A Simple Method to Quantitate Iodine-124 Contamination in Iodine-123 Radiopharmaceuticals

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Iodine-123 (^{123}I) produced by the $^{124}Te(p,2n)^{123}I$ reaction contains several percent ^{124}I radionuclidic contamination at the time of imaging. Since ^{124}I degrades the quality of the images and causes unnecessary radiation absorbed dose to the patient, it is important to know the amount present in radiopharmaceuticals at the time of administration. A simple approach is described which uses a radionuclide dose calibrator and lead shield. The sample is assayed both shielded and unshielded and the ratio of readings depends uniquely upon the percent ^{124}I present. The technique can be adopted for any type of dose calibrator, sample container, and Pb shield, but use of the numeric constants reported here should be restricted to the specified equipment.

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Iodine-123 (^{123}I) is the radionuclide of choice for a growing number of nuclear medicine procedures. This is due to its desirable physical properties (half-life 13.2 hr, photon energy 159 keV:84%) which provide excellent diagnostic information at low absorbed dose, and the ease with which iodine labels a variety of pharmaceuticals. Unfortunately, most of the ^{123}I available today is produced by the $^{124}Te(p,2n)^{123}I$ reaction which also produces several percent iodine-124 (^{124}I) radiocontamination due to the competing reaction $^{124}Te(p,n)^{124}I$ (*1–3*).

Iodine-124 is an undesirable contaminant for several reasons. Its energetic photons (603 keV:62%; 723 keV:10%. . .) more readily penetrate the collimator septae than those of ^{123}I, thereby degrading both resolution and contrast in the resulting images, and its relatively long half-life (101 hr) causes the situation to worsen with delayed administration of the radiopharmaceutical since the $^{124}I/^{123}I$ activity ratio trebles each day. Hence, even for a relatively pure source of ^{123}I (4.1% ^{124}I contamination) the ^{124}I has been shown to contribute as much as 36% of the detected events when using a low-energy collimator and about 15% for a medium-energy collimator (*4*). Finally, ^{124}I produces considerably higher radiation dose per unit activity to the patient than does ^{123}I, and because of this, the Food and Drug Administration mandates that no more than 5% ^{124}I be present in injected doses of [^{123}I] iodoamphetamine.

Clearly, it is desirable to find a means to assay ^{124}I activity in the presence of ^{123}I. Though this can be accomplished with a solid state detector/multichannel analyzer spectrometry system, such systems are not usually available in nuclear medicine facilities. A convenient method is presented here, similar to the molybdenum-99 breakthrough test (*5*), which requires making only two measurements on the sample in question.

MATERIALS AND METHODS

As will be seen, assessment of the percent ^{124}I contamination in a sample of ^{123}I will require only that it be assayed in a radionuclide dose calibrator both inside and outside of the lead canister (6 mm thickness) normally used for the "Moly breakthrough test." However, a series of preliminary measurements must be made—one time only—to characterize the response of the assay system to these radionuclides with and without the shielding.

Characterization of the dose calibrator/lead canister response to ^{123}I and ^{124}I

The values of three constants suffice to predict the response of a dose calibrator to either ^{123}I or ^{124}I, either inside or

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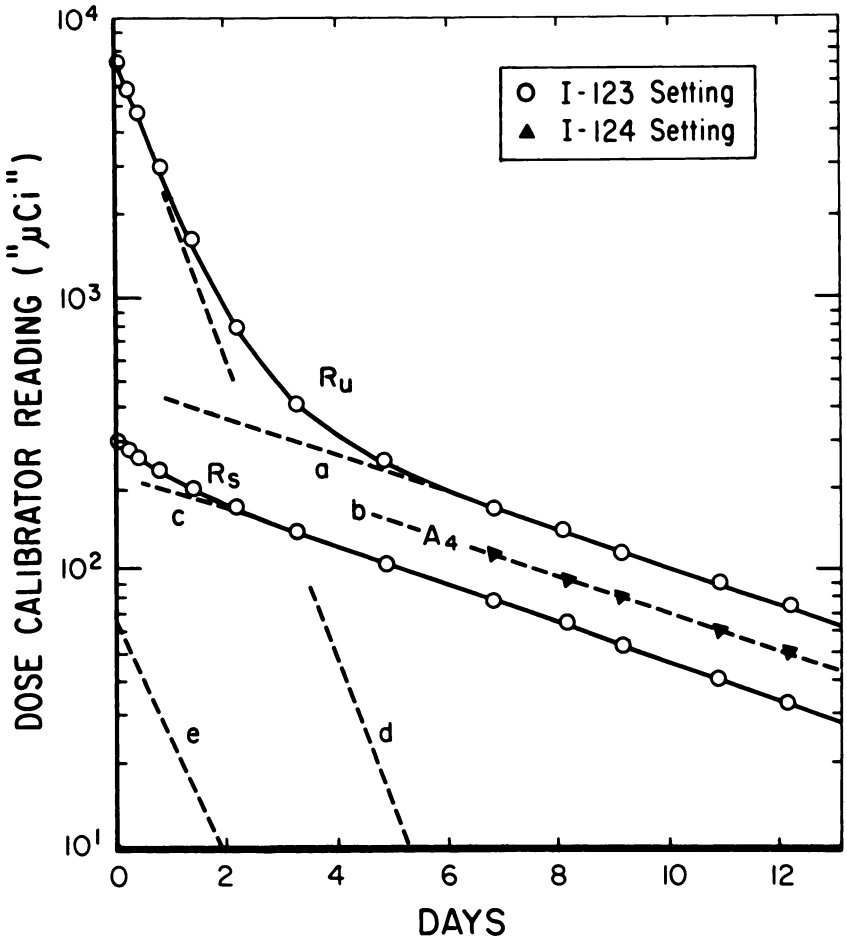

