Bioassay for Iodine-125

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The use of the volatile form of iodine-125 (^{125}I) in clinics and laboratories often imposes the responsibility of bioassay on nuclear medicine personnel. We reviewed several methods with respect to regulations and guidelines. Urinalysis is sufficiently sensitive when performed within two days of accidental ingestion; however, an action level cannot be set unambiguously. In vivo measurement is preferred. Discussion of this method was illustrated by the calibration of our detector system.

The usage of the volatile forms of iodine-125 (^{125}I) in the fields of nuclear medicine and research in medical centers requires monitoring of the thyroid burden. Bioassay is a task frequently assigned to the nuclear medicine department, where Iodine-131 (^{131}I) is used routinely. Iodine-125 has a longer half-life, with lower energy radiation than ^{131}I and the limits on thyroid burden, instrumentation, and methods of assay of these two isotopes are, therefore, quite different. The following is a review of bioassay techniques for ^{125}I with our own work as an example.

REGULATION AND GUIDELINES

The maximum permissible thyroid burden (MPTB) for ^{125}I as set by the United States Nuclear Regulatory Commission (USNRC) (*1*) is 0.5 μCi (18.5 kBq). The maximum permitted annual thyroid dose for ^{125}I recommended by the International Commission on Radiological Protection (ICRP) (*2*) is 50 rem (0.5 Sv). This has been translated by Bartolini et al. (*3*) to be 1.85 μCi (68.45 kBq) of thyroid burden. Other recommended MPTB values are: 0.4 μCi (14.8 kBq) from Bordell et al. (*4*) and 0.77 μCi (28.5 kBq) from Gavron and Feige (*5*). According to the latest NRC guidelines (*1*), bioassay should be performed whenever the individual handles in "open form" (e.g., an open bottle or container) more than 50 mCi (1.85 GBq) at any one time. Immediate action has to be taken if the thyroid burden at any time exceeds 0.5 μCi (18.5 kBq). Measurements need to be repeated at approximately one-week intervals until the thyroid burden falls below the action level of 0.12 μCi (4.44 kBq). A bioassay program should therefore have a sensitivity better than 0.12 μCi (4.44 kBq). Moreover, an agreement state may have stricter requirements in bioassay. Baseline studies of personnel are desirable and may be necessary.

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METHODS OF BIOASSAY

Direct and indirect measurements of thyroid uptake have been described by others (*6–11*). The methods fall into two categories: in vitro assay by urinalysis, and in vivo assay by a radiation detector.

Urinalysis Method

After an accidental or incidental ingestion of radioactive iodine, the amount not taken up by the thyroid will be excreted mostly in urine. Therefore, the concentration of iodine in urine is related to thyroid burden. Urine can be collected either in 24 hr or 48 hr postingestion to determine the amount of radioactive iodine retained in the body. Action level in this protocol can be estimated by the following sample computation. Let us assume that the subject has a thyroid burden of 0.12 μCi (4.44 kBq), the thyroid uptake is 25% after 24 hr, total body water output of 2,500 ml (including perspiration and 1,400 ml of urine) is passed in a 24-hr period (*8*) following accidental ingestion. The amount of ^{125}I excreted in urine could be as much as 0.20 μCi (7.4 kBq). The average amount in a 5-ml sample would be 0.71 nCi (26.27 Bq). However, the percentage of thyroid uptake and urine excreted in a 24-hr period will reflect individual variation. Vohs and Petersen (*11*) reported that the variation of normal thyroid uptake was between 10% and 35%. Urine excretion from normal individuals may range from 750 ml to 2,000 ml (*12*). Therefore, the amount of ^{125}I in a 5-ml sample could vary from 0.36 nCi (13.32 Bq) to 3.07 nCi (113.59 Bq). This uncertainty must be considered if one measures thyroid uptake by the urinalysis method. Conservatively, we can set an action level of 0.36 nCi (13.32 Bq) in a 5-ml sample from a 24-hr urine collection, in correspondence with limiting the thyroid burden to 0.12 μCi (4.44 kBq). The action level would be 1.5 nCi (55.5 Bq) for a thyroid burden limit of 0.5 μCi (18.5 kBq).

Collection of urine over an extended time frame discourages compliance with routine assay. Moreover, it is more convenient for the subject to give only one sample. If it is

known when the radioiodine is accidentally ingested, one can compute the thyroid burden with a reasonable model of kinetics. Recent guidelines for radioiodine bioassay from Canada (*9*) computed the relation of the total radioiodine content of the thyroid and the concentration in urine as a function of time after an acute intake of radioiodine. One mathematical model (*9*) enables determination of thyroid burden without knowing the initial time of exposure. If several measurements are made within five days of the intake, the thyroid burden, the time of initial exposure, and the amount ingested may be obtained. This model indicates that the initial concentration of ^{125}I in urine will fall to 10%, 0.6%, and 0.015%, respectively, after one day, two days, and five days. With the thyroid burden at the action level of 0.12 μCi (4.44 kBq), the maximum concentrations of ^{125}I in 5 ml urine after one day, two days, and five days are calculated as 0.24 nCi (8.88 Bq), 0.0143 nCi (0.53 Bq), and 0.00035 nCi (0.013 Bq), respectively. A typical gamma counter* has a sensitivity of 0.01 nCi (0.37 Bq) for a counting period of one minute. Therefore, bioassay of ^{125}I by urinalysis is possible for the first two days after intake. However, the sensitivity of the gamma counter will not be enough in urinalysis for more than two days after intake. Instead of urinalysis, in vivo measurement of the thyroid burden is more suitable.

