Effect of a Diagnostic Dose of 185 MBq ^{131}I on Postsurgical Thyroid Remnants

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Stunning of thyroid remnants after diagnostic scanning with ^{131}I may limit ^{131}I therapy. The follow-up scans and serum thyroglobulin levels of such patients have been studied. **Methods:** Three-hundred seventy-eight patients who underwent thyroidectomy for differentiated thyroid carcinoma were studied. Diagnostic scans were obtained with 185 MBq ^{131}I; 7.2 wk afterward, the patients received 489 ablative treatments with 4 GBq ^{131}I. A total of 1575 scans were obtained (pre- and posttreatment scans and 615 follow-up scans). The evolution of serum thyroglobulin levels was determined. **Results:** In all patients, the thyroid-stimulating hormone level was more than 30 µIU/mL. Posttherapy scans showed less uptake than did diagnostic scans or even showed negative findings in 99 patients (21%). In these patients, the mean time between diagnostic scanning and therapy was 7.9 wk. In 61 of these 99 patients (61.6%), follow-up scans have shown negative findings, serum thyroglobulin was less than 3 ng/mL, and antithyroglobulin antibodies were not present. Twenty-three patients (23.2%) have not undergone follow-up scanning yet. In 8 patients (8.1%), follow-up scans showed negative findings but serum thyroglobulin was more than 3 ng/mL. In 7 patients (7.1%), follow-up scans showed less uptake than posttherapy scans, but the findings were not yet negative and thyroglobulin was less than 3 ng/mL. **Conclusion:** Our data suggest that a stunning effect does not exist for doses of 185 MBq ^{131}I for diagnostic scans. However, a therapeutic effect may exist.

Key Words: stunning effect; diagnostic dose; ^{131}I treatment; differentiated thyroid carcinoma

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The treatment of differentiated thyroid carcinoma with total or near-total thyroidectomy is well accepted. Even after total thyroidectomy, thyroid remnants are usually present (*1*). Diagnostic scans are used to determine the appropriate therapeutic dose (*2*,*3*).

Several studies concerning the best tracer and the optimal dose of ^{131}I for diagnostic scans have been published (*4*–*7*). Different administered activities yield differences in diagnostic information; with higher activities, more lesions and more advanced stages of disease can be shown (*4*,*5*,*8*,*9*). However, a subject of debate is whether a high imaging dose of ^{131}I can decrease the uptake of a subsequent ablative radioiodine dose by normal thyroid remnants and thereby reduce therapeutic efficacy (*10*–*12*). This effect has been called thyroid stunning. A possibility is that those higher tracer doses are capable of ablating or affecting thyroid remnants, because these diagnostic activities are commonly used therapeutically for thyrotoxicosis.

Knowing the follow-up findings of patients in whom the stunning effect exists would help in ascertaining whether thyroid stunning is a real phenomenon. Therefore, the aim of this study was to determine whether lesions that show less uptake on posttherapy scans than on diagnostic scans stay the same or become more intense on subsequent follow-up scans.

MATERIALS AND METHODS

Subjects

We studied 378 patients (299 females, 79 males; age range, 18–83 y; mean age, 45.9 y) who underwent total or nearly total thyroidectomy for differentiated thyroid carcinoma. Three hundred one patients (79.6%) had papillary carcinoma, 76 (20.1%) had follicular carcinoma, and 1 (0.3%) had sclerosing mucoepidermoid carcinoma with eosinophilia. Seventy (23.3%) of the 301 patients with papillary carcinoma had local lymphatic invasion, and 5 (1.7%) had distant metastases (2 in bone and 3 in lung). Three (3.9%) of the 76 patients with follicular carcinoma had local lymphatic invasion, and 9 (11.8%) had distant metastases (7 in bone and 1 in lung).