FIGURE 1
Dose calibrator readings plotted against time. For data R_S, sample was shielded by Pb canister; for data R_U and A_4 no shielding was used. Dashed straight lines (a–c), representing ^{124}I contributions, are fits to data beyond Day 7; lines (d) and (e), representing ^{123}I, are fits to data obtained by subtracting (a) and (c) from R_U and R_S data, respectively

outside of a lead canister: T_3, the effective transmission of the canister for the ^{123}I radiation (dose calibrator set to assay ^{123}I); T_4, the effective transmission of the canister for ^{124}I radiation (dose calibrator set to assay ^{123}I); and D, the ratio of ^{124}I activity in a pure sample to the reading obtained when the sample is placed in the dose calibrator (set to assay ^{123}I). Two methods can be used to obtain these necessary characterization constants.

Method 1. If pure samples of ^{123}I and ^{124}I can be secured, then T_3, T_4, and D are easily measured. For T_3, the dose calibrator is set to assay ^{123}I, and readings are taken for the pure sample of ^{123}I both shielded by the lead canister, R_S, and unshielded, R_U. The ratio R_S/R_U equals the effective transmission of the canister for ^{123}I, T_3. The procedure is repeated for the pure ^{124}I sample to obtain T_4 (dose calibrator set to assay ^{123}I). For D, the pure ^{124}I sample is read in the dose calibrator set for ^{123}I, R_4, and with the calibrator set to assay ^{124}I, A_4. The ratio A_4/R_4 equals D.

Method 2. Usually pure samples of ^{123}I and ^{124}I cannot be obtained, so an alternate approach has been developed for determining T_3, T_4, and D which uses a sample of ^{123}I contaminated with ^{124}I. For this method a series of readings must be made over a period of about 11 days of the shielded and unshielded sample vial placed in the well of the dose calibrator. These readings, R_S and R_U, respectively, are made with the dose calibrator adjusted to assay ^{123}I. At Day 6, and thereafter, a third set of readings is taken along with the first two: the unshielded vial is read, A_4, with the dose calibrator adjusted to assay ^{124}I.

For each of the three sets of data (R_U, R_S, A_4) the separate contributions of ^{123}I and ^{124}I are deduced by using the conventional stripping technique. The ratio of the ^{123}I contributions to the R_S and R_U data is T_3. T_4 is the corresponding ratio for the ^{124}I contributions, and D is the ratio of the ^{124}I contributions to A_4 and R_U.

Percent ^{124}I contamination of an ^{123}I sample

The same dose calibrator that was characterized above is adjusted to assay ^{123}I. The sample vial in question is placed into it, and readings are made with the vial both shielded and unshielded. The ratio of the shielded and unshielded readings allows immediate determination of the ratio of activities of ^{124}I to ^{123}I, A_4/A_3, either by calculation from the formula

$$A_4/A_3 = D(R_S/R_U - T_3)/(T_4 - R_S/R_U),$$

where T_3, T_4, and D were determined by the method described above, or from a graphical representation of the dependence

