Potential Errors Caused by Variable Radionuclidic Purity of Iodine-123

Judy A. Hughes, Craig C. Williams, Stephen R. Thomas, Harry R. Maxon III, Rosemary H. Basiewicz*, and William J. Love†

University of Cincinnati Medical Center, Cincinnati, Ohio

The commercial accelerator production of iodine-123 in the United States has changed from the Te-122 (d,n) I-123 reaction to the Te-124 (p,2n) I-123 reaction—and a greater amount of I-124 contamination results. This impurity causes only slight elevation in thyroid uptake value when counted 24 hr after calibration time of the capsule, but a significant elevation in uptake value 48 hr after calibration time (when I-123 is administered 24 hr after calibration time). There is no image degradation on 24- and 48-hr scintigraphs obtained with a pinhole collimator. A significant time-dependent change in potentiometer settings on dose calibrators is required to assay the capsules.

With the change in U.S. commercial production of I-123 from the Te-122 (d,n) I-123 reaction to the Te-124 (p,2n) I-123 reaction (*1*), higher yields of I-123 with a smaller number of radioiodine contaminants—but with a higher percentage of the longer-lived I-124 contaminant and a slight elevation of radiation absorbed dose to the patient (*2*)—have resulted. Production of commercial I-123 by both of these reactions typically gives a variety of radiocontaminants, as determined by assay with a calibrated Ge(Li) detector (Table 1), which may affect clinical use of the radiopharmaceutical. The purpose of our work was to determine which parameters could be affected by these contaminants and propose methods to correct these differences if they exist.

TABLE 1. Typical and Maximal Radiocontaminants in Commercially Produced I-123 at Calibration Time.

	Production method			
Radiocontaminant	Te-122 (d,n)	I-123	Te-124 (p,2n)	I-123
	Mean and range*	Maximal†	Mean and range	Maximal†
I-124	0.9%(0.4 1.2)	1.1%	3.8%(3.7 4.2)	5.0%
I-126	0.5%(0.2 0.8)	1.1%	ND	NS
I-130	3.1%(2.8 4.0)	3.2%	ND	NS
I-131	0.4%(0.2 0.6)	0.8%	ND	NS
Na-24	ND	0.5%	ND	0.5%

*As determined by our assay [n=4, Te-122 (d,n); n=7, Te-124 (p,2n)].
†As specified by the manufacturer's product literature (*1*).
ND = none detected.
NS = not specified.

Evaluation by Dose Calibrator Assay

In the interest of patient care, as well as meeting the appropriate state regulatory agency's requirements as exemplified by a federal regulatory guide (*3*), the activity of I-123 administrations must be measured. Ideally, with radionuclidically impure I-123 samples, one should use a calibrated Ge(Li) detector in a fixed geometry, summing the counts in the 159-keV photopeak of I-123 for each assay. The assay of activity may also be performed with an ion chamber dose calibrator. It is also possible to calibrate an uptake system or other device that measures activity if an accurately calibrated capsule is obtainable. Since accurately calibrated capsules were not available, we chose to use the dose calibrator as our means of satisfying this requirement. We also feel it is more convenient and reliable to use a single method to assay all radiopharmaceuticals before administering them to patients.

Because of radionuclidic impurities and differences in geometry, the isotope factors specified by dose calibrators for I-123 will not be accurate. We therefore modified our dose calibrator potentiometer settings to correct these differences based on the results obtained from a Ge(Li) detector calibrated sample. Effects of radionuclidic impurities on dose calibrator assays have been noted elsewhere (*4*).

Our assays of I-123 and its radiocontaminants were per-

For reprints contact: Judy A. Hughes, The Eugene L. Saenger Radioisotope Laboratory, University of Cincinnati Medical Center, Cincinnati, OH 45267.

*Present address: Radioisotope Laboratory, University Hospitals of Cleveland, Cleveland, OH.