^{131}I Treatment

All patients were referred to our department for radioiodine therapy. They received 489 treatments with ^{131}I in doses of 1850–7400 MBq (50–200 mCi). The mean dose was 3996 MBq (108 mCi). Two hundred ninety-three patients (77.5%) were treated 1 time with^{131}I; 69 (18.3%) were treated 2 times, 10 (2.6%) were treated 3 times, 2 (0.5%) were treated 4 times, and 4 (1.1%) were treated 5 times (Table 1). If radioiodine treatment was not administered immediately after the diagnostic scan and, hence, administration of thyroxine hormone was needed, this hormonal treatment was interrupted 3 wk before therapy.

Scans

We obtained 1575 whole-body scans. Pre- and posttreatment scans were obtained for all except 18 patients; those 18 underwent only posttreatment scanning. Moreover, 615 follow-up scans were obtained.

Diagnostic scanning was performed for at least 4 wk after surgery, and the scans were obtained 48 h after administration of 185 MBq ^{131}I. If thyroxine hormone replacement was need, it was

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TABLE 1
Number of Patients and Number of Treatments

Number of treatments (doses)	Number of patients	% of patients
1	293	77.5
2	69	18.3
3	10	2.6
4	2	0.5
5	4	1.1

discontinued 3 wk before the diagnostic scan. The mean time between the pretreatment scan and the ^{131}I therapy was 7.2 wk (range, 1–16 wk). Posttreatment scans were obtained a mean of 6.2 d after the ablative dose of ^{131}I. Like the pretherapy scans, follow-up scans were obtained 48 h after administration of 185 MBq ^{131}I. During the previous 3 wk, the patients did not receive thyroid hormone replacement.

All scans were performed with a computerized gamma camera (SP4; Elscint, Haifa, Israel) equipped with a high-energy parallel-hole collimator. Four images were obtained for 10 min each: head and neck, anterior thorax, posterior thorax, and pelvis. The scans were evaluated visually by 2 experienced physicians. Any scan with ^{131}I uptake out of physiologic locations was considered to show positive findings.

Thyroid-Stimulating Hormone, Thyroglobulin, and Antithyroglobulin Antibodies

A blood sample was obtained just before the ^{131}I administration for the diagnostic and follow-up scans to determine the levels of serum thyroid-stimulating hormone (TSH) (immunoradiometric assay) and thyroglobulin and to determine whether antithyroglobulin antibodies were present (radioimmunoassay).

Follow-Up

In our protocol, the first follow-up examination was 6 mo after ^{131}I therapy. The second was 1 y later, and the third, fourth, and fifth were also at 1-y intervals. Afterwards, we obtain a scan at 2-y intervals until 10 y.

At each follow-up examination, we scanned the patient, measured the levels of TSH thyroglobulin, and checked for antithyroglobulin antibodies. A study was classified as negative—that is to say, radioiodine treatment was successful—if the scan findings were negative, the serum thyroglobulin level was less than 3 ng/mL, and antithyroglobulin antibodies were absent. A study was classified as showing decreased uptake if it had fewer foci of pathologic uptake or if it had foci of equal number but less intensity.

RESULTS

In all patients, the TSH level was more than 30 μIU/mL. On diagnostic scans, 373 patients (98.7%) showed uptake of ^{131}I in the thyroid bed and only 5 patients (1.3%) had negative pretreatment scan findings. For 2 of these 5 patients (1 with papillary carcinoma and 1 with follicular carcinoma), activity could be seen in the thyroid bed on the posttherapy scan. For the other 3 patients (2 with papillary carcinoma and 1 with follicular carcinoma), the posttreatment and follow-up scans showed negative findings, serum thyroglobulin was less than 3 ng/mL, and antithyroglobulin antibodies were absent.

For 99 patients (21%), posttherapy scans showed less thyroidal uptake than did diagnostic scans. These patients were the so-called stunned patients. Seventy-seven (77.8%) had papillary carcinoma, and 22 (22.2%) had follicular carcinoma. The proportion of both types of differentiated thyroid carcinoma was similar between the whole group and this subgroup. We saw no variations in the uptake of distant metastases between pre- and posttreatment scanning. In this subgroup of patients, the mean therapeutic dose was 4033 MBq (109 mCi) ^{131}I, which did not significantly differ from the dose of the whole group (3996 MBq; 108 mCi).

