
Iodine-131 Treatment of Thyroid Cancer: Absorbed Dose Calculated from Post-Therapy Scans

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The radiation absorbed dose for nine neck lesions distributed among four thyroid-cancer patients was measured directly from images taken after administration of a treatment dose of ^{131}I . The tumor volume was measured with anterior plus lateral pinhole images by determining magnification and assuming an ellipsoidal shape. Uptake and effective half-life were determined from serial anterior images by use of a calibration curve. Dose lower limits ranged from 2,400 to 29,900 rad. Response to treatment was judged on the basis of one or more follow-up scans at least 8 mo later. All lesions responded to the therapy administration which ranged from 150 to 175 mCi.

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The quantification of radiation absorbed dose delivered by therapeutic activities of administered iodine-131 (^{131}I) to lesions in thyroid cancer patients is of importance in their treatment. The ultimate aim is to know the minimum administered activity necessary to eliminate the disease with a given confidence level and to determine this activity from the administration of a small tracer dose before onset of treatment.

In a study of 76 patients, Maxon et al. (1) sought to obtain the relation between outcome of therapy and radiation absorbed dose. They made the usual assumption that patient tracer and therapeutic activities behave similarly and made their calculations based on measurements with the tracer. One can question, however, whether the ratio of radiation absorbed dose after therapy over that after tracer equals the ratio of millicuries for therapy over millicuries for tracer as assumed by Maxon et al. For example, Benua et al. found that the average values for total radiation delivered to the blood and for uptake at 48 hr, as determined from a therapy dose, were significantly less than predicted from measurements after a tracer dose (2).

We report here the direct measurement of radiation absorbed dose after ^{131}I therapy administration and

make a preliminary correlation of that dose with response to treatment.

PATIENTS AND METHODS

Patients

The patients involved were those already scheduled for therapy who volunteered to undergo the extra imaging procedures to carry out the dosimetry. The four patients, all of whom had previously had surgical removal of the thyroid, exhibited a total of nine areas of focal uptake of radioiodine in the neck region. They included three females and one male and covered an age range of 28 to 47 yr (Table 1). The diagnosis of their cancer was well-differentiated papillary in two (Patients 2 and 3), follicular with local invasion to capsule in one (Patient 4) and mixed papillary-follicular, locally invasive to left recurrent laryngeal nerve in one. The ^{131}I uptake values measured by a calibrated probe 24 hr after administration of a 2 mCi tracer are shown in Table 2. The low values argue for assigning the uptake as due to local metastases rather than to thyroid remnants. The patients had no evidence of distant metastases. The treatment doses were 150 mCi of ^{131}I sodium iodide in one and 175 mCi in the other three patients. These values were chosen without reference to the calculated radiation absorbed doses presented here.

Measurements

The procedure for the dosimetry measurements and calculations has been outlined in detail elsewhere (3). A summary description is as follows.

The technique consists of a sizing measurement 24 hr after administration of the therapy activity of radioisotope. This measurement involves anterior and lateral images of the pa-

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TABLE 1
Patient Data and Time(s) of Follow-up Showing
no Residual Disease

Patient	Sex	Age (yr)	Probe uptake (%)	Therapy injection	Time of follow-up after therapy
1	F	44	0.24	175 mCi	8 mo
2	M	37	1.9	175 mCi	1 yr
3	F	28	1.8	150 mCi	1 yr and 3 yr
4	F	47	3.5	175 mCi	1 yr and 2 yr

tient. The anterior measurement is the first in a series of daily, if possible, uptake measurements with the patient repositioned at the same distance from the camera. This series of measurements continues through as many as 9 days post-therapy administration.

Equipment

All images were made with a high-energy pinhole collimator. An early version of a rotating Anger camera tomograph was utilized to provide the capability for rotation between views. The patient and supporting table were positioned at a large angle ($\sim 30^\circ$) with respect to the axis of camera rotation so that the pinhole collimator fit snugly between the head and shoulder for the lateral view during sizing. This patient orientation is shown in Fig. 1. The tomograph permitted the camera to be moved directly toward and away from the axis of rotation and use was made of this capability.

Magnification

The employment of the pinhole collimator permitted image magnification of the lesion in at least the anterior view. This magnification was necessary for direct sizing of the small lesions as their image size only then exceeded the resolution of the camera. The amount of magnification itself had to be determined by locating the lesions in three dimensions so that the perpendicular distance to the camera face could be determined. The location was done by (a) carefully aligning the camera with respect to the axis of rotation, (b) keeping track of the amount of camera motion in or out between anterior and lateral views, (c) employing a marker source on the neck which is imaged in both views with perpendicular distance to the pinhole face measured with calipers, and (d) use of the distance of closest approach of backprojected lines to associate projected lesions as belonging to the same lesions.

