PREDICTING THE MINIMUM ACTIVITY REQUIRED FOR THYROID-UPTAKE STUDIES

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In the diagnostic use of radioisotopes, one must strive to administer to the patient the smallest amount of radioactivity consistent with the demands of the study. The activity required for a satisfactory thyroid-uptake study is the activity that reduces the statistical counting uncertainty in the uptake result to an acceptable level in a reasonable counting time. Additional activity results in unnecessarily good statistics and increases the radiation dose to the patient.

In general, the activity required depends on the sensitivity of the detector used, the counting times, the room background and the fraction of the tracer taken up by the thyroid. Doses of 5–20 μCi of ^{131}I are usually recommended in the literature for use in thyroid-uptake studies. Since 10 μCi of ^{131}I produces a thyroid dose of about 15 rads in a normal uptake study (*1*), one should ask whether the commonly recommended amounts of radioactivity are necessary. Although most sources of error in thyroid-uptake studies have been thoroughly investigated (*2,3*), the quantitative control of counting statistical errors is neglected in the literature. Some authors remark that the activity required depends on detector sensitivity, but no one has analyzed the dependence of the required activity on the several variable factors. Cameron and Bell (*4*) studied the use of very small amounts of ^{131}I with conventional instrumentation but did not show how their experimental parameters affected the activity required.

This paper develops an expression which permits calculation of the activity required for an uptake study using any given set of clinical parameters. We have found that the amount of activity required in our laboratory is much less than is generally recommended. Since our equipment and clinical procedure are not unusual, we feel that others may also find that they can markedly reduce patient dose in thyroid-uptake studies with no change in instrumentation and with little or no additional clinical effort.

CLINICAL PROCEDURE

In our thyroid-uptake procedure the patient swallows a capsule of ^{131}I which has been calibrated by the manufacturer and checked in our laboratory. The patient is counted after 2 hr and again after 24 hr with a 2-in. $\times$ 2-in. NaI(Tl) scintillation detector in a flat-field collimator; the front surface of the crystal is positioned 25 cm from the skin surface. The detector calibration factor is measured by counting an accurately assayed capsule at a depth of 2 cm in a 20 $\times$ 20 $\times$ 27 cm pressed-wood phantom. Counting is performed with a 100 keV pulse-height analyzer window centered on the 364-keV photopeak. The counting rate over the patient's thigh is assumed to indicate the background counting rate over the neck due to body background plus room background.

The percent uptake is calculated from the equation:

$$P = \frac{100(R_N - R_T)}{A\epsilon e^{-\lambda t}} \qquad (1)$$

in which R_N is the counting rate over the neck (cpm), R_T is the counting rate over the thigh (cpm), A is the activity administered (μCi), ϵ is the detector calibration factor (cpm/μCi), λ is the decay constant of the isotope and t is the time between the administration of the activity and counting.

If the total background counting rate over the neck is measured over the neck with a lead thyroid shield rather than over the thigh, then the following analysis should also apply if shielded counting rates and counting times are substituted for the appropriate thigh terms.

ERROR IN UPTAKE MEASUREMENT DUE TO COUNTING STATISTICS

We intend to develop an expression to relate the activity given the patient to the uncertainty in the uptake result due to counting statistical uncertainties in measurement of the net thyroid counting rate $R = R_N - R_T$.

Although other sources of error affect the uptake

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measurement, only the uncertainty in determining the net thyroid counting rate depends directly on the activity which the patient receives.

Equation 1 could be written as

$$P = \frac{R}{kA} \qquad (1a)$$

in which $k \equiv 0.01\,\epsilon e^{-\lambda t}$. Then the standard deviation in the uptake result due to uncertainty in measuring the net counting rate R is given by

$$S_P = \frac{1}{kA} S_R \qquad (2)$$

in which S_R is the standard deviation of the measurement of the net counting rate. Note that S_P is measured in units of percent uptake.

