Development of an accelerator based determination of aluminum burden in peripheral bone by neutron activation analysis

ARTICLE *in* APPLIED RADIATION AND ISOTOPES · MAY 1998

Impact Factor: 1.23 · DOI: 10.1016/S0969-8043(97)00092-4 · Source: PubMed

David Robert Chettle
McMaster University

Pergamon

Appl. Radiat. Isot. Vol. 49, No. 5/6, pp. 717–719, 1998

Printed in Great Britain
0969-8043/98 $19.00 + 0.00

PII: S0969-8043(97)00092-4

Development of an Accelerator Based Determination of Aluminum Burden in Peripheral Bone by Neutron Activation Analysis

A. PEJOVIC-MILIC[1], F. E. MCNEILL[1], W. V. PRESTWICH[1], A. J. WAKER[2] and D. R. CHETTLE[1]*

[1]Department of Physics and Astronomy, McMaster University, Hamilton, Ont., Canada and
[2]A.E.C.L. Research, Chalk River Laboratories, Chalk River, Ont., Canada

Introduction

Aluminum toxicity has been of interest since 1976, when the metal was first associated with a neurological syndrome called dialysis encephalopathy (Alfred, 1984). Since then it has been shown that an increase of aluminum burden in persons with kidney failure is the cause of renal osteodystrophy and osteomalacia (Wills and Savory, 1983). Alzheimer's disease has also been associated with aluminum, due to both finding aluminum in the brain of patients and studies showing an increased risk of AD in regions with high concentrations of aluminum in drinking water (Martyn *et al.*, 1989).

Noninvasive *in vivo* aluminum measurement based on neutron activation analysis of ^{27}Al in bones is presented as a feasible and practical technique of monitoring aluminum levels in the body. Previous studies have been undertaken at Brookhaven (Ellis *et al.*, 1988) and McMaster (Palerme *et al.*, 1993) using reactor based sources, at Swansea (Wyatt *et al.*, 1993) using a ^{252}Cf source and at Birmingham using a Dynamitron accelerator to produce neutrons via the ^{3}H(p,n)^{3}He reaction (Green *et al.*, 1993). Aluminum is measured as either total body Al or Al in the bone of the hand via the thermal neutron reaction ^{27}Al(n,γ)^{28}Al. Aluminum-28 is radioactive, with a half life of 2.25 min, emitting 1.78 MeV gamma rays. Fast neutrons also produce the interfering reactions ^{31}P(n,γ)^{28}Al and ^{28}Si(n,p)^{28}Al, with thresholds of 1.95 MeV and 4 MeV, respectively.

System Design

Prior to exposing aluminum doped phantoms to the neutron beam we have characterized our neutron source, a neutron-accelerator in which the production of neutrons is based on the ^{7}Li(p,n)^{7}Be reaction.

The energy distribution of the neutrons was measured using a ^{3}He spectrometer placed 20 cm from the ^{7}Li target for various angles of deflection from the incident beam direction. Protons of 2.25 ± 0.02 MeV energy produce a maximum neutron energy of 340 keV along the beam axis. Therefore, the resulting neutrons do not have sufficient energy to activate phosphorus or silicon in the hand through the reactions previously mentioned.

The thermal neutron flux within the irradiation cavity was measured using an ^{115}In foil (1 cm × 1 cm) via the ^{115}In(n,γ)^{116}In reaction. The variation in flux with different thicknesses of polyethylene pre-moderator indicates that the highest thermal flux was achieved with two shields on each side of the indium foil. The distance from the ^{7}Li target was 42 cm and the foils were centred on the neutron beam axis. The results were as expected, showing the same trends with incident proton energies ranging from 2.00 to 2.25 MeV, with the highest thermal flux being achieved with the 2.25 MeV protons.

As a result of these measurements we have built a simple irradiation cavity with each wall being made of polyethylene shields (2 mm × 12.6 mm thick). All further experiments were performed using 2.25 ± 0.02 MeV protons.

Since a uniform distribution of thermal flux is desired, we have measured the spatial variation of thermal flux inside the cavity 42 cm from the ^{7}Li target. The average thermal flux was $(6 \pm 2) \times 10^{6}$, ranging from $(5 \pm 2) \times 10^{6}$ to $(9 \pm 3) \times 10^{6}$ n/cm^{2} s. These flux measurements allow us to estimate that the dose delivered to the hand during a 3 min irradiation would be 12 mSv, using the fluence to equivalent dose conversion factor from ICRP 26. Assuming that 1.5% of total body skeleton and skin is in one hand, and that 0.1% of the hand dose will be delivered to

Table 1. Performance of different methods for *in vivo* measurement of aluminum in bone

Place	Source	Hand dose (mSv)	Effective dose* (μSv)	Detection limits (mg)
Brookhaven	Nuclear reactor	< 20	26	0.4
Swansea	Moderated ^{252}Cf	36	47	2.2
Birmingham	^{3}H(^{1}H,n)^{3}He	50	65	2.0
Birmingham	$E_p = 1.2$ MeV	20	32 (22†)	1.8
McMaster	Nuclear reactor	43	56	2.8
McMaster	Accelerator			
	(cylindrical pantoms)	12	16	13
	(flat phantoms)			2.5

*Assuming that 1.5% of total body skeleton and skin is in one hand, and that 0.1% of the hand dose will be delivered to the rest of the body.

