9. Sherman SI, Tielens ET, Sostre S, Wharam MD Jr, Ladenson PW. Clinical utility of post-treatment radioiodine scans in the management of patients with thyroid carcinoma. *J Clin Endocrinol Metab* 1994;78:629–634.
10. Thoresen SO, Myking O, Glattre E, Rootwelt K, Andersen A, Foss OP. Serum thyroglobulin as preclinical tumour marker in subgroups of thyroid cancer. *Br J Cancer* 1988;57:105–108.
11. Panza N, Lombardi G, De Rosa M, Pacilio G, Lapenta L, Salvatore M. High serum thyroglobulin levels—diagnostic indicators in patients with metastases from unknown primary sites. *Cancer* 1987;60:2233–2236.
12. De Vathaire F, Blanchon S, Schlumberger M. Thyroglobulin level helps to predict recurrence after lobo-isthmusectomy in patients with differentiated thyroid carcinoma. *Lancet* 1988;2:52–53.
13. McHenry CR, Rosen IB, Walfish PG. Prospective management of nodal metastases in differentiated thyroid cancer. *Am J Surg* 1991;162:353–356.
14. Mazzaferri EL. Treating differentiated thyroid carcinoma: where do we draw the line? [Editorial]. *Mayo Clin Proc* 1991;66:105–111.
15. Tenenbaum F, Corone C, Schlumberger M, Parmentier C. Thyroglobulin measurement and postablative iodine-131 total body scan after total thyroidectomy for differentiated thyroid carcinoma in patients with no evidence of disease [Letter]. *Eur J Cancer* 1996;32A:1262.
16. Ronga G, Fiorentino A, Paserio E, et al. Can iodine-131 whole-body scan be replaced by thyroglobulin measurement in the postsurgical follow-up of differentiated thyroid carcinoma? *J Nucl Med* 1990;31:1766–1771.
17. Pacini F, Lippi F, Formica N, et al. Therapeutic doses of iodine-131 reveal undiagnosed metastases in thyroid cancer patients with detectable serum thyroglobulin levels. *J Nucl Med* 1987;28:1888–1891.
18. Grunwald F, Menzel C, Fimmers R, Zamora PO, Biersack HJ. Prognostic value of thyroglobulin after thyroidectomy before ablative radioiodine therapy in thyroid cancer. *J Nucl Med* 1996;37:1962–1964.
19. Edmonds CJ, Kermode JC. Thyrotropin receptors, tumour radioiodine concentration and thyroglobulin secretion in differentiated thyroid cancer. *Cancer* 1985;52:537–541.
20. Ericcson UB, Tegler L, Lennquist S, Borup Christensen S, Stahl E, Thorell JI. Serum thyroglobulin in differentiated thyroid carcinoma. *Acta Chir Scand* 1984;150:367–375.
21. Ryff de Lèche A, Staub JJ, Kolmer-Faden R, Muller-Brand J, Heitz PU. Thyroglobulin production by malignant thyroid tumors. An immunocytochemical and radioimmunoassay study. *Cancer* 1986;57:1145–1153.
22. Aiello DP, Manni A. Thyroglobulin measurement vs. iodine-131 total body scan for follow-up of well-differentiated thyroid cancer. *Arch Intern Med* 1990;150:437–439.
23. Ruiz Garcia J, Ruiz de Almodovar JM, Olea N, Pedraza V. Thyroglobulin level as a predictive factor of tumoral recurrence in differentiated thyroid cancer. *J Nucl Med* 1991;32:395–398.
24. Ronga G, Fiorentino A, Fragasso G, Fringuelli FM, Todino V. Complementary role of whole body scan and serum thyroglobulin determination in the follow-up of differentiated thyroid carcinoma. *Ital J Surg Sci* 1986;16:11–15.
25. Blahd WH. Management of thyroid cancer. *Compr Ther* 1993;19:197–202.