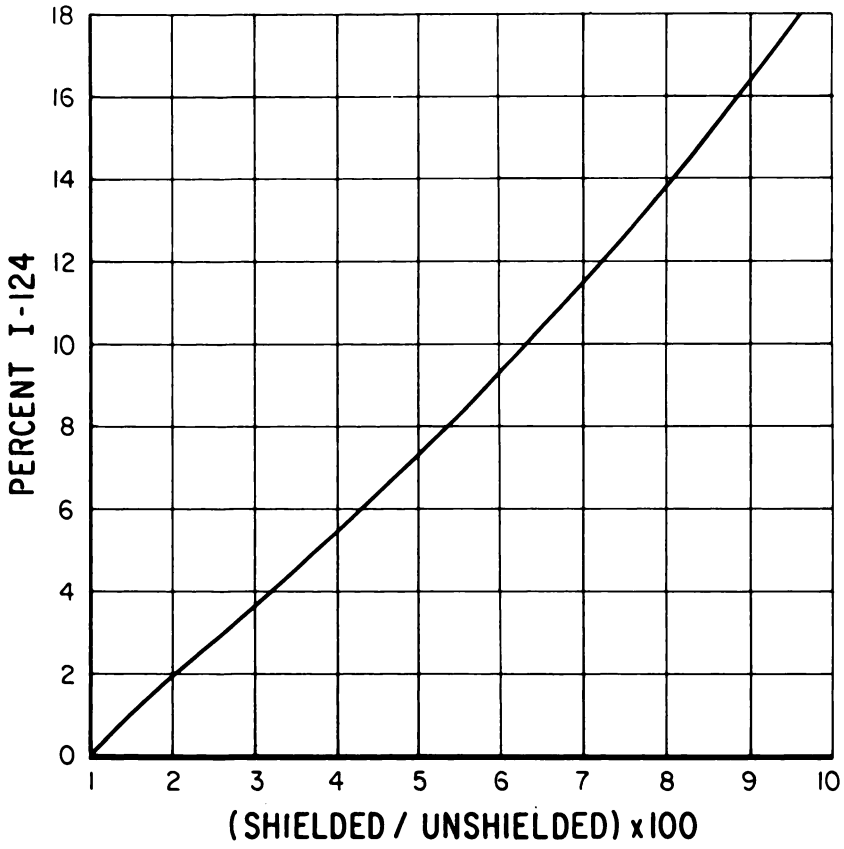

FIGURE 2
Calculated percent ^{124}I contamination in sample of ^{123}I compared with ratio of dose calibrator readings when shielded (R_S) and unshielded (R_U). Shield was Pb canister used for molybdenum breakthrough test. As sample decays, shielded-to-unshielded ratio increases because percent ^{124}I increases. (See text for description of required equipment and limits of applicability)

of A_4/A_3 on the value of R_S/R_U. (See the appendix for a derivation of the formula.)

RESULTS AND DISCUSSION

The three characterization constants

Since it appears that Method 1 can be pursued by only those few laboratories which have access to pure ^{123}I and ^{124}I, only Method 2 was attempted for this work. Iodine-123 produced by the (p,2n) reaction on tellurium-124 was obtained from a commercial supplier.* The original glass vial was placed in the well of a radionuclide dose calibrator of the gas ionization chamber type† to obtain the data shown in Fig. 1. The readings commenced soon after delivery of the sample in order to maximize the contribution of the 13.2 hr ^{123}I, and were taken with greater frequency during the first 48 hr so that several data points could be used to fit the ^{123}I contributions. The reading depicted by circles (Fig. 1) were taken with the calibrator set for ^{123}I, the lower set being taken with the sample inside the shield; for the triangles, the calibrator was set for ^{124}I, and the sample was unshielded.

Fits to the data beyond Day 7 are shown by the dashed lines (a-c) in Fig. 1 and provide the ^{124}I contributions to the readings; dashed lines (d) and (e) provide the ^{123}I contributions. Values T_4, T_3, and D were calculated as described in the Materials and Methods section. A second set of values was obtained for these constants by following the same procedure for another sample from the same supplier. The average values and standard deviations from the two sets of measurements are: $T_3 = 0.0079 \pm .0006$, $T_4 = 0.363 \pm 0.004$, and $D = 0.543 \pm 0.001$.

Percent ^{124}I contamination of a sample

Such elaborate data need not be taken anymore. The actual ratio of ^{124}I to ^{123}I activities for any sample, A_4/A_3, as well as the separate values of A_3 and A_4 can be calculated using Eqs. (3-5) of the appendix merely using the results of two readings: one with the sample shielded, R_S, and one with it unshielded, R_U. For example, the sample used for the data in Fig. 1 gave initial readings $R_U = 7.095$ and $R_S = 0.245$ mCi. From this we find $A_4 = 0.288$ mCi, $A_3 = 6.56$ mCi and $A_4/A_3 = 4.4\%$.

The dependence of A_4/A_3 upon R_S/R_U, described by Eq. (5) of the appendix, can also be displayed graphically (Fig. 2). Only a clinically relevant range of values for the ratio of A_4/A_3 is shown in the figure so that the percent ^{124}I radiocontamination can be reported with greater precision. From this graph we obtain the same percent ^{124}I contamination for the sample as was calculated above, 4.4%.

