Absence of Thyroid Stunning After Diagnostic Whole-Body Scanning with 185 MBq ^{131}I

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There has been recent controversy regarding the optimal protocol for imaging and ablation of post-thyroidectomy patients. Several authors have suggested that a scanning dose of 185–370 MBq (5–10 mCi) ^{131}I may be capable of producing a stunning effect on thyroid tissue that may interfere with the uptake and efficacy of the subsequent ablation dose of radioiodine. The purpose of this study was to determine whether a 185-MBq (5 mCi) diagnostic dose of ^{131}I produces a visually apparent stunning effect 72 h before ^{131}I ablation therapy. **Methods:** One hundred twenty-two consecutive post-thyroidectomy patients for differentiated thyroid carcinoma received a 185-MBq (5 mCi) diagnostic dose of ^{131}I followed by a whole-body diagnostic scan at 72 h. On the same day the diagnostic scan was completed, the patient was admitted to the hospital and received an ^{131}I ablation therapy dose of 5550 MBq (150 mCi) in most cases. A postablation, whole-body scan was obtained at 72 h and compared with the previous diagnostic scan for any visual evidence of stunning. **Results:** No cases of visually apparent thyroid stunning were observed on any of the postablation scans with regard to the number of ^{131}I foci identified or the relative intensity of ^{131}I uptake seen. **Conclusion:** Diagnostic whole-body scanning can be performed effectively with a 185-MBq (5 mCi) dose of ^{131}I 72 h before radioiodine ablation without concern for thyroid stunning.

Key Words: thyroid stunning; radioiodine ablation; ^{131}I diagnostic imaging

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The incidence of thyroid carcinoma is estimated at approximately 40 cases per million people per year (*1*). Approximately 10,000 patients are treated annually for thyroid carcinoma, accounting for 0.2% of all cancer deaths (*2*). Thyroid carcinoma is generally classified by histologic criteria into papillary (70%–80%), follicular (15%), medullary (5%), and undifferentiated (5%) types. The incidence of differentiated thyroid carcinoma is uncommon in children and increases with advancing age. Papillary carcinoma has a peak incidence in the third and fourth decades, whereas follicular carcinoma is most common in the fifth decade of life. Thyroid carcinoma also has a higher incidence in women than in men with a 2:1 ratio (*3*).

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The cornerstone of management of differentiated thyroid carcinoma has been near-total thyroidectomy followed by radioiodine scanning and ablation as indicated. Most protocols use a scanning dose of 74–185 MBq (2–5 mCi) ^{131}I followed 2–7 d later by a whole-body diagnostic scan for evaluation of residual thyroid tissue and any functioning thyroid metastases. After the need for radioiodine ablation is confirmed by the diagnostic scan, the patient receives an ablative dose of ^{131}I ranging from 1850 to 7400 MBq (50–200 mCi) depending on various factors, such as tumor size, histologic grade, presence of lymph node involvement, extrathyroid extension, and distant metastases.

Several authors have reported that a diagnostic dose of ^{131}I radioiodine may produce a stunning effect on residual thyroid tissue and functioning metastases (*4–10*). The concept of stunning is generally defined as a diagnostic dose of ^{131}I that inhibits the uptake of the subsequent therapy dose of radioiodine by remnant thyroid tissue or functioning metastases. By inhibiting the uptake of the subsequent ablative radioiodine dose, the diagnostic dose could potentially impair the diagnostic and therapeutic efficacy of the ablation dose. Park et al. (*5*) described a visible stunning effect using various ^{131}I scanning doses ranging from 111 to 370 MBq (3–10 mCi). They noted that stunning was not observed with ^{123}I, making it the preferable radiotracer for diagnostic scanning after thyroidectomy despite its greater cost.

The purpose of this study was to determine whether a 185-MBq (5 mCi) ^{131}I scanning dose used at our institution produces a stunning effect that could impair the uptake of the subsequent ablation dose administered 72 h later.

