Assessment of the Efficacy of Iodine-131 for Thyroid Ablation

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It is customary to ablate residual tissue after near-total thyroidectomy for thyroid carcinoma by administering ^{131}I. A recent trend has been to use lower ^{131}I doses. This study was designed to assess the efficacy of thyroid ablation by 1110 MBq of ^{131}I (30 mCi) in patients who had near-total thyroidectomy for papillary, mixed or follicular thyroid carcinoma. Four months after surgery, a whole-body scan was done using 185 MBq (5 mCi) of ^{131}I after withdrawal of L-thyroxine for 5–6 wk. Residual thyroid area was then measured by planimetry of the thyroid scan. Patients received ablation therapy within 5 days after scanning and one or more subsequent scans were performed 6 mo later. Forty-four patients were treated to ablate residual functional thyroid tissue. Of these, 12 (27%) had successful ablation. Total body areas (1.63 ± 0.16 versus 1.83 ± 0.30, $p < 0.03$) and residual thyroid tissue (1.4 ± 1.4 versus 2.0 ± 1.2 cm^2, $p < 0.05$) were less in patients with total thyroid ablation while there was a trend for a smaller incidence of associated goiter in those patients (1/12 versus 13/32, $p < 0.07$). Nine of the 17 (53%) patients with a total body area less than 1.9 m^2 and/or with a residual thyroid tissue less than 2.1 cm^2 and/or without associated previous associated diffuse or multinodular goiter had a total thyroid ablation, while 3 of the 27 (11%) patients who did not have these characteristics had a successful therapy ($p < 0.005$). Our data suggest that 1110 MBq (30 mCi) of ^{131}I can achieve total ablation of residual thyroid tissue after near-total thyroidectomy particularly in patients with lower total body area and smaller residual thyroid tissue without associated previous diffuse or multinodular goiter.

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Iodine-131 has been recommended to ablate residual thyroid functional tissue after thyroidectomy for well-differentiated thyroid carcinoma (*1–3*). However, there are various opinions on which patients should be given ^{131}I and the amount administered. The doses that are used range from 925 to 7400 MBq (25–200 mCi) (*4–5*). During the last two decades, a trend has been to use 1110 MBq (30 mCi) of radioiodine in order to avoid hospitalization (*6*). However, the result of thyroid ablation after 1110 MBq of ^{131}I are highly variable without clear explanation (*6–15*). In order to assess the effectiveness of this method of ablation and the factors that may explain why this technique may be successful in some and unsuccessful in others, we conducted this prospective study.

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PATIENTS AND METHODS

From 1984 to 1990, 57 consecutive patients with surgically proven papillary and follicular thyroid carcinoma were seen for ^{131}I treatment. The surgeon intended to perform a subtotal or total thyroidectomy in all of these patients. Clinicopathologic stages of thyroid carcinoma were determined during surgery according to Smedal's classification (*16*). Thus, the lesion was intrathyroidal only in Stage I; nonfixed cervical metastases were documented in Stage II; fixed lymph node metastases or invasion into the neck outside the thyroid were noticed in Stage III and metastatic thyroid disease was present in Stage IV. In addition, associated diffuse or multinodular goiter was documented on pathological findings. Four months after surgery, a whole-body scan was done using 185 MBq (5 mCi) of ^{131}I after withdrawal of L-thyroxine for 5–6 wk. Residual thyroid tissue area was then measured by planimetry of the thyroid scan. Five days after scanning, a dose of 1110 MBq of ^{131}I was given to all patients except in six where distant metastases were documented and in one where no residual thyroid tissue was seen (Fig. 1). A subsequent 185 MBq (5 mCi) ^{131}I scan was performed 6 mo later in all patients except five who refused to become hypothyroid again and in one who was hemodialysed. Consequently, 44 patients were completely evaluated in order to assess the efficacy of thyroid ablation with 1110 MBq of ^{131}I. All scans were independently reviewed by two physicians. Ablation was defined as complete absence of any focal uptake in the anterior neck area. Any residual functioning tissue was seen as failure of ablation. A second dose of 30 mCi was given 6 mo after the first dose in 21 of the 32 patients without total thyroid ablation after the first radioactive treatment. Of the 11 subjects who did not have a second 1110-MBq treatment, 10 refused to prolong their hypothyroid period related to ^{131}I administration, and a second dose of 4440 MBq (120 mCi) of ^{131}I was administered in one patient. A third dose of ^{131}I was given in 8 of the 11 patients who had incomplete ablation after a second dose of ^{131}I. A whole-body scan with 185 MBq (5 mCi) of ^{131}I was performed 6 mo after ^{131}I treatment.

