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# Is Diagnostic Iodine-131 Scanning Useful after Total Thyroid Ablation for Differentiated Thyroid Cancer?

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**ABSTRACT**

A diagnostic iodine-131 ($^{131}$I) total body scan (TBS) is usually recommended 6 to 12 months after thyroid ablation for differentiated thyroid carcinoma. Its usefulness was evaluated in 256 consecutive patients treated and followed up at the Institut Gustave Roussy for papillary (n = 200), well differentiated (n = 27), or poorly differentiated (n = 29) follicular thyroid carcinomas.

All patients underwent a near-total or total thyroidectomy and $^{131}$I ablation with 3.7 GBq (100 mCi). No TBS was performed before $^{131}$I ablation. The TBS performed after the administration of $^{131}$I to destroy the thyroid remnants showed uptake (<2%) limited to the thyroid bed. A diagnostic $^{131}$I-TBS was obtained after withdrawal of $T_4$ treatment, with either 74 MBq (2 mCi; n = 82) or 185 MBq (5 mCi; n = 174), 6 to 12 months after initial treatment, with serum thyroglobulin (Tg) determination. No interference in the Tg assay was found in these 256 patients.

Uptake in the thyroid bed was not detected (total ablation) in 236 patients, was visible but too low to be measured in 19 patients, and attained 1% in only 1 patient. No uptake was found outside the thyroid bed. The serum Tg level, once thyroid hormone treatment had been withdrawn, was below 1 ng/mL in 210 patients, ranged from 1–10 ng/mL in 31 patients, and was above 10 ng/mL in 15 patients. A $^{131}$I-TBS performed with 3.7 GBq in nine patients with a Tg level above 10 ng/mL, showed foci of uptake outside the thyroid bed in three patients ; lung metastases were demonstrated by a CT scan in another patient, and palpable lymph node metastases were found in one patient.

In conclusion, a diagnostic $^{131}$I-TBS with 74–185 MBq performed 1 yr after thyroid ablation demonstrated no abnormal uptake; it did not correlate with results of Tg determination and only confirmed the completeness of thyroid ablation. The serum Tg level obtained after withdrawal of $T_4$ treatment permits the selection of patients with a Tg level exceeding 10 ng/mL, for scanning with 3.7 GBq (100 mCi). (*J Clin Endocrinol Metab* **85:** 175–178, 2000)

AFTER TOTAL OR near-total thyroidectomy, followed by iodine-131 ($^{131}$I) ablation of thyroid remnants, for differentiated thyroid cancer (DTC) (1–8), the follow-up protocol is: if no uptake is seen outside the thyroid bed on the total body scan (TBS) performed 4–7 days after the administration of $^{131}$I to destroy the thyroid remnants, $T_4$ treatment is initiated. Serum FT3, TSH, and thyroglobulin (Tg) are measured 3 months after initial treatment. Even in patients with no evidence of disease, including an undetectable serum Tg concentration, a diagnostic $^{131}$I-TBS with 74–185 MBq (2–5 mCi) and a serum Tg determination are obtained after withdrawal of $T_4$ treatment within 12 months after $^{131}$I treatment. If no uptake is then detected, subsequent follow-up is based on prognostic factors and on the serum Tg concentration (9).

However, the yield of routine control $^{131}$I-TBS with 74–185 MBq during the 1st yr of follow-up is assumed to be very low: total ablation is achieved in the majority of patients after near total or total thyroidectomy (4), and abnormal foci of uptake that were not depicted on the TBS performed after the administration of 3.7 GBq of $^{131}$I to destroy the thyroid remnants are rarely discovered.

Previous studies have shown that serum Tg measured after withdrawal of thyroid hormone treatment was detectable and often at a high level in most patients with foci of uptake outside the thyroid bed on diagnostic $^{131}$I-TBS (9–11). When the Tg level obtained after withdrawal of thyroid hormone treatment is above some arbitrary limit (*i.e.* 10 ng/mL in our institution), even in the absence of any other evidence of disease, 3.7 GBq (100 mCi) of $^{131}$I are administered with a TBS performed 4–7 days later; this will demonstrate foci of uptake outside the thyroid bed in 60–80% of patients (12–14).

