

Statistical Evaluation of 125-I vs 131-I for Scanning Cold Lesions¹

Raymond L. Libby, Ph.D.

Los Angeles

This report is concerned with a statistical evaluation of the use of 125-I and 131-I for the detection and delineation of "cold" lesions using ordinary scan techniques. The experimental data provided in this report indicates a more extensive role for 125-I in the discrimination of "cold" lesions at depths up to several centimeters below the surface than has been indicated previously (2),(3).

The success or failure to detect a "cold" lesion in organs such as the thyroid and liver by commonly used radioisotope scanning techniques involves a diverse number of parameters such as: the absolute count rate; the "Target/Nontarget" ratio (1); the resolving capability of the detector system; the scan speed; the energy of the emitted photon, together with its absorption and scatter properties in tissue; and, finally, the visual interpretation of the recorded scan. To evaluate the contribution of each of the above variables is a difficult task. However, appropriate phantom studies can shed considerable light on the probability of detecting lesions in various organs and tissues and can indicate, under various specified conditions, which of two or more radioisotopes has the most favorable potential for detecting a lesion.

EXPERIMENTAL

The following symbols will be used throughout this report:

N_t = Nontarget

T = Target ("cold" lesion)

ϵ = Fractional standard deviation of the difference (N_t -T)

Figure 1 depicts photographically the phantom arrangement used in this study. A one-liter beaker was filled with 800 ml of water containing 80 μ c (0.1 μ c/ml) either of 125-I or 131-I. The radioactive solution represents the Nontarget (N_t) volume of interest.

The Target (T), shown in Fig. 1, is a 3 cm-diameter lucite sphere with a small hole drilled through the center. The lucite sphere was suspended at various levels by means of a nonwetttable string of dental floss. The one-centimeter markings on the string used to establish the depth of T can be seen in the photograph. The "cold" Target was set at the surface and at successive one-centimeter depths below the surface down to 6 cm. Sufficient total counts were accumulated on a RIDL scaler so that the standard error in all cases was less than one percent.

¹From the Department of Radiology, The University of California Center for the Health Sciences, Los Angeles, California 90024.