A Mann-Whitney U-test was used to assess the significance of differences between the two groups. Normal scale data were analyzed with chi-square and Fisher exact tests. Pearson's correlation rank was also calculated. Results are expressed as means ± s.d. and significance was accepted when $p < 0.05$.

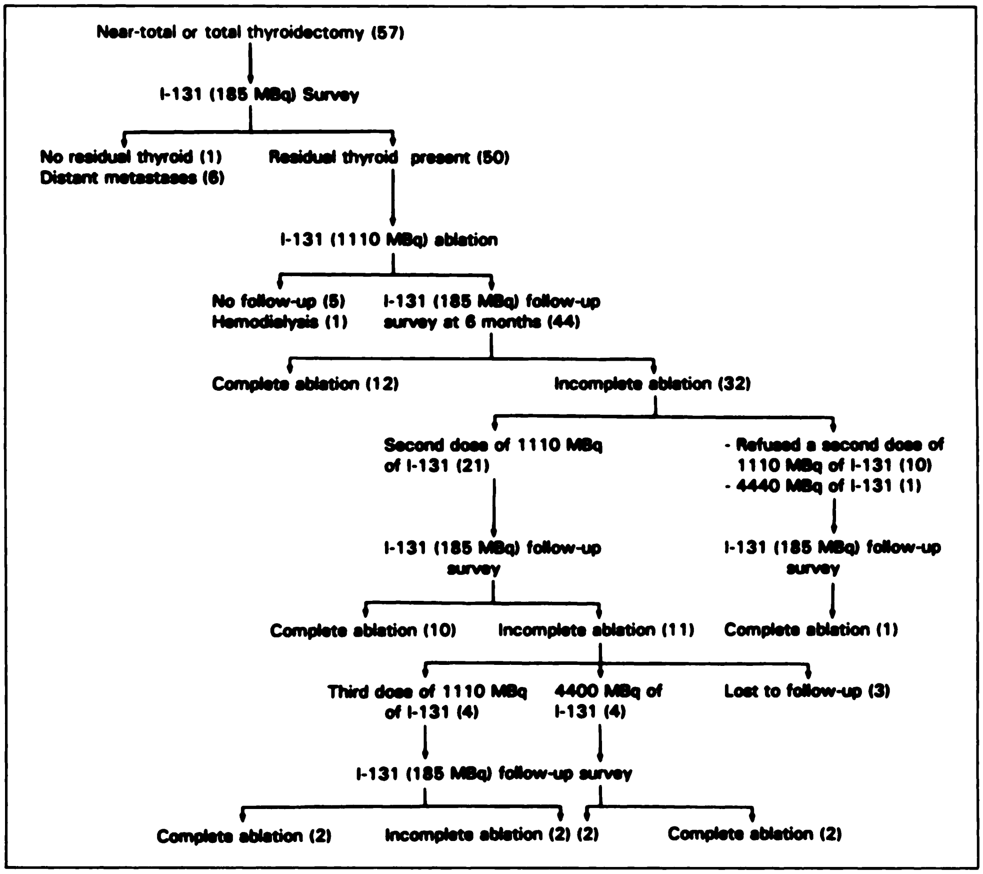

FIGURE 1. Iodine-131 therapy and follow-up scan results of the selected population.