The aims of the present study were to assess: 1) whether routine control $^{131}$I-TBS should be routinely performed within 1 yr after initial treatment; and 2) whether the serum Tg level measured after withdrawal of thyroid hormone treatment permits the selection of the small percentage of patients in whom a detectable Tg level suggests the persistence of neoplastic tissue. A total of 256 consecutive patients treated and followed up at the Institut Gustave-Roussy (Villejuif, France) were included in the present study.

## Patients and Methods

Between 1990 and 1997, 256 consecutive patients fulfilled the following criteria. First, a near-total or total thyroidectomy was performed in all, with lymph node dissection in 225 patients (9). Second, one month after surgery, during which no thyroid hormone treatment was given, 3.7 GBq (100 mCi) $^{131}$I were administered; the TSH level was above 30 $\mu$U/mL in all patients. No diagnostic $^{131}$I-TBS was performed before $^{131}$I administration, which was decided on the basis of prognostic factors such as an age above 45 yr, a poorly differentiated carcinoma, or a large extent of the disease. Patients were not placed on low iodine diet, but were asked to avoid iodine-containing drugs, and, in case of doubt, urinary iodine was measured. A TBS was performed 4 days after the administration of $^{131}$I and showed uptake confined to the thyroid bed, representing less than 2% of the administered activity; patients with

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uptake outside the thyroid bed were not included in the study because they required other therapeutic procedures, such as surgery or further $^{131}I$ treatments (8, 9). Third, $T_4$ treatment was then initiated with the aim of decreasing serum TSH to low levels (<0.1 $\mu$U/mL), without inducing clinical thyrotoxicosis. This was controlled 3 months later by measuring serum FT3 and TSH levels (15). Fourth, a control TBS was performed 6–12 months after initial treatment, depending on the preference of each patient. LT4 treatment was withdrawn, and LT3 was given for 3 weeks and then withdrawn for 2 weeks. Serum TSH was then measured and exceeded 30 $\mu$U/mL in all patients; 74 MBq $^{131}I$ (2 mCi) were administered in 82 patients, and 185 MBq (5 mCi) in 174 patients with high risk factors, and a TBS was performed 3 days later. A double-head gamma camera (DHD-SMV, Buc, France) equipped with high-energy collimators and thick crystals was used at a constant low speed, over 30 min. The least detectable uptake in small sources that was visible on TBS was 1 $\mu$Ci; the least detectable uptake that could be measured was 5 $\mu$Ci, representing 0.3% and 0.1% after the administration of 2 and 5 mCi, respectively. Finally, serum Tg levels were measured during thyroid hormone treatment 3 months after initial treatment and again after withdrawal of thyroid hormone treatment at the time of the control $^{131}I$-TBS. A commercial kit, with a sensitivity of 1 ng/mL was used (Dynotest Tg; Brahms, Berlin, Germany) (10). A recovery test was performed in all Tg assays and did not show interferences (recovery >80%) in the 256 patients under study. The eight patients with interferences in the Tg assay were not included in the study.

Complete remission was defined as a normal clinical examination, a negative control $^{131}I$-TBS (*i.e.* no uptake outside the thyroid bed), and an undetectable Tg level after withdrawal of thyroid hormone treatment.

When abnormalities were detected on clinical examination, on the diagnostic $^{131}I$-TBS or when the Tg level after withdrawal of thyroid hormone treatment was above 10 ng/mL, patients underwent further diagnostic and/or therapeutic procedures, including the administration of 3.7 GBq (100 mCi) of $^{131}I$, conventional imaging modalities, and/or surgery.

## Results

### *Patients*

A total of 256 patients ranging in age from 13–75 yr (mean age, 45 yr) were included; there were 201 female and 55 male patients. Thyroid carcinomas were classified as papillary in 200 patients, well differentiated follicular carcinomas in 27 patients, and poorly differentiated follicular carcinomas in 29 patients (16). The pTNM classification of these tumors is reported in Table 1 (17). Patients were followed up for 6 months to 9 yr (median, 5 yr) after the control TBS. Seven patients were lost to follow-up after the first control TBS.