Influence of Scanning Doses of Iodine-131 on Subsequent First Ablative Treatment Outcome in Patients Operated on for Differentiated Thyroid Carcinoma

Jean-Pierre Muratet, Alain Daver, Jean-Françqis Minier and Francis Larra
Médecine Nucléaire, Centre Paul Papin, Cedex, France

The therapeutic outcome after ^{131}I first ablative treatment in patients operated on for nonmedullary differentiated thyroid carcinoma was compared after both the currently used scanning dose of 111 MBq ^{131}I and a scanning dose of 37 MBq ^{131}I. **Methods:** Two-hundred twenty-nine consecutive patients with no known metastases were retrospectively studied. They were divided in two populations according to the scanning dose (127 patients with 111 MBq and 102 patients with 37 MBq). All patients received 111 or 37 MBq ^{131}I for diagnostic purposes and 3.7 GBq ^{131}I for ablative therapy 9 days later. To assess the efficacy of the treatment, all patients were studied with ^{131}I and with thyroglobulin plasma assays 6–17 mo later. **Results:** Successful outcome was significantly more frequent after a scanning dose of 37 MBq ^{131}I than after a scanning dose of 111 MBq (76% versus 50%, $p < 0.001$). The treatment efficacy was particularly enhanced after 37 MBq in patients with associated lymphocytic thyroiditis. **Conclusion:** In patients with no known metastases, our data suggest that the impairment of the treatment efficacy observed after a scanning dose of 111 MBq ^{131}I is related to a stunning effect on the thyroid remnants. The threshold amount above which this effect begins to occur in thyroid remnants could be between 37 and 111 MBq ^{131}I. Consequently, a scanning dose of only 37 MBq ^{131}I could be recommended before first ablative treatment. The absence of metastatic patients in our study prevents any conclusion about the possible stunning of the neoplastic tissue. Nevertheless, we must suspect such an effect and try to avoid it, especially during follow-up after first radioiodine therapy. For instance, one may consider postponing radioiodine treatment several weeks or even months after scanning dose administration or using only thyroglobulin measurement for patients who are likely to receive a subsequent radioiodine treatment.

Key Words: iodine-131 treatment; thyroid cancer; scanning dose; stunning effect

J Nucl Med 1998; 39:1546–1550

Despite some controversies, radioiodine treatment is frequently performed after total or subtotal thyroidectomy for nonmedullary differentiated thyroid cancer even if radioiodine accumulation is limited to the thyroid bed and is not specific for tumor (*1–7*). The success of the ^{131}I ablative treatment depends on different factors (such as size of the remnants, thyroid-stimulating hormone (TSH) stimulation, iodine diet, etc.), and currently accepted guidelines have recently been published on this issue (*8–10*). One of these guidelines concerns the scanning dose to use before possible ^{131}I treatment. A dose of no more than 74–185 MBq is advocated because higher doses have been shown to impair the ability of the remnant tissue to take up the subsequent therapeutic dose of ^{131}I (*11,12*). The purpose of this study is to know if this impairment, the so-called stunning effect, could appear with the currently used scanning dose of 111 MBq ^{131}I and could reduce the efficacy of subsequent radioiodine treatment. This is a retrospective study on two consecutive populations, the first treated after a scanning dose of 111 MBq ^{131}I, the second after a scanning dose of 37 MBq ^{131}I.

Received Sep. 22, 1997; revision accepted Dec. 19, 1997.
For correspondence or reprints contact: Jean-Pierre Muratet, MD, Centre Paul Papin, Médecine Nucléaire, 2, rue Moll, 49033 Angers Cedex 01, France.