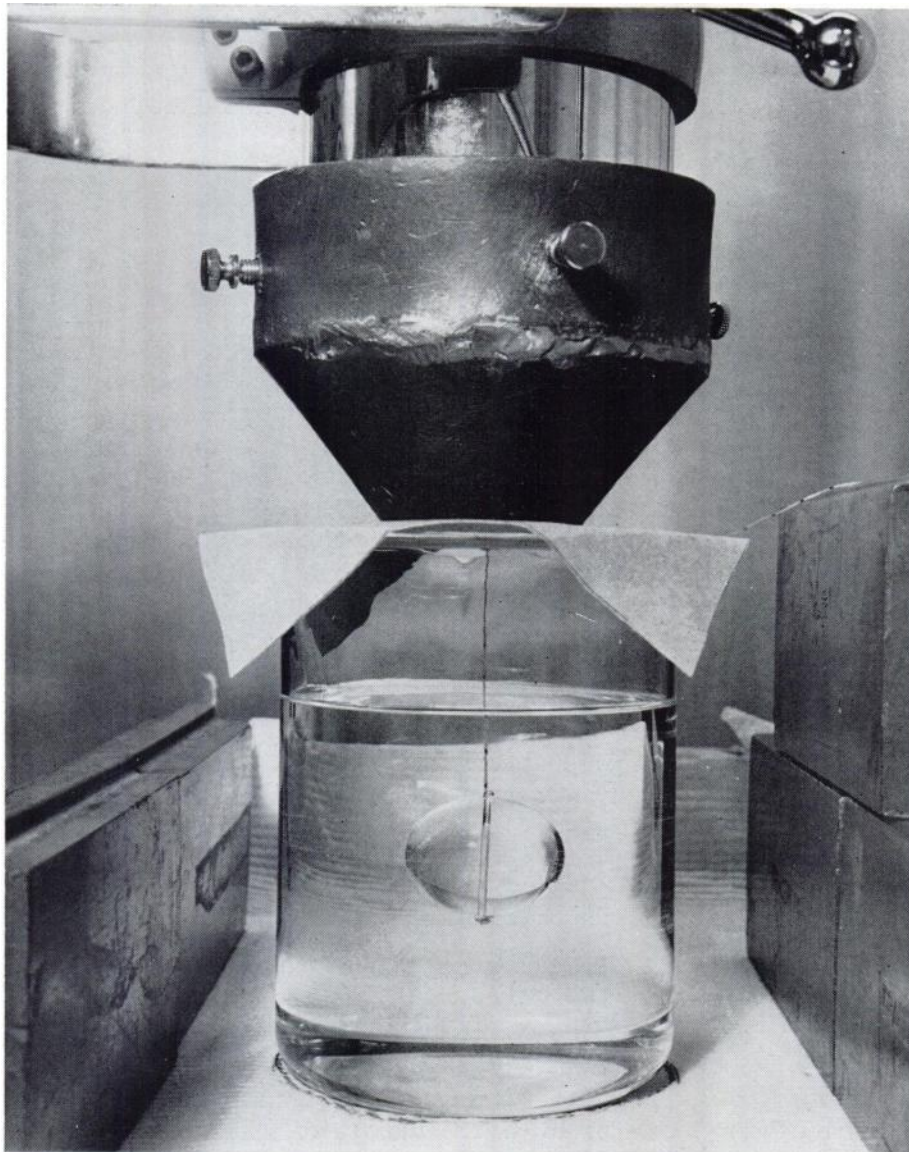


Fig. 1. Phantom used to evaluate relative merits of ^{125}I and ^{131}I for scanning "cold" lesions.

A nineteen-hole focussing collimator was used for all measurements with the focal point of the collimator 2.4 cm below the surface of the water. As shown, an additional half-centimeter of lead shielding was fitted around the sides of the collimator to minimize any radiation emanating from outside of the volume being counted.

The count rates both for ^{125}I and for ^{131}I were determined under identical geometrical conditions, with one exception. The ^{131}I detector was a 2-inch-diameter by 2-inch-thick NaI crystal, whereas, a 2-inch-diameter by $\frac{1}{4}$ -inch-thick NaI crystal with a 0.001-inch-thick aluminum shield was used for counting the ^{125}I .

A single channel pulse height analyzer was used to minimize background and scattered radiation. For 131-I, the analyzer was set to observe only the counts from the 0.364 mev photopeak for 131-I; and, for the measurement of 125-I, the analyzer was set to observe both the principal photopeak at ~28 kev and the coincidence photopeak at ~56 kev.

RESULTS

In Table I, columns 2 and 3 show the observed net counts per minute both for 125-I and for 131-I, for the N_t situation (radioactive-solution phantoms only) and for each radioisotope with T ("cold"-lesion-lucite sphere) interposed at the surface and at increasing one-cm depths down to 6 cm below the surface. In the fourth and fifth columns the ratios of the T-to- N_t counts per minute for the various depths of T are calculated.

From the data in Table I the following observations may be made:

1. Under the conditions adopted for this experiment, the N_t net counts per minute both for 125-I and for 131-I are essentially identical and reproducible (6124 c/m for 131-I and 6115 c/m for 125-I).

TABLE I

EXPERIMENTAL DATA

Counts per Minute T and N_t and the Ratio of T to N_t c/m

Depth of Target cm	Target Net counts per minute		Ratios c/m Target Nontarget	
	131-1	125-1	131-1	125-1
	0	4698	3474	0.77
1	4936	4280	0.81	0.70
2	5112	4956	0.84	0.81
3	5460	5334	0.89	0.87
4	5518	5630	0.90	0.92
5	5663	5813	0.93	0.95
6	5802	5942	0.95	0.97
	N_t c/m			
	6124	6115		

Nontarget specific activity 0.1 $\mu\text{c/ml}$ for both 131-I and 125-I.

Focal depth of collimator 2.4 cm below surface.

2. A comparison of the ratios of T-to- N_t counts per minute for 125-I and for 131-I are of considerable interest without further analysis. It has already been reported that 125-I provides an improved scan contrast over 131-I for a "cold" surface lesion (2),(3). A comparison of the ratios, 0.77 for 131-I and 0.57 for 125-I is consistent with these reports.

If the ratios (T/N_t) for the two isotopes for T depths of 1, 2 and 3 cm below

the surface are compared, it would appear that even under these conditions 125-I would be expected to provide as good if not a better scan contrast than 131-I.