### *$^{131}I$-TBS*

The $^{131}I$-TBS performed 4 days after the administration of 3.7 GBq (100 mCi) $^{131}I$ showed uptake confined to the thyroid bed in all 256 patients. Uptake was below 0.5% of the administered activity in 140 patients, ranged from 0.5% to less than 1% in 49 patients and from 1–2% in 67 patients.

The control $^{131}I$-TBS performed 6–12 months later with 74–185 MBq (2–5 mCi) showed no uptake at all in 236 patients (92%); an uptake confined to the thyroid bed was found in the other 20 patients; it was low and not measurable in 19 patients, and was equal to 1% of the administered activity in only one patient. No uptake was found outside the thyroid bed.

**TABLE 1.** pTNM classification of the 256 patients with DTC (17)

| | N0 | N1 | Nx |
|---|---|---|---|
| $T_1$ | 30 | 19 | 6 |
| $T_2$ | 49 | 36 | 8 |
| $T_3$ | 12 | 3 | 5 |
| $T_4$ | 18 | 51 | 10 |
| Tx | 3 | 4 | 2 |

### *Serum Tg level*

The Tg level was measured 3 months after the initiation of $T_4$ treatment in 203 patients and was undetectable in 195 patients. It was detectable in eight patients, ranging from 2–10 ng/mL in six and exceeding 10 ng/mL in two.

The Tg level was measured in all patients, at the time of the administration of $^{131}I$ for the control TBS after withdrawal of thyroid hormone treatment: it was undetectable in 210 patients (82%), ranged from 1–5 ng/mL in 27 patients, 6–10 ng/mL in 4 patients, and was above 10 ng/mL in 15 patients (13–170 ng/mL) (Fig. 1).

There was no relationship between the Tg level and detectable uptake in the thyroid bed on the control TBS, since Tg was detectable in 25% of patients with visible uptake in the thyroid bed and in 17% of patients in the absence of such uptake, as shown in Table 2.

### *Additional procedures*

A $^{131}I$-TBS was performed with 3.7 GBq in 9 of the 15 patients with Tg levels above 10 ng/mL after thyroid hormone treatment had been withdrawn. The TBS performed 4 days later showed uptake in the neck corresponding to lymph node metastases in two patients and uptake in the chest corresponding to lung metastases in one patient. No uptake was found in the other six patients, among whom computed tomography scan demonstrated lung metastases in one patient.

Of the other six patients, one had palpable neck lymph nodes at the time of the diagnostic scan that proved to be metastases at surgery. Among the other five patients, three whose Tg level attained 27, 27, and 72 ng/mL, respectively, had another diagnostic $^{131}I$-TBS within a year. After withdrawal of thyroid hormone treatment, the Tg level became

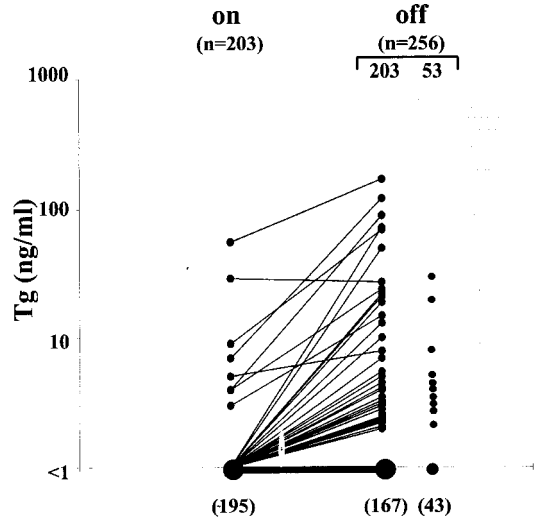


FIG. 1. Serum Tg level during $T_4$ treatment and after withdrawal of thyroid hormone treatment in 203 patients. In the other 53 patients (*right column*), Tg measurement was obtained only after withdrawal of thyroid hormone treatment.