MATERIALS AND METHODS

Patients

Two-hundred twenty-nine consecutive patients referred for first ^{131}I ablative treatment were included. All patients had undergone a total thyroidectomy for thyroid carcinoma with lymph-node dissection when indicated. All patients received a scanning dose of 111 or 37 MBq ^{131}I 9 days before the administration of a therapeutic dose of 3.7 GBq ^{131}I. To assess treatment efficacy, all patients were studied with ^{131}I 6.0–16.8 mo later. Patients referred for surgery for local or distant spread after first radioiodine treatment and before follow-up were not included. Patients with known distant metastases were also not included because there were not enough to constitute a separate group. The 229 patients were divided in two populations according to the scanning dose. The first population (P1) was composed of the first 127 patients (110 females, 17 males; age range 17–79 yr) who received a scanning dose of 111 MBq before treatment. The second population (P2) was composed of the other 102 patients (76 females, 26 males; age range 14–75 yr) who were treated after a scanning dose of 37 MBq. The following data were recorded for each patient: age and sex, histological type and size of primary tumor, lymph-node status, American Joint Committee on Cancer (AJCC) stages, TSH and thyroglobulin (Tg) levels just before scanning dose administration and presence of anti-Tg autoantibodies (aAbs). Primary tumors were classified as papillary carcinoma with or without follicular pattern and follicular carcinoma. Associated histological abnormalities as lymphocytic thyroiditis and nodular goiters were also noted. Nodular goiter diagnosis was retained only when one or more benign nodules ($\geq$10 mm) had been found on histological examination.

First Iodine-131 Treatment

Patients were referred for treatment 4 wk to 21.8 mo (mean 3.7 mo) after surgery. On the first day, patients received 111 or 37 MBq ^{131}I. Rectilinear scan of the neck and diagnostic whole-body scan were performed 3 days later. Spot images were obtained for 10 min with a high-energy, parallel-hole collimator on an analogic or computerized gamma camera. No quantitative dosimetric study was performed, nevertheless, radioiodine cervical uptake at 72 hr was measured using a probe system. Radioiodine treatment (3.7 GBq ^{131}I) was given 6 days later. Post-therapeutic whole-body scan was performed 5 days after treatment administration. Exogenous thyroxine replacement was discontinued 5 wk before diagnostic whole-body scan and replaced by triiodothyronine for 3 wk. Triiodothyronine was stopped 2 wk before the diagnostic whole-body scan.

Thyroid-Stimulating Hormone, Thyroglobulin and Thyroglobulin Autoantibody Measurements

Blood samples for serum TSH, Tg and Tg aAbs assays were drawn just before any radioiodine administration. TSH measurement was performed using a radioimmunoassay (CT Ultra-sensible Riagnost; Behring, Frankfort, Germany) on diluted samples (1:10) to take into account high values of TSH (above 50 μIU/ml). For Tg measurement, we used consecutively two commercialized radioimmunoassays [ELSA-HTG; CIS Bio International, Gif-sur-Yvette, France (A) and TG IRMA; ERIA Diagnostics Pasteur, Marnes la Coquette, France (B)]. These Tg assays are different in terms of calibration and also of sensitivity [0.5 ng/ml (A) and 0.2 ng/ml (B)]. We have found a strong correlation between them (correlation coefficient of 0.96, linear regression curve: $B = 1.84 A + 3.55$; $p = 0.0001$). However, in the range 0.5–1.5 ng/ml (A), the relationship was different ($B = 2.58 A + 0.59$; $r = 0.82$; $p = 0.006$). Consequently, we have considered that the concentration of 1 ng/ml with A, chosen as a threshold, was equivalent to 3 ng/ml with B. Tg aAbs measurement was performed with two other radioimmunoassays (ELSA-AB-HTG; CIS Bio International or TGAB IRMA; ERIA Diagnostics Pasteur).

Iodine-131 and Thyroglobulin Follow-Up

All patients were studied with ^{131}I 6.0–16.8 mo (mean 8.0 mo) after radioiodine ablative treatment. Patients were taken off their thyroid hormone therapy according to the protocol above. Blood samples for serum TSH, Tg and Tg aAbs assays were drawn before radioiodine administration for diagnostic whole-body scan. Whole-body scans were obtained 3 days after administration of a scanning dose of 111 MBq ^{131}I and were classified as positive if they showed focal abnormal uptake in a pattern of residual or metastatic disease. Radioiodine treatment was considered successful if the ^{131}I whole-body scan was negative, with no detectable uptake in the regions where it was observed on the preablation scan nor anywhere else, and if Tg level was $<$ 1 ng/ml (A) or $<$ 3 ng/ml (B).

