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Assessing the ^{210}At impurity in the production of ^{211}At for radiotherapy by ^{210}Po analysis via isotope dilution alpha spectrometry

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Abstract

A method for assessing the impurity ^{210}At in cyclotron-produced ^{211}At via isotope dilution alpha spectrometry is presented. The activity of ^{210}At is quantified by measuring the activity of daughter nuclide ^{210}Po. Counting sources are prepared by spontaneous deposition of Po on a silver disc. Activity of ^{210}At (at the time of ^{210}Po maximum activity) is found to be 83.5 ± 9.0 Bq, corresponding to an atom ratio (^{210}At:^{211}At at the time of distillation) of $0.010 \pm 0.007\%$ ($k = 2$). The method produces high-quality alpha spectra, with baseline alpha-peak resolution and chemical yields of greater than 85%.

Keywords: Astatine-211; Cyclotron production; Radiotherapy; Impurity analysis; Astatine-210; Polonium-210; Isotope dilution; Alpha spectrometry

1. Introduction

The use of α-emitters for radiotherapy of certain cancers continues to receive considerable attention (Yordanov et al., 2001; Hermanne et al., 2005) because of the relatively high linear energy transfer (LET) of alpha particles in human tissue (Stavroula et al., 2004; Apostolidis et al., 2005). Astatine-211 is particularly attractive due to a relatively short half-life (7.2 h), which is nonetheless long enough to allow high tumour uptake (Schwarz et al., 1998). In addition, the branching decay scheme yields not only α-emissions of 5.87 and 7.45 MeV (^{211}Po daughter), but also K X-ray emissions which may allow for external imaging of ^{211}At tissue distributions.

Although the use of ^{211}At is promising for radiotherapy applications, co-production of ^{210}At is known to occur in the production process (Schwarz et al., 1998). Although the co-production of ^{210}At is small (at beam energies of <30 MeV) and the half-life of this radionuclide is relatively short (8.1 h), the decay of ^{210}At leads primarily to the α-emitting daughter ^{210}Po ($E_\alpha = 5.304$ MeV; Fig. 1), which reaches a maximum theoretical activity at approximately 70 h post-production and then decays with a relatively long half-life (for most radiotherapeutic applications) of 138 d (Fig. 2). In this paper, a method is presented for estimating the ^{210}At impurity in the production of ^{211}At by analysis of ^{210}Po via isotope dilution alpha spectrometry.

2. Materials and methods

2.1. Production of ^{211}At (^{210}At)

The ^{211}At material was prepared at the cyclotron facilities at the National Institutes of Health (NIH), Bethesda, MD, USA via the ^{209}Bi(α, 2n)^{211}At reaction and was achieved by irradiation with an α-beam from a CS-30 Cyclotron (The Cyclotron Corporation, Berkeley, CA USA). A radiolabeling procedure was performed to ensure that At would be present in a bound form, which is relevant to current clinical procedures and minimizes volatility. The bound form employed in this

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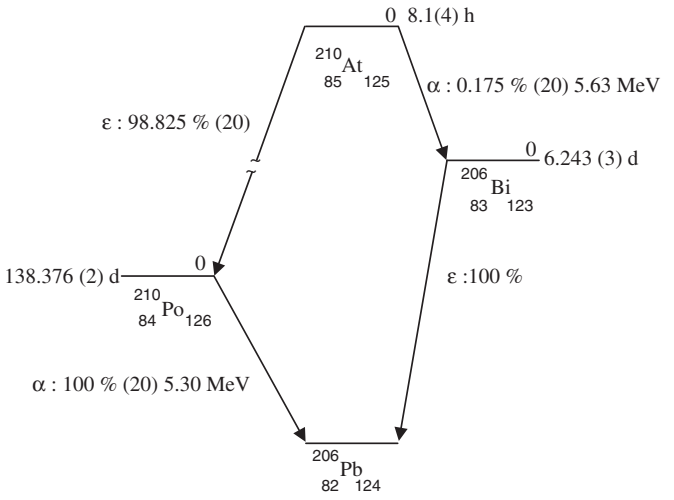

Fig. 1. Decay scheme for ^{210}At. Data are obtained from ENSDF (Chu et al., 1999).

