



# Production of Positron-emitting $^{110m}\text{In}$ via the $^{110}\text{Cd}(^3\text{He}, 3n)^{110}\text{Sn} \rightarrow ^{110m}\text{In}$ Process

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Positron-emitting  $^{110m}\text{In}$  was produced in a two-step process. Irradiation of highly enriched  $^{110}\text{Cd}$  with  $^3\text{He}$ -particles over an energy range of 36–25 MeV led to the formation of  $^{110}\text{Sn}$ , which after its fast radiochemical separation from the target material was used to prepare a  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  generator. The radiochemical separation consisted of a thermochromatographic volatilization of  $^{110}\text{SnCl}_4$  from metallic  $^{110}\text{Cd}$  targets in a small quartz apparatus at  $800 \pm 10^\circ\text{C}$  within 20 min, followed by its removal from the quartz tube via dissolution in hydrochloric acid. The  $^{110}\text{Sn}$  separation yield was > 98% and the fraction contained only  $< 10^{-4}\%$  of the target material. The solution was then transferred to a small Kieselgel 40 column to prepare a  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  elution generator. The  $^{110m}\text{In}$  was eluted quantitatively within 1 ml of 0.02 M hydrochloric acid. The only detectable isotopic impurity was  $^{111}\text{In}$ , generated from the co-formed  $^{111}\text{Sn}$ -contamination. Its percentage decreased from about 0.8% at 1 h after the end of bombardment to  $< 0.01\%$  at 7 h. The final solution was free of any traces of Cd. In the first experiments more than 15 mCi of  $^{110m}\text{In}$  was delivered per generator. Copyright © 1997 Elsevier Science Ltd

## Introduction

Most of the isotopes routinely applied in nuclear medicine for clinical diagnosis, especially via single photon emission tomography (SPET) are single photon-emitting isotopes of metals. The corresponding radiometal-labelled radiopharmaceuticals provide important diagnostic information. For some special purposes, however, more quantitative data are needed, which are available in general using positron emission tomography (PET). One approach consists of the incorporation of a positron-emitting radioisotope of the same element as that used in the SPET radiopharmaceutical. This bridging of SPET and PET may provide more quantitative information on the diagnostic potential of a given radiopharmaceutical as well as on the *in vivo* quantification of the uptake kinetics of that radiopharmaceutical in individual patients.

Some of these SPET–PET pairs such as  $^{123}\text{I}$ – $^{124}\text{I}$  (see for example Langen *et al.*, 1990), have already been studied; others such as  $^{99m}\text{Tc} \rightarrow ^{94m}\text{Tc}$  (Nickles *et al.*, 1993; Rösch *et al.*, 1994) or  $^{123}\text{I} \rightarrow ^{120}\text{I}$  (Zweit *et al.*, 1995) are only just coming under investigation.

Another pair available for bridging SPET and PET is  $^{111}\text{In} \rightarrow ^{110m}\text{In}$ . Various radiopharmaceuticals labelled with the single-photon emitter  $^{111}\text{In}$  ( $t_{1/2} = 2.81$  d) are used in the diagnosis of cancer and other diseases. In particular for receptor-type studies, the quantification of the uptake of the pharmaceutical via PET measurements may be important. The corresponding indium isotope of choice is  $^{110m}\text{In}$ . It has a half-life of 69.1 min and decays 62% via positron emission with  $E_{\beta^+ \text{ max}} = 2.3$  MeV.

The direct production of  $^{110m}\text{In}$  via  $^{110}\text{Cd}(p,n)$ -,  $^{107}\text{Ag}(\alpha, n)$ - and  $^{109}\text{Ag}(^3\text{He}, 2n)$ -processes leads to the co-formation of the isomer  $^{110g}\text{In}$  ( $t_{1/2} = 4.9$  h). This co-formation increases with increasing projectile energy. Isotopically pure  $^{110m}\text{In}$  could only be prepared via the generator system  $^{110}\text{Sn}$  ( $t_{1/2} = 4.11$  h; EC)  $\rightarrow ^{110m}\text{In}$ . The principal routes for producing  $^{110}\text{Sn}$  consist of the following reactions: (i)  $^{108}\text{Cd}(\alpha, 2n)$ ; (ii)  $^{110}\text{Cd}(^3\text{He}, 3n)$ ; and (iii)  $^{113}\text{In}(p, 4n)$ . Nuclear reaction cross-section data for route (ii) over the  $^3\text{He}$  particle energy range of 27–16 MeV in irradiation of  $^{nat}\text{Cd}$  have been reported (Szelecsényi *et al.*, 1991), and the first experiments on the production of  $^{110m}\text{In}$  via the generator route have been performed by irradiating natural indium at  $E_p = 80$  MeV (Lundqvist *et al.*, 1991).

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The aim of the present work was to determine the production yield and the isotopic purity for route (ii), i.e. the  $^{110}\text{Cd}(^3\text{He},3\text{n})$ -process on enriched  $^{110}\text{Cd}$ . Moreover, a radiochemical separation should be developed which would lead to high yield and radiochemical purity of  $^{110}\text{Sn}$ , and allow a quantitative recovery and cyclic use of the highly enriched and rather expensive  $^{110}\text{Cd}$  material. Previous attempts to evaluate the production of  $^{110\text{m}}\text{In}$  via the  $^{110}\text{Sn} \rightarrow ^{110\text{m}}\text{In}$  generator system involved the separation of  $^{110}\text{Sn}$  either from macroscopic indium targets (Lundqvist *et al.*, 1991) or from cadmium targets (Szelecsényi *et al.*, 1991). Both groups applied wet chemical techniques using anion or cation exchangers and HBr or HF solutions, respectively, as eluents. Recently a direct separation of  $^{110\text{m}}\text{In}$  was reported by Lundqvist *et al.* (1995), making use of the diffusion of  $^{110\text{m}}\text{In}$  in metallic cadmium targets.