Since the standard deviation of the sum or difference of two independent quantities x and y is given by $(S_{x\pm y})^2 = S_x^2 + S_y^2$, and since $R = R_N - R_T$, we can write

$$S_R = (S_{R_N}{}^2 + S_{R_T}{}^2)^{1/2} \qquad (3)$$

so

$$S_P = \frac{1}{kA}\left(S_{R_N}{}^2 + S_{R_T}{}^2\right)^{1/2}. \qquad (3a)$$

According to Poisson counting statistics the estimated standard deviations in the neck and thigh counting rates are:

$$S_{R_N} = \left(\frac{R_N}{\tau_N}\right)^{1/2} \text{ and } S_{R_T} = \left(\frac{R_T}{\tau_T}\right)^{1/2} \qquad (4)$$

in which τ_N and τ_T are the times spent measuring the counting rates R_N and R_T. Thus the estimated standard deviation in the uptake result due to counting statistical uncertainties is

$$S_P = \frac{1}{kA}\left(\frac{R_N}{\tau_N} + \frac{R_T}{\tau_T}\right)^{1/2}. \qquad (5)$$

Using Eq. 1a and the fact that $R = R_N - R_T$, we find

$$S_P{}^2 = \left(\frac{1}{kA}\right)^2 \left[\frac{kAP}{\tau_N} + \left(\frac{1}{\tau_N} + \frac{1}{\tau_T}\right) R_T\right]. \qquad (6)$$

The dependence of S_P on the activity A given to the patient is not explicit in Eq. 6 since the counting rate over the thigh R_T depends in general on how much activity the patient receives. The counts registered over the thigh are due both to radioactivity in the patient's thigh and to room background. The counting rate over the thigh can be written

$$R_T = R_{BB} + R_{RB} \qquad (7)$$

in which R_{BB} is the counting rate due to radioactivity in the thigh and R_{RB} is the room background counting rate. The body background counting rate R_{BB} should be proportional to the amount of radioactivity in the patient's thigh. We therefore propose the mathematical *model* that the body background counting rate can be expressed by

$$R_{BB} = fA(100 - P_{EX} - P) \qquad (8)$$

in which f is a constant of proportionality and P_{EX} is the percent of the administered activity which is either excreted or concentrated in some part of the body other than the thyroid and not in the thigh.

If we accept the model given by Eq. 8, then Eq. 6 can be written

$$S_P{}^2 = \left(\frac{1}{kA}\right)^2 \left\{\frac{kAP}{\tau_N} + \left[\frac{1}{\tau_N} + \frac{1}{\tau_T}\right] \left[fA\left(100 - P_{EX} - P\right) + R_{RB}\right]\right\}. \qquad (9)$$

Equation 9 gives the expected standard deviation in the uptake result due to counting statistical uncertainty as an explicit function of the activity A given to the patient. Equation 9 can be solved for A, yielding

$$A = \frac{100\,[1 + (\tau_T/\tau_N)]}{2\epsilon T S_P{}^2 e^{-\lambda t}} \left[P + \frac{Tf}{\tau_T k}\left(100 - P_{EX} - P\right)\right] \left[1 + \left(1 + \frac{4R_{RB}TS_P{}^2\,(\tau_N/\tau_T)}{\left[P + \frac{Tf}{\tau_T k}\left(100 - P_{EX} - P\right)\right]^2}\right)^{1/2}\right] \qquad (10)$$

in which $T = \tau_N + \tau_T$ is the total time spent counting the patient. Equation 10 gives the activity A which will result in an expected standard deviation S_P in the uptake result due to counting statistical uncertainty.

CALCULATION OF THE ACTIVITY REQUIRED

Unfortunately, Eq. 10 cannot be used directly to calculate the activity required for an uptake study since values are not known for all of the factors on the right side of the equation. The percent uptake P is not known before the uptake study is performed; the value of the constant f is not known; and P_{EX} cannot be confidently predicted in the individual case before the uptake study is done because of the wide variation in plasma and urine activities after administration of ^{131}I (*5*).

However, Eq. 10 can be used to compute the *upper limit* of the activity required to produce a standard deviation S_P. Since from Eq. 10 the activity required is maximum if P is maximum, that is if $P = 100$, then a calculation performed assuming $P = 100$ will somewhat overestimate the activity required to produce a standard deviation S_P in the real situations when the uptake is less than 100%. In all cases of less than 100% uptake, the standard deviation in the uptake result due to counting statistical uncertainty should be *less than* S_P since the required activity was overestimated. Thus if a calculation is performed assuming $P = 100$, S_P in Eq. 10 should be interpreted as the *maximum allowable* standard deviation in the uptake result due to counting statistical uncertainties.