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**TABLE 2.** Absence of relationship between the Tg level obtained after withdrawal of $T_4$ treatment and the presence of uptake in the thyroid bed on the control $^{131}$I-TBS; visible uptake in the thyroid bed was too low to be measured, except in one patient[a] in whom it represented about 1% of the administered activity. Demonstrated disease is presented according to the time of its discovery after initial treatment. This included lymph node metastases (in six cases), and lung metastases, shown either by thoracic uptake of $^{131}$I or by CT-scan (two cases[b]).

| Tg level (ng/mL) | Diagnostic $^{131}$I-TBS | | Demonstrated disease after initial treatment | |
|---|---|---|---|---|
| | No detectable uptake | Uptake in thyroid bed | <1 yr | >3 yr |
| <1 | 195 | 15 | | 2 |
| 1–10 | 29 | 1 + 1[a] | | 1 |
| >10 | 12 | 3 | 5[b] | |
| Total | 236 | 20 | 5 | 3 |

undetectable in one patient and was still detectable in the other two patients at 13 and 23 ng/mL, respectively; the other two patients, with Tg levels attaining 19 and 21 ng/mL after withdrawal of thyroid hormone treatment, are being followed up annually.

Disease was, therefore, demonstrated in 5 of the 15 patients (33%). After surgery for lymph node metastases, the serum Tg level during $T_4$ treatment became undetectable in two patients and ranged 2 ng/mL in one. The other 10 patients are followed up annually on $T_4$ treatment; they have no evidence of disease, and serum Tg is undetectable in this situation.

Among the 31 patients with a Tg level ranging from 1–10 ng/mL after withdrawal of thyroid hormone treatment, 29 had no evidence of disease, with a Tg level below 1 ng/mL during $T_4$ treatment. One patient was lost to follow-up after the first diagnostic scan. In one patient, the Tg level (which was at 1.5 ng/mL at the first $^{131}$I TBS), rose to 10 ng/mL during $T_4$ treatment 3 yr after initial treatment: $^{131}$I treatment was then administered, and the posttherapy TBS showed uptake in the neck outside the thyroid bed that proved to be lymph node metastases at surgery, after which the serum Tg level became undetectable during $T_4$ treatment.

Among the 210 patients with a Tg level below 1 ng/mL after withdrawal of thyroid hormone treatment, two had a palpable neck lymph node 3 and 4 yr after initial treatment, respectively. In one patient, the Tg level had attained 19 ng/mL during $T_4$ treatment at that time; the other patient had an undetectable Tg level during $T_4$ treatment and a detectable Tg level (3 ng/mL) after withdrawal of thyroid hormone treatment. $^{131}$I-TBS with 3.7 GBq showed foci of uptake in the neck in both patients that proved to be lymph node metastases at surgery; in both patients, the Tg became undetectable after surgery both during $T_4$ treatment and after its withdrawal.

The Tg level was measured during $T_4$ treatment in 249 patients at the end of the study, 6–118 months (mean, 60 months) after initial treatment and was undetectable in 242 patients (93%). It ranged from 1–10 ng/mL in five patients and was above 10 ng/mL in two patients who had demonstrated lung metastases.

## Discussion

This study concerned 256 consecutive patients with DTC who were initially treated by near-total or total thyroidectomy, followed by the administration of an ablative dose of 3.7 GBq (100 mCi) of $^{131}$I to destroy the thyroid remnants. If no uptake was found outside the thyroid bed on the $^{131}$I-TBS performed 4–7 days after the administration of $^{131}$I to destroy the thyroid remnants, a diagnostic $^{131}$I-TBS was obtained with 74–185 MBq (2–5 mCi) and serum Tg was measured after withdrawal of thyroid hormone treatment, 6–12 months after initial treatment (9).

Ablation was achieved in 92%, as shown by the absence of detectable uptake on the control diagnostic $^{131}$I-TBS. The other 8% had visible, but low, uptake in the thyroid bed that was not measurable, except in one patient in whom it attained 1%. This high ablation rate is related to the solid experience of the surgeon who performed the near-total or total thyroidectomy, resulting in a low (<2%) uptake in the thyroid bed on the initial TBS; it is in close agreement with previous reports that used activities based on dosimetric studies or of either 30 or 100 mCi $^{131}$I to ablate thyroid remnants (4). This suggests that similar results can be obtained after the administration of 1.1 GBq (30 mCi) for ablation. Furthermore, several authors (6, 7, 12–14) have shown that $^{131}$I-TBS performed with 3.7 GBq (100 mCi) or more is the most sensitive tool for localizing neoplastic foci with $^{131}$I uptake, demonstrating foci of uptake that were not shown by a $^{131}$I-TBS performed with 2–5 mCi, in more than 50% of patients with elevated Tg levels.