Size

The estimate of lesion size was made by assuming an ellipsoidal shape and using both views unless there is overlap of two lesions or poor magnification characteristics in a view. For both views, nothing needs to be assumed about orientation and the result is an upper bound on volume. For one view, the average of two possible orientations is employed to estimate the volume. Use is made of the previously determined magnifications.

Uptake

Uptake was determined from the anterior view by use of a premeasured calibration curve of counts versus distance in front of the pinhole, for a fixed-activity source. Attenuation was corrected for by using an assumed linear attenuation

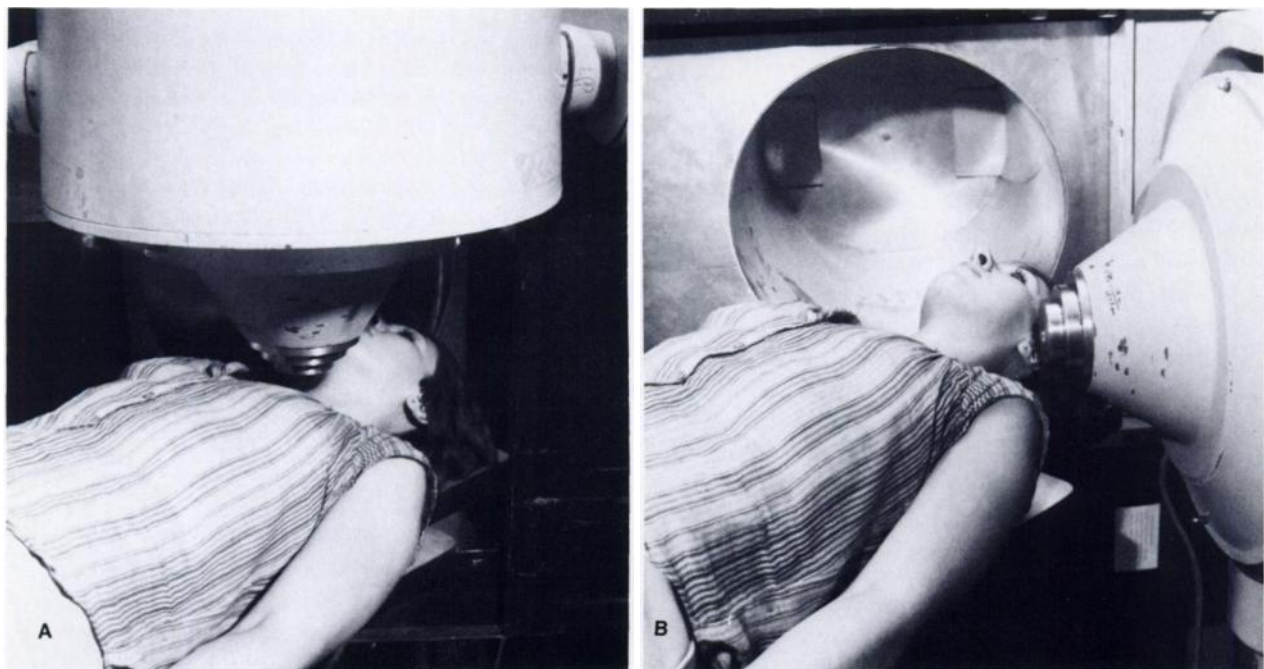


FIGURE 1
Anterior (A) and lateral (B) position of pinhole collimator and Anger camera for sizing measurements. Photos are taken looking along axis of 90° rotation. Patient is positioned at angle to this axis so collimator fits between head and shoulder for lateral view

TABLE 2
Uptake as Function of Time After Ingestion of Therapy Dose

Patient		Time (days) and Dose (μCi)						
1		1.04 days	2.04 days	3.04 days	—	—	—	—
1	1	130 μCi	151 μCi	158 μCi	—	—	—	—
1	2	140 μCi	173 μCi	174 μCi	—	—	—	—
2		1.15 days	2.15 days	3.23 days	4.21 days	6.87 days	—	9.23 days
2	1	153 μCi	119 μCi	115 μCi	85 μCi	30.1 μCi	—	6.8 μCi
2	2	333 μCi	270 μCi	248 μCi	180 μCi	67.9 μCi	—	15.8 μCi
2	3	338 μCi	364 μCi	374 μCi	269 μCi	62.9 μCi	—	23.0 μCi
3		1.0 days	2.0 days	—	—	—	7.9 days	—
3	1	1,170 μCi	1,590 μCi	—	—	—	547 μCi	—
4		1.18 days	2.01 days	3.17 days	—	—	8.18 days	—
4	1	500 μCi	471 μCi	233 μCi	—	—	3.7 μCi	—
4	2	162 μCi	155 μCi	100 μCi	—	—	4.4 μCi	—
4	5	178 μCi	172 μCi	150 μCi	—	—	4.3 μCi	—

