jnm/INSTRUMENTATION AND PHYSICS

Estimation of Thyroid Depth and Correction for I-123 Uptake Measurements

Peter M. Martin and F. David Rollo

Veterans Administration Hospital, San Francisco, California

A new technique has been developed to correct I-123 uptake measurements for the effect of gland depth. The method uses the effect of differential tissue absorption and/or scatter of photons of different energies, and measures the ratio of counts of the primary I-123 emission to the counts of the tellurium K shell x-ray to determine a depth-correction factor. A comparison of this new method against three previously reported methods indicates that the present method provides the most sensitive index of gland depth. The method is sensitive to depth changes, is not significantly dependent on detector distance ($p > 0.05$) for distances greater than 18 cm, and is not dependent on gland size ($p > 0.25$), within the range 20–40 ml. In a group of 40 patients, the ORINS phantom method was found to underestimate the mean gland depth by about 1 cm, thereby causing an average uptake error of 23%. The application of the depth-correction factor was found to change the interpretation of uptake estimates in approximately 10% of the cases in this limited series.

J Nucl Med 18: 919–924, 1977

Thyroid uptake measurements with radioiodine have been performed with several radionuclides (*1–4*). Several sources of inaccuracy and inconsistency have been noted with all of these agents. For example, the effect of encapsulation of iodine-123 has been shown to generate results inconsistent with those of iodine-131 (*1*). Radionuclide purity has also been shown to affect the estimation of uptake (*2*).

Gland depth is another factor that can affect thyroid uptake estimates. The magnitude of the effect varies with the radionuclide used. The effect of neck tissue on the count rate is estimated to be −15%/cm for I-123, −50%/cm for I-125, and −11%/cm for I-131, based on absorption at photopeak energies by intervening soft tissue. The position of the gland can also affect uptake. For example, a substernal thyroid can result in low uptake estimates when low-energy radionuclides are used.

Efforts have been made to correct for variations in gland depth for I-131 (*3,6*), I-125 (*4*), and I-123 (*2*). The methods include the use of a ratio of counts obtained at different detector distances or at different energy selections. All methods rely on the generation of a calibration curve from phantom measurements. This curve is used to determine a correction factor that corrects for the variation of the patient's thyroid gland depth from the normal, or reference, thyroid depth.

Iodine-123 is becoming increasingly popular for thyroid uptake measurements. The purpose of this paper is to describe a simple and sensitive new method of correcting uptake measurements for the effect of gland depth when this radionuclide is used. The results of a comparison between this new method and three previously reported methods of corrections for depth will also be discussed. These

Received July 12, 1976; revision accepted April 11, 1977.

For reprints contact: Peter M. Martin, Veterans Administration Hospital, 4150 Clement St., San Francisco, CA 94121.

methods we will call the two-peak (2P) method, the two-distance (2D) method, the peak-to-scatter (PS) method, and the standard ORINS method.

Finally, the effect of depth correction on uptake measurements will be presented.

METHODS AND MATERIALS

The detector system used in this study was a 2 in. × 2 in. NaI(Tl) crystal restricted by a flat field 11.5-cm-long collimator. The detector was interfaced to a multichannel pulse-height analyzer and scaler. Background and dead-time corrections were made, as were decay corrections for the 13.3-hr half-life of I-123. The dead-time correction was accomplished by live-time counting. The energy windows used were: 136–175 keV (25%) for the 159-keV photopeak, 20–40 keV (75%) for the 28-keV x-ray peak, and 82–112 keV for the Compton scattering range. No correction was made for the contribution of scattered photons to the counts in the 18-keV window.

The I-123 was produced using the $^{122}Te(d,n)^{123}I$ reaction.* At the time of calibration, it included the following impurities: I-130 < 3.2%, I-124 and I-126 < 1.1%, I-131 < 0.8%, Na-24 < 0.5%.

