

Article

## Dry Distillation of Radioiodine from TeO<sub>2</sub> Targets

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**Abstract:** As medical cyclotrons are becoming more abundant, <sup>123</sup>I and <sup>124</sup>I are getting more attention as alternatives to <sup>131</sup>I for diagnostics of thyroid disease. Both <sup>123</sup>I and <sup>124</sup>I provide better diagnostics, deliver less dose to patients and both reduce the risk of thyroid stunning, facilitating subsequent therapy. Dry distillation of radioiodine from tellurium dioxide targets has become the standard approach to producing these radioiodines. Setting up such a production of radioiodine is associated with a lengthy optimization of the process and for this purpose natural tellurium is often used for economical reasons. In this paper, the distillation parameters are scrutinized to ensure optimal distillation temperature, in order to minimize time spent and prevent loss of expensive target material. It is further demonstrated how the individual iodine isotopes, produced from proton bombardment of <sup>nat</sup>Te, will diffuse out of the target in a time dependent ratio. We believe the effect is due to the isotopes having their maximum cross section at different energies. The individual isotopes produced will thus have their highest concentration at different depths in the target. This results in individual mean diffusion lengths and diffusion times for the different isotopes.

**Keywords:** cyclotron; radioiodine; production; distillation; iodine-124; tellurium dioxide

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### 1. Introduction

Due to the increasing number of medical cyclotrons and the growing demand for more specialized radio tracers, an increasing number of sites are producing radioiodine, namely <sup>123</sup>I and <sup>124</sup>I. While <sup>131</sup>I is still the workhorse in diagnostics of thyroid disease, <sup>123</sup>I ( $T_{1/2} = 13.2$  h) is increasingly used instead,

due to better diagnostic features.  $^{123}\text{I}$  has a better suited decay energy of 159 keV vs. 364 keV for  $^{131}\text{I}$ , providing higher sensitivity in SPECT due to thinner camera collimators [1]. In addition, since  $^{123}\text{I}$  has no  $\beta$  component, it delivers significantly less dose to the thyroid tissue. This minimizes the risk of thyroid stunning, a phenomenon rendering the thyroid tissue unable to take up iodine, and thus complicates subsequent radiotherapy [2,3].  $^{124}\text{I}$  ( $T_{1/2} = 4.18$  days) has its own merits as a radionuclide for diagnostics. With a half-life of more than 4 days it allows PET studies of processes with slow biokinetics, as well as allowing for more complicated and time consuming labeling synthesis [4–6] (Table 1).

**Table 1.** Properties of the most common medical iodine isotopes [7].

Radionuclide	$T_{1/2}$	Mode of decay (%)	$E_{\beta}$ (max) keV	Main $\gamma$ -rays [keV] (%)	Application
$^{123}\text{I}$	13.2 h	EC (100)		159 (83.0)	SPECT
$^{124}\text{I}$	4.18 days	$\beta +$ (22) EC (78)	2140	603 (61.0); 723 (10.0); 1691 (10.4)	PET
$^{131}\text{I}$	8.02 days	$\beta -$ (100)	606	284 (6.1); 364 (81.2); 637 (7.3)	SPECT/Therapy

A method for producing  $^{123}\text{I}$  and  $^{124}\text{I}$  available to many cyclotron labs, is bombardment of tellurium dioxide and production of iodine via (p,n) reactions. There are several advantages to this approach. Both  $^{123}\text{Te}(p,n)^{123}\text{I}$  and  $^{124}\text{Te}(p,n)^{124}\text{I}$  have maximum cross sections below 14 MeV [8], which is within reach of many medical cyclotrons, and only a general solid target setup is needed. The downside is the price of the enriched target material (10–50 \$/mg). The entire optimization process associated with setting up an in-house production of iodine can however be done using natural tellurium, in order to keep development costs low. This paper summarizes the findings from research carried out at Herlev Hospital during this optimization process.