## Experimental

### Target material

In preliminary studies on chemical separations, Cd of natural isotopic composition was irradiated in the form of a foil or as CdO powder. The targets were prepared either by rolling metallic cadmium to thin foils (200 mg, foil diameter 13 mm, 0.14 mm thickness) or by pressing 200 mg of CdO powder at 10 ton/cm<sup>2</sup> to pellets (13 mm  $\varnothing$ , 0.17 mm thickness). However, 200 mg of highly enriched  $^{110}\text{Cd}$  ( $^{110}\text{Cd} = 91.5\%$ ,  $^{106}\text{Cd} = 0.02\%$ ,  $^{108}\text{Cd} = 0.05\%$ ,  $^{111}\text{Cd} = 4.00\%$ ,  $^{112}\text{Cd} = 1.99\%$ ,  $^{113}\text{Cd} = 0.76\%$ ,  $^{114}\text{Cd} = 1.45\%$ ,  $^{116}\text{Cd} = 0.21\%$ ) in the form of a foil was used in production runs for experiments. The latter target was prepared from metallic  $^{110}\text{Cd}$  by pressing. Uniformity of the target (foil diameter 13 mm, foil thickness 0.14 mm) was measured to be  $\pm 5\%$ .

### Irradiations

The targets were irradiated at the Jülich compact cyclotron CV28 with 36 MeV  $^3\text{He}^{2+}$  particles for 1 h at beam currents of 1–5  $\mu\text{A}$ . For some investigations

on the behaviour of radioindium alone, Cd and CdO targets were irradiated with 20 MeV protons to obtain the radioisotopes of indium via the  $^{110}\text{Cd}(p, xn)$  reactions.

The degradation of the  $^3\text{He}$  particle energy in the 200 mg Cd foils was calculated using the stopping powers by Williamson *et al.* (1966).

### Measurement of radioactivity

Table 1 summarizes the isotopes of tin and indium relevant to the study of  $(^3\text{He}, xn)$ -reactions on enriched  $^{110}\text{Cd}$ .

In general, a HPGe detector was used which was coupled to an EG&G ORTEC MCA plug-in card, connected to an IBM-compatible PC-AT. The peak area analysis was done using Maestro II MCA emulation software. The efficiency of the detector was determined using known standards supplied by the Physikalisches-Technische Bundesanstalt Braunschweig. The count rates were corrected for pile-up losses as well as for  $\gamma$ -ray abundances and the efficiencies of the detector. Since the distance between the sample and the detector was always  $> 10$  cm, the correction for real coincidence losses was negligible. For some qualitative measurements, well-type NaI detectors were used.

### Thermochromatographic isolation of $^{110}\text{Sn}$ from Cd targets

In experiments to study the different absorption temperatures of the chlorides formed within this separation scheme, initially a horizontal quartz tube ( $3 \times 300$  mm) was inserted into an electric resistance oven. The maximum oven temperature at the place of the irradiated target was varied between 600 and 1100°C, while a moderate flow of chlorine (10–20 ml/min) was led through the quartz tube. Experimental time was varied between 15 and 60 min. In these experiments about 5 mg of metallic cadmium or its oxide was used. Volatilization kinetics were measured on-line at the original place of the target material using a NaI detector. After the experiments, the distribution of the volatilized products along the

Table 1. Nuclear decay parameters of the relevant tin and indium<sup>a</sup> isotopes (Browne and Firestone, 1986)

Reaction	Product isotope (decay mode; half-life)	Major $\gamma$ -lines in keV (abundance)	Generated indium isotopes (decay mode; half-life)	Major $\gamma$ -lines in keV (abundance)
$^{110}\text{Cd}$ ( $^3\text{He}, 4\text{n}$ )	$^{109}\text{Sn}$ (EC; 18.0 min) (30%)	649.9 (28%); 1099.3 (30%)	$^{109\text{m}}\text{In}$ (IT; 1.34 min)	649.9 (93.7%)
$^{110}\text{Cd}$ ( $^3\text{He}, 3\text{n}$ )	$^{110}\text{Sn}$ (EC; 4.11 h)	283 (97.0%)	$^{109\text{g}}\text{In}$ (EC, 7.9% $\beta^+$ ; 4.2 h) $^{110\text{m}}\text{In}^a$ (EC, 62% $\beta^+$ ; 69.1 min)	203.3 (73.5%); 426.2 (4.23%); 657.8 (98%)
$^{110}\text{Cd}$ ( $^3\text{He}, 2\text{n}$ )	$^{111}\text{Sn}$ (EC; 35.3 min)	762.0 (1.44%); 1153.2 (2.7%)	$^{111\text{m}}\text{In}$ (IT; 7.7 min)	336.7 (87.0%); 171.3 (90.2%)
$^{112}\text{Cd}$ ( $^3\text{He}, 2\text{n}$ )	$^{113}\text{Sn}$ (EC; 115.1 d)	391.7 (64%)	$^{113\text{g}}\text{In}$ (IT; 2.81 d) $^{113\text{m}}\text{In}$ (IT; 1.66 h)	245.4 (94.0%); 391.7 (64.2%)

<sup>a</sup>The designation of the two isomers of  $^{110}\text{In}$  as  $^{110\text{m}}\text{In}$  for the 69 min, 62%  $\beta^+$ -emitting isomer and  $^{110\text{g}}\text{In}$  for the 4.9 h, 100% EC isomer is due to a 62 keV higher level of the positron emitting isomer; see De Frenne and Jacobs, 1992; Bertschy *et al.*, 1995.

inner surface of the quartz tube was measured  $\gamma$ -spectrometrically using Ge(Li)-detectors.