The calibration measurements are made with a neck and thyroid gland phantom in which the "gland" phantom depth may be varied. The neck phantom is a water-filled plastic cylinder 17 cm in height and 15 cm in diameter. Within this, the gland phantom consists of two test tubes, each 2 cm in diameter and 6 cm long. Each tube is filled with I-123-labeled solution and suspended with a ringstand and dowels. The tubes are mounted on an air-filled plexiglass tube in order to simulate the trachea. By moving the gland phantom relative to the neck phantom and detector, various gland depths are simulated. The size of the gland in the phantom is varied by distributing the same amount of activity among varying numbers of test tubes. Volumes of 10, 20, and 40 ml are used. Gland depths ranging from 2 to 10 cm in 1-cm increments are used for each volume. The detector-to-phantom distance was normally 25 cm.

Two-peak method (2P). In the two-peak method, the counts for the two spectral peaks of I-123 (Fig. 1) are recorded simultaneously from the neck-and-gland phantom for calibration, and from the ORINS phantom as a reference. The ratio of counts for the two peaks, gamma/x-ray, is used as an index, ρ_P, which varies with gland depth. The detector is located at 25 cm from the surface of the neck phantom, and counts are recorded for 1 min. The ratio of the gamma counts from the ORINS phantom to the gamma counts under the various calibration conditions provides a depth-correction factor, K. The calculations consist of (a) plotting the count ratio, ρ, versus the distance, d, and fitting the data to a linear model; and (b) lotting the correction factor, K, compared with the ratio, ρ, and fitting the data to an exponential model.

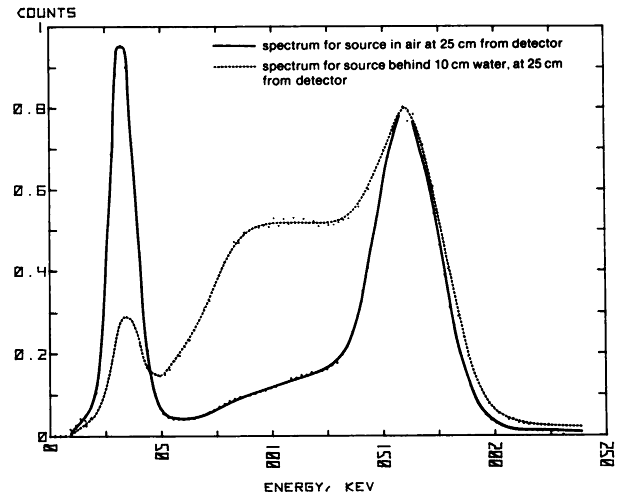

FIG. 1. Spectrum of iodine-123 with NaI(Tl) crystal detector at 25-cm distance, in air (solid), and with 10 cm H_2O absorption medium surrounding (dashed). Peaks are normalized to the same height at 159 keV.

For patient measurements, the counts for the two spectral peaks are recorded for the ORINS phantom, and again for the patient at 24 hr. The counts used for uptake determination are then multiplied by the correction factor to correct for depth. For the patient, since the factor, K, cannot be determined directly, it is determined indirectly through the measurement of the depth index ρ_P for that patient, and the use of the calibration curve, K (ρ_P).

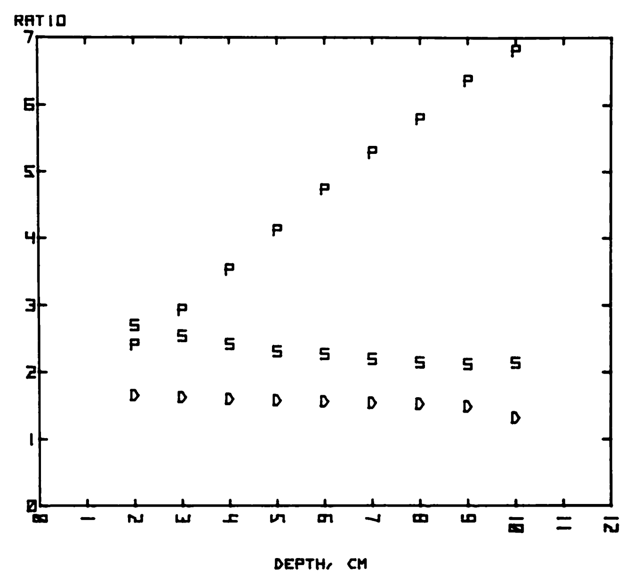

FIG. 2. Count ratios, ρ_P, ρ_s, ρ_D, for three methods vs. phantom gland depth, d, 25-cm detector distance. Two-peak method = ρ_P (P); peak/scatter method = ρ_s (S); two-distance method = ρ_D (D).