The mean interval between the diagnostic scan and treatment was 7.9 wk, and the mean time between treatment and the posttreatment scan was 5.3 d. Neither of these intervals was significantly different from the whole group (7.2 wk and 6.2 d, respectively).

The follow-up status of these 99 patients is as follows (Table 2): 23 patients (23.2%) have not yet undergone follow-up scanning or are not being followed up. For 61 patients (61.6%), follow-up scan findings became or continued to be negative, the serum thyroglobulin level became or continued to be less than 3 ng/mL, and antithyroglobulin antibodies were absent. These patients had no evidence of disease. For eight patients (8.1%), although follow-up scan findings were negative, the level of serum thyroglobulin was greater than 3 ng/mL. Therefore, we could classify the study as negative. For 7 patients (7.1%), follow-up scans showed less uptake than did the posttherapy scan but were not yet negative, the serum thyroglobulin level was less than 3 ng/mL, and antithyroglobulin antibodies were absent.

None of the 99 patients who showed less uptake on the posttherapy scan than on the diagnostic scan showed increased uptake on follow-up scans. All these patients showed decreased uptake or no uptake on the follow-up scan 6 mo after treatment and on posterior follow-up scans. Table 3 shows the follow-up findings for the nonstunned patients.

DISCUSSION

The classic approach to the use of ^{131}I in detecting and treating differentiated thyroid cancer is changing. One of the issues currently under review is the optimal dose of ^{131}I for diagnostic scans.

Perhaps the first point to consider is whether the diagnostic scans are needed. Remnants are almost always present

TABLE 2
Evolution of the 99 Stunned Glands

Stunned glands	Follow-up scan	Thyroglobulin	Thyroglobulin antibodies
61 (61.6%)	Negative	<3 ng/mL	Negative
8 (8.1%)	Negative	>3 ng/mL	Negative
7 (7.1%)	Less intensity	<3 ng/mL	Negative
23 (23.2%)	Not yet		

TABLE 3
Evolution of the 390 Nonstunned Glands

Nonstunned glands	Follow-up scan	Thyroglobulin
144 (36.9%)	Negative	<3 ng/mL
130 (33.3%)	Positive	>3 ng/mL
14 (3.6%)	Negative	>3 ng/mL
102 (26.1%)	Not yet	

after total or near-total thyroidectomy and must be destroyed with a therapeutic dose of ^{131}I (*3,13*). Consequently, some authors have abandoned tracer scanning and treat their patients systematically with ^{131}I after surgery without scanning first (*1*). We also found that some thyroid tissue usually remains after total thyroidectomy; the pretreatment scan showed negative findings on only 5 occasions (1.3%). But studies have shown that with a high tracer dose, the information obtained is more diagnostic and the staging of disease is more advanced (*4,5,8,9*). Therefore, a low scanning dose (37–74 MBq) is less useful.

A high dose (185–370 MBq), although producing a beneficial scan, seems also to produce thyroid stunning (*1,7,14*). Thyroid stunning can be defined as reduced iodine uptake by normal thyroid remnants and tumor after administration of ^{131}I (*15*). Stunning may also change the tumor kinetics of radioiodine subsequently given for therapy by reducing its efficacy (*16*).

A solution to this problem may be to scan with ^{123}I, which appears to give the same diagnostic information as ^{131}I. ^{123}I is a pure gamma emitter that delivers a low radiation dose to the thyroid and does not decrease the uptake of a subsequent therapeutic dose of ^{131}I, but ^{123}I has some disadvantages. One is its high cost. Moreover, a study (*17*) showed that ^{123}I is less sensitive and less accurate than ^{131}I. Therefore, routine scans with large doses (185–370 MBq) would be too expensive (*1*).

Another disadvantage is that ^{123}I has a short half-life (13 h). Whole-body imaging requires an interval of at least several hours for the thyroid metastases to take up iodine, so ^{123}I is not ideal for whole-body imaging. ^{123}I presents another drawback. In follow-up of patients who have undergone radioablation, accuracy is less with ^{123}I than with ^{131}I (*17*). Consequently, diagnostic scans would be useful with ^{131}I and with large doses, with the drawback of the supposed stunning effect.

