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A Comparison of Iodine-125 and Iodine-131 as Tracers in the Diagnosis of Thyroid Disease. II. Clinical Aspects[1,3]

M. Ben Porath[2], A. Hochman and J. Gross

Jerusalem, Israel

The physical aspects of the use of ^{125}I for thyroid studies have been investigated in a previous paper (4). It was shown that ^{125}I theoretically has many desirable characteristics for this purpose. In this work, we compare the utility of this isotope with iodine-131 under the conditions of routine clinical examinations of thyroid function.

MATERIALS AND METHODS

The result of 229 tracer studies for thyroid function evaluation with ^{125}I were compared with the results of 229 randomly chosen studies with iodine-131. Patients over the age of 60 and patients showing symptoms of psychoneurosis were excluded. In the ^{125}I group, 50% were clinically euthyroid, 18% hypothyroid and 32% hyperthyroid. Forty-five percent of the ^{131}I tests were performed on clinically euthyroid individuals, 24% on hypothyroid and 31% on hyperthyroid patients. In addition, 20 patients were given a mixed dose of 10 μC ^{125}I and 50 μC ^{131}I and the counts were performed simultaneously. Two-hour and 24-hour uptakes, 24-hour urine excretions, total plasma concentrations and PBI conversion ratios (CR), were measured. Two hundred and forty-eight thyroid scans and 12 scans of lungs were performed with iodine-125. Some of the scans were repeated after ^{131}I administration. The doses used for the various tests are listed in Table I.

The standard for the uptake measurements was a plastic tube, 3.1 cm diameter and 4.3 cm (32.5 cc), filled to the top. The standard was counted in a five inch diameter lucite neck phantom at 0.5 cm depth, as described in the previous article (4).

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[2]Present Address: Medical Physics Section, Radioisotope Service, Hines, VA Hosp., Hines, Ill.

[3]The Medical Physics Section, the Department of Oncology, and the Department of Experimental Medicine and Cancer Research, The Hebrew University Hadassah Medical School, Jerusalem, Israel.

The standard for urine measurements was a plastic container of one liter volume. All urines were collected in plastic containers of the same diameter as the standard. The crystal-sample distance was 30 cm and at this distance the counts were independent of volume in the range of 0.8-2.0 liters.

Two-ml plasma samples were counted in plastic test tubes in a 1¾″ × 2″ Well Counter.

PBI conversion ratio was determined with an ion-exchange resin (Squibb Rezikits).

Scannograms were performed with a FH96 Scintiscanner (Frieseke Hoepfner), with a 2″ × 2″ Crystal, and a 31-hole focussing collimator. Mechanical and photoscans were obtained simultaneously. The magnetic memory feature of this scanner was used for detailed localizations and profile scans. The base line setting for ^{125}I was 15 KeV with a channel width of 35 KeV. The base line for ^{131}I was 330 KeV with a channel width of 50 KeV. The scanning speed was 2.5 mm/sec. Distances between rows was 3 mm for thyroids and 6 mm for metastases outside the thyroid. The speed of replay from the memory was 10–20 mm/sec.

TABLE I

THE DOSES OF ^{125}I AND ^{131}I USED FOR VARIOUS TESTS

Test	^{125}I	^{131}I
Uptake and Urine	0.5 μC	2.0 μC
PBI conversion ratio	10	50
Thyroid Scanning	25	75
Scanning of Metastases from Thyroid Carcinoma	500	500

RESULTS

Uptake, excretion and protein-bound-conversion ratio.

In Table II the results are given as averages ± standard deviations. The distributions are shown in Figure 1. As the number of studies compared were equal in both the ^{125}I and the ^{131}I groups, the distribution is represented in percent of patients in each group, in five percent steps of the uptake or PBI-conversion ratio. The results of the 20 consecutive studies with *cocktails* of ^{125}I + ^{131}I are given in Table III. No statistically significant differences are demonstrable. However, there is an indication of a systematic negative difference in the two-hour uptake.

Scanning

In Fig. 2, a chest x-ray picture of a patient suffering from follicular adenocarcinoma of the thyroid, is shown. No metastases were seen in his lungs (a).

However, metastases are clearly visualized on an anterior (d) and posterior (e) photoscan of the lungs with iodine-125. Superimposing these two scans (c) results in a picture similar to the anterior photoscan of the lungs with ^{131}I (b).