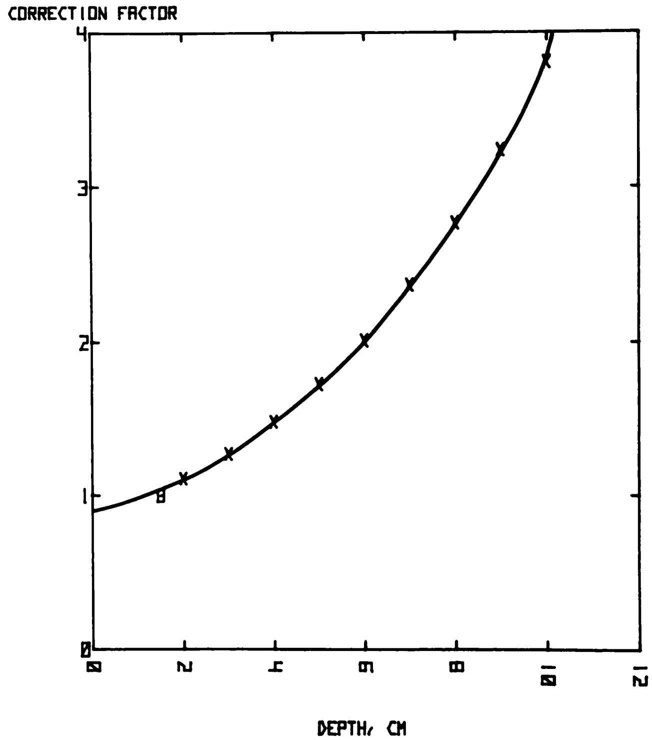

FIG. 3. Depth-correction factor, K, vs. phantom gland depth, d, for distance of 25 cm. ORINS phantom is indicated by ⊙.

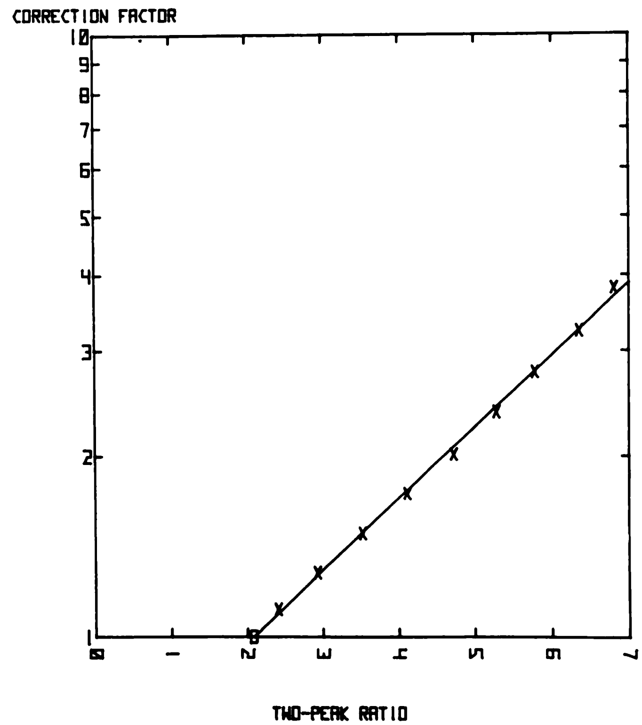

FIG. 4. Calibration curve: K(ρ), for D = 25 cm, using two-peak method. ORINS phantom is indicated by ⊙.