MATERIALS AND METHODS

This retrospective study consisted of 122 consecutive patients with well-differentiated thyroid carcinoma who were referred to our department between January 1990 and December 1996 for radioiodine ablation of thyroid remnant or metastases. The carcinoma was initially diagnosed in all patients by fine-needle aspiration before surgery, and all patients were referred to the nuclear medicine department by the primary care physician or surgeon approximately 6 wk after undergoing surgery. A near-total thyroidectomy had been performed in 107 patients, whereas 15 had undergone a lobectomy. All surgically resected thyroid tissue was examined by the surgical pathology department at our institution for definitive pathologic classification, and the pathology reports for all resected specimens were available for review. All patients received an oral dose of 185 MBq (5 mCi) ^{131}I followed by a 72-h diagnostic scan to confirm the presence of thyroid remnant or functioning metastases. After confirming the presence of functioning thyroid tissue and an adequate hypothyroid state using clinical and laboratory criteria (thyroid-stimulating hormone > 30 μU/mL), the patients were admitted to Strong Memorial Hospital for ^{131}I ablation therapy on the same day. Radioiodine ablation doses ranged from 1110 to 7400 MBq (30–200 mCi), with 5550 MBq (150 mCi) used in 104 of the 122 total cases. All postablation scans were obtained at 72 h.

The patients ranged in age from 17 to 80 y (mean age, 41 y). There were 92 women (mean age, 37 y) and 30 men (mean age, 53 y). Histologic classification consisted of 96 papillary (79%), 5 follicular (4%), 16 mixed papillary-follicular (13%), and 5 Hürthle cell carcinomas (4%).

Radioiodine scans were obtained using 1 of 3 large field-of-view gamma cameras equipped with a high-energy, parallel-hole collimator. Cameras used were an ADAC Argus (ADAC Laboratories, Milpitas, CA), a Trionix BIAD (Trionix Research Laboratory, Inc., Twinsburg, OH), and a Technicare 438 (Technicare, Inc., Solon, OH). All diagnostic and postablation scans consisted of an anterior and posterior whole-body scan with anterior and posterior spot views of the neck. An additional anterior spot view of the neck was obtained using radioactive anatomic markers on the chin and suprasternal notch. Additional spot views were obtained at the discretion of the reviewing physician. Whole-body scans were acquired in a 512 × 1024 matrix, and spot images were obtained in a 128 × 128 matrix. The camera linear tracking speed was 10–12 cm/min for diagnostic whole-body scans and 20 cm/min for postablation whole-body scans.

Two or more experienced nuclear medicine physicians in the department interpreted all scans. Postablation scans were compared visually with each patient's diagnostic scan obtained 3 d earlier. The reports for the diagnostic and ablation scans of each patient were also evaluated for any discrepancy. Stunning was considered to be present on any postablation scan that revealed either fewer foci of radioiodine uptake or relatively less prominent uptake compared with the corresponding diagnostic scan from 3 d earlier. Radioiodine uptake within the thyroid bed or regional nodes was visually compared with soft-tissue background activity in the upper chest. Our observations were evaluated statistically using Fisher's exact test by the University of Rochester biostatistics department.

RESULTS

Of the 122 patients reviewed, all had some residual thyroid tissue in the neck after surgery. In addition, 17 patients had functioning metastases involving 20 different sites, including the cervical lymph nodes (n = 11), lung (n = 5), and bone (n = 4). Three patients had 2 or more metastatic sites. Of the 17 patients who were initially shown to have functioning metastases, 14 were eventually rendered free of disease on the basis of follow-up scans, clinical follow-up, and serum thyroglobulin criteria. All patients with metastases limited to the regional cervical nodes were also eventually rendered free of disease. Three patients had persistent metastatic disease despite multiple ablations, including 2 patients with multiple bone metastases and 1 patient with diffuse lung metastases (Table 1). After careful visual review of all diagnostic scans with the corresponding ablation scans, no thyroid stunning was observed that involved either remnant thyroid tissue or functioning metastases (Figs. 1 and 2).

TABLE 1
Ablation Success Rate by Metastatic Site

Metastatic site	Rendered disease free/total
Thyroid remnant only (no metastases)	103/105 (98)
Cervical lymph node metastases	11/11 (100)
Lung metastases	4/5 (80)
Bone metastases	2/4 (50)

Values in parentheses are percentages.