For the separation of high activities of radiotin from larger amounts of  $^{110}\text{Cd}$  targets in a production scale experiment a vertical quartz tube system was designed according to a prototype developed recently for the thermochromatographic separation of  $^{94m}\text{Tc}$  from  $^{94}\text{MoO}_3$  targets (Rösch *et al.*, 1994). It consisted of three quartz tubes of different diameters. After the separation the tubes were disconnected and analysed separately in order to determine the separation coefficients for all the three elements (Sn, In, Cd). The amount of cadmium in the separated radiotin fraction was determined via high resolution inductively coupled plasma source mass spectrometry (HR-ICP-MS).

#### $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$ generator system

Elution generators have been described for the  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  system (Szelecsényi *et al.*, 1991; Lundqvist *et al.*, 1991) as well as for the  $^{113}\text{Sn} \rightarrow ^{113m}\text{In}$  system. In the present work, small glass columns of 4 mm inner diameter were filled with Kieselgel 40 (37–70 mesh; Merck); bed length 50 mm. The column was conditioned by washing with 10 ml of 0.02 M HCl. The radiotin fraction was evaporated to dryness and redissolved in 1 ml of 0.02 M HCl. This solution was then transferred to a small Kieselgel 40 column. The column was subsequently washed with another 5 ml of 0.02 M HCl. While radiotin remained at the top of the column, all the radioindium isotopes (mainly  $^{111}\text{In}$ ) as well as traces of cadmium were washed from the column. Elution was performed at low pressure at a rate of about 0.5 ml per min.

#### Recovery of the enriched target material, $^{110}\text{Cd}$ , for cyclic use

In order to prepare new targets for further irradiations, the cadmium chloride is converted into the metal via electro-deposition. After dissolution of the condensed  $^{110}\text{Cd}$  chloride, the compound is converted into the sulphate. Electrolysis using this compound in an  $\text{H}_2\text{SO}_4\text{-Na}_2\text{SO}_4$  electrolyte in a PTFE device (volume 10 ml) at 100 mA provides > 99% deposition of  $^{110}\text{Cd}$  on an aluminium cathode within a few hours. The amorphous cadmium metal can be pressed easily into metallic foils, which are ready for further irradiations.

## Results and Discussion

#### Thick target yields of Sn-isotopes and isotopic composition of the radiotin

In the case of  $^{110}\text{Cd}$  targets weighing about 200 mg (foil diameter 13 mm, foil thickness 0.14 mm), the yield of  $^{110}\text{Sn}$  amounted to  $\approx 9 \text{ MBq}/\mu\text{Ah}$ . An extrapolation to 100% enrichment of  $^{110}\text{Cd}$  resulted in an expected yield of about  $75 \text{ MBq}/\mu\text{Ah}$ . No special

efforts were made to increase the accuracy of these data. This result, however, was fairly well reproduced in the irradiation of the 91.5% enriched  $^{110}\text{Cd}$  target at  $1 \mu\text{A}$ , which yielded  $81 \text{ MBq}$  ( $2.2 \text{ mCi}$ )  $^{110}\text{Sn}$  per  $\mu\text{Ah}$  at EOB. This represents an amount of  $20 \pm 5\%$  of the total radioactivity of the isotopes at EOB.  $^{109}\text{Sn}$ ,  $^{111}\text{Sn}$  and  $^{113}\text{Sn}$  represent  $17 \pm 5$ ,  $61 \pm 10$  and  $0.4 \pm 0.1\%$  of the total radioactivity at EOB, respectively. The percentage of  $^{111}\text{Sn}$  could be reduced by choosing a somewhat higher energy range instead of the one used here (36–25 MeV). However, cross-section data of the corresponding nuclear reactions over this energy range of the  $^3\text{He}$  particles have not been measured in detail hitherto.

#### Thermochromatographic separation of chlorides of radiotin and radioindium from macroscopic cadmium

The results of the basic thermochromatographic experiments using a horizontal quartz tube are illustrated in Figs 1 and 2. They represent distributions of the corresponding chlorides as generated in a  $\text{Cl}_2$  flow at  $T_{\text{max}} = 900^\circ\text{C}$  and 20 min experimental time, starting from either metallic cadmium or  $\text{CdO}$  targets. According to the thermal properties of the most probable chlorides of these elements, one would expect adsorption zones as follows:  $\text{CdCl}_2 \cdot x\text{H}_2\text{O}$  (macroscopic),  $T_{\text{sub}} = 568^\circ\text{C}$ ;  $\text{SnCl}_4 \cdot x\text{H}_2\text{O}$  (no carrier added—n.c.a.),  $T_{\text{ads}} < 80^\circ\text{C}$ ;  $\text{InCl}_3$  (n.c.a.),  $T_{\text{ads}} < 400^\circ\text{C}$ .

