LAAC-5794 (Publication Version)
CONF-66-8

SEP 12 1963

79665

LEGAL NOTICE

This report was prepared as an account of Government sponsored work. Neither the United States, nor the Commission, nor any person acting on behalf of the Commission:

A. Makes any warranty or representation, expressed or implied, with respect to the accuracy, completeness, or usefulness of the information contained in this report, or that the use of any information, apparatus, method, or process disclosed in this report may not infringe privately owned rights; or

B. Assumes any liabilities with respect to the use of, or for damages resulting from the use of any information, apparatus, method, or process disclosed in this report.

As used in the above, "person acting on behalf of the Commission" includes any employee or contractor of the Commission, or employee of such contractor, to the extent that such employee or contractor of the Commission, or employee of such contractor prepares, disseminates, or provides access to, any information pursuant to his employment or contract with the Commission, or his employment with such contractor.

MASTER

THYROID METABOLISM IN CHILDREN AND ADULTS USING
VERY SMALL (NANOCURIE) DOSES OF IODINE¹²⁵ AND IODINE¹³¹*

I-125 and I-131

By

M. A. Van Dilla and M. J. Fulwyler

Los Alamos Scientific Laboratory
University of California
Los Alamos, New Mexico

*Work performed under the auspices of the U. S. Atomic Energy Commission.

Facsimile Price \$ 3.60

Microfilm Price \$ 1.31

Available from the
Office of Technical Services
Department of Commerce
Washington 25, D. C.

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

INTRODUCTION

In order to estimate properly the dose to the human thyroid resulting from ingestion of radioiodine, it is necessary to know the retention of iodine by the thyroid as a function of time. In the case of children, there is a scarcity of such data. It has recently been shown possible to measure much less than 1 nanocurie of fallout I^{131} in people (1,2). These facts have encouraged us to set up an experiment to accumulate radioiodine retention data for children using doses in the 10-nanocurie range.

One of the problems encountered in measuring thyroid radioiodine is the uncertainty of thyroid depth in neck tissue. This uncertainty can lead to error due to the unknown attenuation of radiation by overlying tissue and unknown thyroid-to-detector geometry. Errors due to geometry can be large because of the small neck-to-crystal distance necessary at these low dose levels. This paper describes a method of measuring thyroid radioiodine at the nanocurie level which determines and corrects for variations in thyroid depth. Also presented are preliminary results obtained by this technique.

METHODS

The method employs a mixture of two isotopes of iodine: 60-day I^{125} and 8-day I^{131} . Iodine¹²⁵ decays solely by electron capture to the first excited level (35.4 kev) of Te^{125} , which in turn decays to its stable ground state. In this process, the total radiative yield of 27.4-kev X rays and 35.4-kev gamma rays is $143. \pm 12$ photons per 100 disintegrations, of which 96 per cent are of 27.4-kev energy (3). Iodine¹³¹ decays by beta emission to various excited states of Xe^{131} ; decay to the ground state results in emission of 364-kev gamma rays (79 per cent yield) and 27.4-kev k_{α} X rays (5 per cent yield), among others (4). Thus, a mixture of I^{125} and I^{131} constitutes a tracer with two abundant photon yields (27 kev and 364 kev) widely separated in energy. Because of this energy separation, these photons have very different attenuation (i.e., half-thicknesses of 2.2 cm and 6.3 cm of water, respectively). The relative attenuation of the 27-kev X rays and the 364-kev gamma rays gives a measure of thyroid depth. To establish this relationship, a polystyrene neck mockup similar to the ORINS standard (5) and shown in Fig. 1 was constructed. Overlying tissue was simulated by layers of lean beefsteak pressed to uniform

Fig. 1. Polystyrene neck mockup.

POLYSTYRENE NECK MOCK-UP

THYROID "LOBE"
(10 ml.)