RESULTS

Figure 1 illustrates the treatment and outcome of the patients in a flow diagram. Forty-four patients were treated to ablate cervical residual functional thyroid tissue. Of these, ablation was achieved in 12 (27%). As summarized in Table 1, patients with total thyroid ablation after a single dose of ^{131}I had smaller total body area and residual thyroid tissue after surgery while there was a trend for a lower incidence of associated goiter in these patients. Nine of the 17 (53%) patients with a total body area less than 1.9 m^2 and/or residual tissue less than 2.1 cm^2 on planimetry of thyroid scan after surgery and/or without associated goiter on pathological findings had a total thyroid ablation, while 3 of the 27 (11%) who did not have these characteristics had successful radioactive therapy (X^2, $p < 0.005$). The tumor clinicopathological stages of patients with successful and unsuccessful ablation were similar. In patients where ablation respectively achieved or failed, Stage I was observed during surgery in Patients 6 and 9; Stage II in Patients 1 and 7, Stage III in Patients 5 and 16 and Stage IV in any of both groups. In the 15 patients where both tests were performed, there was no significant difference in thyroid-stimulating hormone (TSH) (41 ± 14 versus 45 ± 28 mU/liter) and ^{131}I uptake (3% ± 3% versus 7% ± 8%) between patients with successful and unsuccessful radioactive therapy. A second dose 1110 MBq of ^{131}I was given in 21 of the 32 patients without total thyroid ablation after the first radioactive treatment. Characteristics of patients

TABLE 1
Clinical Data of Patients Where 1110 MBq (30 mCi) Doses of ^{131}I Achieved Ablation of Thyroid Functioning Remnant Compared to Those Where Ablation Failed

Clinical characteristics	Ablation achieved n = 12 (27%)	Ablation failed n = 32 (73%)	p value
Sex (M/F)	3/9	13/19	NS
Age (yr)	38.5 ± 15.7	39.3 ± 12.3	NS
(Age range)	(21–70)	(19–72)	
Total body area (m^2)	1.63 ± 0.16	1.83 ± 0.30	<0.03
Tumor (papillary/follicular)	6/6	25/7	NS
Clinical stages	1.9 ± 1.0	2.2 ± 0.9	NS
Associated goiter	1 (11%)	13 (40%)	<0.07
Residual thyroid area (cm^2)	1.4 ± 1.4	2.0 ± 1.2	<0.05

with or without a second treatment were similar except for total body area which was smaller in those with a second treatment (1.8 ± 0.3 versus 2.0 ± 0.2 m^2, $p < 0.02$). Of the 21 patients, a second treatment was successful in 10 (48%) (Fig. 1). Patients with total thyroid ablation after 2220 MBq (60 mCi) had a smaller thyroid tissue area before the second dose of 1110 MBq (0.4 ± 0.1 versus 1.1 ± 0.7 cm^2, $p < 0.003$), while total body area was similar (1.66 ± 0.27 versus 1.72 ± 0.24 m^2, ns) to those with an unsuccessful second treatment. Associated histological goiter was present in three patients of each group (ns). There was no significant difference in the frequency of total thyroid ablation rate between the first (27%) and second treatment (48%).

After 1 or 2 doses of 1110 MBq, the success rate of ablation of functional thyroid remnant was 50% (22/44) with a mean ^{131}I dose of 1554 ± 592 MBq (42 ± 16 mCi). Residual thyroid tissue after surgery (1.4 ± 1.1 versus 2.3 ± 1.3 cm^2, $p < 0.04$) and total body area (1.65 ± 0.21 versus 1.9 ± 0.28 m^2, $p < 0.004$) were smaller in patients with successful first and second treatment. Associated histological goiter was present in 4 of the 22 patients with successful ablation compared to 10 of the 22 patients with unsuccessful treatment (ns).