This was true for the cadmium chloride fraction, which was detected (via  $\gamma$ -ray spectrometry using the co-produced  $^{105,107}\text{Cd}$  isotopes) over a distance of 5–10 cm from the original place of the irradiated target material. This location corresponded to a temperature of  $580 \pm 120^\circ\text{C}$ . The temperatures of adsorption of radiotin correspond to the values derived from the boiling temperature of  $\text{SnCl}_4$ . However, in order to avoid a further transport of the n.c.a. radiotin tetrachloride and to focus the adsorption zone, quartz wool was inserted at the end of the quartz tube at a temperature between about 50 and  $20^\circ\text{C}$ . Some differences in the adsorption behaviour of the chlorides were observed at the position between 13 and 19 cm of the quartz tube (corresponding to temperatures of  $230 \pm 20^\circ\text{C}$ ). In the case of  $\text{CdO}$  targets, about 15–25% of the radiotin was adsorbed at this zone. For  $\text{Cd}^\circ$  as target, however, this fraction amounted to about 1% only. Thus the separation of radiotin from the cadmium targets was quantitative.

For radioindium, which was formed directly during the irradiation as well as via the decay of the corresponding tin isotopes, two zones of adsorption were observed. The fraction at higher temperature of  $230 \pm 20^\circ\text{C}$  can be easily attributed to  $\text{InCl}_3$ . Its amount is greater in the case of  $\text{CdO}$  targets than that in  $\text{Cd}^\circ$  targets. The major fraction, however, is adsorbed at a much lower temperature of about  $50^\circ\text{C}$ , or even less when no quartz wool was inserted into the quartz tube. This result is consistent with some

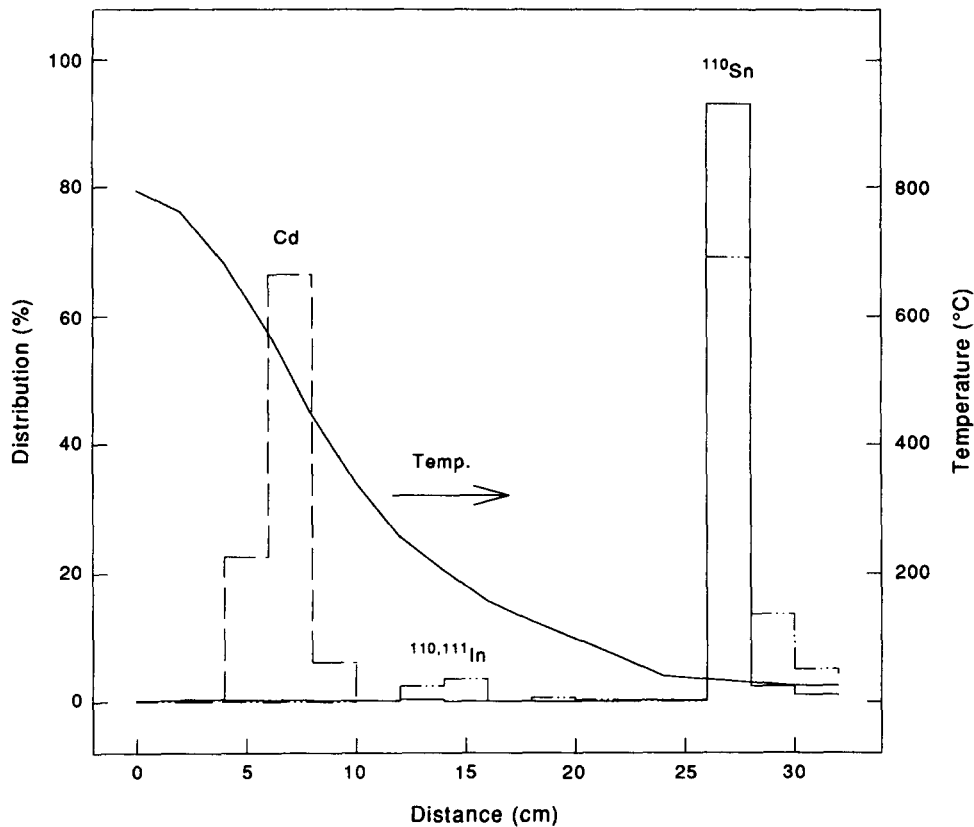


Fig. 1. Thermal adsorption of n.c.a. indium and tin chlorides as well as of macroscopic cadmium chlorides (all generated from  $\text{Cd}^\circ$  in a  $\text{Cl}_2$  flow at  $T_{\text{max}} = 900^\circ\text{C}$  and 20 min experimental time) on the inner surface of the horizontal quartz tube at different distances from the original target position. The temperature distribution within the quartz tube is also shown.

similar observations reported by Novgorodov *et al.* (1986), Rudstam and Grapengiesser (1973) and Westgaard *et al.* (1969), who also measured the thermochromatographic behaviour of indium chlorides. This fraction occurs in the case of n.c.a. radionuclidic species and is usually denoted as  $\text{InCl}_x$ . Schomäcker *et al.* (1988) even observed the coexistence of different chemical forms of n.c.a. radioindium chlorides. The species were dissolved in 0.05 M HCl and identified by electrophoresis.