Two-distance method (2D). In the two-distance method, the counts for the primary peak of the I-123 spectrum are recorded for the detector at two different distances, 18 cm and 25 cm, from the surface of the neck or neck phantom. The ratio of counts for 18 cm to those for 25 cm is used as an index of gland depth, ρ_D, as described by Rollo and Schulz (*4,6,7*). In other respects this method proceeds as in the two-peak method.

Peak-scatter method (PS). In the peak-scatter method, the counts are recorded for an energy window centered on the primary peak of I-123 and for another window within the Compton scatter region lying below that peak. The ratio of peak counts to scatter counts is then used as an index, ρ_S, for the gland depth. Sodd et al. (*2*) used this method with I-123, although they placed a Ge(Li) detector at the neck surface. Wellman et al. (*3*) used this method with I-131, both for a NaI(Tl) detector located 25 cm in front of the neck, and for two NaI(Tl) detectors located obliquely at the neck surface. In other respects, our PS method follows the 2P procedure.

ORINS method. In the ORINS method, a cylindrical plexiglass phantom is used to make a standard correction for gland depth. The dose is placed in a hole in the phantom at a standard depth of 1.5 cm. The 1-min counts are used as a 100% value for uptake calculations.

Patients. For each patient study, the patient's dose of I-123 was counted in the ORINS phantom before being given to the patient. The dose was placed in a single hole in the phantom at a depth of approximately 1.5 cm from the surface. One-minute counts were recorded for the spectral peaks, with the detector at its usual 25-cm distance. At 24 hr after dose, 1-min counts were recorded for the two peaks derived from the thyroid region. These data were then corrected for background by using counts from the thigh.

RESULTS

Calibration. As the simulated thyroid depth was varied from 2.0 to 10.0 cm, the 2D ratio, ρ_D, was observed to decrease slightly from 1.66 to 1.32; the PS photopeak/scatter ratio, ρ_S, decreased slightly from 2.70 to 2.12; but the 2P gamma/x-ray peak ratio, ρ_P, increased linearly and significantly from 2.41 to 6.81 (Fig. 2). The depth-correction factor was observed to increase from 1.1 to 3.8 (Fig. 3). Figure 4 presents the computed calibration curve, a plot of the depth-correction factor, K, compared with count ratio, ρ_P. The correction factor varied with depth by 16.2%/cm, yielding the simple exponential curve in Fig. 3. The two-peak count ratio,

ρ_P, appears to be the index most sensitive to depth changes. The calibration curve of K compared with ρ_P (hereafter, ρ) in Fig. 4 thus presents itself as the best source for gland-depth correction.

The point-source assumption was tested by measurements of the thyroid phantom in air at various distances, R, from 20 to 30 cm. Applying a linear regression analysis to a logarithmic transformation of the data, the count rate was found to vary with distance to the -1.67 ± 0.01 (SE) power. The count rate from a point source varies with R to the -2 power.

The dependence of K upon detector distance, D, was investigated by comparing the straight lines of best fit of ln K(d) for D = 18 cm and for D = 25. The slopes of the lines [0.177 ± 0.001 (SE) cm^{-1} and 0.162 ± 0.001 cm^{-1}, respectively, for a phantom volume of 20 ml] were compared by analysis of variance and were found to be significantly different ($p < 0.01$).

The dependence of K upon phantom volume was investigated in the same manner. Volumes of 20 and 40 ml were compared. The slopes (0.162 cm^{-1} $\pm$ 0.001 and 0.162 cm^{-1} $\pm$ 0.001, respectively, for a detector distance of 25 cm) were identical, to the degree of accuracy permitted.

The elevations of these lines differed, but the differences were considered to result from systematic errors, and hence no analysis was made of them.

The dependence of the calibration curve, $K(\rho)$, on detector distance and phantom volume was investigated by the same process. The straight lines of best fit for ln K compared with ρ were compared for D = 18 and 25 cm, and for V = 20 and 40 ml. Dependence on detector distance was not significant ($p > 0.05$), and dependence on phantom volume was also not significant ($p > 0.05$). That the lines compared were linear under the logarithmic transformation within the range of the data was tested by the correlation coefficient, r. In all cases, $r > 0.995$.