Of the 104 patients treated with 5550 MBq (150 mCi) ^{131}I, 82 patients (79%) had successful ablation after a single dose and 22 patients required additional radioiodine therapy. The success rate of radioiodine ablation appeared to be related to the type of surgery performed and the amount of postsurgical remnant thyroid tissue. Of the 92 patients who underwent a near-total thyroidectomy followed by a 5550-MBq (150mCi) ablation dose, 77 patients (84%) had successful ablation after a single radioiodine treatment. Of the 12 patients who underwent thyroid lobectomy, only 5 patients (42%) had successful ablation after a single 5550-MBq (150 mCi) therapy dose (Table 2). The difference in single-dose ablation success rate between patients who underwent a near-total thyroidectomy versus a lobectomy was statistically significant ($P = 0.003$).

A review of the patients' clinical charts revealed no major complications resulting from the radioiodine ablation, such as thyroid storm, severe radiation thyroiditis, sialadenitis, or emesis after treatment. We believe that sialadenitis was averted by the aggressive encouragement of oral fluids and hard candy or gum to maintain good salivary gland function. All side effects, consisting of mild transient nausea or mild swelling of the salivary glands or neck, were considered minor. All symptoms resolved within 1 or 2 d without residual sequelae. Patients were started on supplemental thyroid hormone approximately 1 wk after receiving the ablation dose. All patients returned to the Strong Memorial Hospital nuclear medicine department 6 wk after their therapy for follow-up. All subsequent clinical follow-up was performed by the nuclear medicine department or the referring endocrinologist.

DISCUSSION

Thyroid stunning has been described in patients who received diagnostic doses of ^{131}I (*5,6*). A study by Park et al. (*5*) consisted of 40 subjects, 26 of whom received a diagnostic dose of ^{131}I and a comparison group of 14 scanned using ^{123}I. Thyroid stunning was observed in 2 of 5 patients after a 111-MBq (3 mCi) dose of ^{131}I, in 2 of 3