†Present address: Pharmatopes Inc., Cincinnati, OH.

formed with a calibrated Ge(Li) detector within 4 hr of the manufacturer's stated calibration time. Initially, capsules from several different batches of I-123 produced from Te-122 in May 1975, were assayed and then used to calibrate four factory-shielded dose calibrators (one CRC®-2N and three CRC®-6's [Capintec, Inc., Montvale, NJ]). The average potentiometer setting varied considerably depending on the particular calibrator tested. In a given calibrator, the potentiometer setting varied somewhat from batch to batch of I-123, presumably because of slight differences in quantities of radiocontaminants found. Use of the average setting value for each calibrator of 406 to 454, however, usually gave results for capsule assays accurate to ± 10% of the activity determined on the Ge(Li) detector. It is of interest that the activities we determined were approximately 31% less than would have been obtained using the dose calibrator manufacturer's potentiometer setting of 277 listed for pure I-123 in a 5-ml borosilicate ampule.

Six capsules from four daily batches of I-123 produced from Te-122 in November 1977 were assayed in the Ge(Li) detector and used to recalibrate the same dose calibrators. The variation in potentiometer settings in any calibrator among batches was minimal since the I-124 activity at calibration time remained relatively constant at 3.8% (range: 3.7-4.2%) of the total I-123 activity. The variation between calibrators still required determining a separate potentiometer setting for each device. This measured activity was approximately 19% less than that using the dose calibrator manufacturer's potentiometer setting for pure I-123.

These data indicate that, regardless of the production method, the dose calibrator setting determined was different from that which the manufacturer recommended for pure I-123. Since the potentiometer settings were modified for the impure I-123 formulations in capsules and plastic bottles rather than for liquid in a borosilicate ampule, these numbers will also be higher than the modified settings that can be empirically determined by the method of Suzuki (5). This time dependent response to impure I-123 as 5 g of liquid in a borosilicate ampule is shown in Table 2 and is based on the impurities found in one capsule from each production method.

Table 2. Empirically Determined Dose Calibrator Settings for Impure I-123 as a Function of Time*.

Time (hours post calibration)	I-123 (from Te-124)		I-123 (from Te-122)
0	301	(309*)	330*
4	306	(314*)	331*
8	312	–	—
12	319	(328*)	333*
18	333	(341*)	335*
24	351	(360*)	337*
36	405	—	—
48	499	(509*)	362*

*Includes contribution from 0.5% Na-24.

The experimentally determined settings are useful only when the level of radiocontaminants remains constant. We recommend, therefore, that the settings be used only when the capsule is assayed within 4 hr of its calibration time. A new potentiometer setting would need to be determined for capsules 24-hr-old or others at significantly different time intervals. The variation between dose calibrators requiring the determination of a modified potentiometer setting for each is not understood; all four calibrators are routinely tested for accuracy with NBS standard reference materials as they become available and no abnormal results have been obtained with these standards. An I-123 standard reference material has not yet been tested.

Evaluation by Thyroid Uptake Studies

All patients referred for thyroid uptakes in our laboratory have been given approximately 100 μCi of I-123. Each individual capsule is counted upon receipt in the laboratory and is administered to the patient shortly thereafter. Uptake studies are performed 18–28 hr later. All uptakes are performed on an integral counter with the dis-