Figure 3 shows (a) a diagram of a scanned thyroid, indicating the location of nodules by palpation, (b) the photoscan with ^{125}I and (c) the photoscan with iodine-131.

DISCUSSION

From Table II and Fig. 1 we see that there is no significant difference between the results obtained with ^{125}I and iodine-131. The slightly higher ^{131}I uptakes of clinically euthyroid patients may be due to a higher extrathyroidal contribution of ^{131}I than ^{125}I, and to the larger absorption of the ^{125}I x-rays in the thyroid. In patients who received mixed doses of ^{125}I and ^{131}I (Table III), there is no statistically significant difference between the thyroid parameters measured with the two isotopes. The *in vivo* uptakes tend to indicate a greater uptake of ^{131}I than iodine-125. The difference is particularly obvious in the two-hour uptake comparison given in Table III and is probably due to the extrathyroidal contribution to the count. Since this contribution is present in a larger volume than the thyroid it would according to curve 2 (4), result in a relatively lower count for iodine-125. It is clear that there is no isotope effect occurring in the metabolic utilization of these two isotopes of iodine by the human thyroid.

From these results it is apparent that thyroid function studies are as easily performed with ^{125}I as they are with iodine-131. For uptake measurements with ^{125}I, it is essential to use a proper neck phantom and an approximate 30 ml standard in a plastic container. While for ^{131}I, a phantom and standard of these sizes is desirable, only slight errors are introduced when a 5 ml standard in a glass container is used instead. Differences up to 30% in the uptake results with

TABLE II

COMPARISON OF THE DISTRIBUTIONS OF ^{125}I AND ^{131}I GIVEN SEPARATELY, MEANS ± STANDARD DEVIATION OF VARIOUS GROUPS AND TESTS.

Clinical Diagnosis	*24-h Uptake % Dose*		*24-h Urinary Excretion % Dose*		*24-h PBI-Conversion Ratio*	
	^{125}I	^{131}I	^{125}I	^{131}I	^{125}I	^{131}I
Hypothyroid	16 ± 9	17 ± 7	59 ± 11	57 ± 15	8 ± 4	7 ± 6
Euthyroid	32 ± 7	36 ± 8	49 ± 8	47 ± 10	28 ± 11	27 ± 12
Hyperthyroid	64 ± 11	65 ± 13	25 ± 13	22 ± 14	76 ± 17	74 ± 18

TABLE III

COMPARISON OF THE DISTRIBUTION WITH ^{125}I AND ^{131}I GIVEN SIMULTANEOUSLY TO THE SAME PATIENT

Case No.	^{125}I	^{131}I	R^*	^{125}I	^{131}I	R^*	*24-h Urinary Excretion*			*24-h Plasma, % dose/liter*			*24-h Conversion Ratio*		
							^{125}I	^{131}I	R^*	^{125}I	^{131}I	R^*	^{125}I	^{131}I	R^*
1.	10	14	0.71	29	30	0.97	50	58	0.86	0.30	0.28	1.07	15	15	1.00
2.	10	12	0.83	27	30	0.90	55	60	0.90	0.30	0.24	1.25	4	6	0.67
3.	85	85	1.00	88	91	0.97	8	9	0.89	1.20	1.30	0.92	100	100	1.00
4.	48	46	1.04	80	77	1.04	18	19	0.95	0.30	0.30	1.00	80	90	0.89
5.	7	7	1.00	95	82	1.16	—	—	—	0.18	0.22	0.82	99	99	1.00
6.	38	38	1.00	60	74	0.81	25	25	1.00	0.10	0.10	1.00	60	57	1.05
7.	10	15	0.67	32	37	0.87	49	50	0.98	0.13	0.10	1.30	20	16	1.25
8.	17	18	0.94	48	50	0.96	36	41	0.88	0.14	0.12	1.17	47	50	0.94
5.	7	7	1.00	95	82	1.16	—	—		0.18	0.22	0.82	99	99	1.00
6.	38	38	1.00	60	74	0.81	25	25	1.00	0.10	0.10	1.00	60	57	1.05
7.	10	15	0.67	32	37	0.87	49	50	0.98	0.13	0.10	1.30	20	16	1.25
8.	17	18	0.94	48	50	0.96	36	41	0.88	0.14	0.12	1.17	47	50	0.94
9.	23	27	0.85	15	17	0.88	19	19	1.00	0.72	0.73	0.99	2	3	0.67
10.	10	11	0.91	27	24	1.13	56	52	1.08	0.40	0.34	1.18	10	10	1.00
11.	10	11	0.91	32	35	0.91	40	40	1.00	0.90	1.00	0.90	14	12	1.17
12.	—	—	—	96	97	0.99	6	7	0.86	0.25	0.30	0.83	84	85	0.99
13.	24	25	0.96	64	65	0.98	25	23	1.09	0.20	0.25	0.80	—	—	—
14.	—	—	—	20	17	1.18	54	59	0.92	0.60	0.59	1.15	5	5	1.00
15.	—	—	—	26	28	0.93	45	49	0.92	0.40	0.38	1.05	14	10	1.40
16.	—	—	—	28	30	0.93	42	37	1.14	0.30	0.25	1.20	11	14	0.79
17.	68	72	0.94	92	92	1.00	10	8	1.25	0.70	0.60	1.17	76	70	1.09
18.	18	19	0.95	90	65	0.92	22	27	0.83	0.30	0.25	1.15	58	57	1.02
19.	10	12	0.83	38	35	1.09	55	44	1.25	0.40	0.30	1.33	14	10	1.40
20.	46	50	0.92	90	96	0.94	20	17	1.18	0.30	0.32	0.94	84	84	1.00
			0.90±0.11			0.98±0.09			1.00±0.13			1.06±0.15			1.00±0.19