## 2. Experimental Section

### 2.1. Targetry

$^{\text{nat}}\text{TeO}_2$  (99.9995% Sigma-Aldrich, Brøndby, Denmark) was mixed with 5% w/w  $\text{Al}_2\text{O}_3$  (99.99%, Sigma-Aldrich, Brøndby, Denmark) in a small beaker with a 2 mL of methanol. It is common practice to mix the  $\text{TeO}_2$  with 5%–10%  $\text{Al}_2\text{O}_3$ . This not only enhances the adherence of the glass layer to the target backing, but also makes the tellurium glass less brittle and thus less prone to break. To ensure homogeneity the suspension was magnetically stirred and evaporated to dryness on a heat plate at 90 °C. This approach was used instead of mixing in a mortar, because using a mortar resulted in large (20–30 mg) losses of target material. Next the target material was distributed evenly in a cylindrical groove, either 1 mm or 1.8 mm deep, with diameter of respectively 11 or 10 mm in a platinum disc ( $\varnothing = 24$  mm) and melted at approximately 695 °C. The melting was done in a laboratory oven from Nabertherm, which had previously been subjected to a one point calibration, done by measuring the

melting point of pure  $^{\text{nat}}\text{TeO}_2$ . A 20 °C offset was found between the set temperature and the actual target temperature, which all data in this paper have been corrected for.

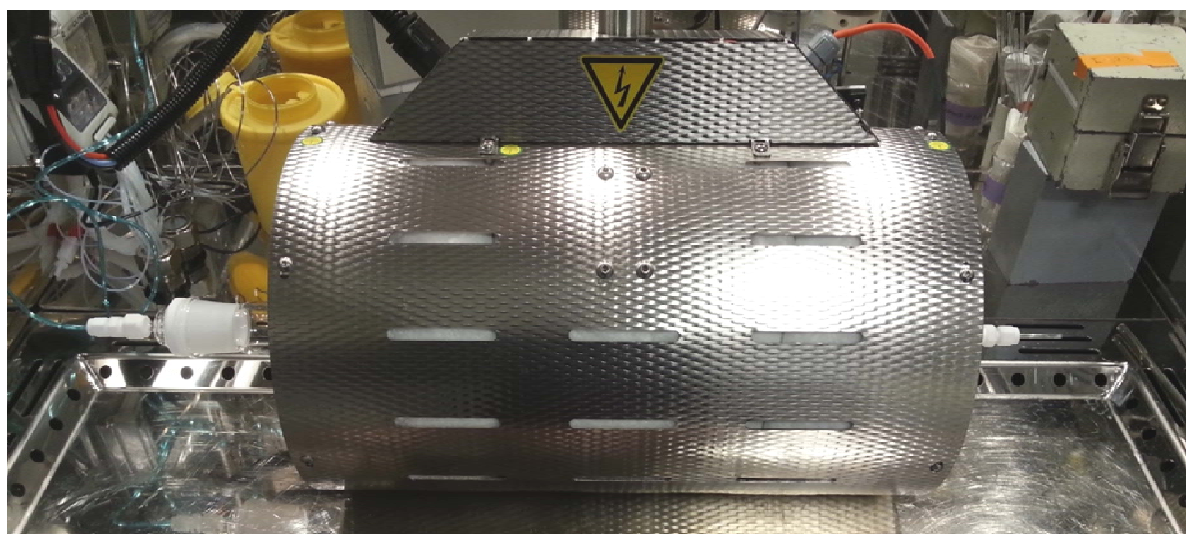
## 2.2. Bombardment

The target was loaded in a COSTIS solid target system bought from IBA (Louvain-la-Neuve, Belgium), and bombarded with 14.8 MeV protons on an IBA Cyclone 18/18 cyclotron. During bombardment the target material was cooled with helium on the front and a water flow of 3 L/min on the platinum backing.