coefficient of 0.110 cm^{-1} and the difference of the perpendicular distance to the marker source and to the lesion as the attenuation distance, d . The correction factor was then

$$A = e^{0.110 \text{ cm}^{-1} d} \quad (1)$$

Absorbed Dose

The radiation absorbed dose, D , was calculated from a sum of two terms:

$$D = D_o^c + D_c^\infty \quad (2)$$

where D_o^c is the result of numerical integration of the dose rate compared with time curve from time 0 to c and D_c^∞ is a closed-form dose depending on: (a) the measured uptake concentration in $\mu\text{Ci/g}$ at time c , (b) the measured effective half-life, T_{eff} , for exponential decay from that time on, and (c) known and approximated constants for ^{131}I dose absorption. An example dosimetric calculation is detailed in Appendix A.

An early patient had the imaging for sizing done with the tracer administration. In that case, a smaller magnification was used for the anterior uptake measurements after the therapy administration. This procedure made repositioning less important because of being on a less rapidly changing part

of the calibration curve. This advantage, however, was offset by difficulty in detecting the edge of the lesion for the sizing due to poor statistics. For the other patients, advantage was taken of the good statistics available with the therapy injection for the edge detection and sizing. A single high-magnification position was chosen to avoid the necessity of extra imaging and calculations associated with two positions.

Follow-up

The response of a patient to treatment was judged on the basis of a follow-up scan 8 mo to 3 yr after administration of the treatment dose. The scan was acquired with a tracer administration of 2 mCi of ^{131}I and a pinhole collimator. No recurrent disease was assumed if there was no focal accumulation of uptake above background.

RESULTS

The uptake values for the individual lesions as a function of time are shown in Table 2. The exact times are listed but uptakes for a given time rounded to the nearest day are shown in the same column for different patients.

TABLE 3
Calculational Parameters and Calculated Absorbed Dose

Patient	Lesion	d (cm)	A	V (cm^3)	T_c (days)	D_o^c (rad)	T_{eff} (days)	D_c^∞ (rad)	D (rad)
1	1	14.0	1.50	≤ 3.8	3.5	$\geq 1,220$	3.5*	$\geq 2,240$	$\geq 3,460$
1	2	16.0	1.88	≤ 3.1	3.5	$\geq 1,650$	3.5*	$\geq 3,000$	$\geq 4,650$
2	1	6.1	1.17	≤ 2.9	4.0	$\geq 1,800$	1.42	≥ 600	$\geq 2,400$
2	2	9.0	1.60	2.9	4.0	3,900	1.52	1,400	5,300
2	3	9.0	1.60	2.1	4.0	6,800	1.43	2,700	9,500
3	1	8.5	1.41	≤ 4.2	2.0	$\geq 8,000$	3.83	$\geq 21,800$	$\geq 29,900$
4	1	4.7	1.09	0.8	3.2	16,300	0.84	3,700	20,000
4	2	7.2	1.43	1.1	3.2	6,100	1.11	2,300	8,400
4	5	6.5	1.33	0.8	3.2	7,800	0.98	3,600	11,400

* Assumed value.

Table 3 gives measured parameter values, the effective half-life and the early, late, and total radiation absorbed dose. Note that these radiation absorbed doses agree with those given in (3), but update incorrect values listed in (4) and (5). The upper bounds on volume lead to lower bounds on absorbed dose while the approximate values for volume lead to approximate values for dose. For Patient 1, T_{eff} could not be determined due to lack of data. It was assumed to be 3.5 days, a value chosen from a single case in Ref. (6) but close to the average value of 3.28 ± 1.33 days given for responding lesions by Maxon et al. as well (1).

As shown in Table 1, the follow-ups showed no recurrent disease in all cases. The date of follow-up ranged from a minimum of 8 mo to a maximum of 3 yr.

DISCUSSION

The data shown in Table 2 deviates from a model that assumes instantaneous uptake followed immediately by a single-exponential decay. In three of the lesions, the uptake is greater on Day 3 than it is on Day 1 and for all of them a semilog plot shows that a straight line is not a particularly good fit.

The complexity of the uptake versus time curve following therapy does not rule out that the curve following a tracer dose may be instantaneous with a single-exponential decay. If that is true, however, then the usual scaling assumption fails because the curve shape is different. Therefore, it appears that a direct comparison of uptake behavior for the tracer administration and for the therapy administration needs to be made with the same measuring equipment, procedure, and patients.

The lower dose limits in our measurements range from 2,400 to 29,900 rad. A similar wide variation is found by Maxon et al. In our results, a combination of variations in uptake, T_{eff} , and volume is responsible, i.e., 130 to 1,170 μCi on Day 1, 0.84 to 3.83 days, and 0.8 to $\leq 4.2 \text{ cm}^3$. We did not estimate how much these variations depend on experimental error.