At T depths of 4, 5 and 6 cm below the surface, it is doubtful whether either isotope would delineate a "cold" lesion under the conditions of this experiment.

The probability of detecting a "cold" lesion within a given time interval depends on the magnitude of the count rate as well as the difference in count (N_t-T). Table II shows the computed Fractional Standard Deviations¹ (ϵ) for the difference in counts between N_t and T for a one-minute and for a five-second count for a series of observations where T is set at the surface and at 1, 2, 3, 4, 5 and 6 cm below the surface. The five-second count interval was adopted on the assumption that in a normal scan procedure the scan speed per centimeter of path would be approximately 2.5 seconds, and that for the 3-cm-diameter T, only the center 2 cm would contribute to the maximum change in count rate.

By comparing the fractional standard deviations of the difference in count (N_t-T) it is possible to make reasonably confident statements as to the relative merits of 125-I vs 131-I for detecting "cold" lesions. For equal specific activities

TABLE II
FRACTIONAL STANDARD DEVIATIONS (ϵ) FOR DIFFERENCE IN COUNTS BETWEEN
 N_t AND T FOR ONE-MINUTE AND FIVE-SECOND COUNTS
AT VARIOUS TARGET DEPTHS
(Derived from Data Table I)

Depth of T _{cm}	For One-Minute Count		For Five-Second Count	
	131-1	125-1	131-1	125-1
0	0.07	0.04	0.25	0.13
1	0.09	0.06	0.31	0.19
2	0.11	0.10	0.36	0.32
3	0.16	0.14	0.57	0.48
4	0.18	0.22	0.62	0.78
5	0.24	0.36	0.83	1.26
6	0.34	0.63	1.17	2.26

¹Standard Deviation of the difference in count (N_t-T) divided by (N_t-T).

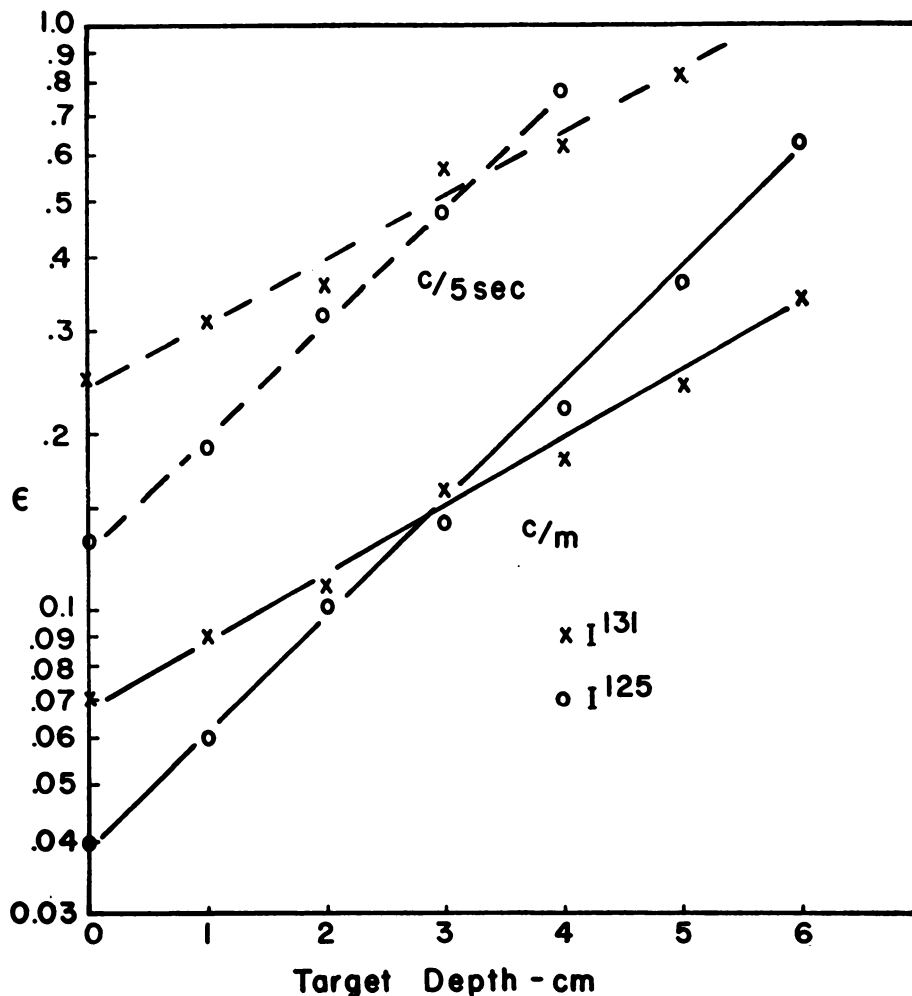


Fig. 2. Semilogarithmic plot of fractional standard deviations (ϵ) for difference in counts between N_t and T for one-minute and five-second counts at various T depths.

