MEASUREMENT OF ^{127}I CONCENTRATION IN THYROID TISSUE BY X-RAY FLUORESCENCE

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X-ray fluorescence was used to determine the iodine content of surgically removed thyroids which had been preoperatively scanned with ^{131}I. Iodine concentrations were determined for tissues classified as normal, papillary-follicular carcinoma, chronic thyroiditis, and colloid nodules of adenomatous thyroids. The iodine concentration of these thyroid states varied, with carcinomatous tissue having the lowest concentration and normal tissue the highest. There was considerable overlap among the various pathological states. Nodules showing increased ^{131}I activity on the presurgical thyroid scan contained no more iodide than normal tissue, while nodules showing decreased ^{131}I activity contained considerably less iodine. The residual ^{131}I from the presurgical dose showed a distribution similar to the distribution of stable iodine.

The iodine concentration of normal thyroid tissue obtained from autopsy specimens was determined to be about 2.5 times greater than the levels reported in the older literature.

K_α x-ray fluorescence is produced when a gamma ray reacts with high-Z atoms ejecting a K-shell electron. The K_α x-ray is characteristic of the atom in which the interaction occurs. Since for a given gamma-ray flux, the number of K_α x-rays produced is proportional to the number of atoms irradiated, quantitation of these x-rays can be used to determine the concentration of the irradiated element.

When thyroid tissue is bombarded with photons, the ionization of iodine atoms results in a characteristic x-ray of 28.5 keV. Hoffer, et al have demonstrated that this process can be used as a new means of imaging the thyroid (*1–4*). It is apparent that if x-ray fluorescent scanning is to come into general clinical use there must be detectable differences in the distribution of stable iodine in macroscopic areas of the thyroid, and these differences should correlate with the various pathological thyroid states. Additionally, if fluorescent scanning is to be used as a supplement to ^{131}I scanning, an important consideration is whether the ^{127}I distribution determined by fluorescent scanning is measurably different from the ^{131}I distribution determined by conventional scanning.

It was the purpose of this study to determine what difference may exist between ^{131}I and ^{127}I thyroid concentrations in various pathological states. Using x-ray fluorescence, iodine levels were determined in surgically removed thyroid tissue. The ^{127}I levels were compared with the pathological diagnosis, a presurgery radionuclide thyroid scan, and when possible, the in vitro ^{131}I distribution.

METHOD

Specimens were obtained from 60 surgically removed thyroids and from 9 thyroids obtained from cadavers with no known history of thyroid disease. All nodular tissue was diagnosed by a microscopic examination. When possible, both non-nodular and nodular tissue from each thyroid gland was obtained. All patients had presurgery ^{131}I thyroid scans. No attempt was made to control the time interval between the ^{131}I administration and surgery. For over half of the patients the interval was 3 days but the range extended from 1 to 29 days. The ^{131}I tissue activity was determined in a conventional well scintillation detector. X-ray fluorescence was used to determine the iodine concentration of the surgical

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specimens and normal thyroid tissue obtained from autopsy specimens.

X-ray fluorescence was produced by exposing thyroid tissue to a 100-mCi collimated source of ^{241}Am. The K_α x-rays were detected with a Kr-CO_2 gas-filled proportional detector. The proportional detector which was uncollimated had a thin Be window 1 in. in diam (4.9 cm^2) and 0.005 in. thick. The angle formed by the source, sample, and detector was 30 deg. The arrangement of the ^{241}Am source and detector was such that only Compton-scattered photons and the K_α x-rays could reach the detector. The output from the amplifier was split and fed into two single-channel analyzers. One analyzer was set with a wide window (40–55 keV) to accept Compton-scattered photons while the second analyzer was set with a 2–3 keV window on the 28.5 keV ^{127}I K_α peak. The FWHM for the 28.5 keV photons was 12%.

The amount of detected scattered photons was a function of the size of the sample since the relationships of source, detector, and shielding material were constant. To determine the effect of sample size on the number of Compton-scattered photons, various volumes of distilled H_2O were counted. The number of Compton-scattered photons detected in the wide window and in the narrow K_α window was determined. Taking a ratio of these two counting rates (narrow-to-wide) gave a factor which was used to obtain a background correction factor for varying sample size. The background counting rate in the narrow window was a linear function of the counting rate in the wide window while the ratio (narrow-to-wide), i.e., background correction factor, varied typically from 0.098 for 0.5 ml to 0.101 for 1 ml. For this same range in sample size, the background count varied approximately 30%.

To standardize the sample, 0.5–1 gm of thyroid tissue was weighed, cut into small pieces, and tightly compacted into plastic test tubes and frozen. One to six tissue samples from each thyroid were irradiated and counted for 5–10 min using the dual-window system.

