EVALUATION OF CLINICAL VALUE OF ^{123}I AND ^{131}I IN THYROID DISEASE

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Comparison of ^{123}I and ^{131}I for thyroid scans and uptakes was undertaken to evaluate their diagnostic values in conjunction with instrumental efficacy for ^{123}I. By far the superior quality images were obtained with ^{123}I. Further, both the lower absorbed radiation dose and the shorter scanning time required indicate that ^{123}I is the radionuclide of choice for thyroid studies.

Uptake studies and scans continue to be valuable tools for detailed functional and morphological evaluation of the thyroid. The widely adopted radionuclide for this purpose is ^{131}I despite certain disadvantages (*1*). The isotope ^{123}I has ideal physical characteristics for this use ($T_{1/2} = 13.2$ hr, EC, no β^- or β^+, E_γ 159 keV, 83%); however, problems with product yield and purity delay its routine clinical use. Iodine-123 has been produced directly by several nuclear reactions (*2–4*). The product which contains longer lived radioiodine contamination, notably ^{124}I, has been clinically compared to ^{131}I (*5*). More recently, pure ^{123}I has been prepared by Sodd, et al (*6*) and others (*7,8*). By using pure ^{123}I instead of ^{123}I which contains impurities, scanning resolution is improved and absorbed radiation dose further reduced. This communication compares the use of pure ^{123}I and ^{131}I for thyroid studies in various clinical situations.

MATERIALS AND METHODS

Iodine-123, containing less than 0.005% higher energy radioiodine contaminants, was made with the gas-flow target assembly using the $^{122}Te(^4He,3n)$ ^{123}Xe reaction (*6*). Xenon-123 decays to ^{123}I, and the time necessary for ^{123}I in growth can be used to transport the isotope to the user. The radionuclidic purity of the ^{123}I used in this work was 99.7% as determined by Ge(Li) gamma spectroscopy. The major contaminant was 0.3% ^{125}I which emits only 30-keV photons (*6*). Other radioiodine contaminants which have higher energy gamma rays, such as ^{124}I, account for 0.005% of the ^{123}I activity so that even at 48 hr after production, when the scans are done, their total activity is still less than 0.1%. Thus the use of pure ^{123}I eliminates collimation problems associated with the higher energy gamma-ray emitters: ^{124}I, ^{126}I, ^{130}I, and ^{131}I.

Iodine-131 was obtained from a commercial source. All patients tested were suspected of having functional and/or anatomical pathology. Studies consisted of a 3-day procedure: dose of ^{123}I on the first day; uptake and two scans with ^{123}I followed by a dose of ^{131}I on the second day; and uptake and scan with ^{131}I on the third day. Both ^{123}I and ^{131}I were administered in liquid form. All scan and uptake procedures were performed 24 hr postdose by a technician. The standard doses used in this study for ^{123}I and ^{131}I were 200 and 100 μCi, respectively. Uptake studies were carried out with standard techniques (*1*), and all scans were obtained with the Picker Magna Scanner III*. Either the low-energy, fine-focus collimator (LEFF) or the low-energy, medium-focus collimator (LEMF) was used for one ^{123}I scan, and the fine-focus collimator (FF) with an energy range of 100–400 keV was used for both an ^{123}I and an ^{131}I scan. The information density was set for 500 ± 200 counts/cm² whenever possible or the scan speed was not less than 25 cm/min. No contrast enhancement or background suppression was used. Seventy-two scans (three per patient) and an uptake study obtained from 24 patients com-

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* Mention of commercial product does not imply endorsement by the Department of Health, Education, and Welfare.