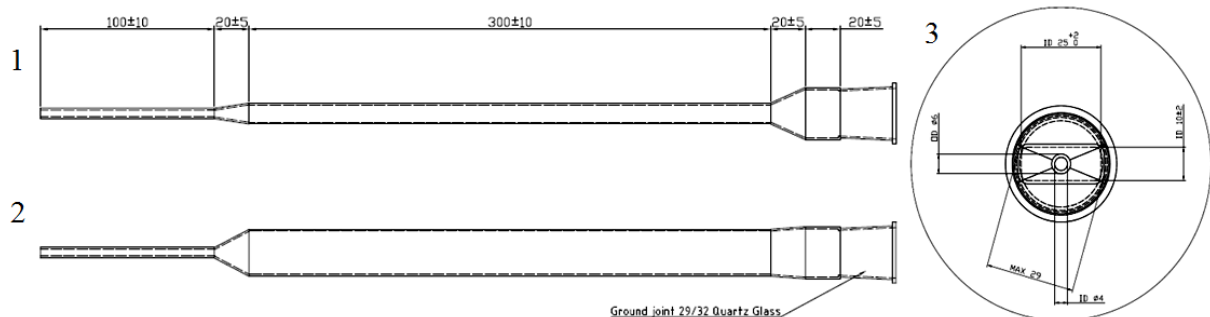
## 2.3. Dry Distillation

After bombardment the produced iodine was separated from the target by dry distillation (Figure 1). Dry distillation is commonly preferred over wet chemical processing, as it is reasonably straight forward and allows for immediate reuse of the target. The target was heated in a quartz tube (Figure 2), and as the temperature surpassed the critical temperature of iodine (546 °C), iodine started diffusing out of the tellurium glass [9]. Carried by a flow of air, the iodine was passed through a capillary glass tube outside the oven, on which it adsorbed. Prior to distillation the capillary tube had been coated with NaOH to facilitate trapping [10]. The melting was done in a tube furnace (Nabertherm, Lilienthal, Germany), which like the oven, had previously been subjected to a one point calibration, done by measuring the melting point of pure  $^{\text{nat}}\text{TeO}_2$ . Here a 50 °C offset was found between the set temperature and the actual target temperature, which all data in this paper have been corrected for. All radioactivity measurements were performed using a calibrated HPGe detector (Canberra, Meriden, CT, USA).

**Figure 1.** Image of the setup in use. Air introduced from the left carried the distilled iodine from the target in the middle of the tube furnace, to the capillary tube on the far right, on which it adsorbed.



**Figure 2.** Computer-aided design (CAD) drawing of the quartz distillation tube designed to hold a target of 24 mm in diameter. The actual length of the distillation tube can be changed to fit the length of the tube furnace. **1:** Side view **2:** Top view **3:** End view. (Unit: mm).

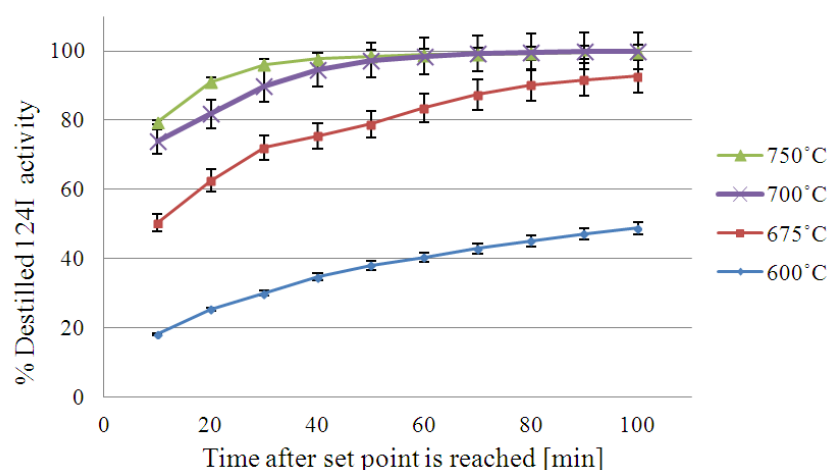


### 3. Results and Discussion

We began by examining the distillation profile for different distillation temperatures. This was done using targets produced from natural tellurium dioxide. The targets were bombarded with approx. 1.5  $\mu$ Ah of 14.8 MeV protons and subsequently distilled, using temperatures of 600 °C, 675 °C, 700 °C and 750 °C. The collection tube was changed every 10 min, the first one changed 10 min after the oven had reached the set temperature. The distillation tubes were subsequently measured and the produced isotopes quantified by gamma spectroscopy. Because gamma spectroscopy was performed several days after EOB, the measurements of  $^{123}\text{I}$  were associated with very large uncertainties due to low residual activity. The data obtained of  $^{123}\text{I}$  activities were therefore omitted.