In five patients, the second (*1*) or third (*4*) dose of ^{131}I was 4400 MBq (100 mCi), as illustrated in Figure 1. The ablation response following this larger dose was 60% (3/5) which was similar to the success rate of 50% (22/44) when only low doses of ^{131}I were administered. There was no statistical difference between characteristics of patients with low and high doses, although residual thyroid tissue tended to be larger in those treated with 4400 MBq (100 mCi) (2.6 ± 1.4 versus 1.7 ± 1.2 cm^2).

DISCUSSION

Ablation of thyroid functioning remnant with a single dose of 1110 MBq was achieved in 27% of the subjects. In the medical literature, the success rate in thyroid ablation ranges from 7% to 83% with doses of 925–1110 MBq (25–30 mCi) of ^{131}I (*6–15*) and from 60% to 100% for doses equal or greater than 1850 MBq (50 mCi) (*9,12–14,18,19*). We observed a success rate of 50% (22/44) with a mean dose of 1554 ± 592 MBq (42 ± 16 mCi) when we globally evaluated the patients who were treated once (*21*) and those treated twice (*23*). This ablation success rate would have probably been greater if all patients with an unsuccessful first treatment had a second dose of radioiodine. However, the six patients who refused to have a second ablation dose had a larger total body area than those who had a second treatment which, according to our data, was associated to a lower incidence of successful functional remnant ablation. Ramanna et al. reported that 2 of 19 (15%) patients treated after total or near-total thyroidectomy for differentiated thyroid carcinoma with 1110 MBq had successful residual thyroid ablation, while 3 of 12 (25%) additional patients were ablated after a second, low dose of radioiodine (*15*). These ablation rates were observed with a 187 MBq (5 mCi) to 394 MBq (10 mCi) diagnostic ^{131}I scan. However, the choice of ablation dose, between 1110 MBq and 3700 MBq (100 mCi), was not randomized in this study. In addition, no data was given in the Ramanna's series regarding residual thyroid area, total body area and associated goiter. Consequently, it is difficult to compare our results to those of Ramanna et al. Arad et al. reported that it was possible to achieve thyroid ablation with multiple 1110-MBq doses as frequently (75%) as with a single dose (80%) with a lower total radioiodine dose ((3108 versus 5254 MBq) (84 versus 142 mCi)) (*17*). However, multiple radioiodine treatments may be more inconvenient and time-consuming because episodes of hypothyroidism are more numerous. In our study, 6 of 50 patients and 10 of 32 refused to have a second and third period of hypothyroidism, respectively. Multiple doses of radioiodine, according to Arad's series, do not seem to induce a radio-resistance since thyroid ablation was achieved with multiple low doses as frequently as with one single high dose. However, radio-resistant patients are regularly noticed. For instance, Johansen et al. (*13*) reported that after two and three doses of 1073 MBq (30 mCi) or 3700 MBq (100 mCi), thyroid ablation was achieved in 33% (3/9) and 44% (4/9), respectively. After the first dose, the success rate was 81% (21/26) and 84% (14/17), respectively.

Variations in radioactive doses have been reported previously to be associated to variations in ablation rate success. Maxon et al. have shown that an initial radioiodine treatment resulting in radiation doses of at least 30,000 cGy (rad) to thyroid remnants was associated with a significant increase in the rate of response to therapy (*19*). In contrast, Snyder et al. reported that effectiveness of 1110-MBq doses did not correlate with ^{131}I uptake (as in our study), surgeon's estimate of remnant size and ^{131}I delivered dose to the remnants (*11*). In order to explain the absence of relationship between ^{131}I uptake and ablation results, Snyder et al. advocate that errors in measuring thyroid uptake less than 5% can be as much as 10%–100% (*11*). In addition, it is not surprising that remnant size estimated by the surgeon did not correlate with the radioactive ablation results since total thyroidectomy rarely results (≤5%) in absence of iodine-avid tissue on diagnostic ^{131}I scan (*20*). In fact, the surgeon's estimate seems particularly inaccurate for small size remnants (*20*).