If $P = 100$, then $P_{EX} = 0$ and Eq. 10 reduces to

$$A = \frac{5{,}000\,[1 + (\tau_T/\tau_N)]}{\epsilon T\, S_P^2\, e^{-\lambda t}} \left\{ 1 + \left[1 + \frac{4R_{RB} T\, S_P^2}{(\tau_T/\tau_N) \times 10^4} \right]^{1/2} \right\}. \quad (11)$$

All of the factors on the right side of Eq. 11 can be either measured or clinically determined before the uptake study is performed so the equation can be used to calculate the activity required for an uptake study to ensure a standard deviation less than S_P in the uptake result due to counting statistics.

FACTORS INFLUENCING THE ACTIVITY REQUIRED

To calculate the activity required, one must, of course, measure or choose values for the factors on the right side of Eq. 11.

The room background counting rate R_{RB} can be easily measured to any desired accuracy. Although room background should be fairly constant from day to day, it should be checked periodically to guard against any marked change.

The detector calibration factor ϵ is fixed by the detector and counting distance used in the study and can be measured to any desired accuracy by counting a neck phantom containing an accurately assayed source.

The acceptable standard deviation S_P in the uptake result due to counting statistical uncertainty in the measurement of the net counting rate must be chosen in the perspective of other errors in thyroid-uptake studies. The recommendations of consultants for the International Atomic Energy Agency state (*6*): "In view of the number and magnitude of other errors involved in thyroid-uptake measurements, it is not necessary to aim at a less than three percent error in counting statistics." If we interpret "error" to mean the 95% (2σ) confidence limits of the uptake result due to counting statistics, then an error of 3% uptake corresponds to $2S_P = 3$ or to a value of $S_P = 1.5$ in Eq. 11.

Choice of the total time T to be spent counting the patient must be made on the basis of practical considerations. In most cases the first (T^{-1}) factor in Eq. 11 will predominate, and the activity required will be roughly inversely proportional to the total counting time T. In any case, the rate of reduction of required activity diminishes as the total counting time is increased. Reduction in patient dose must be balanced against the increased time required for each study. In light of the total time spent registering and preparing the patient, we have found that 5 min is an acceptable total counting time.

The ratio (τ_T/τ_N) is determined by the division of the available counting time between neck and thigh. Although one could simply take $\tau_N = \tau_T = T/2$ and calculate the required activity from Eq. 11, equal division of the total counting time is not maximally efficient. Generally, the most efficient division of total counting time, $\tau_N + \tau_T$, in the measurement of a net counting rate $R_N - R_T$ is (*7*)

$$\frac{\tau_N}{\tau_T} = \left(\frac{R_N}{R_T}\right)^{1/2} \quad (12)$$

It is clear from Eq. 12 that equal division of the available counting time is efficient only if $R_N = R_T$; that is, for zero uptake. For all cases in which the uptake will be greater than zero, R_N should be greater than R_T, and more than half of the available time should be spent counting over the neck.

The counting rate ratio R_N/R_T will depend on the percent uptake P and on the activity administered A. Assuming the model for the body background counting rate developed above, we can write

$$\frac{R_N}{R_T} = 1 + \frac{kAP}{R_{RB} + fA(100 - P_{EX} - P)} \quad (13)$$

The ratio should vary from unity for low uptakes ($P \rightarrow 0$) to approximately $1 + (kAP/R_{RB})$ for high uptakes ($P + P_{EX} \rightarrow 100$). For low uptakes ($P \rightarrow 0$), we might expect that the ratio is approximately given by:

$$\frac{R_N}{R_T} \doteq 1 + \frac{kAP}{R_{RB} + fA(100 - P_{EX})} \quad (14)$$

Thus R_N/R_T should be roughly a linear function of P for low uptakes.