LOS ALAMOS
PHOTO LABORATORY

NEG. NO. 633874

PLEASE RE-ORDER
BY ABOVE NUMBER

thickness and frozen to the contour of the neck mockup. These uniform "tissue" layers were added to obtain a relationship between X/γ^* and thickness of overlying tissue and the corresponding correction factor. The results are given in Figs. 2 and 3, from which can be determined both depth and the factor needed to correct the observed count rate to zero overlying tissue.

The solutions of I^{125} and I^{131} were calibrated with an I^{125} standard obtained from the National Bureau of Standards, and I^{131} standards obtained from the Radiochemical Center, England, and Nuclear-Chicago. The latter two agreed to 2 per cent.

The detector chosen was an 8 x 4-in. NaI crystal (with a 0.005-in. entry window to minimize attenuation of the soft X rays) mounted in a steel room as a whole-body spectrometer. The decision to use a large crystal rather than a pair of smaller (3 x 3-in.) crystals was based on the following considerations:

- (a) Minimum detectable amount** of I^{131} was found to be

*More precisely, the ratio of photopeak areas for a source containing equal activities of I^{125} and I^{131} . If unequal activities are employed in a given experiment, correct the observed X-ray photopeak area by the factor $1 - (k-1)(0.0350)$, where k = the ratio of I^{131} activity to I^{125} activity administered.

**"Minimum detectable amount" is that quantity of I^{131} which can be detected with a standard deviation of 50 per cent for source and background counting times of 30 minutes.

Fig. 2. Relationship of $\frac{\text{X-ray photopeak area}}{\gamma\text{-ray photopeak area}}$ to

thyroid depth in neck tissue for equal activities of I^{125}

and I^{131} .

LOS ALAMOS
PHOTO LABORATORY

NEG.
NO. 633880

PLEASE RE-ORDER
BY ABOVE NUMBER

Fig. 3. Relationship of $\frac{\text{X-ray photopeak area}}{\gamma\text{-ray photopeak area}}$ to correction factor for equal activities of I^{125} and I^{131} .

LOS ALAMOS
PHOTO LABORATORY

NEG. NO. 633876

PLEASE RE-ORDER
BY ABOVE NUMBER

similar for both systems, the smaller crystals being only 20 per cent more sensitive.

(b) A simple water mockup was used to measure the effect of perpendicular displacement of the source from the crystal axis, since actual thyroid position in the neck is usually uncertain. Figure 4 shows the result (a 9 x 6-in. NaI was used, the 8 x 4-in. NaI being unavailable). Note that uncertainty in thyroid position introduces considerably less error in the case of the large crystal.

(c) Another advantage of the single large crystal is that whole-body spectrometers presently in operation are able to make use of this system.

The pulses are analyzed by a RIDL 400-channel pulse height analyzer. In order to delineate clearly both peaks, the system is calibrated at 1.05 kev per channel, and all 400 channels are used.

To account for room and subject (non-thyroid) background, a thyroid eclipsing lead shield, as described by Brucer (5), is used. The shield is placed between the crystal and the subject, eclipsing the thyroid area of the neck from the view of the crystal, as shown in Fig. 5. The dimensions are 4 x 4 x 1/2 in. for adults and 3 x 3 x 1/2 in. for children. That this is effectively accomplished can be seen from Fig. 6, which shows the uneclipsed and eclipsed

Fig. 4. Response of large (9 x 6-in.) crystal and two small (3 x 3-in.) crystals to perpendicular displacement of source from axis.

LOS ALAMOS
PHOTO LABORATORY

NEG.
NO. 633878

PLEASE RE-ORDER
BY ABOVE NUMBER

Fig. 5. Subject in tilting chair during background count
(with lead shield).

Fig. 6. Gamma-ray spectra with and without lead shield
(subject LVD, dose 11.9 nanocuries I^{125} , 15.3 nanocuries I^{131} ,
third day).