The narrow-window background count of each thyroid sample was determined by multiplying the appropriate background correction factor times the counts collected in the wide window. This derived background was subtracted from the gross counts in the narrow window. Because the analyzer windows were narrow, a constancy check was performed by counting a concentrated solution of ^{127}I before and after each thyroid tissue determination. A result was considered satisfactory only if the counts in the wide and narrow windows did not vary before and after each determination. To compare counts from day to day, standard solutions of ^{127}I were irradiated with each batch of thyroid tissue. The sensitivity of the system was such that a standard 1-cc solution containing 0.38 mg of ^{127}I gave 1,000 cpm above background. The background count for a 1-cc sample was approximately 4,000 cpm. All data were normalized to net counts per gram of tissue or milligrams of iodine per gram of tissue.

TABLE 1. RATIO OF NON-NODULAR TISSUE TO NODULAR TISSUE

Pathology	Thyroid scan	N	^{131}I	^{127}I
Benign nodules	Cold area	9	4.7 ± 0.9	6.7 ± 1.4
	Hot area	6	1.1 ± 0.3	0.9 ± 0.3
Carcinomatous nodules	Cold area	4	132	≤104*

* In these four cases the ^{127}I levels of the carcinomatous nodular tissues were below the detection level of our system (≤0.04 mg of ^{127}I per gm of thyroid). The 104 value was obtained by assuming that the levels were 0.04. If the actual value were less, the ratio would be greater.

Studies were made to estimate the magnitude of error involved in these measurements. A 3% maximum difference from the mean was found among five successive measurements of a 1-cc solution containing 0.38-mg iodine. A 7% maximum difference from the mean was found in the counting rate of six 1-gm samples of normal thyroid tissue taken from the same gland, and an 11% difference was obtained from the mean of ten determinations repeated 1 year apart.

RESULTS

The ratios shown in Table 1 are from thyroids which were diagnosed by pathology as nodular goiter or carcinoma. These are categorized according to the relative ^{131}I concentration of palpable nodules seen on the presurgery thyroid scan.

The results are expressed as the ratio of ^{127}I and ^{131}I in vitro activity in non-nodular tissue to that in the nodular tissue of the same gland. The mean for each category is shown and also the standard error when the number of determinations allowed this calculation. A value close to unity indicates that the iodine content of the nodular tissue was the same as the surrounding non-nodular tissue. Where cold areas were found on the thyroid scan, the ^{131}I ratio indicates a considerably lower iodine content in the nodular tissue. The ^{127}I ratios confirm that there is a real difference in iodine content in these two types of tissues. In the group where hot areas were found on the scan, both the ^{131}I and ^{127}I ratios indicate that

the iodine content of the nodule is nearly the same as the surrounding thyroid tissue.

There were only four carcinomatous tissues in which we were able to do both ^{131}I and ^{127}I determinations, all of which were papillary-follicular carcinomas. Both the ^{131}I and ^{127}I ratios indicate that the iodine content of thyroid carcinomatous nodules is very low when compared with the normal part of the same thyroid gland. None of these ratios were within the range of the noncarcinomatous cold nodules.

Table 2 shows the milligrams of iodine per gram of thyroid tissue calculated from the irradiated samples. The data are grouped according to pathological diagnosis and relative concentration of ^{131}I as seen in the presurgery thyroid scan. The highest iodine contents were found in the normal tissue and nonnodular tissue of nodular goiters. Low iodine content was found in the cold areas of nodular goiters, thyroiditis, and carcinomatous tissue. The range of values found for normal thyroid tissue does not overlap into the range of values found for the carcinoma or the Hashimoto's thyroiditis groups. On the other hand, the range of values for the non-nodular tissue of nodular goiters completely covers the normal range and extends into both of the other pathological states. The carcinomas tested here were all papillary-follicular in type.

Three hyperplastic thyroids from patients treated with antithyroid (propylthiouracil) drugs were irradiated. Iodine concentrations in milligrams per gram of thyroid were 0.36, 0.57, and 0.56.

TABLE 2. CONCENTRATION OF IODINE IN THYROID TISSUE (mgI/gm TISSUE)

	Colloid nodular goiters			Hashimoto's thyroiditis	Papillary-follicular carcinoma (cold*)
Normal	Non-nodular	Nodule (hot*)	Nodule (cold*)		
1.34	1.83	1.18	0.74	0.48	0.37
1.27	1.57	1.10	0.38	0.39	0.30
1.27	1.41	0.93	0.29	0.17	0.11
1.06	1.32	0.81	0.24	0.16	0.11
1.02	1.23	0.75	0.20	0.15	0.08
0.95	1.06	0.68	0.17	0.10	ND
0.67	0.97	0.65	0.15	ND	ND
0.66	0.84	0.63	0.14	ND	ND
0.61	0.83	0.56	0.12	ND	ND
	0.67	0.37	0.11		ND
	0.62	0.32	0.08		ND
	0.57	0.22	ND		
	0.47		ND		
	0.45		ND		
	0.42				
	0.40				
	0.38				
	0.35				
	0.23				
	0.19				
	0.18				
	0.08				
Mean					
0.98	0.73	0.68	0.20†	0.17†	0.12†

* As seen on the presurgery ^{131}I thyroid scan.
† The mean was calculated by assuming ND = 0.04.
ND = Nondetectable (≤0.04 mg ^{127}I/gm of thyroid).