No difference was observed for  $\text{Cd}^\circ$  and  $\text{CdO}$  targets regarding this zone of sublimation. The volatilization kinetics, however, were different. Whereas chlorination of metallic cadmium occurred fast and quantitatively, that of  $\text{CdO}$  target was slower. This was measured on-line with a NaI-detector, mounted at the place of the target material. Using this technique, the decrease in the overall radioactivity (represented by the sum of all the tin and indium isotopes produced in the nuclear reactions on  $^{115}\text{Cd}$ ) was detected as a function of experimental time. In these experiments, volatilization yields were determined for 15 min heating periods at various but constant temperatures.

In order to distinguish between the thermal release of radioindium and radiotin, the individual be-

haviour of radioindium was measured using cadmium targets after irradiation with protons. In these experiments almost all the radioactivity measured on-line by a NaI(Tl) scintillation detector is represented by radioindium. The targets were placed into the electric oven and the temperature was raised slowly from 0 to  $800^\circ\text{C}$  for  $\text{Cd}^\circ$  and a bit faster from 0 to  $860^\circ\text{C}$  for  $\text{CdO}$ . The time to reach the final temperature was 60 min in both cases. The results are summarized in Fig. 3 for two separate experiments on metallic cadmium and one experiment on  $\text{CdO}$ . For  $\text{Cd}^\circ$  the thermal release starts at about  $570 \pm 10^\circ\text{C}$ . Temperatures of about  $680 \pm 10^\circ\text{C}$  seem to be sufficient to volatilize radioindium quantitatively in relatively short experimental periods. For  $\text{CdO}$ , the release of radioindium only becomes measurable at about  $640 \pm 20^\circ\text{C}$ , and even at  $750^\circ\text{C}$  the kinetics of its thermal volatilization from  $\text{CdO}$  targets is slow. A similar volatilization kinetics was measured in the case of  $\text{Cd}^\circ$  or  $\text{CdO}$  targets immediately after irradiation with  $^3\text{He}$  particles, when the dominating radioactivity was represented by the radiotin isotopes.

In general, this behaviour is not due to the individual characteristics of radioindium (or radiotin) chlorides, but reflects the delayed chlorination

kinetics of metals ( $\text{Cd}^0$ ) and metal oxides ( $\text{CdO}$ ) when using a pure chlorine gas flow in the thermochromatographic studies. Although the volatilization kinetics were thus comparable for n.c.a. radioindium and radiotin chlorides, the separation efficiency is finally guaranteed by the different temperatures of adsorption of these compounds in different parts of the thermochromatographic apparatus.

#### Routine production of $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$

For routine production, the  $^{110}\text{Cd}$  target foil was irradiated in a  $2\pi$  water-cooled target system (cf. Blessing *et al.*, 1982) for 4 h at a beam current of  $3 \mu\text{A}$ . The on-target energy of the  $^3\text{He}$  particles was 36–25 MeV. For subsequent chemical processing, a vertical quartz apparatus was designed (Fig. 4). The irradiated target was transferred to the outer quartz tube (20 mm diameter, 200 mm long) with a small inlet for a low chlorine gas flow (15 ml/min). Thereafter, a twin quartz tube system was connected to it. This consisted of a middle tube for sublimation of the cadmium chloride and a small inner quartz tube, filled with quartz wool, to adsorb the volatilized  $^{110}\text{SnCl}_4$ . The whole device was inserted into an electric resistance oven having its maximum temperature of  $800 \pm 10^\circ\text{C}$  at the target position. In

experiments with  $T_{\text{max}} = 700^\circ\text{C}$  and  $T_{\text{max}} = 800^\circ\text{C}$  and heating periods of 10 and 20 min, respectively, the separation yields of radiotin and radioindium were investigated. The results are given in Table 2. Almost all of the  $^{110}\text{Sn}$ -chloride was transported relatively fast into the inner quartz tube at  $800^\circ\text{C}$ , and the process can be terminated after 20 min. The inner tube was then disconnected and radiotin dissolved from the quartz surface using 3–4 ml of warm 2 M HCl ( $90 \pm 5\%$  recovery). Subsequently, the separation yields of radiotin and radioindium were determined  $\gamma$ -spectrometrically and the cadmium content in this separated fraction was analysed using HR-ICP-MS.

The results on the thermal volatilization of radiotin, i.e. its quantitative separation from the cadmium chlorides and its adsorption on the inner quartz tube at temperatures close to room temperature, are consistent with those obtained in the model experiments using the horizontal quartz tube system. This was, however, not the case for the radioindium fraction.

The major adsorption of radioindium chlorides was expected to be within the inner quartz tube (see Fig. 1). However, in the vertical quartz tube system a surprisingly low amount of only about 10% of radioindium was co-adsorbed with the radiotin

