



High efficiency production and purification of ^{86}Y based on electrochemical separation

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ABSTRACT

As an intermediate half-life positron emitter ^{86}Y is an attractive radioisotope for positron emission tomography (PET) studies, particularly for patient specific dosimetry planning of ^{90}Y -based radiotherapy procedures. It can be conveniently produced by a small-sized cyclotron via the $^{86}\text{Sr}(p,n)^{86}\text{Y}$ nuclear reaction. The optimization of the electrochemical separation of ^{86}Y from the target material and its purification was done by modeling the whole production cycle using ^{90}Y . The radionuclide was isolated using four electrodes in two electrolytic steps. In the first step two Pt plate anodes and a Pt Winkler cathode were used and the electro-deposition yield was determined in constant current mode of operation. In addition, the influence of pH on the efficiency of this first step was investigated. The second electrolysis, with Winkler electrode as anode and a Pt wire as cathode, was also performed in constant current mode of operation. The kinetics of recovery of the deposited activity on the Pt wire was investigated in acidic solutions. The optimized electrochemical method was then applied for ^{86}Y separation and purification. This modified procedure was proved to be faster and simpler than the previously proposed electrochemical techniques and is more convenient for automation of the routine production of ^{86}Y .

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1. Introduction

Due to its availability and favorable radio-physical properties, ^{90}Y ($T_{1/2} = 64.24$ h, $\beta^- = 100\%$, $\beta_{\text{max}}^- = 1.3$ MeV) is today widely used in targeted radioimmunotherapy (Oyen et al., 2007). However, being a pure β^- emitter it is not applicable for tomography studies. β^+ -emitting radioisotopes linked to the same targeting molecule in combination with positron emission tomography (PET) can provide the necessary information on biodistribution and kinetics required for dose planning, due to the quantitative nature of PET imaging. ^{86}Y ($T_{1/2} = 14.7$ h, $I_{\beta^+} = 33\%$, $E_{\beta^+}^{\text{max}} = 1.2$ MeV) is reported to be suitable for accurate dosimetry planning of ^{90}Y -labeled radiopharmaceuticals (Herzog et al., 1993; Rösch et al., 1996, 1999; Pentlow et al., 2000). This radionuclide can be produced via the (p,n) or (d,2n) nuclear reaction on enriched ^{86}Sr , ($^3\text{He},2n$) on natural rubidium, (p,3n) on enriched ^{88}Sr , or (d,x) reaction on natural zirconium (Rösch et al., 1993a,b; Sachdev et al., 1967; Tarkanyi et al., 2004). However, only the $^{86}\text{Sr}(p,n)^{86}\text{Y}$ reaction can be applied at small-sized cyclotrons. The target material is typically enriched $^{86}\text{SrCO}_3$ or ^{86}SrO . After irradiation, ^{86}Y is separated from the target material and purified in order to accomplish efficient radio-labeling. Based on a procedure

described earlier (Lange et al., 1957; Herrmann, 1958) an electrochemical method was developed recently (Reischl et al., 2002; Yoo et al., 2005) providing no-carrier-added ^{86}Y of high purity. As compared to other separation techniques such as the combination of co-precipitation and cation-exchange chromatography (Rösch et al., 1993b) and ion specific resin chromatography (Finn et al., 1999), or paper filtration from alkaline solution (Avila-Rodriguez et al., 2008), the electrochemical method is much easier to handle. In just two electrolytic steps, ^{86}Y can be separated from the target material and produced in a form suitable for labeling bioactive molecules with high specific activity and high concentration. Modifying and optimizing the previously reported methods, an effective procedure for isolation, purification and concentration of ^{86}Y is advanced. The critical phases of the process were studied using ^{90}Y and the optimal conditions were verified in real production runs resulting in high quality ^{86}Y preparations.

