Applied Radiation and Isotopes 95 (2015) 114–121

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

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

Standardisation of ^{223}Ra by liquid scintillation counting techniques and comparison with secondary measurements

John Keightley*, Andy Pearce, Andrew Fenwick, Sean Collins, Kelley Ferreira, Lena Johansson

National Physical Laboratory, Hampton Road, Teddington, Middlesex TW11 OLW, UK

HIGHLIGHTS

- An aqueous solution of ^{223}Ra chloride was standardised by liquid scintillation counting.
- CIEMAT/NIST efficiency tracing and Digital Coincidence Counting were utilised.
- Calibration factors for a variety of radionuclide calibrators were calculated.
- A discrepancy of around 9% was identified utilising existing published calibration factors.
- γ-spectrometry measurements exhibited a large spread (18.3%) in the individual activity estimations using published γ-emissions.

ARTICLE INFO

Article history:
Received 30 June 2014
Received in revised form
10 October 2014
Accepted 10 October 2014
Available online 23 October 2014

Keywords:
Ra-223
Calibration figure
Dial setting
Radioactivity
Primary standardisation
Liquid scintillation counting
Digital coincidence counting
DCC

ABSTRACT

An aqueous solution of ^{223}Ra chloride in equilibrium with its decay progeny was standardised by liquid scintillation counting techniques. Since secular equilibrium with the decay progeny of ^{223}Ra had been established by the time of measurement, the apparent detection efficiency of ^{223}Ra was approximately 6 and was determined by both the CIEMAT/NIST efficiency tracing technique and the 4π(LS)-γ digital coincidence counting techniques. The results obtained were compared with γ-spectrometry and ionisation chamber measurements. Whilst the γ-spectrometry measurements were in agreement (albeit exhibiting a large spread (18%) in the individual activity estimations using the main γ-emissions), a significant discrepancy of the order of 9% was identified between the liquid scintillation counting results and those obtained using published calibration factors for a variety of radionuclide calibrators.

1. Introduction

Since radium exhibits similar chemical properties to calcium, the short-lived α-emitting radioisotope ^{223}Ra exhibits elevated uptake in regions of the body undergoing new bone formation. Radium-223 has recently been utilised (in the form of $^{223}RaCl_2$) to treat skeletal metastases associated with advanced castration-resistant hormone refractory prostate cancer in a series of clinical trials (Parker et al., 2013a; Parker et al., 2013b, Michalski et al., 2013; Nilsson et al., 2013) and has been approved for use in the USA by the Food and Drug Administration in May 2013 (FDA, 2013). In November 2013, the European Commission granted marketing authorisation for the use of $^{223}RaCl_2$ in Europe following a positive recommendation from the European Committee for Medicinal Products for Human Use in September 2013 (EMA/CHMP, 2013).

In order to correctly calculate the dose delivered to patients, accurate measurements of administered activity are required and these are typically achieved in hospitals via the use of radionuclide calibrators (IAEA, 2006; NPL, 2006; Zimmerman and Judge, 2007).

The aim of the work reported here was to support operators of radionuclide calibrators in the UK by providing estimations of ^{223}Ra calibration factors for some commonly used radionuclide calibrators, comparing these results to the previously published calibration factors from which (to date) calculation of the administered activity of ^{223}Ra to patients have been based (Bergeron et al., 2010), and instigating a new calibration service for user-supplied solutions of this radionuclide.

The first step in achieving these aims was to obtain an accurate primary standardisation of a solution of ^{223}Ra to facilitate the

* Corresponding author. Tel.: +44 208 943 6398.
E-mail address: john.keightley@npl.co.uk (J. Keightley).

http://dx.doi.org/10.1016/j.apradiso.2014.10.009
0969-8043/

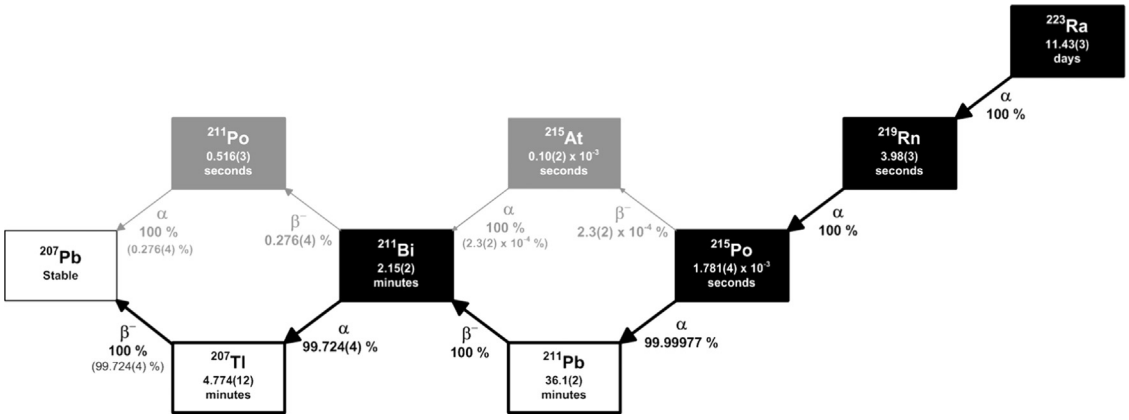

Fig. 1. Simplified schematic of the decay chain for ^{223}Ra and its progeny. Half-lives and branching data are taken from Kellett and Nichols (2011). The main decay path is indicated with black bold arrows. Isotopes undergoing α-decay are indicated in black boxes, and those undergoing β-decay in white boxes with a bold border. Where branching occurs, the smallest branch is indicated in a grey box (and the overall branching relative to ^{223}Ra decay is given in parentheses).

calibration of a suite of instruments at NPL. Details of the calibration of the ionisation chambers will be reported in detail separately, only the figures are reported here.