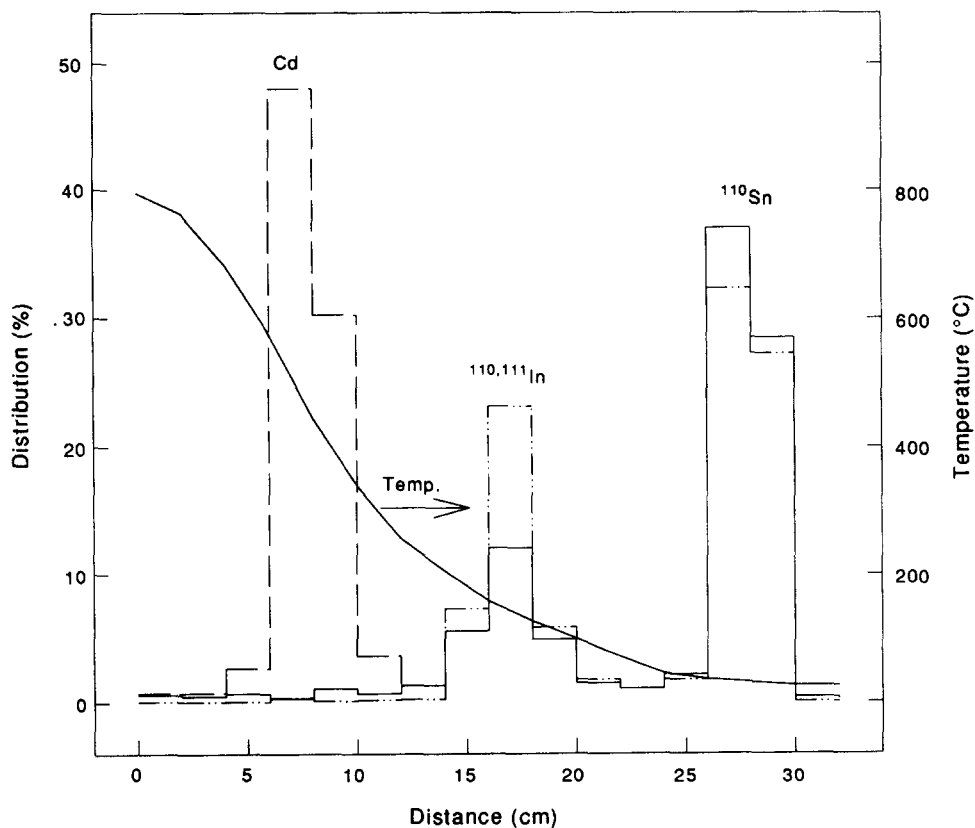


Fig. 2. Thermal adsorption of n.c.a. indium and tin chlorides as well as of macroscopic cadmium chlorides (all generated from  $\text{CdO}$  in a  $\text{Cl}_2$  flow at  $T_{\text{max}} = 900^\circ\text{C}$  and 20 min experimental time) on the inner surface of the horizontal quartz tube at different distances from the original target position. The temperature distribution within the quartz tube is also shown.

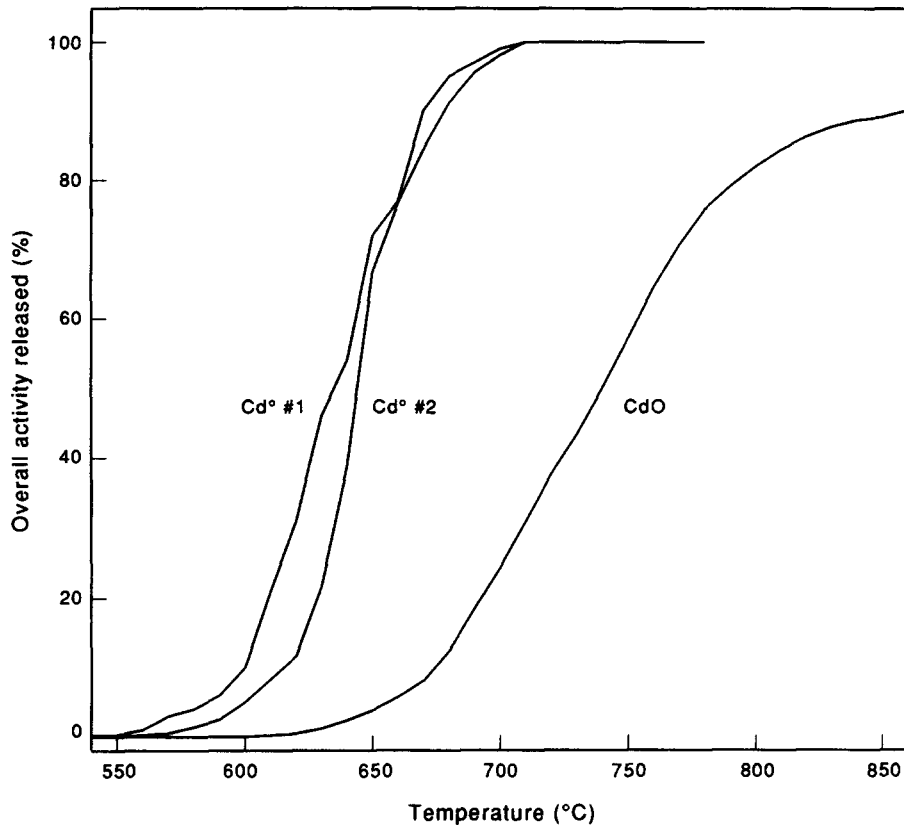


Fig. 3. Volatilization kinetics of radioindium from Cd° and CdO targets in a slow chlorine gas flow of 15 ml/min at  $T = 0\text{--}800^\circ\text{C}$  (Cd°) and  $T = 0\text{--}860^\circ\text{C}$  (CdO). In all experiments, a time of 1 h was fixed to reach slowly the maximum temperature. Cd° no. 1 and Cd° no. 2 denote two independent experiments.

fraction; the greater part being adsorbed with the sublimated cadmium chloride. Presumably, the increased gas volume of the vertical system ( $\approx 200\text{ cm}^3$ ) compared to that of the horizontal ( $\approx 2\text{ cm}^3$ ) provides a greater reservoir of air, which may create a characteristic pattern, more similar to that obtained for CdO targets. Additional contributing factors may be the formation of radioindium oxochlorides as well as the 'trapping' of radioindium species within the much higher mass of cadmium chloride (about 325 mg used in the production experiment as against about 8 mg cadmium chloride in the model experiments). Yet another possible explanation may lie in the increased amount of the cadmium target material which may lead to higher indium impurities, sufficient to form carrier-added  $\text{InCl}_3$  (see Westgaard *et al.*, 1969). Altogether, this effect is useful for the separation, since it facilitates the radiotin-radioindium separation, which would otherwise have to be managed subsequently in the preparation of the generator system.