TABLE 1. COMBINED SCAN AND UPTAKE INTERPRETATION

Interpretation	No. of patients
Euthyroid, normal glands	5
Euthyroid, diffuse goiter	7
Euthyroid, functional nodule	1
Euthyroid, nonfunctional nodule	1
Euthyroid, agenesis of right lobe	1
Euthyroid, multinodular goiter	5
Euthyroid, postlobectomy	1
Hyperthyroid, diffuse goiter	1
Hypothyroid, diffuse goiter	2
Total	24

FIG. 1. 28-year-old euthyroid female (uptake at 24 hr: 22% with ^{131}I and 24% with ^{123}I) with nodular goiter. Nonfunctioning lesions are well delineated with ^{123}I but poorly defined with ^{131}I. Scanning time was 25 min by FF with ^{131}I, 25 min by FF with ^{123}I, and 15 min by LEFF with ^{123}I.

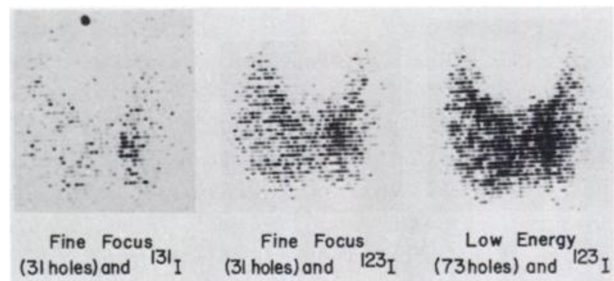

FIG. 2. 42-year-old hypothyroid female (uptake at 24 hr: 10% with ^{131}I and 12% with ^{123}I) with diffuse goiter. There is hardly any structural delineation with ^{131}I but well-defined anatomy with ^{123}I. Scanning time was 32 min by FF with ^{131}I, 25 min by FF with ^{123}I, and 15 min by LEMF.

prise the data for this report. In addition, thyroid images obtained from most of the patients studied with the gamma camera were evaluated if scan interpretation was questionable.

A panel of six physicians independently evaluated each patient's set of three scans, rating them from best to worst according to diagnostic quality by assigning corresponding point values of 3 to 1. Clinical history and collimator and isotope combinations were not given to the panel. Any structural difference between scans was also recorded. To avoid bias in interpreting the results of the study, the senior author who evaluated patients clinically was not included in the panel.

RESULTS

The final interpretation on these 24 patients is shown in Table 1. Agenesis of the right lobe was later verified by TSH stimulation study. A case with functional nodule was lost for followup, and a case with nonfunctional nodules was diagnosed as Hashimoto's thyroiditis by the partial lobectomy (see Fig. 3). The number of scans graded "best" by the panel is shown for each of the three scanning procedures in Table 2. Scans obtained with ^{123}I and LEFF or LEMF collimators were rated the "best" quality, an average of 14.3 of the total 24 (59.6%) for an average score of 2.5. Similarly, the average score for ^{123}I and FF was 1.8 and for ^{131}I and FF, 1.7. No attempt was made on this rating to determine which collimator (LEFF or LEMF) is better.

TABLE 2. NUMBER OF SCANS RATED BEST BY THE PANEL

Physician	Low energy (LEFF or LEMF) collimator & ^{123}I	Fine focus (FF) collimator & ^{123}I	Fine focus (FF) collimator & ^{131}I
A	12	8	4
B	13	2	9
C	10	5	9
D	17	4	3
E	16	3	5
F	18	5	1
Average	14.3 (59.6%)	4.5 (18.7%)	5.2 (21.7%)

Two examples showing marked structural differences in each scan of the set are shown in Figs. 1 and 2. Figure 1 clearly illustrates the superior quality of the scan with ^{123}I and the low-energy collimator in comparison with the rest. The most important aspects of these scans are the serial changes from poorly delineated anatomy with ^{131}I to well-delineated multiple lesions with ^{123}I. If a routine study using ^{131}I alone is carried out, at least one lesion in the left upper pole of the lobe might be overlooked. In Fig. 2, the thyroid glands are well defined with ^{123}I but with ^{131}I there is hardly any structural delineation because of hypothyroidism and the dose used. Figure 3 shows a set with no structural differences between scans; however, a nodule in the upper pole of the right lobe detected clinically was not well delineated. An additional scintiphoto was obtained with the gamma camera collecting 100,000 counts. There is an area of vague uptake in the upper pole of the right lobe where there was a nodule of 1.6 cm in diam in the surgically resected lobe. There was no detectable abnormality in the left lobe by palpation. Followup scan with ^{99m}Tc-pertechnetate after about a year indicates normal uptake in the remaining left lobe including the lower pole. This illustrates the usefulness of the gamma camera despite criticism of an inherent peripheral distortion produced with the pinhole collimator (*9,10*). Figure 4 illustrates a case with a high normal uptake value, and there is no appreciable structural difference in a set of scans; however, a clearer anatomy in ^{123}I with the low-energy collimator is demonstrated. This case exemplifies scans obtained from euthyroid patients where there is little morphological discrepancy of the gland.