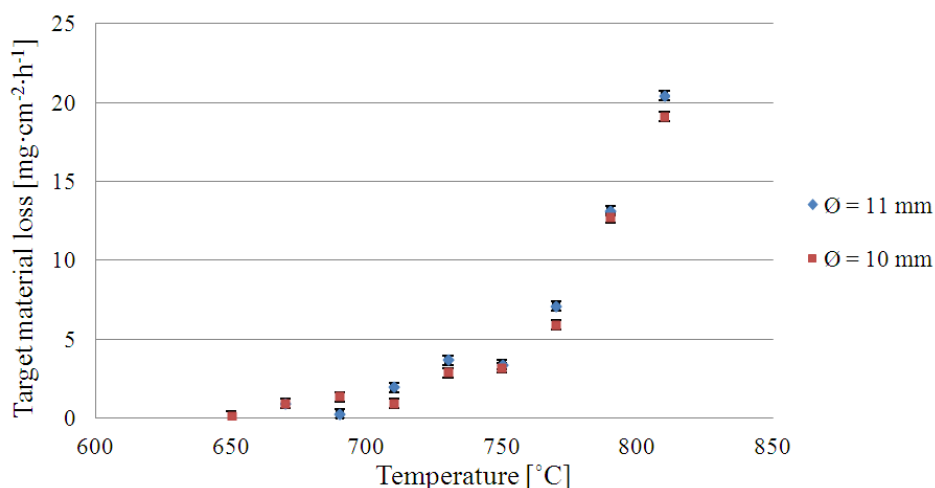
As described by others [5], we found that distillation speed increases rapidly when the glass melts. It should be noted that the melting point of the 95%  $\text{TeO}_2$ /5%  $\text{Al}_2\text{O}_3$  mix, is significantly lower than that of pure  $\text{TeO}_2$  (733 °C), and has a measured value around 685–690 °C. Above this temperature, ~95% of the  $^{124}\text{I}$  activity is distilled out of the target material in 40 min and more than 98% of the  $^{124}\text{I}$  activity is distilled in 60 min (Figure 3).

**Figure 3.** Graph showing the percent  $^{124}\text{I}$  distilled as a function of time. The first collection tube was mounted at room temperature and changed 10 min after the set temperature was reached.



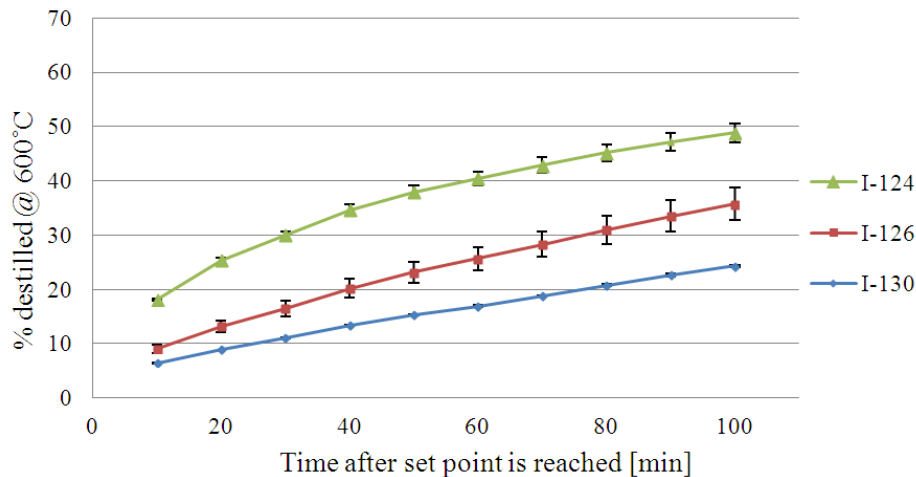
Loss of target material is not only expensive, but can also lead to inconsistent production yields due to thinning of the target. To estimate the loss of target material associated with distillation temperatures, two targets made from natural tellurium dioxide with 5% aluminum oxide were prepared. The target backings were of slightly different designs; One with a groove, diameter of 10 mm and depth 1.8 mm, and one of diameter 11 mm with depth of 1 mm and both targets approximately  $280 \text{ mg/cm}^2$  thick. The targets were heated in intervals of 1 hour, at temperatures ranging from 650 to 810 °C and weighed between each heating stage. It was found that as long as the temperature is below melting point there is no significant loss of target material. However, as the temperature rises above 750 °C, the losses start rising exponentially (Figure 4). When we got these results they were initially difficult to compare to results in literature, where losses are often given as a percentage of total target weight. As evaporation is a function of surface area and not mass, we believe a better unit is loss/time/area. Loss given as percentage of total mass, is acceptable as long as the targets discussed are of similar thickness. A slanted target however will have a very high surface to volume ratio, compared to a normal target of the same effective thickness, and will therefore lose a larger percent of target mass during distillation. Using loss/time/area will make it easier to estimate and compare losses of different target designs.