Highly variable rates in response to radioiodine treatment may be related to other factors. For instance, the doses of ^{131}I used for total body scan may range from 7.4 to 185 MBq (200 μCi to 5 mCi), with most reports using 37–74 MBq (1–2 mCi). This difference in ^{131}I doses may result in differences in the sensitivity of residual-iodine avid tissue detection. Waxman et al. reported a 400% increase in sensitivity with a 370-MBq (10 mCi) dose to a 74-MBq (2 mCi) dose (*21*). In our study, we used a 185-MBq (5 mCi) scan. In the medical literature, the higher ablation rates after radioiodine treatment were observed with a 37–74 MBq (1–2 mCi) diagnostic scan (*6,8–12,14,17,18*) and the lower ablation rates after a dose scan of 185 MBq (5 mCi) or greater (*7,13,15*). Variable responses to radioiodine treatment can also be explained by the fact that the thyroid may be stunned after a high dose of ^{131}I (*22*). Pretherapy scanning with a high dose of ^{131}I may suppress the thyroid and prevent uptake of a subsequential therapy dose of ^{131}I. However, this possible suppression of ^{131}I uptake does not explain the variable responses to radioiodine treatment observed in our patients since the time between scanning and treatment was the same for all patients. According to our data, it seems that more remnant tissue was left by the surgeon, making it difficult to have successful total thyroid ablation after 1110 MBq. Thus, the area of residual thyroid tissue assessed by planimetry was a predictive factor of ablation success rate, even though this technique does not assess the thickness of thyroid remnant. In fact, the trend to a decreased incidence of successful thyroid ablation rate in patients with associated goiter may be related to a greater thickness of the remnant in these patients or to heterogeneous distribution of radioiodine in abnormal thyroid tissue.

Our data also suggest that 1110 MBq of ^{131}I were more effective in patients with small total body area. Increased sensitivity to radioiodine has been described in children with hyperthyroidism (*23*). In smaller patients, there is probably an increase in absolute iodine uptake because plasma ^{131}I concentration is likely greater since the same ^{131}I dose is diluted in a smaller plasma volume in those subjects (*24–25*). Consequently, the efficacy of ^{131}I is better in patients with smaller total body area since the relative radioiodine dose, to destroy thyroid remnant, is probably greater in these cases.

In conclusion, our data suggest that 1110 MBq of ^{131}I can achieve total ablation of residual thyroid tissue after mean-total thyroidectomy patients with lower total body area and smaller residual thyroid tissue without associated previous goiter. Patients who did not have characteristics may need higher doses of ^{131}I to achieve total thyroid ablation.

