF techniques for elemental measurements in human tissue.

The purpose of this study was therefore to evaluate the feasibility of measuring and quantifying Cr levels in skin using portable X-ray fluorescence (XRF) technology. The goal is to determine whether this can be a useful monitoring tool that can assess either Cr deficiencies or instances of increased exposure. The early application of the technology would be in studies of population health, aiming to determine whether increased exposure is correlated with health effects. In this study we assessed a portable hand-held X-ray fluorescence (XRF) system in its performance in measuring Cr in tissue phantoms, and applied the system to the detection of Cr levels in the dermis of cadavers.

2. Materials and methods

A hand-held XRF system was used to develop calibration lines using skin phantoms made from fiberglass resin. The phantoms' true concentrations were verified using delayed Neutron activation analysis (NAA) using the McMaster Nuclear Reactor pneumatic 'rabbit' facility. Once the calibration line and the MDL of the system were established, the system was used to measure several sites on the skin of multiple cadavers. A more detailed description is outlined in the following sections. Concentrations in the data presented are referred to as parts per million (ppm) and μg/g when referring phantoms and tissues respectively. In each case the two units express the quantity, μg of Cr per g of material, which can be aqueous solution, phantom, and human tissue.

2.1. Ethics approval

Since this study measures data from human cadavers, ethics approval was required before experiments could be performed. The ethics approval for this study was obtained through the Hamilton Integrated Research Ethics Board (HiREB), by an amendment to a previously approved study. The previous study sought approval for 'Characterisation of the Depth Distribution of Toxic and Biometals in Skin Samples.' The approval was granted on 27 April 2011 under HiREB file # 11–209-T. The amendment request was granted on 17 July 2014, allowing this study to be conducted.

2.2. Tissue phantoms

A set of calibration phantoms was prepared from fiberglass resin manufactured by Bondo (3 M, London, ON). We have successfully used this material as a model for skin in previous studies of arsenic XRF [21,22]. The phantoms were doped with chromium using a 1000 μg/L Chromium atomic absorption standard (AAS) for low concentration phantoms and a stock solution of Cr(III) chloride hexahydrate for higher concentrations. The substrate solutions were mixed in fiberglass resin by hand for several minutes to ensure a homogeneous distribution. Once the mixture was thoroughly mixed, the hardener was added and the mixture was poured into 4.8 cm diameter circular petri dishes up to a depth of 3.1 ± 0.2 mm. Each concentration of the mixture was poured into two separate petri dishes in order to make two identical sets of phantoms. The resin was left to set for 12 h. Once the resin had hardened, one set of disks was broken up and fragments from each quadrant of the disk were sent to the McMaster Nuclear Reactor for NAA to provide a validation of the Cr concentration in each sample. Table 1 shows the NAA verified phantom concentrations. The reason behind taking a fragment from each quadrant was to assess the spatial distribution of Cr in the phantoms. Due to the high viscosity of the fiberglass resin, mixing an aqueous solution in the resin raised a concern that despite mixing for several minutes, the distribution of the solution in resin may still not be completely homogeneous. Keeping this in mind, when data were acquired from these phantoms, X-ray spectra were similarly taken from different locations on the phantoms (one from each quadrant of the disc). A plot of measured and target concentrations as shown in Fig. 1 shows a linear fit with a slope of 1.24 ± 0.03. This is significantly different from 1 and the deviation can be attributed to error propagations in the phantom preparation process. As described below, three different Cr solutions were used in the phantom preparation process. One of which was the Cr AAS, while the other two solutions were prepared using a $CrCl_3$ salt. Both the measuring scale used for weighing the salt and the pipettes used for adding the solutions to the resin were only coarsely calibrated. This was deemed acceptable during the preparation stage since NAA was going to be used to verify the concentrations of the final phantoms. Note that phantom 1 had no Cr added to it. Any measurement of Cr is either due

Table 1
Fibreglass Resin Concentrations. The δ represents the measurement uncertainties of the NAA system, while the σ represents the standard deviations between the various fragments of same phantom. $\frac{2\sigma}{\mu}$ represents the percent variation at 95% confidence level.

Serial	Targeted Conc. (ppm)	NAA Concentration (ppm)		
		$\mu \pm \delta\mu$	σ	$\frac{2\sigma}{\mu}(\%)$
1	0	0.68* ± 8.42	1.023	300.88
2	5	8.82 ± 0.87	0.276	6.26
3	7	9.50 ± 0.85	1.571	33.07
4	10	14.20 ± 5.46	3.336	46.99
5	20	30.91 ± 1.17	0.924	5.98
6	30	42.86 ± 1.56	3.328	15.53
7	50	70.54 ± 7.48	1.724	4.89
8	100	142.26 ± 6.32	11.204	15.75
9	150	175.53 ± 6.44	8.877	10.11
10	200	243.22 ± 6.96	22.764	18.72