Urinalysis has several disadvantages (*8,10*), including the inaccuracy of urine collection, sample preparation procedures, and great uncertainty of thyroid burden inferred from the results. One advantage is that no additional equipment is required. The gamma counter used for work with ^{125}I can be used for urinalysis.

In-Vivo Assay Method

Iodine-125 emits gamma photons and x-rays with energies of ~30 keV. Therefore, the window of the detector must be sufficiently thin to ensure transmittance of the low-energy photons. The enclosure of the NaI crystal in a detector used for ^{131}I thyroid uptake studies may be too thick for this purpose.

With a detector probe, there are two methods of measurement. The first method is single-photopeak counting. That is, an energy window is selected to accept the x-rays and gammas of 28-30 keV. These low-energy photons can also be easily absorbed and scattered by the tissues between the thyroid and the neck surface. This reduction in photon intensity must be corrected for the determination of thyroid burden. A detailed study of the absorption by tissues using ^{125}I and ^{131}I was presented by Porath et al. (*13*). Schulz and Rollo (*14*) proposed a two-distance method, in which they related the ratio of counts obtained from two prescribed distances of a subject to the effective thyroid depth. With this method, the activity can be measured without taking the thyroid depth into consideration. The simplest and most commonly used protocol to correct for tissue attenuation would be a calibration with a neck phantom. This procedure is sufficiently accurate for most purposes.

The second method of measurement is coincidence counting. It has been in use with ^{125}I in vitro and in vivo assay for more than two decades (*4,15–19*). Iodine-125 decays 100% by electron capture into tellurium-125, followed by a 35.5 keV gamma emission and two K x-rays with energies of 27.4 and 31 keV. This unique decay scheme of ^{125}I results in a primary single photopeak centered at 28.5 keV and a sum peak around 62 keV. The method of coincident detection of one gamma photon and one or more K x-rays can be used to determine the "absolute" amount of thyroid burden. Harper et al. (*15*) presented a simplified equation for coincidence counting which required only the total amount of photons and coincidences detected to calculate the absolute activity of an ^{125}I source. By making several assumptions, Eldridge and Crowther (*16*) extended the idea from Harper et al. and formulated this method with an equation for single detector as follows:

$$N_0 = [(N_p + 2 \times N_c)^2]/(4 \times N_c), \qquad \text{Eq. 1}$$

where N_0 is the disintegration rate of the source, and N_p and N_c are the measured counting rates from the primary and coincidence peaks, respectively.

The advantages of the coincidence method, in theory, are: (a) no standard sources are required, (b) precise positioning of the source in front of the detector is not necessary, and (c) the disintegration rate of a source is not dependent on the emission probabilities of photons and x-rays or on the resolution of the detectors. However, in practice there are limitations on accuracy and precision. Bordell et al. (*4*) suggested that the utilization of the coincidence method would be accurate only when the activity of the ^{125}I source was of the order of 1.5 μCi (55.5 kBq) or less. When the activity is high, the resolving time of the detecting system may not be short enough to distinguish between two emitting photons. Van Damme (*20*) showed that a counting error would result if the incident rate of photons were not sufficiently low to make the accidental coincidences negligible. Burns and Peggie (*21*), in their study with an arrangement of two detector probes, pointed out that accidental coincidence correction would be significant when the measuring activities exceeded 2.7 μCi (100 kBq). In a medical center, the amount of accidental ingestion is expected to be small. Thyroid burden of the personnel should be within the limitation mentioned previously.

CALIBRATION OF A THYROID PROBE DETECTOR

We put together a detector system with the following components: a 2M2 detector with a photomultiplier tube (PMT) and a 5×5 cm sodium iodide crystal†, a high-voltage power supply,‡ a preamplifier,§ an amplifier,¶ and a nuclear personal computer analyzer** (PCA) interface card. The detector has an aluminum entrance window of 0.01 in (0.254 mm) thickness and a removable flat-field collimator 5 cm in length and an inside diameter of 1 in. (2.54 cm). The analyzer circuit was installed in an IBM PS/2 Model 30 microcomputer to serve as a multichannel analyzer (MCA).

For single-photopeak counting, we adopt the definition of minimum detectable activity (MDA) as the counting rate of

three standard deviations (s.d.) above background. Absorption of the low-energy photons from a calibrating source by air and neck tissue is significant. Therefore, MDA for a particular working distance cannot be extrapolated from a measurement in air or by the inverse-square of distance. Discrepancies are illustrated in Figure 1, where values were obtained with and without a neck phantom and at various distances. The source used for calibration was a reference standard iodine-129 (^{129}I) with known activity of 0.098 μCi (3.63 kBq). The optimum viewing distance for our system was found to be 12 cm.