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REFERENCES

1. Pochin EE. Radioiodine therapy of thyroid cancer. *Semin Nucl Med* 1971; 1:503–515.
2. Tubiana M, Lacour J, Monnier JP, et al. External radiotherapy: radioiodine in the treatment of 359 thyroid cancers. *Br J Rad* 1975;48:894–907.
3. Krishnamurthy GT, Blahd WH. Radioiodine ^{131}I therapy in treatment of thyroid cancer. *Cancer* 1977;40:195–202.
4. Beierwaltes WH. The treatment of thyroid carcinoma with radioactive iodine. *Semin Nucl Med* 1978;8:79–94.
5. Blahd WH. Treatment of malignant thyroid disease. *Semin Nucl Med* 1979; 9:95–99.
6. McCowen KD, Adler RA, Ghaed N, Verdon T, Hofeldt FD. Low dose radioiodine thyroid ablation in postsurgical patients with thyroid cancer. *Am J Med* 1976;61:52–58.
7. Kuni CC, Klingensmith WC. Failure of low doses to ablate residual thyroid tissue following surgery for thyroid cancer. *Radiology* 1980;137:773–774.
8. Siddiqui AR, Edmonson J, Wellman HH, et al. Feasibility of low doses of ^{131}I for thyroid ablation in postsurgical patients with thyroid carcinoma. *Clin Nucl Med* 1981;6:158–161.
9. Degroot LJ, Reilly M. Comparison of 30- and 50-mCi doses of iodine-131 for thyroid ablation. *Ann Intern Med* 1982;96:51–53.
10. Ramacciotti C, Pretorius HT, Line BR, Goldman JM, Robbins J. Ablation of non-malignant thyroid remnants with low doses of radioactive iodine: concise communication. *J Nucl Med* 1982;23:483–489.
11. Snyder J, Gorman C, Scanlon P. Thyroid remnant ablation: questionable pursuit of an ill-defined goal. *J Nucl Med* 1983;24:659–665.
12. Creutzig H. High- or low-dose radioiodine ablation of thyroid remnants. *Eur J Nucl Med* 1987;12:500–502.
13. Johansen K, Woodhouse NJY, Odugbesan O. Comparison of 1073 MBq and 3700 MBq iodine-131 in postoperative ablation of residual thyroid tissue in patients with differentiated thyroid cancer. *J Nucl Med* 1991;32:252–254.
14. Maxon HR, Thomas SR, Hertzberg VS, et al. Relation between effective radiation dose and outcome of radioiodine therapy for thyroid cancer. *N Engl J Med* 1983;309:937–941.
15. Ramanna L, Waxman AD, Brachman MB, Tanasescu DE, Sensel N, Braunstein GD. Evaluation of low-dose radioiodine ablation therapy in postsurgical thyroid cancer patients. *J Nucl Med* 1985;10:791–795.
16. Leung SF, Law MWM, Ho SNW. Efficacy of low-dose iodine-131 ablation of postoperative thyroid remnants: a study of 69 cases. *Br J Radiol* 1992; 65:905–909.
17. Smedal ML, Saltzman FA, Meissner WA. The value of 3 mv roentgen-ray therapy in differentiated thyroid carcinoma. *Am J Roentgenol* 1967;99:352–364.
18. Arad E, Flannery K, Wilson GA, O'Mara RE. Fractionated doses of radioiodine for ablation of post surgical thyroid tissue remnants. *Clin Nucl Med* 1990;15:676–677.
19. Maxon HR, Englaro EE, Thomas SR, et al. Radioiodine-131 therapy for well-differentiated thyroid cancer. A quantitative radiation dosimetric approach: outcome and validation in 85 patients. *J Nucl Med* 1992;33:1132–1136.
20. Fratkin MJ, Newsome HH, Sharpe AR, Tatum JL. Cervical distribution of iodine-131 following total thyroidectomy for thyroid cancer. *Arch Surg* 1983;118:864–867.
21. Waxman A, Ramanna L, Chapman N, et al. The significance of ^{131}I dose in patients with thyroid cancer: determination of ablation. *J Nucl Med* 1981; 22:861–865.
22. Park HM. Stunned thyroid after high dose ^{131}I imaging. *Clin Nucl Med* 1992;17:501–502.
23. Werner SC, Hamilton H, Nemeth MR. Therapeutic effects from repeated diagnostic doses of ^{131}I in adult and juvenile hyperthyroidism. *J Clin Endo Metab* 1952;12:1349–1355.
24. Freedberg AS, Kurland GS, Blumgart HL. The pathologic effects of ^{131}I on the normal thyroid gland of man. *J Clin Endocrinol Metab* 1952;12:1315–1348.
25. Oliner L, Kohlenbiener RM, Fields T, Kinstodter RH. Thyroid function studies in children: normal values for thyroidal ^{131}I uptake and PB ^{131}I levels up to the age of 18. *J Clin Endocrinol Metab* 1957;17:61–75.