Within experimental error, and without extrapolation, this linearity permits an analytical expression of the calibration curve:

$$K(\rho) = K_0 e^{a\rho}, \quad (1)$$

where

$a = 0.276 \pm 0.002$ (SE) and

$$K_0 = 0.56 \times (1 \pm 0.024).$$

One may also express the depth estimation as:

$$\rho = 0.560\ (\pm 0.003) d + 2.10\ (\pm 0.05), \text{ for } V = 20 \text{ ml.} \quad (2)$$

Patients. In a sample of 40 patients, the ratio of counts of the gamma rays to those of x-rays ranged from 1.9 to 5.1, with a mean of 2.80. By using a linear regression analysis of $d(\rho)$ to determine the depth, and an exponential regression analysis of $K(\rho)$ to determine the correction factor, a set of corresponding depths and corrections were calculated (Fig. 5).

The estimates of gland depth, d, ranged from 1.0 to 6.6 cm, with a mean of 2.74 cm. In almost all cases, the ORINS phantom underestimated the gland depth.

The correction factor, K, ranged from 0.97 to 2.3, with a mean of 1.23. Thus, on the average, the correction due to depth increased the measured uptake by 23% and, at the extreme, increased the measured uptake by 130% (Fig. 6).

DISCUSSION

The application of the two-window method using the scattering region differs in this study from that reported earlier (*3*). In the current study, a single NaI(Tl) probe was used for all measurements at a distance of not less than 18 cm from the neck, whereas previously multiple detectors or the better energy-resolving, less sensitive Ge(Li) detector was

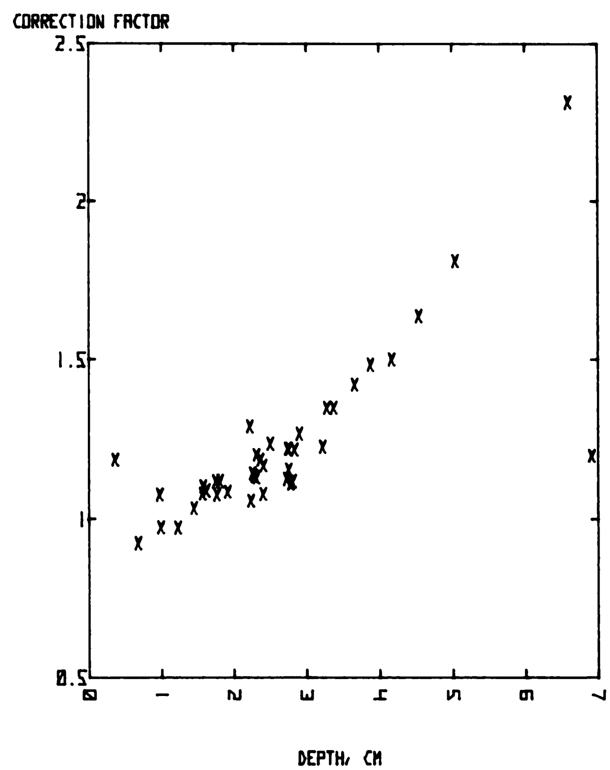

FIG. 5. Distribution of correction factors and depths in a sample of 40 patients. The plot is from phantom studies.