LOS ALAMOS
PHOTO LABORATORY

NEG.
NO. 633881

PLEASE RE-ORDER
BY ABOVE NUMBER

spectra for subject LVD 3 days after ingestion. The contributions to background, sensitivity to radioiodine, and minimum detectable amount of I^{131} are shown in Table 1.

The subjects recline in a tilting chair so that the head is tipped back fully exposing the thyroid area. During the thyroid count, neck-to-crystal distance is maintained constant by a Lucite spacer rod 3-1/4 in. long fixed to the center of the crystal (Figs. 7 and 8). The crystal is positioned so that the spacer rod lightly touches the subject's neck. Counting children in the age group of 4 to 9 years is complicated by the need to keep them still during the 15-minute count. To attract and to hold their attention, a small Sony television set is mounted above the crystal in such a way that good viewing requires that the head be kept in the desired position (Fig. 9). This has proven very successful, although occasionally it is difficult to remove the child during a particularly fascinating cartoon. With this arrangement, considerably longer counting times appear to be entirely feasible. During the measurement, an adult remains in the steel room shielded from the crystal by a steel partition. With the aid of a mirror, he is able to see the Lucite spacer rod lightly touching the child's neck. If the child moves, a reminder to sit still and to watch the T. V. is usually adequate.

TABLE 1. BACKGROUND AND SENSITIVITY OF THE 8 x 4-IN. SODIUM
IODIDE THYROID SPECTROMETER

	I ¹²⁵ Band (15 to 44 kev)	I ¹³¹ Band (320 to 415 kev)
Steel room background	54 c/m	144 c/m
Subject contribution to back- ground (LVD) 1 day before dose	20 c/m	45 c/m
Subject contribution to back- ground (LVD) with lead shield 3 days after dose	39 c/m	79 c/m
Net subject thyroid count (thyroid only) with no shield 3 days after dose	719 c/m	394 c/m
Counting sensitivity via neck mockup (no overlying tissue)	274 c/m/nc	153 c/m/nc
Minimum detectable amount*	16 pc	52 pc

*The minimum detectable amount is based on the criterion that the signal must equal twice its standard deviation. Counting time is 30 minutes for both signal and background.

Fig. 7. Subject in tilting chair during thyroid count (no lead shield).

Fig. 8. Subject in tilting chair during thyroid count (no lead shield).

Fig. 9. Subject in tilting chair viewing television.

EXPERIMENTAL RESULTS

Before trying this system out, it was thought desirable to measure anyone available that had taken I^{131} recently for other purposes. When about $0.1 \mu\text{c}$ of I^{131} is present, the X-ray peak is quite prominent and gives a good X/ γ ratio. Two such adults and 3 children were found, the I^{131} having been administered for circulation studies or thyroid diagnosis. The results are summarized in Table 2. The 2 adults were of quite opposite build, BS being short and stocky and JL quite slender, which is consistent with the thyroid depth values found. Although uptake for these 2 adults could not be measured because the administered dose was unknown, the correction factors were appreciably different, being in the ratio 1.37. None of the 3 children can be considered normal from the viewpoint of thyroid function. PM had a history of hyperthyroidism; Tapazole treatment stopped about 10 days before taking an oral dose of about $0.5 \mu\text{c}$ I^{131} . His relatively high uptake may be the result. PB and DD have small goiters but no treatment during (and for several weeks preceding) the measurements. Their uptakes were normal, although reaching the extremes of the euthyroid range, as

TABLE 2. THYROID DEPTH MEASUREMENT WITH IODINE¹³¹ ONLY

Subject	Age (years)	Sex	Weight (kg)	Height (cm)	X/ γ	Thickness Overlying Tissue (cm)	Uptake Correction Factor	Uptake at 7 days (per cent)
BS	36	M	70	173	0.038	2.0	0.68	--
JL	38	F	57	171	0.058	0.40	0.93	--
PM	15	M	48	166	0.050	1.0	0.83	42
PB	8	M	40	141	0.051	0.90	0.85	10
DD	10	F	39	145	0.051	0.90	0.85	18

stated by Werner (6). All 3 had similar thyroid depths and correction factors. Retention as a function of time after oral administration for the 3 children is shown in Fig. 10. Note that another administration of Tapazole to PM at 15 days seems to have decreased the biological half-life of the I^{131} thyroid burden to the shortest value of the 3 (22 days), the other values being 34 and 42 days.