DISCUSSION

These studies indicate that normal thyroids contain on the average 0.98 mg iodine per gram of tissue. This value is about 2.5 times the value reported for iodine concentration of thyroids obtained from U.S. residents in studies a decade or more ago (*5*). As has been noted in other parts of the U.S., the mean 24-hr ^{131}I uptake has decreased in Houston during the past 10 years. Our laboratory now reports a normal mean uptake value of 10% while the normal mean value reported 10 years ago was 20%. The lowering of the mean uptake indicates that the iodine content of the Houston diet is two times that of 10 years ago.

These in vitro studies also indicate that the iodine content of a pathological area (colloid nodular goiter, thyroiditis, carcinoma) is generally below the iodine content of normal thyroid tissue. Some exceptions to this were found in hot nodules and nonnodular tissue from nodular goiters. While the lowest mean concentration was found in carcinomatous tissues, the range of values found for this group overlapped into the range of iodine concentrations found in cold areas of colloid nodular thyroids and in Hashimoto's thyroiditis. These data suggest that an extremely low concentration of iodine in a nodule might increase the probability of that nodule being carcinoma. However, due to the overlap in ranges of values found in the pathological conditions studied, it would be almost impossible to separate them on an individual basis.

Hoffer and Gottschalk have described their results of a survey of 159 patients who received a fluorescent scan in addition to a conventional ^{131}I scan (*1,2*). It is useful to compare the results of their in vivo study with the results of our in vitro study. In the studies of Hoffer, et al, the thyroid scans of Hashimoto's thyroiditis patients showed ^{127}I concentrations less than the normal thyroid concentrations. Low iodine content was particularly prevalent in those patients who were hypothyroid (*1*). Low iodine concentration is in agreement with our in vitro results where none of the Hashimoto thyroiditis tissue had iodine concentrations equal to that found in normal tissue.

In attempting to correlate increased thyroid function with iodine content as determined by fluorescent scans, Hoffer, et al, found that only 40% of his hyperthyroid patients had high iodine content (*1*). Also they report that one of three autonomous nodules had decreased iodine content (*2*). In our study we found that both the ^{131}I and ^{127}I ratio data indicate that the iodine content of a hot nodule is nearly the same as the surrounding thyroid tissue. These results would seem to indicate that these nodules were seen as hot areas on the ^{131}I scan due to increased iodine turnover rates rather than increased iodine content. This observation is confirmed by the data shown in Table 2 since the hot nodule group did not have the highest concentrations of iodine.

Hoffer and Gottschalk, using fluorescent scanning, detected 60 of 61 cold nodules which were localized by conventional radionuclide scanning (*1*). Our results show that the mean concentration of iodine in cold nodules is considerably lower than the mean concentration for either paranodular tissue of the same gland or normal thyroid tissue.

These data indicate that combining an x-ray fluorescent scan with an ^{131}I thyroid scan should not greatly improve the clinician's ability to separate thyroid carcinoma from benign forms of palpable thyroid nodules. On the other hand, a fluorescent scan might be used in lieu of a conventional ^{131}I thyroid scan. Fluorescent scanning delivers a lower radiation exposure to the thyroid than does ^{131}I or ^{123}I scanning. In addition, as suggested by Hoffer and Gottschalk, fluorescent scanning would be useful in patients with a flooded iodine pool and in scanning patients being treated with thyroid extract. Therefore, a fluorescent scan would be preferable to an ^{131}I scan if both techniques furnished an equal amount of clinically useful information. Other factors such as cost of equipment, scanning time, and ease of scan interpretation are additional factors to be considered in choosing between the two methods.

REFERENCES

1. HOFFER PB, BERNSTEIN J, GOTTSCHALK A: Fluorescent techniques in thyroid imaging. *Sem Nucl Med* 1: 379–389, 1971
2. HOFFER PB, GOTTSCHALK A: Fluorescent thyroid scanning: Scanning without radioisotopes. *Radiology* 99: 117–123, 1971
3. HOFFER PB, JONES BW, CRAWFORD RB, et al: Fluorescent thyroid scanning: A new method of imaging the thyroid. *Radiology* 90: 342–344, 1968
4. HOFFER PB: Fluorescent thyroid scanning. *Am J Roentgenol* 105: 721–727, 1969
5. MCGAVACK TH: *The Thyroid.* St. Louis, CV Mosby, 1951, p 339