of $0.1 \mu\text{C/ml}$ for both radioisotopes, 125-I would be the isotope of choice for detecting "cold" lesions from the surface down to a depth of 2 cm. At 4, 5 and 6 cm depths 131-I would appear to be the isotope of choice. However, if a fractional standard deviation of $\epsilon \leq 0.50$ is adopted as the criterion of the smallest difference in the count rate ($N_t - T$) which could be detected in a scan, then from the data in Table II one can say:

1. That for one-minute counts T could be detected at 6 cm below the surface using 131-I ($0.1 \mu\text{C/ml}$) and at 5 cm below the surface using 125-I ($0.1 \mu\text{C/ml}$). This time interval of course precludes the use of scanning techniques.
2. That for a five-second-scan time T could be detected down to between a 2-to-3 cm depth using 131-I and down to a depth of 3 cm below the surface using 125-I. Below these levels, i.e. 4 cm to 6 cm, neither isotope would provide any delineation of the lesion by means of common scan techniques. At these

depths, delineation could only be accomplished by increasing the specific activity ($\mu\text{c/ml}$) of the N_t volume for both isotopes.

Figure 2 is a semilogarithmic plot of the fractional standard deviations (ϵ) tabulated in Table II. The fact that the data appears to fit a straight line implies that the difference in counts between N_t and T as a function of the depth of T varies exponentially. The different slopes for the two isotopes is a reflection of the difference in the absorption characteristics of the radiations from 125-I and 131-I.

The following equation formulated by Greenfield and Koontz (4).

$$r_s \epsilon^2 \tau = 1 + \frac{2}{r} [1 + \sqrt{1 + r}]$$

where:

r_s = the net N_t count rate

ϵ = fractional standard deviation of the difference $N_t - T$

τ = total counting time

r = ratio $\frac{N_t - T}{T}$

can be used to calculate what the count rate or the specific activity of the N_t volume would have to be so that the "statistical confidence" ($\epsilon^2 \tau$) for both isotopes is identical.

The factors shown in Table III were calculated by means of the above equation. These factors indicate the amount by which the count rate or the specific activity of the N_t volume would have to be increased in order to maintain equal "statistical confidence" for both radioisotopes for five-second counts with T located at a series of depths from 0 to 4 centimeters. As shown, the

TABLE III
FACTOR BY WHICH 131-I OR 125-I ACTIVITY WOULD HAVE TO BE INCREASED TO MAINTAIN EQUAL "CONFIDENCE LIMITS"

Depth of T cm	Five Second Counts			
	Factor		Specific Activity $\mu\text{c/ml}$	
	131-I	125-I	131-I	125-I
0	3.2	—	0.32	—
1	2.3	—	0.23	—
2	1.5	—	0.15	—
3	1.3	—	0.13	—
4	—	1.5	—	0.15

specific activity ($\mu\text{c/ml}$) of the 131-I would have to be increased by a factor of 3.2. i. e., from 0.1 $\mu\text{c/ml}$ to 0.32 $\mu\text{c/ml}$, for a surface lesion in order to have the same statistical confidence as 125-I with a N_t specific activity of 0.1 $\mu\text{c/ml}$.

At T depth of 1, 2 and 3 cm below the surface the "factors" would be 2.3, 1.5 and 1.3, respectively. Thus the specific activity for 131-I would have to be 0.23, 0.15 and 0.13 $\mu\text{c/ml}$. At a T depth of 4 cm the specific activity of the 125-I would have to be increased by a factor of 1.5 i.e. 0.15 $\mu\text{c/ml}$.

It was of interest to determine whether or not a change in the focal depth setting of the focussing collimator would effect the validity of results given in this report. To test this possibility a second series of measurements were carried out identical to those reported except the focal depth was set at 3.4 cm below the surface instead of the original depth of 2.4 cm.