Mean R, ± S. D.

$*R = \frac{^{125}I \text{ result}}{^{131}I \text{ result}}$ Ratio

^{125}I may occur when inadequate standards are used. This would probably explain the low value of uptakes obtained by Levy *et al* (1). The use of ^{125}I in tracer studies is also of advantage in cases where a long follow-up of iodine metabolism is required. When a second thyroid-uptake study is necessary a short time after the first, it can be carried out by means of iodine-131.

Certain advantages of ^{125}I for scanning have been reported (2,3). In Fig. 2 we see the differences of scannograms with ^{125}I and ^{131}I in a patient with lung metastases of thyroid follicular adenocarcinoma. With ^{125}I the front and back metastases are clearly differentiated, while with ^{131}I a picture is obtained similar to the superimposed picture of the chest and back scans with ^{125}I (equal doses are used). In addition, the background obtained with ^{131}I is much higher and cannot be eliminated by electronic means, else the counting rates over the metastases would be reduced to undetectable levels. The chest x-ray picture of this patient shows no metastases in the lungs (Fig. 2a).

In Fig. 3, the scannogram of the thyroid with ^{125}I clearly shows all three of the nodules present in the gland, while only two can be recognized when ^{131}I is used. This is due to the better resolution obtainable with ^{125}I, as well as to the *fogging* of the ^{131}I scan from functioning thyroid tissue underneath the cold nodules.

The calculated radiation dose to the thyroid is less from ^{125}I than from iodine-131. However, experimental work with animals is now in progress to investigate directly the toxicity and tumorogenicity of ^{125}I in comparison with ^{131}I. If the results of these studies prove there is an equal or a lower effect for ^{125}I, then clearly this isotope should replace ^{131}I for thyroid diagnostic studies.

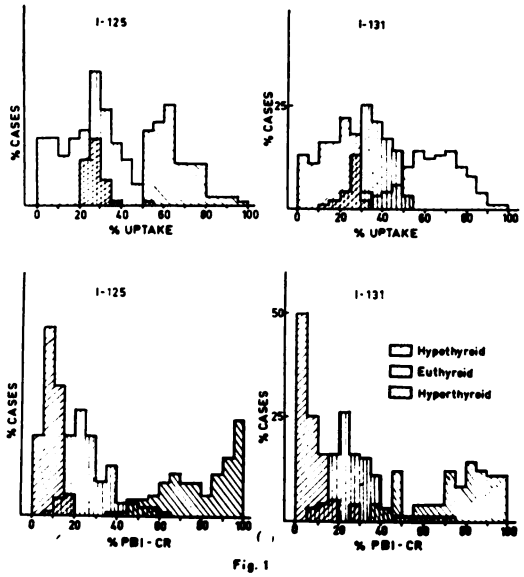

Fig. 1

Fig. 1. The distribution of the results of 229, 24-hour thyroid uptake measurements and PBI conversion ratios carried out with ^{125}I (left) and ^{131}I (right).