Statistical Analysis

To determine if there were any significant differences between populations P1 and P2, quantitative data were compared by Student's t-test or the Mann–Witney U-test. The chi-square test was used for qualitative data.

RESULTS

All 229 patients had accumulation of ^{131}I in the thyroid bed alone with no evidence of lymph node or distant metastasis. They were divided into two populations, P1 and P2, according to the scanning dose (111 MBq and 37 MBq ^{131}I, respectively). Characteristics of P1 and P2 are summarized in Table 1. There was no significant difference between the two populations regarding age, histological type and size of primary tumor, lymph node involvement, TSH and Tg before treatment, incidence of Tg aAbs before treatment and follow-up, time between surgery and radioiodine treatment, and time between radioiodine treatment and follow-up. The distribution of P1 and P2 according to the AJCC classification was nearly the same. The cervical uptake 72 hr after scanning dose administration was comparable. More than 60% of the patients presented a lymphocytic thyroiditis or a nodular goiter associated with the carcinoma. The prevalence of these associated histological abnormalities was not different in the two populations. Conversely, there was a significant difference for male-to-female ratio with 17:110 in P1 and 26:76 in P2 ($p < 0.02$).

Results of first radioiodine treatment in P1 and P2 are summarized in Table 2. Successful treatment was observed for 64 of 127 patients in P1 and for 78 of 102 patients in P2 (50% versus 76%). The difference was significant at $p < 0.001$. The difference remains significant for subgroups composed of only females or males. Significant differences between P1 and P2 with better results in P2 were also found regarding the three histopathologic subgroups of carcinoma (follicular, papillary without and with follicular pattern). When P1 and P2 were compared regarding associated histological abnormalities, difference was significant only for patients with lymphocytic thyroiditis ($p < 0.001$) but not for patients without associated abnormalities ($p = 0.09$) nor for patients with nodular goiter ($p = 0.13$). When patients were divided into subgroups according to AJCC staging, differences remain significant for Stages I and III ($p < 0.01$) but not for Stage II ($p = 0.14$). Additionally, it was observed in P1 that the efficacy of the treatment was significantly impaired in patients with lymphocytic thyroiditis. Radioiodine treatment was successful in only 33% of P1 patients with lymphocytic thyroiditis (9 of 27 P1 patients) compared with 56% of patients with nodular goiter (24 of 43 P1 patients) and 55% of patients without associated

TABLE 1
Characteristics of Populations P1 and P2

Variable	P1 (n = 127)	P2 (n = 102)	p value
Age (yr)	43.7 ± 14.1 (17–79)	44.3 ± 13.3 (14–75)	ns
Sex (male) (%)	13	25	<0.02
Size of primary tumor (mm)	19.4 ± 11.3 (1–70)	20.1 ± 13.6 (2–70)	ns
Histological type (F/P/PF) (%)	73/17/10	65/23/12	ns
Lymph-node status (N+) (%)	35	42	ns
AJCC Stage (I/II/III) (%)	64/19/17	64/17/19	ns
Other abnormalities (No/LT/NG) (%)	38/22/40	36/22/42	ns
Thyroglobulin before treatment (ng/ml)*	3.7 (0–307)	3.1 (0–228)	ns
TSH (mu/liter)	82.0 (32–170)	86.4 (11.7–405)	ns
Cervical radioiodine uptake at 72 hr (%)	1.66 (0.1–10.4)	2.05 (0.1–12.5)	ns
aAbs ratio before treatment (aAbs+) (%)	13	16	ns
aAbs ratio on follow-up (aAbs+) (%)	5	8	ns
Time between surgery and treatment (mo)	4.2 ± 2.7 (1.5–21.8)	3.0 ± 1.4 (0.8–7.5)	ns
Time between treatment and follow-up (mo)	8.3 ± 1.5 (6.0–16.8)	7.6 ± 0.8 (6.0–12.2)	ns