Table IV shows the percent loss in count $(\frac{N_t - T}{N_t} \times 100)$ for 131-I and 125-I both for focal depth and for different T depth. The differences in the percentages for the two focal depths are slight, but undoubtedly real. However, the magnitude of the differences are such that they would not invalidate the statistical evaluation of 125-I vs 131-I for scanning "cold" nodules as presented.

DISCUSSION

The type of phantom measurements and the statistical analysis of the results employed in this study to evaluate the probability of detecting lesions in various organs and tissues can be applied to any of the commonly-used scanning techniques. It is desirable in any scan procedure that the detection limits im-

TABLE IV
PERCENT LOSS IN N_t ONE MINUTE COUNTS DUE TO T AT VARIOUS DEPTHS FOR TWO SETTINGS OF FOCAL DEPTH OF COLLIMATOR

Depth of T cm	131-I Focal Depth cm		125-I Focal Depth cm	
	2.4	3.4	2.3	3.4
0	23	22	43	44
1	19	19	30	32
2	16	15	19	22
3	11	13	13	15
4	10	11	8	10
5	7	8	5	6
6	5	6	3	4

posed by the system are evaluated, as well as the limitations imposed by the application of different isotopes.

It is also of considerable interest to know how one can improve the probability of detecting lesions of various dimensions and at various depths within the organ or tissue of interest. Since the probability of detecting a lesion within a given scan-time interval (such as the five-second time used in this report) depends upon the magnitude of the count rate as well as the difference in count ($N_t - T$), it is important to note that the absolute count rate, or the specific activity ($\mu\text{C/gm}$), that must be used to achieve a given statistical probability for visualization, can be calculated by means of the equation formulated by Greenfield and Koontz (4). One such application is illustrated in Table III.

The linearity of the semilogarithmic plot of the fractional standard deviations (ϵ) for the difference in counts between N_t and T and the depth of T in centimeters, as shown in Fig. 2, indicates an exponential relation between these two parameters. This relationship implies that only two measurements have to be made. In a particular case the T measurement could be made at two different depths and the resultant straight line extrapolated to any T depth of interest. This relationship can thus minimize the time involved in establishing the statistical probability of the detection of a lesion for any scan system.

SUMMARY

A statistical analysis of the relative delineation potentials of ^{125}I and ^{131}I for scanning a "cold" 3-cm-diameter lesion indicates that ^{125}I is better than ^{131}I , not only for a surface lesion, but also for lesions located as much as 2 cm below the surface. For a "cold" 3-cm-diameter lesion located at depths of 3 cm or greater, neither ^{125}I nor ^{131}I would delineate such a lesion under the specific conditions chosen for this study.

The application of the type of measurements made in this report and their statistical analysis is discussed in relation to the probability of detecting a lesion by ordinary scan techniques.

ACKNOWLEDGEMENT

I wish to express my appreciation to Professor M. A. Greenfield, Department of Radiology, The University of California Center for the Health Sciences, for his advice concerning the statistical analysis and to Mrs. Liuda Kaupas for her valuable technical assistance.

REFERENCES

1. BLAU, M. AND BENDER, M. A.: Letter To The Editor, *J. Nuclear Med.*, 5:4, 318, 1964.
2. ENDLICH, H.; HARPER, P.; BECK, R.; SIEMENS, W. AND LATHROP, K.: The Use of I-125 to Increase Isotope Scanning Resolution, *Am. J. Roentgenol., Rad. Therapy & Nuclear Med.*, 87:1, 148, 1962.
3. HARPER, P. V.; SIEMENS, W. D.; LATHROP, K. A. AND ENDLICH, H.: Production and Use of Iodine-125, *J. Nuclear Med.*, 4:277, 1963.
4. GREENFIELD, M. A. AND KOONTZ, R. L.: A Universal Function for Computing Counting Performance, *Int. J. of Applied Rad. & Isotopes*, 8:205, 1960.
5. MYERS, W. G. AND VANDERLEEDEN, C.: Radioiodine-125, *J. Nuclear Med.*, 1:149, 1960.
6. HARPER, P. V. AND LIPSCOMB, C.: The Assay and Dosimetry of Iodine-125, Abstract, *J. Nuclear Med.*, 5:308, 1964.