**Figure 4.** Graph showing the loss of target material associated with 1 h of distillation at a range of temperatures. It should be noted that these experiments were done without any air flow over the target disc.



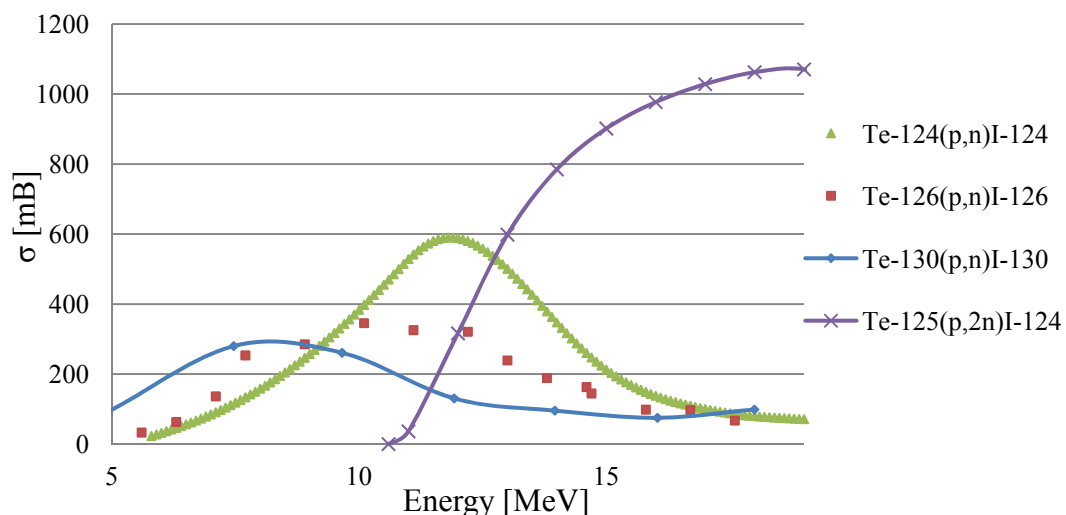
During the distillation tests following proton bombardment of natural tellurium targets, we stumbled on an initially surprising result. We found that  $^{124}\text{I}$ ,  $^{126}\text{I}$  and  $^{130}\text{I}$  were not distilled out of the target at the same rate when distilled at lower temperatures (Figure 5).

**Figure 5.** Graph showing the percentage of the individual iodine isotopes, distilled as a function of time at 600 °C. It is seen that the isotopes do not distill out at the same proportionate rate. At temperatures above melting point this effect almost completely disappears.

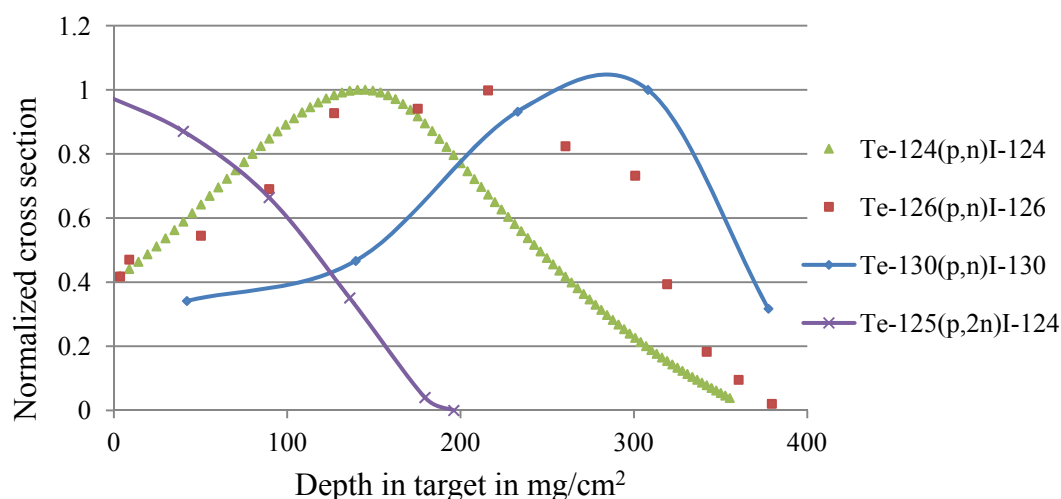


This puzzled us, but examination of the cross section functions in Figures 6 and 7 provides some insight into this phenomenon.