To investigate the best division of the total available counting time, the ratio R_N/R_T was measured as a function of percent uptake. Since the required activity predicted by Eq. 11 is a rather insensitive function of τ_N/τ_T for $\tau_N/\tau_T > 1$, we arbitrarily chose $\tau_N/\tau_T = 4$ as a first approximation and calculated the activity required for this case. For our study parameters ($\epsilon = 2{,}000$ cpm/μCi; $R_{RB} = 150$ cpm; $t = 24$ hr; $T = 5$ min) we calculated from Eq. 11 that 0.89 μCi of ^{131}I was required to ensure a standard deviation of less than 1.5% uptake. The results of 58 uptake studies done using 0.6–1.1 μCi of ^{131}I are plotted in Fig. 1. The ratio R_N/R_T seems to be a roughly linear function of percent uptake. The counting-rate ratio is not appreciably different for 2 or 24-hr studies; with such small amounts of radioactivity the counting rate over the thigh is due

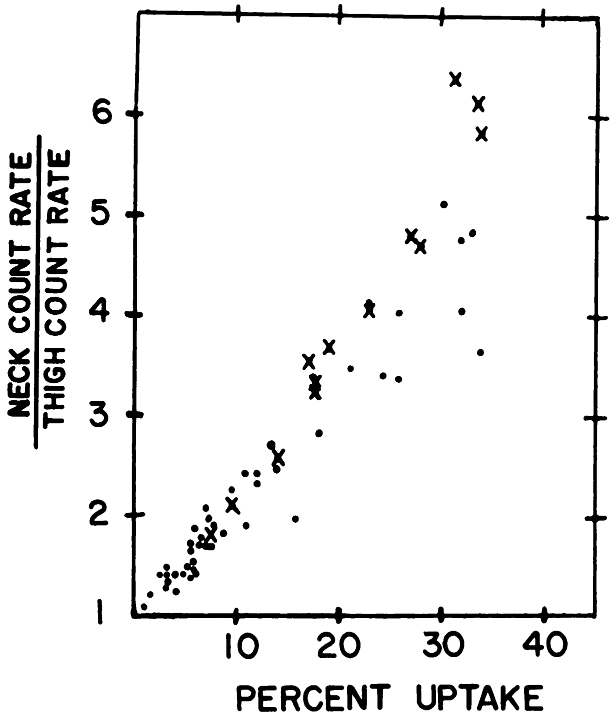

FIG. 1. Neck-thigh counting-rate ratio as function of percent uptake. Dot indicates 2-hr study; X indicates 24-hr study. Subjects ≐ 2,000 received 0.6–1.1 μCi of ^{131}I orally. Detector sensitivity cpm/μCi; room background ≐ 150 cpm.

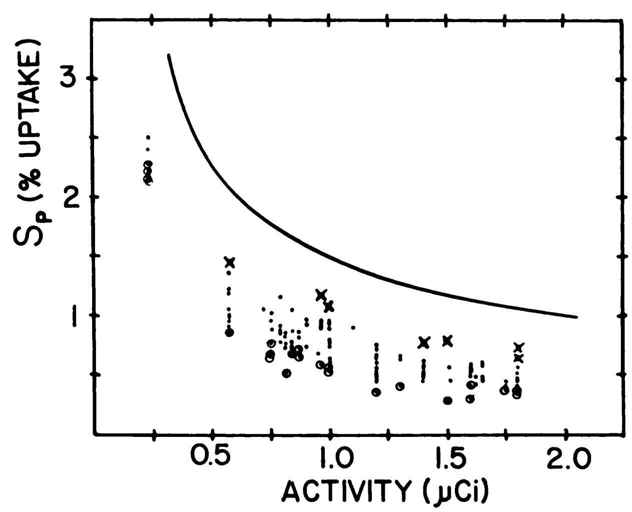

FIG. 2. Comparison between predicted maximum and observed counting statistical standard deviations in the uptake result as a function of ^{131}I activity administered. Solid curve represents predicted maximum S_P calculated from Eq. 11 for 24-hr uptake studies. Individual points are pooled 2 and 24-hr uptake data. ⊙ indicates uptake less than 5%; X indicates uptake greater than 40%. Detector sensitivity ≐ 2,000 cpm/μCi; room background ≐ 150 cpm; neck counting time = 3 min; thigh counting time = 2 min.

almost entirely to room background and is thus essentially independent of plasma activity. For uptakes in the normal range the counting rate ratio is roughly 3, so the most efficient division of counting time $\tau_N/\tau_T = (R_N/R_T)^{1/2}$ is about 1.5. If $\tau_N/\tau_T = 1.5$ is substituted into Eq. 11 as a second approximation, we find that 0.97 μCi is required for that case. Since the counting-rate ratios with 0.89 and 0.97 μCi should be nearly equal, we have converged by successive approximations on the most efficient division of the counting time. Convergence toward the most efficient value of τ_N/τ_T for normal uptake studies was rapid because the activity predicted by Eq. 11 is an insensitive function of τ_N/τ_T and because the maximally efficient ratio τ_N/τ_T, as given by Eq. 12 is an insensitive function of the ratio R_N/R_T and, in turn, of the administered activity.