Maxon et al. divided their patients into those referred for ablation of residual thyroid tissue and those for treatment of recurrent or metastatic cancer. For the patients in the latter category, when 8,000 rad was the dividing line for characterizing their results, 47 out of 48 lesions responded; however, 12 out of 19 lesions that received $< 8,000$ rad also responded. Their division at 8,000 rad is designed to almost assure response. In their discussion, they state "if radiation doses are less than 3,500 rad, there is little chance for success."

Since our results include both lower limits and, in other areas, estimates of radiation absorbed dose, it is difficult to compare to these thresholds. When one combines the lower limits and estimates, four of nine values are $< 8,000$ rad and one of nine is $< 3,500$ rad. We conclude that the thresholds appear slightly high. If

the true dose is about twice the lower limit, however, then there is approximate agreement.

Since the methods are different, it is possible that either or both have a systematic error in obtaining absolute radiation absorbed dose. Moreover, the values of Maxon et al. can, of course, be accurate as an index for handling the results obtained from their method regardless of whether or not a systematic error exists. For our technique, either phantom studies or more patients are needed to draw firm conclusions.

APPENDIX A

In this Appendix, we present a sample calculation of absorbed dose. The lesion chosen is No. 3 for Patient 2. The volume estimation for this lesion has been specified in Ref. (3).

First, the uptakes are determined from the number of counts in the region of interest, N , by use of a constant, C_1 , taken from the calibration curve at the correct lesion to pinhole distance. For example, for lesion 3 at the measured 9.0 cm, $C_1 = 1.59 \times 10^{-3} \mu\text{Ci}/\text{count}$. Then at 27.5 hr, the uptake, U , is:

$$\begin{aligned} U &= C_1 \cdot N \\ U &= 1.59 \times 10^{-3} \cdot 132,075 \\ &= 210 \mu\text{Ci} \end{aligned}$$

For the depth below skin which was measured to be 4.29 cm, the correction factor A is 1.60 [Eq. (1)]. The attenuation corrected uptake, U' , then is:

$$\begin{aligned} U' &= U \cdot A \\ &= 210 \cdot 1.60 \\ &= 338 \mu\text{Ci} \end{aligned}$$

One now assumes that the density of the lesion is $1 \text{ g}/\text{cm}^3$. Then the estimated volume in cubic centimeters can be converted to a mass in grams without change in numeric value. Also, from constants relating curies to disintegrations per sec and rads to ergs of energy deposited per g, and from dosimetric assumptions about the amount of energy absorbed per disintegration of ^{131}I , one determines a second constant C_2 :

$$C_2 = \frac{0.436}{V} (\text{rad g})/(\mu\text{Ci hr}).$$

For lesion 3, $V = 2.13 \text{ cm}^3$ and

$$\begin{aligned} C_2 &= 0.436/2.13 \\ &= 0.205 \text{ rad}/(\mu\text{Ci hr}). \end{aligned}$$

The dose rate, $R_{27.5 \text{ hr}}$, then is

$$\begin{aligned} R_{27.5 \text{ hr}} &= C_2 \cdot U' \\ &= .205 \cdot 338 \\ &= 69.2 \text{ rad/hr.} \end{aligned}$$

Similar rates at Days 2, 3, and 4 are computed.

The dose for the early part of the therapy is then given by

a sum of products of dose rate multiplied by time:

$$D_o^4 = \sum_{i=1}^4 R_i \Delta t_i.$$

For lesion 3,

$$\begin{aligned} D_o^4 &= 69.2 * 27.5 + 74.7 * 24 + 76.7 * 24 + 55.0 * 23.5 \\ &= 6,800 \text{ rad.} \end{aligned}$$

The dose for the later part of the therapy D_4^∞ is given by a closed form

$$D_4 = 15.12 \text{ (rad g)/}(\mu\text{Ci day)} * C_4 * T_{\text{eff}}.$$

Here, C_4 is given by U' on Day 4 divided by the lesion mass:

$$\begin{aligned} C_4 &= U'/V \\ &= 269/2.13 \\ &= 126.3 \mu\text{Ci/g.} \end{aligned}$$

Also, T_{eff} was measured to be 1.43 days. Therefore,

$$\begin{aligned} D_4 &= 15.12 * 126.3 * 1.43 \\ &= 2,700 \text{ rad.} \end{aligned}$$

Finally, then, the total absorbed dose, repeating Eq. (2), is

$$\begin{aligned} D &= D_o^4 + D_4^\infty \\ &= 6,800 \text{ rad} + 2,700 \text{ rad} \\ &= 9,500 \text{ rad.} \end{aligned}$$

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