†Data from (Green *et al.*, 1993); the assumptions were that the hand and lower forearm comprise approximately 3% of the total skin and skeleton, and that the patient's body receives 0.05% of the hand dose.

the rest of the body, we have calculated the effective dose to the patient as 16 μSv.

Phantom Studies

According to the chemical composition of Reference Man cited by ICRP 23 (ICRP, 1975), cylindrical (clenched fist) aluminum doped phantoms (76 mm × 90 mm) were constructed to simulate both soft tissue and bone. Polyester resin was used as substrate, to which a fixed amount of bone ash, NaCl, Na_2CO_3 and varying amounts of $Al(NO_3)_3 \cdot 9H_2O$ were introduced.

After 3 min of exposure to a neutron beam and a 20–30 s transfer time, the γ-ray spectrum was acquired for 5 min using two large NaI (Tl) detectors (200 mm × 50 mm thick) separated by 12 cm, arranged in a quasi-4π geometry, built in a Pb-shield environment.

Data analysis has been done using the non-linear least-squares optimization method first developed by Marquardt and separate fits are applied to the aluminum and calcium characteristic peaks. Since the aluminum signal from the hand depends upon the size of the hand as well as the irradiation and counting geometry, the ratio of the aluminum to calcium signals is taken to derive the aluminum concentration in the hand.

The calibration curves are obtained by plotting the ratio of amplitudes (Al/Ca) vs aluminum concentration and the equation for the cylindrical set of phantoms is $\mathrm{Al/Ca} = (0.39 \pm 0.02) + (0.017 \pm 0.001)\mathrm{Al}$. The minimum detection limit (MDL) is 13 ± 2 mg Al. A significant positive intercept suggests that there is aluminum contamination in these phantoms. Further investigation showed aluminum present in the bone ash, the concentration of which has been estimated as 9 mg in 37.52 g of ash. This improved the calibration line ($\mathrm{Al/Ca} = (0.24 \pm 0.01) + (0.017 \pm 0.001)\mathrm{Al}$), but some aluminum contamination from other chemicals remains.

To investigate different phantom shapes, a second set of flat phantoms (23 cm × 13 cm) simulating an open hand, doped with low concentrations of aluminum, was made with the same procedure as the cylindrical ones to investigate the possibility of improving the system design and lowering the detection limit. This shape of phantom is expected to have a lower screening effect during the irradiation, providing better activation of aluminum, and allowing lower distances between the detectors (4.5 cm) which improves the detection efficiency. Assuming the same slope of the calibration curve and aluminum contamination as found for the cylindrical phantoms, the detection limit is estimated as 2.5 ± 0.4 mg Al. The acquired spectra of flat phantoms have a ^{24}Na double peak at 4.1 MeV, which has not previously been seen, clearly showing the improved detection efficiency.

Conclusion

Overall performances in terms of MDL and the dose achieved are summarized in Table 1.

The results of this preliminary study can therefore be said to indicate that an accelerator based system can provide clinically useful MDLs with low dose delivered to the patient. It is hoped to approach the performances of the Brookhaven system when design studies on the irradiation cavity are improved and a new set of flat phantoms simulating an open hand is constructed, using p.a. chemical compounds to avoid aluminum contamination.

References

Alfred, A. C. (1984) Aluminum in toxicity. *New Engl. J. Med.* **310,** 1113–1115.

Ellis, K. J. *et al.* (1988) *In vivo* monitoring of skeletal aluminum burden in patients with renal failure. *J. Radioanal. Nucl. Chem.* **124,** 85–95.

Green, S. *et al.* (1993) Characteristics of an accelerator based system for *in vivo* aluminum measurement in peripheral bone. In *Human Body Composition*, eds K. J. Ellis and J. D. Eastman, pp. 289–293. Plenum Press, New York.

ICRP (1975) *Report of the Task Group on Reference Man*, No. 23, p. 290. Pergamon Press, Oxford.

Martyn, C. N. *et al.* (1989) Geographical relation between Alzheimer's disease and aluminum in drinking water. *The Lancet* **January 14,** 59–62.

Palerme, S. *et al.* (1993) Pilot studies for *in vivo* bone aluminum measurements. In *Human Body Composition*, eds K. J. Ellis and J. D. Eastman, pp. 303–306. Plenum Press, New York.
Wills, M. R. and Savory, J. (1983) Aluminum poisoning: Dialysis encephalopathy, osteomalacia, and anemia. *The Lancet* **July 2,** 29–33.
Wyatt, R. M. *et al.* (1993) The development of a technique to measure bone aluminum content using neutron activation analysis. *Phys. Meas.* **14,** 327–335.