2. Experimental

2.1. Materials and equipment

^{90}Y was used as chloride form in 0.04 M HCl (YTRACIS, radiochemical purity $\geq 97\%$) obtained from CIS Bio International

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(France). Enriched $^{86}\text{SrCO}_3$ with an isotopic composition of ^{84}Sr (0.00), ^{86}Sr (95.60), ^{87}Sr (1.07), ^{88}Sr (3.33), was supplied by Isoflex (Russia). The sum of the metal impurities, such as Na, Mg, Al, Ca, Cr, Fe, Cu and Pb was specified to be below 0.05%. All reagents used for electrolysis (HCl, HNO_3 , NH_4OH) and $^{\text{nat}}\text{SrCO}_3$ were purchased from Merck (Germany), indicated as highly pure. Water was distilled and deionized by Milli-Q filtration system ($18.3\text{ M}\Omega\text{ cm}^{-2}$), Barnstead (USA).

Platinum target disks ($\varnothing 24 \times 1.90\text{ mm}$ with a $\varnothing 6 \times 1.5\text{ mm}$ cylindrical depression in the center of the disk, made of 99.9% pure Pt) as well as aluminum disks ($\varnothing 24 \times 2\text{ mm}$) were obtained from Hans Wälischmiller GmbH (Germany). Pt plates ($0.1 \times 10 \times 100\text{ mm}^3$), Pt Winkler electrode (150 mm total length, 46 mm spiral length, 4.5 mm internal diameter, 6.7 mm external diameter, 5.5 cm^2 effective surface area in contact with the electrolyte) and Pt wire ($\varnothing 1 \times 180\text{ mm}$, 1.6 cm^2 effective surface area in contact with the electrolyte) were purchased from Ögussa (Austria). The glass beakers used as electrolytic cells ($\varnothing 38 \times 70\text{ mm}$, 36 mm internal diameter) were obtained from Schott (Germany), while the electrolysis was carried out using a Thurlby Thandar Instruments stabilized power supply (UK) in constant current mode of operation.

Measurements of ^{90}Y activity were done by a COBRA II Auto-Gamma detector equipped with a $1.5''$ NaI(Tl) crystal (Packard, USA). The pH of solutions was controlled by a MP 225 pH meter (Mettler, Switzerland).

Irradiations were done by proton beams using an IBA Cyclone 18/9 cyclotron at the Cyclotron Unit of the University Hospital of Geneva (Geneva, Switzerland). The yield of ^{86}Y and the amount of radionuclide impurities were determined based on γ -spectrometric measurements. For this purpose a Ge–Li-detector combined with a Canberra Multichannel Gamma Analyzer was used (Canberra, USA). The beam profile was determined by autoradiographic analysis of aluminum plates irradiated in the same geometry as the production targets by a Packard Cyclone Imager (Perkin Elmer, USA).

2.2. Electrolytic cell with four electrodes

The electrochemical cell is schematically presented in Fig. 1. The Winkler electrode is inserted into a Teflon cup and tightly fixed. The platinum wire is dragged through a removable Teflon cylinder holder and placed along the axis of the Winkler electrode. Two platinum plates are embedded 5 mm apart from the spiral and slightly bended at the top. Using “crocodile” sticks, all four electrodes are connected to the power supply. Ventilation exit is provided by a 3 mm hole in the Teflon cup. The electrode assembly is placed into a standard 50 cm^3 glass beaker. The electrodes were immersed into the electrolyte to a depth of 50 mm.