Radium-223 decays via a series of α and β emitting progeny to stable ^{207}Pb as shown in Fig. 1. All the decay progeny are relatively short-lived with half-lives of less than an hour, thus the standardisation of ^{223}Ra in isolation from the decay products was not considered as a viable option. The first decay product, ^{219}Rn, is a noble gas with a half-life of approximately 4s, and standardisation techniques in which the sample remained in liquid form were preferred to avoid problems with the loss of ^{219}Rn and subsequent short-lived contamination of counting equipment. The techniques selected were efficiency-traced liquid scintillation counting with a commercial scintillation counter (the CIEMAT/NIST technique; Broda et al., 2007) and 4π liquid scintillation–γ digital coincidence counting (Keightley and Watt, 2002), (Keightley and Park, 2007) utilising the computer discrimination technique for efficiency variation detailed in Smith (1975) and Smith (1987).

A similar programme of work has recently been undertaken at NIST (Cessna and Zimmerman, 2010) in which discrepancies were identified between liquid scintillation counting measurements and γ-spectrometry. Therefore, samples were also measured by γ-spectrometry with the aim of investigating such discrepancies and collecting a data set suitable for determining new γ-photon emission probabilities. The γ-emission probability measurements are ongoing and results will be reported separately.

2. Source preparation

The active material was received from Algeta ASA (Norway) with a nominal activity of 50 MBq $^{223}RaCl_2$ in 10 mL of aqueous solution, containing sodium citrate as a pH buffer. Following earlier (unpublished) experiences at NPL with $^{223}RaCl_2$ in a similar format, the material was diluted with an aqueous solution of hydrochloric acid to reduce the risk of precipitation or other losses from solution and any associated loss of activity. The format of the diluted material was nominally 3 MBq g^{-1} in an aqueous solution of 1 M HCl. Aliquots were dispensed to various ISO ampoules (BS EN ISO 9187-2, 2010) in order to calibrate the NPL secondary standard ionisation chambers, enabling future provision of accurate and traceable secondary standardisations of ^{223}Ra as required by the UK user community.

The stock solution was diluted further to a nominal activity concentration of 50 kBq g^{-1}. This diluted solution was dispensed to sixteen 34 mL Wheaton-type liquid scintillation vials with the compositions given in Table 1 (Sets A, B, C … etc), and to three 2 mL ISO ampoules (BS EN ISO 9187-2, 2010) for γ-spectrometry measurements. The gravimetric dilution factor was confirmed by both ionisation chamber and γ-spectrometry measurements of matched ampoules at each dilution level.

In order to minimise the risks of emanation of the gaseous ^{219}Rn, the glass screw threads on the liquid scintillation vials were wrapped with PTFE tape prior to adding the vial caps.

3. Efficiency tracing measurements

All efficiency tracing measurements were performed on a Packard Tricarb 2700TR liquid scintillation counter. The resolving time of the counter was increased from the default 18 to 50 ns in order to ensure that the majority of the decays depopulating the 15 ns excited level of ^{219}Rn occur within the resolving time. The temporal correlations between the decays of ^{219}Rn and its short-lived daughter ^{215}Po (half-life of 1.781 ms) creates an enhanced loss of ^{215}Po counts within the counter dead time following registration of a ^{219}Rn decay. This problem is common to both the CIEMAT/NIST and 4π(LS)-γ coincidence counting techniques, and a discussion on this issue is given in the section on the latter.

The delay-before-burst (DBB) setting, which is associated with background suppression by pulse shape analysis, was increased from the default 75 to 800 ns, following observations at NPL that non-linear behaviour of the apparatus may result from use of the default value. Liquid scintillation (LS) vials (Set C) were counted three times over a one month period to confirm the stability of the samples whilst vials from Set D (the tritium tracer) were counted twice over a shorter period of a few days. Vials from Set E were counted alongside Sets C and D to allow background corrections to be made. Once the stability had been confirmed, varying amounts of 10% (v/v) nitromethane in ethanol were added to each vial to change the level of chemical quench in each set of vials. After quenching, the detection efficiency of ^{3}H varied between 31 and 44%.

The LS counting efficiency was determined with the well-established CIEMAT/NIST standardisation technique (Broda et al., 2007). It was necessary to determine the efficiency for each decay product and perform a summation in order to obtain a combined efficiency for the ^{223}Ra in equilibrium. For the α emissions, a fixed efficiency of 0.998 ± 0.002 ($k=1$) was assumed; this corresponds to a detection probability of approximately unity for α-particles depositing significant energy in the cocktail with 0.2% of all α events being 'lost' to the wall effect as estimated by Cassette (2001). It should be noted that more recently the wall effect was estimated to be considerably lower (Fitzgerald and Fourney, 2010),