If information density is to be consistent in all collimators, the scanning times with a set line space will be proportional to the counting rates. For further verification of counting rates at the time of scanning, doses of the same activity of ^{131}I and ^{123}I were placed in the identical standard neck phantoms. After 24 hr the counting rates with different collimators were measured at the same distance of the focal depth and settings of the scanner as in the

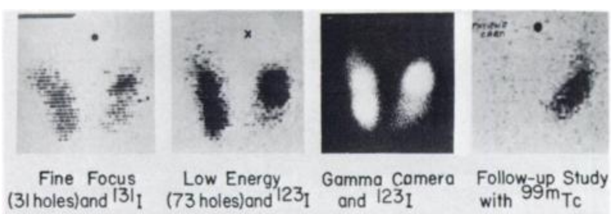

FIG. 3. 59-year-old euthyroid female (uptake at 24 hr: 20% with ^{131}I and 18% with ^{123}I). There is no definite morphological discrepancy between images, but this illustrates better thyroid anatomy using gamma camera with pinhole collimator. Clinically palpable nonfunctioning nodule was noted in right upper pole. Nodule was removed surgically. No palpatory or surgically observable nodule corresponded to apparent defect in left lower pole. Followup study 13 months later shows area to visualize normally. Diagnosis of Hashimoto's thyroiditis was made histologically. Scanning time was 28 min by FF with ^{131}I and 12 min by LEMF with ^{123}I. Camera image required 8 min for 100,000 count collection.

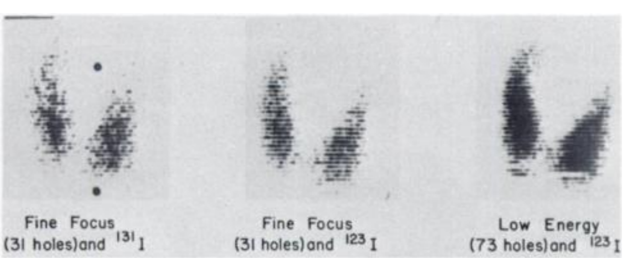

FIG. 4. 43-year-old euthyroid female (uptake at 24 hr: 35% with ^{131}I and 32% with ^{123}I). Enlarged thyroid gland was suspected clinically. Scan was interpreted as being normal. This illustrates case of euthyroid patient with clearer morphology with ^{123}I. Scanning time was 22 min by FF with ^{131}I, 15 min by FF with ^{123}I, and 10 min by LEMF with ^{123}I.

routine clinical procedure. The results, together with collimator specifications, are shown in Table 3.

The uptake values for both ^{123}I and ^{131}I in 22 patients whose studies were completed in 3 days as outlined agreed within the limits of diagnostic values; i.e., hypothyroid, euthyroid, and hyperthyroid defined empirically at this laboratory. In two cases where the studies were done 1–3 months apart, uptake values did not concur with each other. These were later verified as an inadvertent administration of thyroid blocking agents after the ^{123}I study by the referring physicians. Using the paired Student's t-test in the above 22 patients, a t-value of 1.15 was calculated; the critical point being 2.08 at a 95% confidence level. Therefore, no significant difference of uptake values using the two isotopes was observed. The mean uptake value ± 1 s.d. in 18 euthyroid patients was $25 \pm 7\%$ with ^{123}I and $26 \pm 8\%$ with ^{131}I.