These results encouraged us to try out the I^{125}/I^{131} double tracer system, but before using children it was thought advisable to work out the defects first on a group of 6 adults. The I^{131} dose administered was 17.3 nanocuries. Difficulties were encountered with the carrier-free I^{125} solution and hence this dose is not certain; 6.2 nanocuries is the best estimate. Unfortunately, this makes the X/γ ratios of little value, and an uptake correction cannot be derived from the data. However, the biological half-lives determined from the two isotopes are valid and should agree. This was found to be the case. The results are summarized in Table 3, and the data for 2 subjects are shown graphically in Fig. 11. It is to be noted that these subjects all have similar (except JP) and normal uptakes, while the biological half-times vary considerably. According to Lushbaugh et al. (7), the normal biological half-time is about 90 days, so that the values for 2 subjects (MJF and DW) are larger than normal, while the

Fig. 10. Retention of I^{131} by thyroid glands of
3 children (age 8 to 15 years).

LOS ALAMOS
PHOTO LABORATORY

NEG. NO. **633875**

PLEASE RE-ORDER
BY ABOVE NUMBER

TABLE 3. RADIOIODINE METABOLISM IN SIX ADULTS

Subject	Age (years)	Sex	Weight (kg)	Height (cm)	Uptake at 7 days* (per cent)	T _{Bio} (days)	T _{Eff} (days)
MAVD	44	M	71	188	29	107	7.51
MJF	26	M	70	180	23	∞	8.07
DW	38	M	74	180	23	> 200	7.76
HI	46	M	86	179	22	75	7.30
BM	39	M	123	198	26	98	7.46
JP	45	M	88	180	15	27	6.22

* Assumes 1.5 cm overlying tissue.

Fig. 11. Retention of I^{131} and I^{125} by thyroid glands
of 2 adults.

LOS ALAMOS
PHOTO LABORATORY

NEG. NO. 633877

PLEASE RE-ORDER
BY ABOVE NUMBER

value for JP is quite small. It is interesting that JP has a history of low BMR, which is consistent with his relatively low uptake and short biological half-time.

Having obtained reasonable results with adults, only the quantitative difficulty with the I^{125} stood in the way of extending the experiments to children. This problem was solved by adding 0.5 μ g NaI carrier to each dose and then measuring the dose actually ingested by each child. Eight children, ranging in age from 4 to 10 years, each received a nominal 11 nanocuries I^{125} and 15 nanocuries I^{131} oral dose, and 15-minute measurements (10 minutes with no shield, 5 minutes with lead shield) began the following day. It is planned to count 3 times weekly for 6 weeks, and then at less frequent intervals until the I^{125} peak dies away. At the present writing (June 6, 1963), we have about 2 weeks of data processed and summarized in Table 4. Note that uptakes are very similar to those for the adults. Thickness of overlying tissue is small in all cases, resulting in similar correction factors. Figure 12 shows that biological half-lives will be long compared to the 8-day physical half-life, and perhaps similar to adults. Thus far, no differences in radioiodine metabolism have been observed between children and adults.

The uptake results reported here are consistent with those obtained by Saxena et al. (8) on children; 24-hour uptakes by 2-year-old children with normal thyroid function were

TABLE 4. RADIOIODINE METABOLISM IN EIGHT CHILDREN

Subject	Age (years)	Sex	Weight (kg)	Height (cm)	Thickness Overlying Tissue (cm)	Correction Factor	Uptake at 7 days (per cent)
TVD	10	F	32	145	0.45	0.92	22
PVD	7-1/2	M	30	135	0.50	0.91	23
LVD	6-1/2	F	19	117	0.82	0.86	27
WVD	4	F	16	104	0.73	0.88	21
HP	7-1/2	M	29	121	0.90	0.85	18
CP	5-1/2	F	19	116	0.75	0.87	19
JH	8-1/2	M	25	136	0.80	0.86	9.5
MH	7-1/2	M	22	126	0.53	0.91	11

Fig. 12. Retention of I^{131} by thyroid glands of 4 children (age 4 to 10 years).