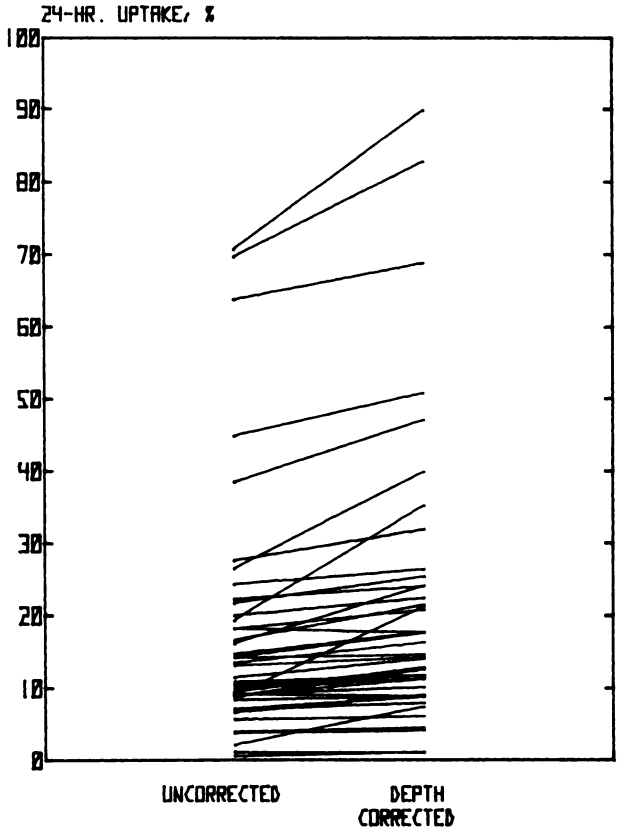

FIG. 6. Effect of correction factor on distribution of 24-hr uptake in patients. Data on left represent the uptakes before correction for gland depth; on right, uptake after correction.

used at the neck surface. The present study was done to simulate a common clinical situation as closely as possible.

The data available from Sodd et al. (*2*) suggest that the count ratio of gamma photons to x-rays may not be a significant index of gland depth. The geometry used in that study, however, put the detector at the neck surface. Locating the detector at some distance from the source (at least four times the gland's transverse dimension) reduces the solid angle subtended by the detector, making the tissue absorption predictable. The ratio of counts for the two energy windows under the present conditions may then be a likely index of gland depth.

Any of the three different methods evaluated in this study may be used to estimate the thyroid depth, and to generate a depth-correction factor. It is clear from Fig. 2, however, where the count ratios are plotted as a function of gland depth, that the methods are not equally sensitive in indicating variations in gland depth. They may be compared by considering the sensitivity for each method, defined as the fractional change in the count ratio for unit change in gland depth—or, in graphic terms, the mean slope of the curve of ln $\rho(d)$, where the count ratio is plotted on a logarithmic scale. For the sake of comparison, a linear approximation for each curve may be made, and the sensitivity of each method may then be expressed as the mean fractional count-rate change per unit change in effective gland depth. The sensitivity is then -0.014 cm^{-1} for the 2D method, -0.03 cm^{-1} for the PS method, and $+ 0.11$ cm^{-1} for the 2P method. The ratio in the 2P gamma/x-ray method is about 7.9 times as sensitive to depth changes as the ratio in the two-distance method. The 2P gamma/x-ray method, having the highest sensitivity in absolute value, is therefore judged to be the preferable method for gland-depth estimation with I-123. A similar analysis may be considered for the variation of the depth correction factor K as a function of each count ratio (not shown). The same conclusion is reached.

Because of geometric considerations, it is quite likely that some systematic error crept into the estimate of effective gland depth, and perhaps this is why the extrapolated regression line does not make $K = 1$ at distance $d = 0$. Imposing such a constraint, however, while maintaining the same slope of the line for ln K compared with d, causes a translation of the line, an estimate of the systematic error, and a method of correcting for it. The determination of the depth-correction factor for uptake (Fig. 4) may be kept separate from the determination of effective gland depth (Fig. 2). The use of the count ratio, ρ_P, as a function of effective depth removes the need to know the depth to make a depth correction. However, the effect of intervening bone will tend to give values of d and K higher than they should be. This can be seen by comparing the attenuation coefficients for bone and muscle at 30 keV and 159 keV. Bone attenuates at 30 keV more than muscle does, by a factor of about 4. But bone attenuates at 159 keV more than muscle by a factor of about 1.6. The proportionally greater attenuation of the low-energy photon will elevate the measured count ratio by up to a factor of about 2.5.

Two remarkably good agreements between theory and experiment occurred. One was in the values of the effect of shielding on the count rate, estimated and measured at -15%/cm; the other was in the ratio of sensitivities of the 2P method and the 2D method, estimated at 8 and measured at 7.9.