The results concerning the stunning effect seem to differ according to the elapsed time between the diagnostic scan and therapy (Table 4). Park et al. (*12*) found stunning within days of a diagnostic scan. O'Mara et al. (*18*) showed no stunning effect from a 185-MBq ^{131}I diagnostic dose on posttreatment scans when the therapy was given shortly after the diagnostic dose. Muratet et al. (*19*) found impairment of treatment efficacy after a 111-MBq diagnostic dose of ^{131}I in comparison with a 37-MBq scanning dose. In their study, the ablative therapy was given 9 d after the diagnostic scan. The results are contradictory. Leger et al. (*1*) found that 185 MBq ^{131}I can impair the subsequent uptake of a therapeutic dose. In that study, the delay between the diagnostic dose and the therapeutic dose varied between 15 and 84 d. In our study, this delay has varied between 1 and 16 wk. For that interval, we have seen so-called stunning in 21% of patients, although it is questionable whether the decreased uptake is, in fact, a stunning effect or a decrease of the tissue remnant. Knowing the evolution of these patients—through both scans and serum thyroglobulin levels—can help us determine whether thyroid stunning is a real phenomenon. In light of our results, the stunning effect is not real, because in no patient did the ''stunned'' lesion become more intense on the follow-up scans or even show the same intensity. All lesions showed less uptake on follow-up scans than on the posttherapy scans or disappeared (Table 2). This finding contrasts with the nonstunned group. As shown in Table 3, only 36.9% of patients in the nonstunned group showed negative findings on the follow-up scans. That the effect is, then, therapeutic is not surprising because the large doses (185–370 MBq) used for diagnostic scans for thyroid carcinoma after thyroidectomy, which leaves only a small mass of thyroid tissue or tumor volume, are usually administered therapeutically for thyrotoxicosis. Although the percentage of the dose taken up is much lower than in thyrotoxicosis, the volume of tissue that receives the dose is also much

TABLE 4
Literature Review

Study	No. of patients	^{131}I dose (scan)	Time from scan to therapy	^{131}I dose (therapy)	% Stunned	Evaluation
Park (*7*)	26	111 MBq	Few hours to days	5550 MBq (average)	40	Visual
		185 MBq			67	
		370 MBq			89	
O'Mara (*18*)	110	185 MBq	3 days	5180 MBq (average)	0	Visual
Muratet (*19*)	102	37 MBq	9 days	3700 MBq	76*	Visual
	127	111 MBq			50*	
Leger (*1*)	17	185 MBq	14–24 days	3700 MBq	29	Visual

*Successful ablative treatment.

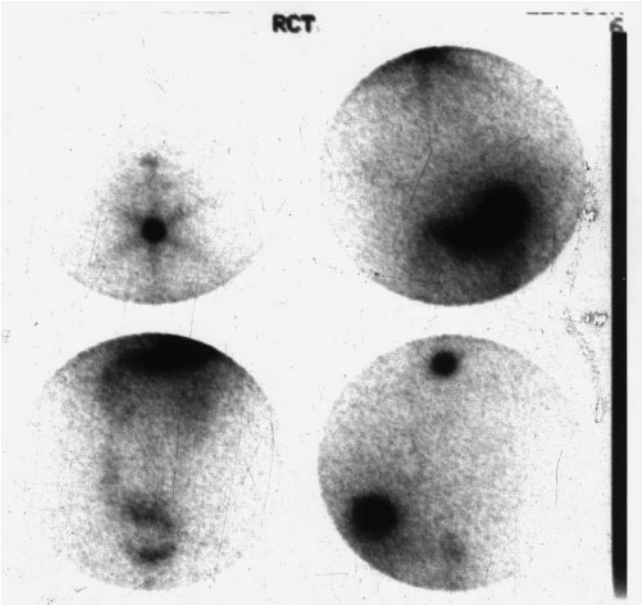

FIGURE 1. Diagnostic scan (185 MBq [5 mCi]) of patient with papillary carcinoma 5 wk after thyroidectomy. TSH level was greater than 30 μIU/mL.

smaller. Therefore, these activities may affect or even ablate such small remnants (Figs. 1–3).