SUMMARY

1) Results of 229 tracer studies with ^{125}I were compared with the results of the same number of studies with iodine-131. Twenty patients were given a mixed dose of ^{125}I + ^{131}I. There was no significant difference in the results, providing appropriate standards are used.

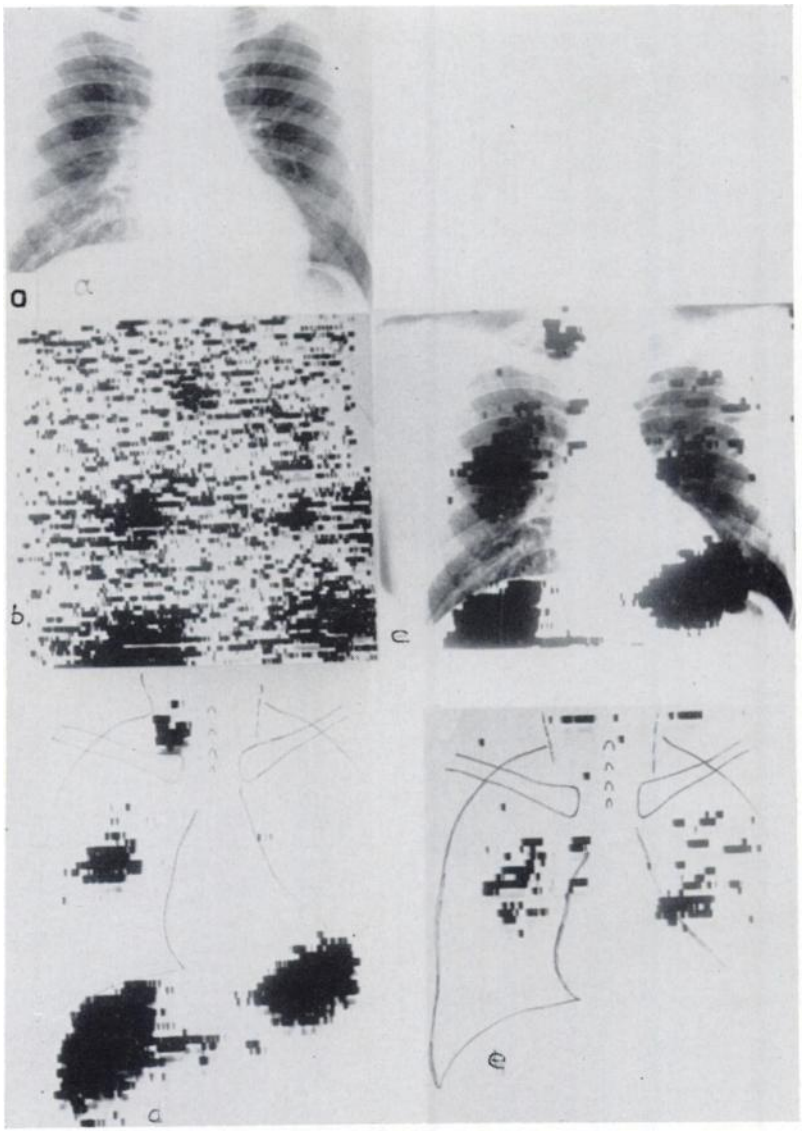

Fig. 2. Lung metastases of follicular adeno-carcinoma of the thyroid, a. Chest x-ray showing no metastases, b. Chest scan with ^{131}I, c. Superposition of chest and back scan with ^{125}I and x-ray picture, d. Anterior scan with ^{125}I, e. Posterior scan with ^{125}I. (This scan is shown from the anterior aspect to permit easy comparison with scan d). Note concentration of radioiodine in stomach and liver in scan d.

Fig. 3. Scan of thyroid with three cold nodules, a. Outline of thyroid and nodules, b. ^{125}I scan of thyroid, c. ^{131}I scan of thyroid.

2) This lack of difference in the metabolism of the two isotopes of iodine by the thyroid, indicates that there is no isotope effect involved.

3) Thyroid scans and thyroid metastases scans with ^{125}I show better resolution, localization and lower backgrounds than with iodine-131.

ADDENDUM

A preliminary report of these findings has been given in the Proceedings of the International Symposium on Medical Radioisotope Scanning, April 20-24, 1964, Athens, Greece, Volume II, pp. 71-77.

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