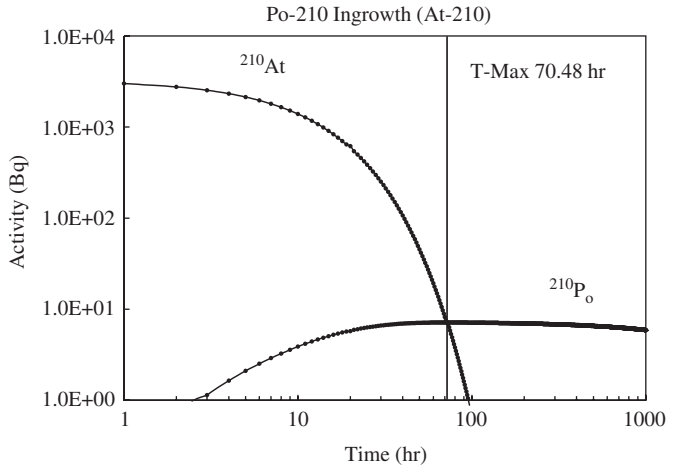

Fig. 2. Theoretical decay/ingrowth of ^{210}At/^{210}Po.

case is *N*-succinimidyl *N*-(4[^{211}At]astatophyenethyl)-succinamate, SAPS). The resulting 1-mL solution was transferred to a screw-top 2-mL v-vial for transport to NIST for dilution and radioactivity measurements. A detailed description of the production techniques is presented elsewhere (Schwarz et al., 1998).

2.2. Gravimetric dilutions and preparation of alpha counting sources

Gravimetric dilutions of the [^{211}At]-SAPS solution were performed using a solution of phosphate buffered saline (PBS, 0.15 M sodium chloride NaCl, 0.15 M ammonium acetate $NH_4C_2H_3O_2$), supplied by NIH. Polonium-210 analyses were performed on a secondary dilution of the [^{211}At]-solution provided to NIST by NIH. Solution transfers to glass ampoules were performed using high-density polyethylene pycnometers (Canus Plastics, Ottawa, Ontario, Canada) to minimize effects of evaporation. Gravimetric determinations were performed by a difference methodology by mass measurements of pycnometers before and after transfers. Confirmational gravimetric measurements were performed by before and after measurements of the glass ampoules with each transfer of activity solution and diluent. A six-decimal-place model M5 microbalance (Mettler-Toledo, Toledo, OH, USA) was employed for measurements with appropriate air-buoyancy and balance-tare corrections applied. The resulting uncertainty from balance measurements is estimated to be approximately 0.1% (coverage factor $k = 2$).

2.3. Radioactivity measurements of ^{210}Po via isotope dilution alpha spectrometry

Sufficient time (3 weeks) was allowed following production such that the ^{211}At and ^{210}At that were present had decayed to negligible amounts (Fig. 2). Based on previous published results (Schwarz et al., 1998), the ^{210}At activity produced under the cyclotron conditions used would be on the order of about 0.01% of the produced ^{211}At. The resulting production of the daughter radionuclide ^{210}Po can be expected to reach a maximum (assuming direct production of ^{210}Po via the irradiation of the ^{209}Bi material is negligible) at approximately 70.5 h post-production (Fig. 2). Based on preliminary measurements of the ^{211}At solution provided by NIH, the anticipated concentration of ^{210}Po, at the time of sample preparation of the ^{210}Po samples for analysis, was estimated to be approximately 32 Bq g^{-1}.

2.4. ^{209}Po tracer solution

Isotope dilution techniques were carried out using a ^{209}Po tracer solution (NIST Standard Reference Material (SRM) 4326; massic activity 85 Bq g^{-1}, Hutchinson et al., 1995; Reference Time March 14, 1994 12:00 Noon EST). The SRM ampoule contains the ^{209}Po in nominally 2 M hydrochloric acid (HCl), with minor constituents nitric acid (HNO_3, $< 3 \times 10^{-3}$ M) and a negligible concentration of the α-emitting radionuclide ^{208}Po ($0.106 \pm 0.017\ \alpha\ s^{-1}\ g^{-1}$ or 0.1% as of the reference date and time, $E_\alpha = 5.115$ MeV, $I_\alpha = 99.9954 \pm 0.0007\%$, $T_{1/2} = 2.898$ a, Hutchinson, et al., 1995; Chu et al., 1999).

2.5. Preparation of samples for alpha counting of ^{210}Po

Reagents employed were American Chemical Society (ACS) or reagent grade. A total of five ^{210}Po samples and three blanks were measured. Background measurements of the detectors were conducted prior to source counting. Appropriate volumes of sample solution and the ^{209}Po tracer were transferred and weighed to reaction cells designed for spontaneous deposition of Po. For this purpose, reaction cells were prepared consisting of 30-mL Nalgene® low-density polyethylene-reagent bottles (Fisher Scientific, Pittsburg, PA, USA), Teflon™ tape, and