#### Elution generator $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$

The generator was allowed to stand for a given period (in these experiments 40–60 min) to accumulate the daughter  $^{110m}\text{In}$  and was then eluted using

2 ml of 0.02 M HCl. The elution of the radioindium fraction was almost quantitative. Considering the half-lives of the two nuclides concerned, the relative maximum  $^{110m}\text{In}$  activities were accumulated at  $t_{\text{max}} = 2.94\text{ h}$  after every generator elution as derived from equation (1). For routine application the generator may be eluted in intervals of 2 h, thus reaching almost 90% of the corresponding maximum theoretical value, see equation (1):

$$t_{\text{max}}(^{110m}\text{In}) = \frac{1}{\lambda(^{110m}\text{In}) - \lambda(^{110}\text{Sn})} \ln \frac{\lambda(^{110m}\text{In})}{\lambda(^{110}\text{Sn})} \quad (1)$$

Due to the co-formation of  $^{111}\text{Sn}$  in the irradiation of  $^{110}\text{Cd}$  with  $^3\text{He}$  particles,  $^{111}\text{In}$  was also detected in the eluted fraction over the first few hours after EOB. However, because of the lower activity and shorter half-life of  $^{111}\text{In}$ , the  $^{111}\text{In}$  contamination in  $^{110m}\text{In}$  decreased significantly. The results are shown in Fig. 5, representing the percentage  $^{111}\text{In}$  impurity in  $^{110m}\text{In}$  for subsequent generator elutions. This radionuclidic impurity decreased continuously from about 0.76% at 1 h after EOB to about 0.008% at about 7 h after EOB, thereby reaching almost the lowest limit of detection.

Additionally, the amount of  $^{110}\text{Sn}$  co-eluted with  $^{110m}\text{In}$  was analysed  $\gamma$ -spectrometrically. On average a

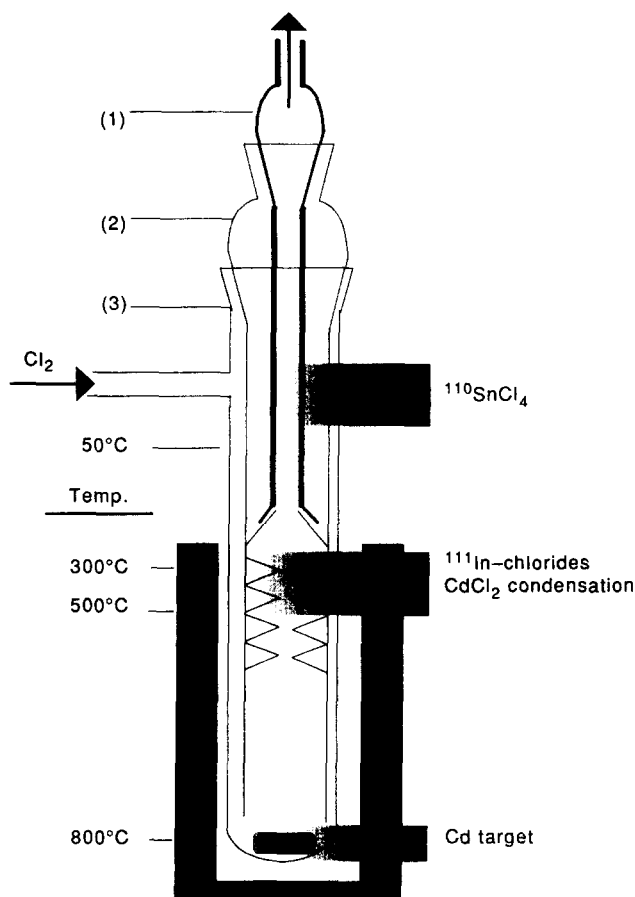


Fig. 4. Apparatus for separation of  $^{110}\text{Sn}$  from irradiated  $^{110}\text{Cd}$ . Indication of zones of  $^{110}\text{Sn}$  adsorption and  $^{110}\text{CdCl}_2$  condensation. (1) Inner quartz tube for the adsorption of  $^{110}\text{Sn}$ ; (2) quartz tube for the condensation of  $^{110}\text{CdCl}_2$  and the co-adsorption of radioindium chlorides; (3) outer tube ( $20 \times 200$  mm).

value of less than 0.003% was measured for the different elutions. This was almost the lowest detection limit. There was no  $^{110}\text{Sn}$ -breakthrough for the prepared column for at least up to 500 ml of elution volume. A  $\gamma$ -ray spectrometric analysis of the eluted indium fraction demonstrated the high isotopic purity of the positron-emitting indium isotope  $^{110m}\text{In}$ . All the lines detected were due to this isotope.