**Figure 6.** Graph showing the excitation functions of  $^{124}\text{Te}(p,n)^{124}\text{I}$  [8],  $^{126}\text{Te}(p,n)^{126}\text{I}$  [11],  $^{130}\text{Te}(p,n)^{130}\text{I}$  [12] and  $^{125}\text{Te}(p,2n)^{124}\text{I}$  [13]. As the beam energy is degraded as it passes through the target,  $^{124}\text{I}$  is produced primarily at the surface of the target, whereas  $^{130}\text{I}$  is produced deep in the target, and will thus have a longer path to the surface during distillation.



**Figure 7.** Using SRIM software by James F. Ziegler, the cross sections were converted from being a function of energy to being a function of depth in the target material, with a starting energy of 14.8 MeV. The cross sections have been summed and normalized to facilitate comparison of depths.



Because the three reactions have their maximum cross sections at different proton energies, the produced isotopes will have maximum concentrations at different depths in the target material and thus have different mean distances to diffuse before reaching the surface. Therefore  $^{124}\text{I}$ , which in  $^{\text{nat}}\text{Te}$  has a maximum cross section at  $>14$  MeV, will be produced very close to the surface of the target and diffuse out the fastest, compared to  $^{130}\text{I}$  which has its maximum cross section at a much lower energy and thus deeper in the target. This demonstrates the importance of optimizing the distillation parameters individually for each isotope of iodine one wishes to produce. Assuming that distillation parameters for all iodine isotopes are identical is an easy mistake to make when optimizing with natural tellurium, but one set of distillation parameters is not representative for all isotopes and assuming so, can have a pronounced effect on the distillation yield.

There is debate about the chemical form of the distilled iodine. Ionic forms must be expected to be less volatile and therefore less consistent with the facile distillation of the iodine which is observed. Molecular iodine seems improbable due to the stoichiometry of the infinitesimal amount of iodine produced. If iodine atoms should encounter by diffusion inside the target material, to unite and form molecular iodine before distilling out, the distillation process would be expected to be very slow, which it is not. If interhalogens were the distilled form, formation of these would furthermore be complicated by gradual exhaustion of halogens such as chlorine and bromine in the target material. A 1 GBq production of  $^{124}\text{I}$  corresponds to approximately 1 nmol of atomic iodine. With targets being used up to 50 times, it seems unlikely that the required amount of halogens should be present in the target matrix. Also due to the volatile character of interhalogens the trapping at room temperature should be hampered; we had an ascarite trap installed and saw no radioactive release during the distillation. Finally there is the possibility that iodine distills as free radicals.  $\text{I}_2$  dissociation into free radicals is 18% at 460 °C [14], indicating that this is a fairly stable species at high temperatures. This

would require no rate limiting formation of chemical species, and should distil easily. As these are the characteristics that we observe, we believe that it is free radicals distilling from the targets.

#### 4. Conclusions

In literature distillation temperatures up to 820 °C have been reported [4], with 750 °C seemingly being the most widely used. In this paper we have demonstrated that when distilling  $^{124}\text{I}$  from  $^{\text{nat}}\text{Te}$ , it is sufficient to distil just above melting point, *i.e.*, at 700 °C. It is only necessary to increase temperature if distillation time needs to be shorter than 40 min. This however is associated with increased loss of target material, a phenomenon which greatly accelerates at temperatures above 750 °C.

Using  $^{\text{nat}}\text{TeO}_2$  is an inexpensive and convenient way of optimizing both bombardment and distillation parameters, when setting up an in-house production of radioiodine. We have however demonstrated the importance of optimizing the distillation parameters for the individual isotopes of iodine. Using a longer lived iodine isotope such as  $^{130}\text{I}$  for optimization, can make activity measurements easier, but applying these results to other iodine isotopes, may result in distillation parameters that either give a low distillation yield or are more time consuming than necessary.

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#### Conflicts of Interest

The authors declare no conflict of interest.

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