Our data clearly show that the routine diagnostic TBS performed with 74–185 MBq 6–12 months after $^{131}$I therapy only confirmed the completeness of thyroid ablation in this selected group of patients, of whom 62% had poor prognostic indicators or a large extent of the disease that exposed to an increased risk of recurrence (Table 1). Detection of foci of uptake on the control TBS with a 74–185 MBq $^{131}$I, that were not shown with 3.7 GBq $^{131}$I some months before was, indeed, highly improbable. These data also confirm the high negative predictive value of the $^{131}$I-TBS performed 4 days after the administration of 3.7 GBq to ablate the thyroid remnants.

When we investigated whether serum Tg determination could obviate the routine use of $^{131}$I TBS, our data confirmed that the sensitivity of serum Tg determination for the detection of persistent or recurrent disease increases following withdrawal of thyroid hormone treatment (9–11): the serum Tg level was detectable in 18% of patients and was above 10 ng/mL in 6%. In this latter group of 15 patients, of whom 6 had undetectable Tg levels during $T_4$ treatment, persistent disease could be demonstrated in 5 patients. These data demonstrate that withdrawal of thyroid hormone treatment should be performed in all patients with thyroid carcinoma to control for the absence of detectable disease. In this situation, the Tg level has a paramount prognostic significance on the risk of recurrence, and only anecdotal cases have been reported with positive $^{131}$I-scan and without elevation of serum Tg level (9–11).

There was no relationship between detectable Tg level and the presence of uptake in the thyroid bed on the control

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diagnostic $^{131}$I-TBS. This signifies that increased Tg values are not due to low uptake limited to the thyroid bed and that the clinical relevance of such low uptake is far from being demonstrated. Detectable Tg levels suggest the persistence of neoplastic tissue. That only 5 of the 15 patients with a Tg level above 10 ng/mL exhibited neoplastic foci may be related to the relatively short follow-up and to the slow growth rate of most differentiated thyroid carcinomas. In these patients, $^{131}$I scanning should be used to localize neoplastic foci. The present data demonstrate that the use of 74–185 MBq does not permit their visualization and favor the administration of 3.7 or more of $^{131}$I to patients with a serum Tg level above some arbitrary limit, even in the absence of any other evidence of disease.

The Tg level may remain detectable for a number of months after initial treatment and, as exemplified by one patient, may become undetectable later. This signifies that serum Tg should not be measured less than 3–6 months after initial treatment.

An undetectable Tg level after withdrawal of thyroid hormone treatment is considered a strong indicator of cure, and only 2 of 210 patients (0.9%) in this situation experienced a late relapse (>3 yr after initial treatment), in accordance with previous reports (8–10). The relapse was located in neck lymph nodes, and follow-up of these patients could be based on neck palpation, neck ultrasound, and, indeed, on serum Tg measurement.

In conclusion, our data confirm the excellent diagnostic value of the TBS performed after the administration of $^{131}$I to destroy the thyroid remnants and suggest that serum Tg measurement obtained after withdrawal of thyroid hormone therapy could serve as a yardstick for the selection of the small percentage of patients with detectable Tg level that suggests the persistence of neoplastic tissue. In this context, the present study shows the poor usefulness of $^{131}$I scanning with 74–185 MBq (2–5 mCi) and suggest that 3.7 GBq (100 mCi) or more of $^{131}$I should be administered when the Tg level increases above some arbitrary limit. This strategy will be easier in the near future with the availability of rh-TSH (18, 19). A strict selection of patients for $^{131}$I ablation, the use of a lower activity for ablation (1.1 MBq; 30 mCi), at least in some patients together with this strategy of follow-up, will significantly reduce both the cost of the treatment and follow-up of DTC patients and, more importantly, their pointless exposure to $^{131}$I.

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