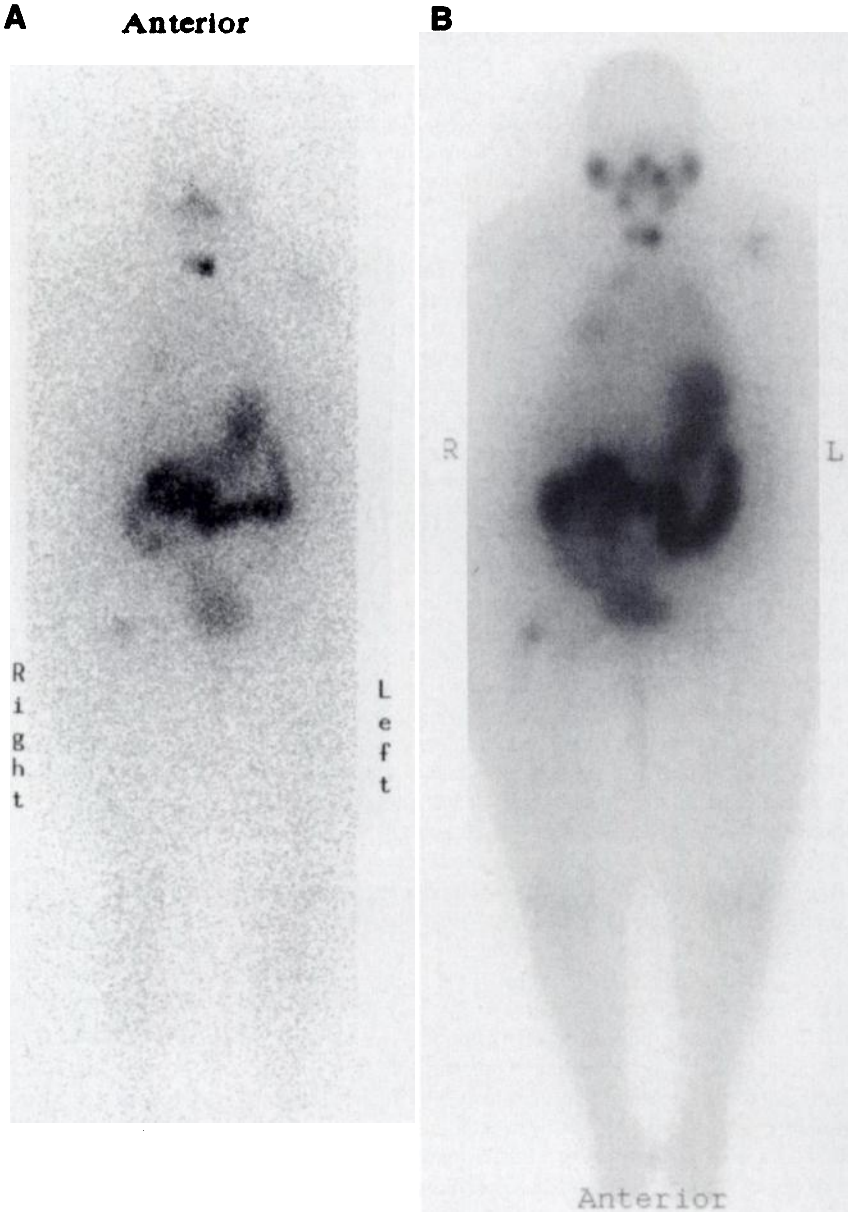

FIGURE 1. Anterior diagnostic whole-body scan (A) and postablation scan (B) of 62-y-old woman with follicular thyroid carcinoma show uptake in thyroid remnant and functioning metastatic disease involving lungs and right hip. Postablation scan at 72 h shows no evidence of thyroid stunning.

patients after 185 MBq (5 mCi), and in 16 of 18 patients after a 370-MBq (10 mCi) diagnostic dose. No stunning effect was evident in the comparison group that received ^{123}I, and ^{123}I was therefore concluded to be the preferable agent for diagnostic whole-body scanning. With our own protocol using a 185-MBq (5 mCi) ^{131}I scanning dose, we were unable to duplicate the thyroid stunning described by these authors.

Numerous differences in imaging protocol may explain the discordant observations regarding thyroid stunning between this study and the findings of others. Most cases of thyroid stunning described by Park et al. (*5*) and Park (*6*) were observed after a 370-MBq (10 mCi) ^{131}I scanning dose (16/18 patients), whereas this study used only a 185-MBq (5 mCi) scanning dose. It is possible that a 370-MBq (10 mCi) dose of ^{131}I will produce an observable stunning effect on thyroid tissue that is not apparent with a 185-MBq (5 mCi) dose. A significant difference between our protocol and that used by Park et al. (*5*) is the time interval between completion of the diagnostic scan and subsequent administration of the ablation dose. This time interval was more variable in the Park et al. study, ranging from several hours to several days, whereas all of our patients received the ablation dose within several hours of completing the diagnostic scan. This protocol difference is probably the most significant factor because the radiation effect to the iodine-concentrating tissue from the scanning dose is related to the effective half-time that the ^{131}I remains within the radioio-