In principle the ratio τ_N/τ_T should be varied for each patient, depending on the expected uptake. However, the data of Fig. 1 and Eq. 12 show that the maximally efficient counting-time ratio τ_N/τ_T is not very different from 1.5 for any commonly observed uptake. We decided to set τ_N/τ_T equal to 1.5 for all uptake studies rather than establish a different clinical procedure for each patient on the basis of predicted uptake. We now routinely count 3 min over the patient's neck and 2 min over the thigh.

RESULTS

The standard deviation in an individual uptake result due to counting statistical uncertainty in the measurement of the net thyroid counting rate can be estimated from the data of the study by using Eq. 5.

Figure 2 illustrates the counting statistical standard deviations observed in a series of 135 consecutive technically satisfactory uptake measurements; the horizontal axis shows the ^{131}I activity used in each study. Equation 11 is plotted as a solid curve on the same figure and shows the relationship between the activity administered in an uptake study and the predicted maximum counting-statistical standard deviation. In each case, the observed standard deviation was found to be less than the maximum expected standard deviation S_P of Eq. 11. Thus the activity calculated using Eq. 11 does result in a standard deviation less than the acceptable limit S_P.

The data of Fig. 2 also seem to verify the functional form of Eq. 11. The experimental points are grouped parallel to and below the line representing the equation. The standard deviations are greatest and closest to the solid curve for high uptakes and are smallest for low uptakes. A hypothetical "best-fit" line through the experimental points might be thought of as the result of Eq. 10 for the "average" percent uptake P, while the solid curve of Eq. 11 represents the limiting case of P = 100.

CONCLUSION

Equation 11 has been shown to successfully predict the activity required in thyroid-uptake studies to ensure a standard deviation due to counting statistics less than a predetermined maximum. Calculations based on this model predicted that an administered activity of only about 1 μCi of ^{131}I is required in our laboratory to produce an uptake result with acceptable counting statistical accuracy. Analysis of the results of 135 consecutive uptake studies has confirmed this approach.

SUMMARY

An expression is developed which permits calculation of the administered activity required for acceptable statistical accuracy in a thyroid-uptake study using any given set of clinical parameters. Approximately 1 μCi of ^{131}I is found to be sufficient for studies done using a scintillation detector with a 2 × 2-in. crystal and a total counting time of 5 min.

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REFERENCES

1. Hine, G. J. and Loevinger, R.: Application and radiation dose of radioisotopes in medicine. In *Instrumentation in Nuclear Medicine*, G. J. Hine, ed., Academic Press, New York, 1967, p. 626.

2. Brucer, M.: Thyroid radioiodine uptake measurement. A standard system for universal intercalibration. *U.S. AEC Report ORINS-19*, June, 1959.

3. Crespo, G. G. and Vetter, H.: The calibration and standardization of thyroid radioiodine measurements. *Intern. J. Appl. Radiation Isotopes* **17**:531, 1966.

4. Cameron, J. R. and Bell, D. B.: Thyroid uptake studies with ^{131}I in very small doses. *Radiology* **79**:452, 1962.

5. Berman, M., Hoff, E., Barandes, M., Becker, D. V., Sonenberg, M., Benua, R. and Koutras, D. A.: Iodine kinetics in man—a model. *J. Clin. Endocrinol.* **28**:1, 1968.

6. Report of consultants of the International Atomic Energy Agency. The calibration and standardization of thyroid radioiodine uptake measurements. *Phys. Med. Biol.* **6**:533, 1962.

7. A manual of radioactivity procedures. NCRP Report No. 28. *National Bureau of Standards Handbook 80*, U.S. Department of Commerce, Washington, D.C., 1961.

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