We cannot draw any conclusion about the behavior of distant metastases because we have only 14 patients with distant metastases, for which uptake on the posttreatment whole-body scans has not varied from that on the diagnostic scans. A study of distant metastases found that they are less sensitive to the stunning effect (*12*), but further studies of distant metastases are needed.

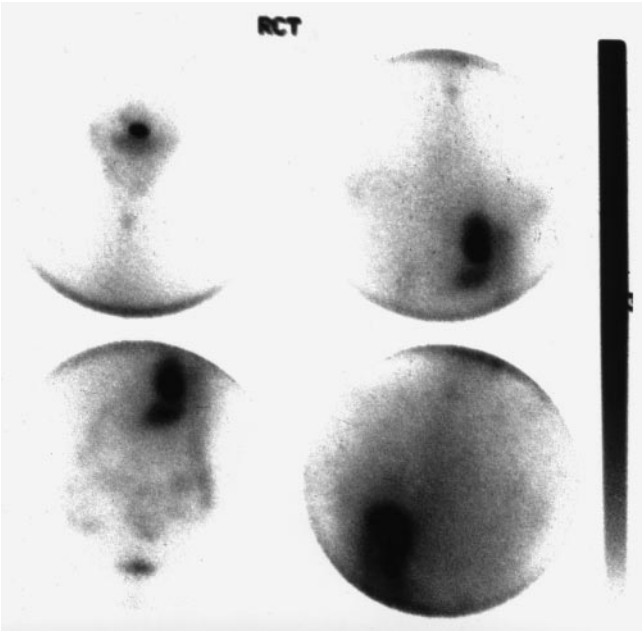

FIGURE 2. Posttherapy scan of patient (same as in Figure 1) 6 d after therapeutic dose (3700 MBq [100 mCi]). TSH level was greater than 30 μIU/mL.

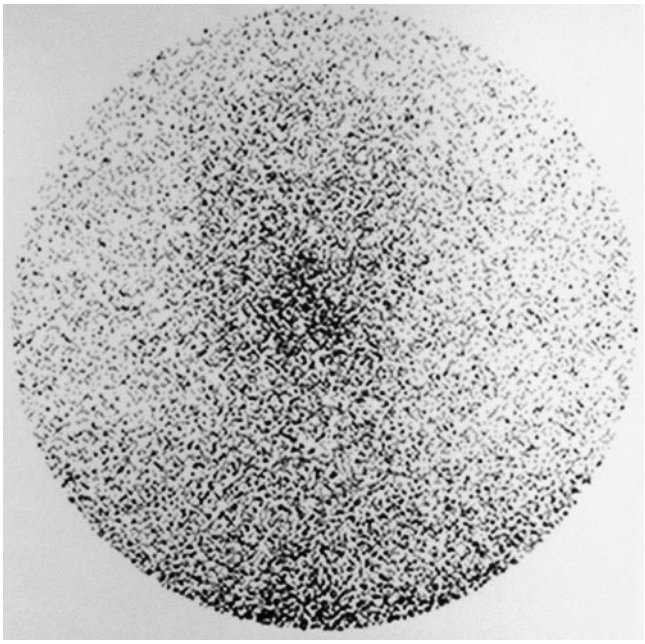

FIGURE 3. Follow-up scan (185 MBq [5 mCi]) of patient (same as in Figures 1 and 2) 6 mo after ablative dose (3700 MBq [100 mCi]), without evidence of disease. TSH was greater than 30 μIU/mL and thyroglobulin was less than 3 ng/mL.

CONCLUSION

No stunning effect was observed when doses of 185 MBq ^{131}I were used to stage differentiated thyroid carcinoma on diagnostic scans. The decreased uptake in thyroid remnants seen in 21% of our patients corresponded to a therapeutic effect through which the diagnostic dose was sufficient for total or partial ablation.

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