Limitations

Use of this technique for assay of ^{124}I contamination of ^{123}I requires a proper determination of the constants T_3, T_4, and D. Those who employ the same type of dose calibrator, Pb canister and sample vial as used in this work can safely adopt the values reported here. However, these constants depend upon the photon energy

distribution presented to the dose calibrator and upon the calibrator's energy response characteristics. Hence, use of either a different type of sample container (e.g., plastic syringe or vial) or a different design Pb shield, both of which affect the energy distribution of the photons entering the chamber gas, will change the values of the constants. Likewise, use of a dose calibrator with a different energy response function (e.g., one that utilizes a plastic scintillation detector, or an ionization chamber detector with different dimensions, etc.) is likely to affect the values of these constants. The significance of using different components can be assessed by obtaining R_S and R_U readings for a sample of ^{123}I with unknown amount of ^{124}I contamination both on the system chosen and on the same type system as used here. Using the values of T_3, T_4, and D given above, if the ratio of A_4 to A_3 calculated from Eq. (5) differs significantly for the two systems, then the proper values of the constants must be obtained for the user's system from either of the two methods described.

The constant D is used to convert the reading of the dose calibrator for a pure sample of ^{124}I (adjusted to assay ^{123}I) to the correct activity value of the ^{124}I. Since a pure ^{124}I sample of known activity is not easily obtained, the method used here to find D takes advantage of the fact that the manufacturer of the dose calibrator has prescribed the proper setting to use for assay of ^{124}I.‡ This allowed determination of the actual amount of ^{124}I present in the sample after the ^{123}I had decayed to a negligible level (data labeled A_4 in Fig. 1). Use of a dose calibrator for which the assay of ^{124}I is not prescribed will require collection of this region of the characterization data on two dose calibrators: the R_U and R_S data will be acquired on the user's system while A_4 must be acquired on a system for which the assay of ^{124}I is possible—using the same sample. Calculation of D will follow otherwise the same procedure.

This assay procedure has been derived assuming that ^{123}I and ^{124}I are the only radionuclides present in the sample. If other radiocontaminants are present to the extent that they contribute to the dose calibrator readings, then the equations in the Appendix are not valid. Confirmation that other radionuclidic impurities were of no consequence in the samples used for this work was provided by examining pulse height spectra taken with a High Purity Germanium detector spectrometry system. At 30 days postcalibration, all major peaks observed were attributable to decay of ^{124}I, ^{126}I, and ^{123m}Te; the latter two were determined to be less than 1% of the ^{124}I activity present when the sample was received.

CONCLUSION

This convenient method of assaying ^{124}I contamination in ^{123}I radiopharmaceuticals can be performed in any clinical nuclear medicine facility. The specific results presented here can be used provided the same type dose calibrator, sample container and lead shield are employed. Use of other equipment may require one-time acquisition of characterization data as described.

FOOTNOTES

* ^{123}I-d,l-*N*-isopropyl-*p*-iodoamphetamine HCl, MediPhysics, Inc., Richmond, CA.

† Model CRC-10, Capintec, Inc., Ramsey, NJ.

‡ 570 on the Capintec CRC-10, Capintec, Inc., Ramsey, NJ.

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APPENDIX

Let R_3 and R_4 be the respective contributions of ^{123}I and ^{124}I to the reading, R_U, of a radionuclide dose calibrator which has been presented with an unshielded sample containing activities A_3 and A_4 of these two isotopes. Assume that the calibrator has been adjusted to assay ^{123}I. Hence $R_U = R_3 + R_4$. If the sample were pure ^{123}I, R_U would correctly equal the activity A_3. If the sample were pure ^{124}I, R_U would be proportional, not equal, to A_4 since the calibrator has been adjusted to assay ^{123}I; therefore one must write $R_4 = A_4/D$, where D is the constant of proportionality. Making these substitutions, the unshielded reading can be written

$$R_U = A_3 + A_4/D. \quad (1)$$

If the sample is now placed inside a closed lead canister (e.g., 6 mm thickness Pb cylinder) and assayed, the shielded reading in the dose calibrator, R_S, will be less than the unshielded reading and can be written

$$R_S = T_3A_3 + T_4A_4/D, \quad (2)$$

where T_3 and T_4 are the effective transmission factors of the shield for the radiations from the two isotopes.

Equations (1) and (2) can be solved simultaneously to eliminate either A_3 or A_4 to obtain:

$$A_4 = DR_U(R_S/R_U - T_3)/(T_4 - T_3), \quad (3)$$

$$A_3 = R_U(T_4 - R_S/R_U)/(T_4 - T_3). \quad (4)$$

Lastly, dividing Eq. (3) by Eq. (4) yields for the ratio of activities

$$A_4/A_3 = D(R_S/R_U - T_3)/(T_4 - R_S/R_U). \quad (5)$$

Equations (3-5) are the essential set for computing the amount and percent ^{124}I contamination of an ^{123}I sample. R_S and R_U are measured for the sample at the time of interest. The constants T_3, T_4, and D, which characterize the response

of the dose calibrator to the shielded and unshielded radiations from ^{123}I and ^{124}I, are determined as described in the Materials and Methods section.

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