Absorbed radiation dose to the thyroid gland and whole body from 100 μCi of the pure ^{123}I used in this study and others currently used for thyroid studies is compared in Table 4. These calculations are based on the highest figure given (*11*).

DISCUSSION

This is the third of a series of thyroid studies using ^{123}I at this laboratory; the first two have been reported elsewhere (*5,12*). No attempt was made in this study to have ^{123}I studies done at 6 hr postdose. It appears to be of little benefit to us to complete the ^{123}I scan and uptake studies in one day since the majority of our patients are referred from outpatient clinics. Either staying at the laboratory or returning, 6 hr postdose was found to be incon-

TABLE 3. COLLIMATOR CHARACTERISTICS AND RELATIVE COUNTING RATES

Description	Energy range (keV)	Width 50% line (in.)	Relative counting rates at 24 hr
Fine focus (FF) 31 holes ^{131}I:100 μCi	100–400	1/4	1.0
Fine focus (FF) 31 holes ^{123}I:100 μCi	100–400	1/4	0.3
Low-energy medium focus (LEMF) 73 holes ^{123}I:100 μCi	<150	1/4	2.3
Low-energy fine focus (LEFF) 73 holes ^{123}I:100 μCi	<150	3/16	1.1

TABLE 4. COMPARATIVE ABSORBED RADIATION DOSE

Source	Radioisotope	Activity	Dose (rads) Thyroid	Dose (rads) Whole body
Pure ^{123}I, Cincinnati General Hospital*	^{123}I	100 μCi	2.000	0.0070
	^{124}I	0.01 μCi	0.012	0.0002
	^{125}I	0.6 μCi	0.720	0.0023
			Total 2.732	0.0095
^{123}I, Commercial†	^{123}I	100 μCi	2.00	0.0070
	^{124}I	<1.0 μCi	<1.20	<0.0142
	^{126}I	<0.5 μCi	<1.15	<0.0028
	^{130}I	<3.0 μCi	<0.56	<0.0026
	^{131}I	<0.5 μCi	<1.05	<0.0018
			Total <5.96	<0.0284
Commercial	^{131}I	100 μCi	210	0.36
Commercial	^{99m}Tc	1,000 μCi	0.5	0.014

* No other radioactive contaminant present.
† Amount of ^{125}I not listed in the product description.

venient to most of the patients. On the other hand, it can be argued that to conduct studies at 6 hr postdose instead of 24 hr is advantageous not only because of completion of the studies in a day but also because of the further reduction of dose (*13*). This possibility was suggested as early as 1968 (*12*) when the radioiodine contained usually 1–2% of ^{124}I at the time of administration but at 24 hr represented about 4–8% of the total activity. The high-energy scatter contributes to the 159-keV photopeak of ^{123}I and increases with time to create problems in obtaining good resolution (*3*). Due to these circumstances, scans with impure ^{123}I were obtained at 6 and 24 hr but with pure ^{123}I at 24 hr.

Absorbed radiation dose from ^{123}I is lower by far than that from ^{131}I; consequently, a relatively large dose can be administered per study. Technetium-99m is a radionuclide currently used for routine thyroid studies including uptake in euthyroid to hyperthyroid individuals (*1*). The dose range of between 1 and 2 mCi of ^{99m}Tc is more acceptable in terms of absorbed radiation dose than that of ^{123}I; however, because of the low uptake of ^{99m}Tc-pertechnetate by the thyroid gland, its higher background activity obscures the image in the majority of hypothyroid individuals. Early uptake tests using ^{99m}Tc in the form of pertechnetate have an obvious advantage but it is unsuitable for the diagnosis of hypothyroidism (*1*).

The dose of ^{123}I does not necessarily have to be 200 μCi; further reduction of the dose is possible. Indeed, we have in a few instances done studies with a 100 μCi dose which in an individual with normal uptake was generally satisfactory.

Five patients in this study, including the two patients listed in Table 1, had uptake values of less than 15% with ^{123}I. Of these five patients, two had ^{123}I scans with the LEFF and three with the LEMF. It is our impression that an individual with low uptake can best be studied with LEMF because of its higher counting rate and, hence, considerably shorter scanning time as compared with the LEFF.