The minimum detectable activity of ^{125}I (measured at 12 cm with a one-minute counting period) was found to be 8 nCi (296 Bq) in air and 10 nCi (370 Bq) inside the neck phantom, respectively. Others (*3,21*) have quoted the MDA to be 1.6 nCi (59 Bq) and 8 nCi (296 Bq) with different experimental set-ups (i.e., size of the detector, optimum measured distance, and time for data acquisition).

The ^{125}I source used in the coincidence study was contained in a capsule 2 cm long. It had 4 μCi (148 kBq) at the time of measurement. After placement of the capsule inside the neck phantom, the experiment was done with the source placed directly under the crystal detector. To achieve a sufficiently high count rate in the coincidence study, we removed the collimator and placed the phantom close to the detector. Results of measurements made at several distances are presented in Figure 2, in which a dependence on distance is apparent. The change of the computed activity over 1 cm distance was calculated to be ~0.13 μCi (4.81 kBq) which was ~3% of the source activity. This error could come from: (a) the simplicity in our method of data analysis in which we did not use any curve-fitting in the spectrum to determine single and coincident counting rates, or (b) a systematic error associated with counting rate which decreases with distance.

To compare sensitivities of the two different techniques, the collimator was re-attached and an ^{125}I source was placed at 12 cm in air. Sensitivity of the coincidence technique is dictated by the count rate in the sum peak which is significantly less than count rate of the primary photopeak. Using three standard deviations above background as a criterion,

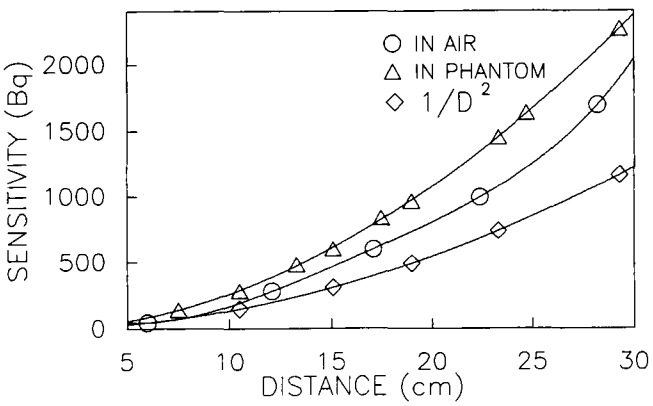

FIG. 1. MDAs of ^{125}I in air and inside a neck phantom. Values predicted by inverse squares of distance are presented for comparison.

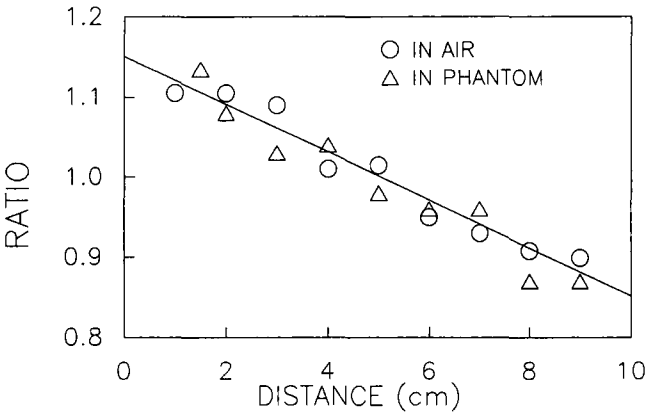

FIG. 2. Results of coincidence technique are presented as the ratios of measurement to the known activity.

the MDA for a one-minute counting period was found to be 1.75 μCi (64.75 kBq). The corresponding parameter in single-photopeak counting was 8 nCi (296 Bq).

SUMMARY

Urinalysis is not a preferred method of bioassay for ^{125}I. Interpretation of its results is affected adversely by the significant biologic variation of each subject. When measurements are made beyond 48 hrs of ingestion, the action level is below the sensitivity of this method. With careful calibration, in vivo measurement with single-photopeak counting can be sufficiently accurate and sensitive. In contrast to the single-photopeak counting, coincidence counting is much less sensitive.

We have presented an overview of bioassay of ^{125}I for readers who are interested in initiating their own programs. Methods of measurement and calibration were illustrated.

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NOTES

* Gamma Tracor 1191, T-M Analytic, Inc., Elk Grove Village, IL.

† Bicron, Inc., Newbury, OH.

‡ ORTEC 556H high-voltage power supply, ORTEC EG&G, Oak Ridge, TN.

§ ORTEC 113 preamplifier, ORTEC EG&G, Oak Ridge, TN.

¶ ORTEC 575 amplifier, ORTEC EG&G, Oak Ridge, TN.

** Nuclear Personal Computer Analyzer interface card, the Nucleus, Inc., Oak Ridge, TN.

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