The amount of inactive cadmium in the eluted indium fractions was determined by HR-ICP-MS. On

average, about  $< 0.1$  ng of cadmium was found. This value, however, was already close to the detection limit of this method. It would correspond to a separation coefficient of  $> 2 \times 10^7\%$  with respect to the original mass of the  $^{110}\text{Cd}$  target used for the irradiation.

#### *Recovery of the enriched target material, $^{110}\text{Cd}$ , for cyclic use*

The recovery of the enriched and expensive target material is an important aspect of the routine

Table 2. Separation yields achieved using the vertical quartz apparatus after 10 or 20 min separation periods at  $T_{\text{max}}$  of 700 and 800°C and 15 ml/min chlorine gas flow

Nuclide	$T_{\text{max}}(^{\circ}\text{C})$	$t(\text{min})$	Distribution of chlorides in % in parts of the thermochromatographic device	
			Inner tube	Middle + outer tube
$^{110}\text{Sn}$	$700 \pm 10$	10	$57 \pm 5$	$43 \pm 5$
$^{111}\text{In}$	$700 \pm 10$	10	$2 \pm 1$	$98 \pm 1$
$^{110}\text{Sn}$	$700 \pm 10$	20	$71 \pm 5$	$29 \pm 5$
$^{111}\text{In}$	$700 \pm 10$	20	$5 \pm 1$	$95 \pm 1$
$^{110}\text{Sn}$	$800 \pm 10$	10	$88 \pm 3$	$12 \pm 3$
$^{111}\text{In}$	$800 \pm 10$	10	$4 \pm 2$	$96 \pm 2$
$^{110}\text{Sn}$	$800 \pm 10$	20	$99 \pm 1$	$1 \pm 1$
$^{111}\text{In}$	$800 \pm 10$	20	$10 \pm 1$	$90 \pm 1$
$^{105,107}\text{Cd}$	$800 \pm 10$	20	$< 0.01^a$	$> 99.99$

<sup>a</sup>The value corresponds to  $< 20$   $\mu\text{g}$  Cd detected in the dissolved radiotin fraction for a 200 mg Cd target.

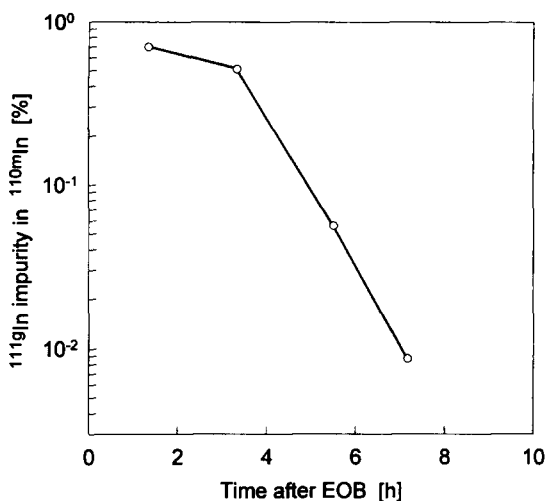


Fig. 5. Amount of  $^{111g}\text{In}$  co-eluted with  $^{110m}\text{In}$  at different times after end of bombardment (expressed as percentage of  $^{110m}\text{In}$ ).

production of the  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  generator, in particular because of the cost of highly enriched  $^{110}\text{Cd}$ . Fortunately, the thermochromatographic separation process provides a well-localized  $^{110}\text{Cd}$  chloride fraction, allowing an overall fractional recovery of the  $^{110}\text{Cd}$  mass of about 95%.

### Conclusion

The  $^{110}\text{Cd}(^3\text{He},3n)^{110}\text{Sn} \rightarrow ^{110m}\text{In}$ -process on highly enriched  $^{110}\text{Cd}$  is suitable for the production of the positron emitter  $^{110m}\text{In}$ . Detailed studies on the cross sections of this process in the 36–25 MeV  $^3\text{He}$ -energy range are not available. Practical experiments using 91.5% isotopically enriched  $^{110}\text{Cd}$  as target material, however, lead to a high  $^{110}\text{Sn}$  yield of 2.2 mCi (81 MBq) per  $\mu\text{Ah}$  and high radionuclidic purity. Chemical separation mainly consists of an initial thermochromatographic step, providing almost 100% separation of  $^{110}\text{Sn}$  within 20 min. The  $^{110}\text{SnCl}_4$  fraction is used to form a  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  elution generator.  $^{111g}\text{In}$  is the only noticeable isotopic impurity, decreasing from about 0.8% (about 1 h after EOB) to < 0.01% (about 7 h after EOB). Batch yields of > 20 mCi  $^{110}\text{Sn}$  allow to run a clinical  $^{110}\text{Sn} \rightarrow ^{110m}\text{In}$  generator for the whole day. The effective ( $\approx 95\%$ ) recovery of the enriched  $^{110}\text{Cd}$  starts with the dissolution of the sublimated  $^{110}\text{CdCl}_2$  deposited within the middle quartz tube, followed by its electrolytic reduction to  $\text{Cd}^0$  for cyclic usage.

Finally, it should be noted that an identical procedure can be applied to produce the analogous  $^{113}\text{Sn} \rightarrow ^{113m}\text{In}$  generator via the  $^{113}\text{Cd}(^3\text{He},3n)^{113}\text{Sn} \rightarrow ^{113m}\text{In}$  process on highly enriched  $^{113}\text{Cd}$  or even  $^{nat}\text{Cd}$ .

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