While the count ratios presented here are difficult to reproduce with different window settings, a different detector distance, or different equipment, the sensitivity should be invariant. Numerical comparison may be possible with normalized count ratios, where the normalization constant is ρ_P at $K = 1.0$.

CONCLUSION

A single probe, using a 2-in.-diam scintillation crystal located at some distance from the neck, with a cylindrical straight-bore collimator and a single-channel analyzer, may be used to make sensitive estimates of a depth-correction factor for uptakes and of the gland depth itself. The method is readily amenable to a clinical facility.

Of three methods tested, the best uses a ratio of counts from the gamma photopeak of I-123 to counts from the daughter's x-ray peak, at a standard distance. This count ratio serves as an index of effective gland depth through a calibration curve. The correction factor, calibrated simultaneously, may be determined from the observed count ratio, without requiring an estimate of the gland depth itself. The method is sensitive to gland depth, with the count ratio giving about a 10% change for a change of 1 cm in depth. The method is insensitive to gland size. The calibration curve for uptake (K vs ρ_P) is not significantly affected by detector distance ($p > 0.05$). The method appears suitable for other in vivo depth or assay procedures, e.g., renal uptake measurements.

In patients, the correction factor increases with uncorrected uptake, indicating greatest significance for suspected or patently hyperthyroid patients.

FOOTNOTE

* Medi-physics, Emeryville, Calif.

REFERENCES

1. Robertson JS, Verhasselt M, Wagner HW: Use of ^{123}I for thyroid uptake measurements and depression of ^{131}I thyroid uptakes by incomplete dissolution of capsule filler. *J Nucl Med* 15: 770–774, 1974

2. Sodd VJ, Wellman HN, Branson BM: ^{123}I thyroid measurements with a Ge(Li) detector. *J Nucl Med* 10: 136–139, 1969

3. Wellman HN, Kereiakes JG, Yeager TB, et al: A sensitive technique for measuring thyroidal uptake of iodine-131. *J Nucl Med* 8: 86–96, 1967

4. Rollo FD: ^{125}I for measuring the radioiodine uptake of the thyroid. *J Nucl Med* 12: 8–13, 1971

5. Silver S: *Radioactive Nuclides in Medicine and Biology; Medicine*, 3rd ed. Philadelphia, Lea & Febiger, 1968, p 87

6. Schulz AG, Rollo FD, Foiber KF: *In vivo* measurements of absolute quantities of radioactivity within an organ. *J Nucl Med* 8: 397–398, 1967 (Abst)

7. Schulz AG, Rollo FD: A method for measuring radioiodine uptake which corrects for thyroid depth. *J Nucl Med* 11: 508–513, 1970

8. Brownell GL, Ellett WH, Reddy AR: Absorbed fractions for photon dosimetry. MIRD Pamphlet No 3, *J Nucl Med* 9: Suppl No 1, 27–39, 1968

9. Lederer CM, Hollander JM, Perlman I: *Table of Isotopes*, 6th ed. New York, Wiley, 1967

10. *Radiological Health Handbook*. Washington, DC, HEW, Jan 1970

11. Van Dilla MA, Fulwyler MJ: Thyroid metabolism in children and adults using very small (nanocurie) doses of iodine-125 and iodine-131. *Proc Hanford Symp Biol Radioiodine Health Phys* 9: 1325, 1963

12. Goolden AWG, Glass HI, Silvester DJ, et al: The choice of a radioactive isotope for the investigation of thyroid disorders. *Br J Radiol* 41: 20–25, 1968

13. Nishiyama H, Sodd VJ, Berke RA, et al: Evaluation of clinical value of ^{123}I and ^{131}I in thyroid disease. *J Nucl Med* 15: 261–265, 1974

ADDRESS CHANGE FOR *JNM* EDITOR

As of July 1, 1977, the address for the editor of *Journal of Nuclear Medicine*, Frank H. DeLand, has been changed from 721 Avalon Park to:

University of Kentucky Medical Center
Medical Annex #5
Lexington, Kentucky 40506
(606) 254-1803