2.3. Electro-deposition of ^{90}Y

Solutions subjected to electrolysis were prepared in a glass beaker by dissolving 50 mg of $^{\text{nat}}\text{SrCO}_3$ in 3 ml of 2.8 M HNO_3 . After dilution with 42 ml of distilled water, ^{90}Y was added using a micropipette in a volume containing activity up to 40 kBq. The pH of solutions was adjusted to 2.8 by adding 5 ml of 3% NH_4OH . The Teflon cup with electrodes was inserted into the electrochemical cell, the Winkler electrode was connected to the power supply as cathode and the platinum plates as anodes and the electrolysis was performed at 30–3000 mA in constant current mode of operation for different time points. In order to determine the influence of the pH on deposition yield of ^{90}Y on the Winkler electrode, the electrolysis was carried out at 2000 mA in constant current mode of operation in a range of pH 1–9. The pH of the

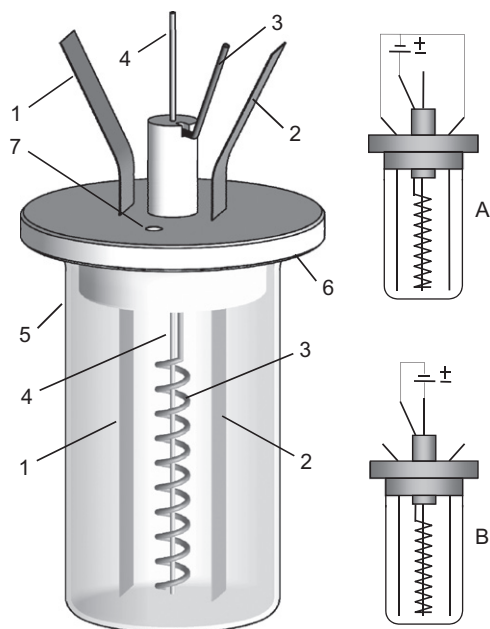


Fig. 1. Electrochemical cell used for the electrochemical separations: 1, 2—Pt plate electrodes, 3—Pt Winkler electrode, 4—Pt wire electrode (for the dimensions of the electrodes see Section 2.1), 5— 50 cm^3 glass beaker, 6—Teflon cap and 7—ventilation opening in the cap. A: wiring during the electrochemical deposition of yttrium on the Winkler electrode and B: wiring during the deep purification of yttrium, i.e. its deposition on the Pt wire electrode.

solutions was adjusted by adding nitric acid and/or ammonium hydroxide while it was measured by the pH meter.

After the first electrolysis the electrode assembly was pulled out from the electrochemical cell with current still on and placed into 50 ml of 0.0035 M HNO_3 . The Winkler electrode (previously used as cathode) was now connected as the anode and the platinum wire was connected as the cathode. During the second electrolytic step ^{90}Y was completely re-dissolved from the Winkler electrode and deposited on the platinum wire. The optimization of this process was carried out by varying the current from 200 to 600 mA and varying the duration of electrolysis. Upon completion of the electrolysis, the electrodes were carefully removed from the electrochemical cell without disconnecting them from the power supply. The kinetics of both of these electrochemical processes was monitored online by taking $20\ \mu\text{l}$ aliquots of the electrolytes at certain time intervals and measuring their activity content by the COBRA II Auto-Gamma detector.

After switching power off, the re-deposited ^{90}Y was recovered by inserting the Pt wire into the barrel of a $250\ \mu\text{l}$ syringe filled with $200\ \mu\text{l}$ of recovery solution. The efficiency of ^{90}Y recovery was investigated using 0.001, 0.005, 0.01, 0.05, 0.1 and 1 M HCl or HNO_3 as solvents and measuring the activity content of the whole solvent expelled from the syringe.

2.4. Target preparation

60 mg of $^{86}\text{SrCO}_3$ powder was manually pressed into the $\varnothing 6 \times 1.5\text{ mm}$ cylindrical depression in the target disk using an aluminum piston. Then, the powder was additionally pressed at 4.3 MPa for 30 min employing specially designed aluminum moulds, resulting in a 212 mg cm^{-2} $^{86}\text{SrCO}_3$ target.

The Pt disk, with compressed strontium carbonate was then inserted into the COSTIS target station described earlier (Čomor et al., 2002, 2004). In order to prevent possible losses of target material due to mechanical stress during the irradiation, the front

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