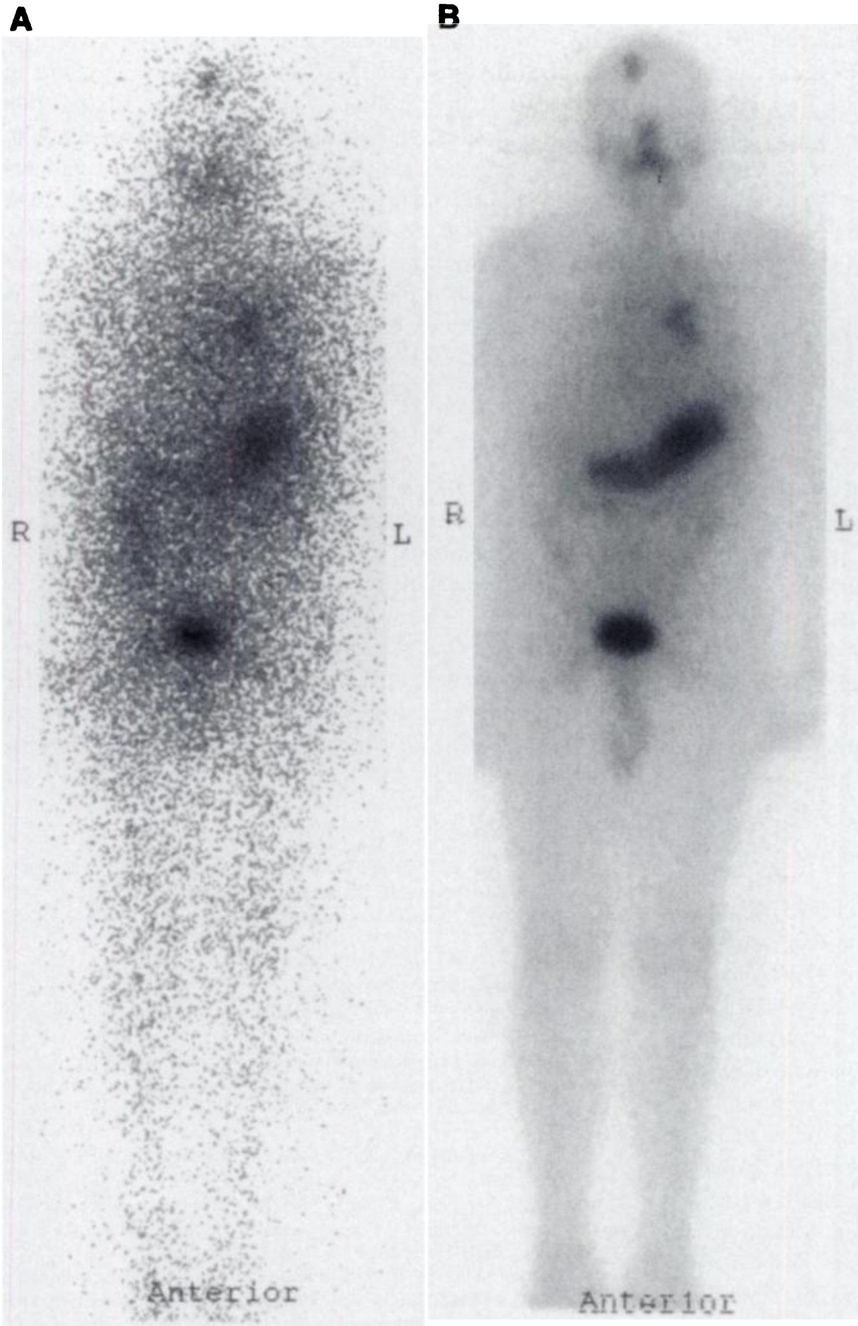

FIGURE 2. Anterior diagnostic scan (A) and postablation scan (B) of patient undergoing third ablation for persistent disease show functioning metastasis in right parietal bone, left mediastinum, and left lung. Comparison of diagnostic and postablation scans shows no stunning of functioning metastatic foci.

TABLE 2
Single-Dose Ablation Success Rate After 5550 MBq (150 mCi) ^{131}I by Type of Preablation Surgery

Type of surgery	Successful ablation/total*
Near-total thyroidectomy	77/92 (84)
Thyroid lobectomy	5/12 (42)

*Difference in single-dose ablation success rate between patients who underwent near-total thyroidectomy versus lobectomy was statistically significant ($P = 0.003$).

Values in parentheses are percentages.

dine uptake sites (*11*). Therefore, a longer time interval between the diagnostic scan and the ablation dose would allow the diagnostic ^{131}I dose a longer period of time to produce a stunning effect on the iodine-concentrating tissue. In fact, many authors who have described thyroid stunning (*7–9*) administered the ablation dose after a longer time interval after the diagnostic scan compared with the protocol used at our institution. For example, Muratet et al. (*7*) observed reduced therapeutic efficacy of ^{131}I ablation after a 111-MBq (3 mCi) ^{131}I scanning dose compared with a comparison group scanned with a 37-MBq (1 mCi) dose. However, these authors administered the ablation dose 9 d after the diagnostic scan. Visual thyroid stunning was also described by Kao et al. (*9*), who administered the ^{131}I ablation dose between 1 wk and 1 mo after the diagnostic scan was completed.