One advantage of LEFF over LEMF with ^{123}I scanning is better resolution; however, when using LEFF, approximately 50% of the sensitivity is sacrificed in comparison with LEMF. It must be remembered, however, that the difference in scan quality appears to be not so great as to cause any discrepancy in interpretation. Fine focus or equivalent collimators designed for energy ranges of 100–400 keV do not seem to be suitable for ^{123}I study. The quality of the ^{131}I and ^{123}I scans using FF were equally rated but more importantly FF for ^{123}I prolongs the scanning time as compared with low-energy collimators. Thick septa may well be advantageous if contamination of higher gamma energies is anticipated; however, this was not the case in this study.

In conclusion, ^{123}I with collimators designed for low-energy isotopes is ideal for thyroid studies in most respects. At this moment, the availability of ^{123}I is limited. Recent reports, however, indicate that the availability of curie quantities of ^{123}I from high-energy photon facilities at competitive prices may soon be realized (*14*).

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REFERENCES

1. Report of an International Atomic Energy Agency Panel: Thyroid radionuclide uptake measurements. *Int J Appl Radiat Isot* 23: 305–313, 1972

2. SILVESTER DJ, SUGDEN J, WATSON IA: Preparation of iodine-123 by particle bombardment of natural antimony. *Radiochem Radioanal Letters* 2: 17–20, 1969

3. SODD VJ, SCHOLZ KL, BLUE JW, et al: Cyclotron production of ^{123}I—an evaluation of the nuclear reactions which produce this isotope. *USPHS, DHEW Report*, BRH/DMRE 70-4, October 1970, (also summarized in) *Isotopes Rad Tech* 9: 154–159, 1971–1972

4. HUPF HB, ELDRIDGE JS, BEAVER JE: Production of iodine-123 for medical applications. *Int J Appl Radiat Isot* 19: 345–351, 1968

5. WELLMAN HN, SODD VJ, MACK JF: Production and clinical development of a new ideal radioisotope of iodine—iodine-123. In *Frontiers of Nuclear Medicine*, Horst W, ed, Berlin, Springer-Verlag, 1971, pp 19–30

6. SODD VJ, BLUE JW, SCHOLZ KL, et al: A gas-flow powder target for the cyclotron production of pure ^{123}I. *Int J Appl Radiat Isot* 24: 171–177, 1973

7. FUSCO MA, PEEK NF, JUNGERMAN JA, et al: Production of carrier-free ^{123}I using the $^{127}I(p,5n)^{123}Xe$ reaction. *J Nucl Med* 13: 729–732, 1972

8. LAMBRECHT RM, WOLF AP: The $^{122}Te(^4He,3n)^{123}Xe \xrightarrow[2.1\ hr]{\beta^+,EC} {}^{123}I$ generator. *Radiat Res* 52: 32–46, 1972

9. HURLEY PJ, STRAUSS HW, PAVONI P, et al: The scintillation camera with pinhole collimator in thyroid imaging. *Radiology* 101: 133–138, 1971

10. CRADDUCK TD: Distortion produced by pinhole collimators. *J Nucl Med* 13: 778–779, 1972

11. ELLIS RE: Protection of the Patient in Radionuclide Investigations. *ICRP #17*, London, Pergamon Press, 1971, pp 41–42, 44–45, 79

12. WELLMAN HN, MACK JF: Study of preliminary experience with the use of ^{123}I for thyroid function and scanning compared to ^{131}I. *J Nucl Med* 9: 359, 1968

13. ATKINS HL, KLOPPER JF, LAMBRECHT RM, et al: A comparison of technetium-99m and iodine-123 for thyroid imaging. *Am J Roentgenol Radium Ther Nucl Med* 117: 195–201, 1973

14. BLUE JW, SODD VJ, SCHOLZ KL, et al: Iodine-123 production for use in nuclear medicine by spallation of xenon. *J Nucl Biol Med* 1: 51–52, 1973