LOS ALAMOS
PHOTO LABORATORY

NEG. NO. 633879

PLEASE RE-ORDER
BY ABOVE NUMBER

15 to 25 per cent. According to Morrison et al. (9), mean uptake in newborn infants receiving oral radioiodine was 45 per cent at 25 hours and 50 per cent at 30 hours; turnover studies indicated a biological half-life of the order of 15 to 25 days. These authors also review the literature and find conflicting reports on uptake by newborn infants, varying between adult values and much higher values. The situation with regard to newborn infants does not seem to be clear.

Cameron and Bell (10) report a series of uptake measurements on 20 normal adults using "very small doses of I^{131} ." Uptake at 24 hours ranged from 8 to 39 per cent, with a mean of 21 per cent; dose was 100 to 200 nanocuries. It would seem that there is good agreement on uptake in children (newborn infants excepted) and adults.

SUMMARY

(a) A new technique for measuring the radioiodine content of the human thyroid in vivo with nanocurie amounts of I^{131} and I^{125} is described.

(b) The technique gives a measure of the thickness of neck tissue over the thyroid; values of 0.4 to 2.0 cm have been found in the subjects studied thus far.

(c) Results on 6 normal adults show uptake at 7 days

after oral ingestion varies between 15 and 29 per cent, with biological half-times between 27 days and infinity.

(d) Results on 8 normal children (ages 4 to 10 years) show little or no difference from adults as far as the data extend at the present writing (15 days post oral ingestion). Uptakes vary between 9.5 and 27 per cent, and biological half-times are long compared to the 8-day physical half-life.

REFERENCES

- (1) H. E. Palmer and F. Swanberg, Jr., Determination of Low Level I¹³¹ in Human Thyroids Resulting from Nuclear Test Fallout, Hanford Atomic Products Operation Report HW-SA-2612 (1962).
- (2) M. Eisenbud, Y. Mochizuki, A. S. Goldin, and G. R. Laurer, Iodine-131 Dose from Soviet Nuclear Tests, Science 136(3514), 370-374 (May 4, 1962).
- (3) W. G. Myers and J. C. Vanderleeden, Radioiodine-125, J. Nucl. Med. 1, 149-164 (July 1960).
- (4) L. Slack and K. Way, Radiations from Radioactive Atoms in Frequent Use, U. S. Atomic Energy Commission (February 1959).
- (5) M. Brucer, Thyroid Radioiodine Uptake Measurement, Oak Ridge Institute of Nuclear Studies Report ORINS-19 (June 1959).
- (6) The Thyroid, S. C. Werner (ed.), Hoeber-Harper, New York, N. Y. (1955), p. 207.
- (7) C. C. Lushbaugh, D. B. Hale, and C. R. Richmond, Los Alamos Scientific Laboratory Report LAMS-2526 (1960), p. 364.

- (8) K. M. Saxena, E. M. Chapman, and C. V. Pryles, Minimal Dosage of Iodide Required to Suppress Uptake of I-131 in Normal Thyroid, *Science* 138(3538), 430-431 (October 19, 1962).
- (9) R. T. Morrison, J. A. Birbeck, T. C. Evans, and J. I. Routh, Radioiodine Uptake Studies in Newborn Infants, *J. Nucl. Med.* 4, 162-166 (1963).
- (10) J. R. Cameron and D. P. Bell, Thyroid Uptake Studies with I¹³¹ in Very Small Doses, *Radiology* 79, 452-455 (1962).