Another protocol difference between this study and that of Park et al. (*5*) is that postablation scans were obtained at 24–48 h after the ablation dose for patients in the latter study, whereas ablation scans at this institution were always obtained at 72 h. This shorter time interval between the ablation dose and scan in the study of Park et al. allows less time for soft-tissue clearance of radioiodine, resulting in relatively higher soft-tissue background, which could make foci of ^{131}I uptake appear less prominent and more difficult to detect (*12*). This was also observed by Pacini et al. (*13*), who obtained diagnostic scans on 17 patients at 48–72 h after a 185-MBq (5 mCi) ^{131}I dose and compared the diagnostic sensitivity with ablation scans obtained 5–10 d after an 1850- to 5550-MBq (50–150 mCi) therapy dose. They observed much higher sensitivity on the ablation scan, which revealed functioning metastases in 16 of 17 patients that were not detected on the diagnostic scan despite positive serum thyroglobulin assays. Furthermore, they observed no evidence of thyroid stunning. An early study by Waxman et al. (*14*) also failed to observe thyroid stunning on ablation scans in a series of 21 patients despite obtaining 2 prior diagnostic scans using both 74-MBq (2 mCi) and 370-MBq (10 mCi) ^{131}I doses. In that study, the diagnostic sensitivity of the scans improved with increasing ^{131}I dose. These authors noted that an ablation scan with 1110–3700 MBq (30–100 mCi) detected foci of radioiodine that were not evident on the prior diagnostic scan using 370 MBq (10 mCi) ^{131}I. They further observed that initial diagnostic scans on the same group of patients using 74 MBq (2 mCi) ^{131}I were less sensitive compared with the comparable diagnostic scans using a 370-MBq (10 mCi) ^{131}I scanning dose.

Our overall ablation success rate after radioiodine therapy was 95%, which indicates adequate uptake of the ablation dose after a 185-MBq (5 mCi) ^{131}I scanning dose 3 d earlier. Of our patients who initially underwent a near-total thyroidectomy, the radioiodine ablation success rate was 84% after a single 5550-MBq (150 mCi) therapy dose. This finding is consistent with the findings of other authors, including Maxon et al. (*11*), who reported initial ablation success rates of 84% for in-patients and 79% for out-patients with a standardized dose of ^{131}I (30,000 cGy). In that study, which included 85 patients, sequential scans were obtained at 24, 48, and 72 h after the administration of 74 MBq (2 mCi) diagnostic ^{131}I. A single administration of ^{131}I resulted in successful ablation in 74% of patients with nodal metastases. The average ablation dose of ^{131}I administered in that study was 3211.6 ± 2297.7 MBq (86.8 ± 62.1 mCi).

Incomplete ablation after a single radioiodine treatment was observed most frequently in patients who initially underwent a thyroid lobectomy; the ablation success rate was only 42%. We observed a statistically significant difference in single-dose ablation success between postlobectomy patients and those who underwent a near-total thyroidectomy. This finding indicates that the amount of postsurgical residual thyroid tissue is a major determining factor in the success rate of ^{131}I ablation. A lower initial success rate of radioiodine ablation was also observed in patients who had functioning metastases compared with that of patients who were free of metastasis (82% versus 87%), although this difference was not statistically significant ($P = 0.70$). Patients with multiple sites of metastases, particularly involving bone, had the lowest ablation success rate. This finding is consistent with the observation of others that bone metastases tend to be more radioresistant than other sites (*15*).

CONCLUSION

Because of the constraints of our protocol, we cannot dispute the occurrence of thyroid stunning if the ^{131}I ablation dose is delayed several days or longer after completion of the diagnostic scan. However, we found no evidence of thyroid stunning when radioiodine ablation was performed on the same day after completion of the diagnostic scan. Therefore, we believe that a 185-MBq (5 mCi) dose of ^{131}I for whole-body scanning can provide excellent diagnostic accuracy and subsequent ablation success without concern for thyroid stunning.

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