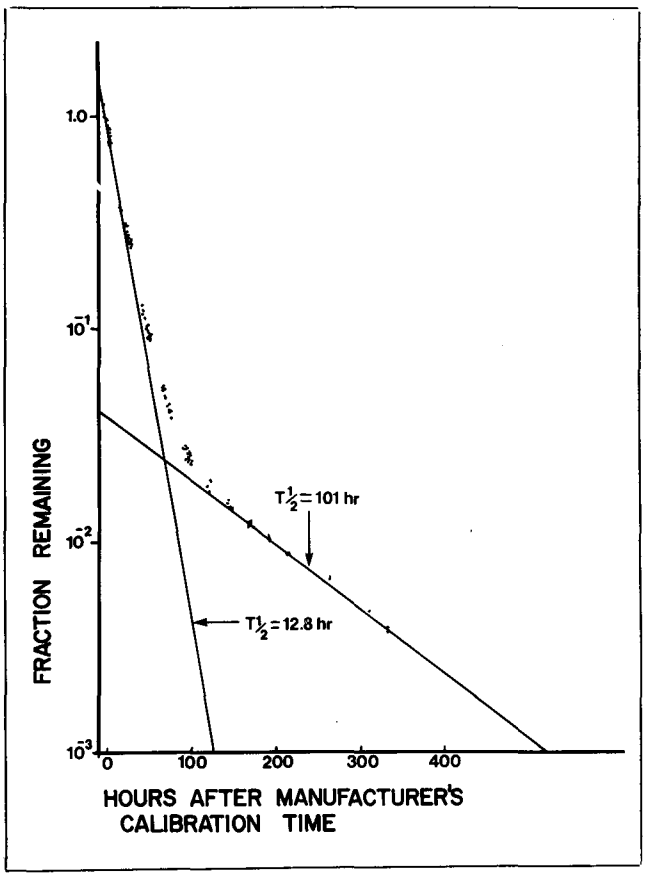

FIG. 1. Experimentally determined biexponential decay curve for I-123 produced from Te-124 using a typical thyroid uptake system utilizing an integral counter. Fraction remaining = $0.0389 \exp\left[\frac{-0.0693t}{101}\right] + 0.965 \exp\left[\frac{-0.693t}{12.8}\right]$ where t = time post calibration in hours.

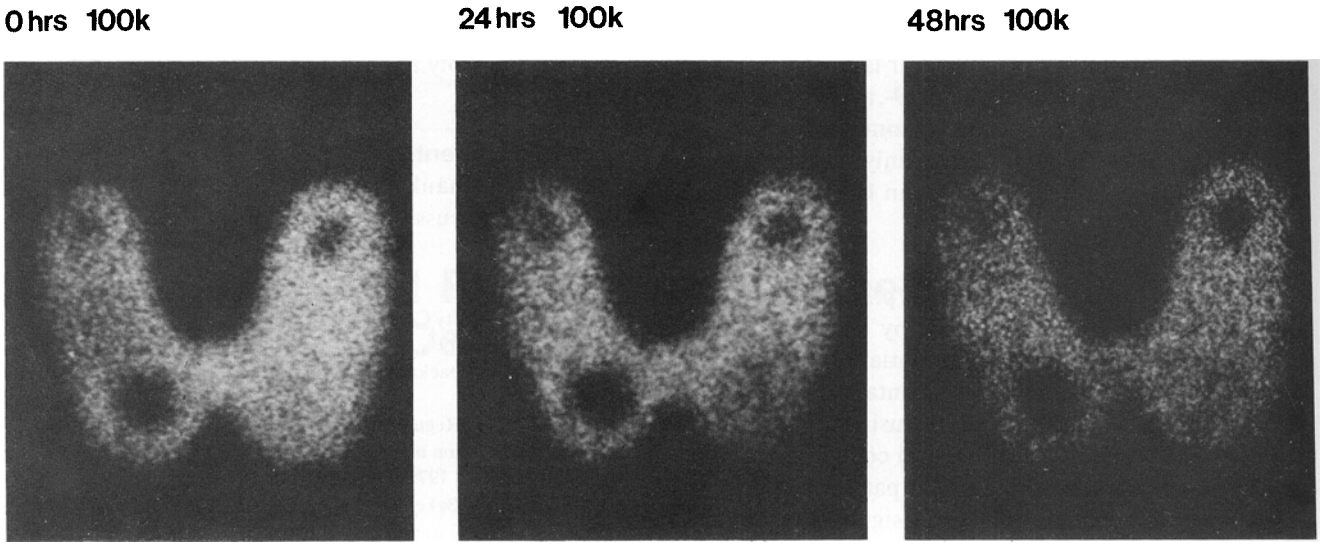

FIG. 2. Phantom images at periodic times after calibration of I-123.

criminator set at 155 keV, interfaced to an uncollimated 2-in. NaI(Tl) crystal. Uptakes are calculated according to the following formula:

$$\% \text{ uptake} = \frac{\text{net cpm neck} - \text{net cpm thigh}}{\text{net cpm standard} \times D(T)^*} \times 100,$$

*where D(T) = the decay factor obtained for the 13.2-hr half-life of I-123.

A critical factor in determining thyroid uptake using I-123 is accounting for loss of activity caused by decay between administering the I-123 and counting the patient about 24 hr later. Figure 1 shows the best-fit curve obtained using our uptake system based on the normalized data from capsules produced from Te-124. Obviously, applying the 13.2-hr decay factor of I-123 to counts contaminated with I-124 will not produce accurate results. This is because contributions from the longer-lived I-124 contaminant become relatively greater with time and will tend to increase the apparent uptake.

We do not consider the difference in uptake to be significant if the capsule is administered at or before the manufacturer's calibration time (I-124 content $< 4\%$) and the patient counted 24 hr later. In our system the following theoretical uptakes were obtained using a plastic neck phantom. When administered at calibration time and counted 24 hr later, a true 45% thyroid uptake would appear to be 47% based on the equation derived for the curve in Fig. 1 by least squares analysis (fraction remaining $= 0.0389 \exp\left[\frac{-0.693\,t}{101}\right] + 0.965 \exp\left[\frac{-0.693\,t}{12.8}\right]$, where t is time in hours). This is not considered to be a significant change.

There is a significant increase in uptake, however, if a capsule is administered 24 hr after calibration time (I-124 content about 15%) and the patient is counted 48 hr post-calibration. Such a procedure is permitted according to the product label (*6*). When administered at 24 hr post-calibration and counted 24 hr later, a true 45% uptake on our system would appear to be 53%, an increase that could be clinically interpreted as being significantly increased. A correction, therefore, must be made for the amount of I-124 in this case. This correction factor will need to be determined for each thyroid uptake system because of differences in detectors and counting electronics.

Correcting these errors in the uptake determination can be accomplished by considering the I-124 contribution at any given time. This step can be accomplished realistically in three ways: first, an extra capsule can be ordered and counted on receipt, immediately before or after the patient is counted, thus serving as a standard to obtain the decay factor. This method requires purchasing an additional capsule. Secondly, a new set of "decay factors," D(T), can be used that incorporates the I-124 contribution to the I-123 at various time intervals, ranging from 0–60 hr after calibration time for the counting system used. Lastly the use of an upper as well as a lower energy window on the uptake system will decrease the contribution from the increase in percent of I-124. A survey of ten hospitals in our geographical area indicates that seven of the nuclear medicine departments use an uptake system without the benefit of an upper window so that this choice of alternatives requires purchasing replacement equipment.

Evaluation by Thyroid Imaging

Despite the fact that the I-124 contaminant can cause interference with uptake counting on an integral counter, it creates very little scatter contribution using a narrow window in a scintillation camera with a pinhole collimator centered around the 159-keV photopeak. Consequently, very little image degradation occurs on thyroid scintigraphs obtained. To illustrate this point, a thyroid phantom was filled with 150 μCi of I-123 made by the new production method and imaged on a Pho/Gamma IV camera, using the pinhole collimator with a 5-mm insert (Searle

Radiographics, Des Plaines, IL). Images were obtained at calibration time (T_0), 24 hr and 48 hr later (Fig. 2). The phantom used had "cold areas" of 5-, 9-, and 12-mm diameters. Even at 48 hr, although there is some minimal degradation, the 5-mm cold area is still plainly visualized. Similar findings were reported by Baker in 1975 (*7*).

Summary

The I-123 produced by the Te-124 (p,2n) I-123 method was compared with that produced by the Te-122 (d,n) I-123 method and evaluated for potential effects resulting from an increased amount of I-124 contamination. Theoretical 24-hr uptake determinations using a plastic neck phantom performed with an integral counter have been shown to be only slightly higher on a patient dosed at the calibration time of the capsule but significantly higher when the patient is dosed 24 hr after the capsule calibration if the pure 13.2 -hr I-123 decay factors alone are used in the calculation. Modified potentiometer settings have been determined to be necessary for accurate assay using several dose calibrators. These settings differ significantly from those for pure I-123 in glass ampules. Lastly, the resolution of the thyroid images performed on the gamma camera using the pinhole collimator with the 5-mm insert is not appreciably altered, even at 48 hr after calibration time.

Acknowledgment

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