*Calculated after transformation of the thyroglobulin values obtained with the A assay in the B assay equivalent values.
Quantitative results are given as mean ± s.d. (range) or as median (range); other results are given as percentages.
F = follicular; P = papillary; PF = papillary with a follicular pattern; No = no associated abnormallity; LT = lymphocytic thyroiditis; NG = nodular goiter; AJCC = American Joint Committee on Cancer; ns = not significant.

abnormality (22 of 40 P1 patients) ($p < 0.05$). This impairment was not found in P2, in which results in patients with lymphocytic thyroiditis were even slightly better than in other subgroups (not significant). No other significant difference was found among subgroups inside each population P1 and P2 according to the success of the treatment.

DISCUSSION

The study of two series of postoperative patients with nonmetastatic differentiated thyroid carcinoma indicates that the success rate of radioiodine ablative therapy is enhanced by using a scanning dose of 37 MBq ^{131}I compared with a scanning dose of 111 MBq ^{131}I. Consequently, the relatively low dose of 111 MBq ^{131}I seems to be sufficient to cause an impairment of the treatment efficacy probably related to the stunning of the thyroid remnants.

In low-risk cancer patients, ablative therapy has not been shown to enhance survival and its effect on recurrence rate is controversial (*1–7*). Nevertheless, many experts recommend one radioiodine treatment for the ablation of thyroid remnants for almost all patients after total or near-total thyroidectomy for nonmedullary differentiated thyroid carcinoma (*9,10*). Further ^{131}I treatments in low-risk cancer patients with persistent uptake limited to the thyroid bed on diagnostic scan is more debatable. Therefore, conditions must be optimal before first treatment to try to obtain complete ablation of remaining thyroid tissue after only one therapeutic dose of ^{131}I. Guidelines have recently been published about optimal preparation for radioiodine treatment in thyroid carcinoma (*8–10*). The mass of the remaining tissue is a critical factor, consequently total or subtotal thyroidectomy is recommended. Levothyroxine and triiodothyronine must be withdrawn 4–6 wk and 2 wk before therapy, respectively. A low-iodine diet is indicated for at least 2 wk. For all our patients, extent of surgery, iodine diet and TSH stimulation followed these guidelines. Lastly, these guidelines suggest a

TABLE 2
Percentage of Successful Radioiodine Treatment in P1 and P2

Variable	P1	P2	p value
Whole population	50% (64 of 127)	76% (78 of 102)	<0.001
Sex			
Male	41% (7 of 17)	77% (20 of 26)	<0.02
Female	52% (57 of 110)	76% (58 of 76)	<0.001
Histological type			
Follicular	38% (5 of 13)	92% (11 of 12)	<0.01
Papillary without follicular pattern	51% (47 of 92)	73% (48 of 66)	<0.01
Papillary with follicular pattern	55% (12 of 22)	79% (19 of 24)	<0.05
Associated histological abnormalities*			
No associated abnormalities	55% (22 of 40)	74% (23 of 31)	0.09
Lymphocytic thyroiditis	33% (9 of 27)	83% (24 of 29)	<0.001
Nodular goiter	56% (24 of 43)	72% (26 of 36)	0.13
AJCC Stage†			
Stage I	56% (45 of 80)	78% (51 of 65)	<0.01
Stage II	50% (12 of 24)	72% (13 of 18)	0.14
Stage III	32% (7 of 22)	74% (14 of 19)	<0.01

*Data not available for 17 patients in P1 and 6 patients in P2.
†Data not available for 1 patient in P1.
AJCC = American Joint Committee on Cancer.

scanning dose of no more than 185 MBq (*8*) or even 74–111 MBq ^{131}I (*10*) because of the results of some previous reports, which describe a stunning effect on remnant tissues when higher doses are used. The first study compared 72 hr ^{131}I uptake by thyroid remnants after scanning doses of 18.5–185 MBq ^{131}I and after subsequent therapeutic doses in 52 patients (*11*). Only patients with an initial uptake of more than 5% were studied. The uptake was much lower after therapeutic doses than after scanning doses. This effect was significantly more frequent when remnants received an absorbed dose of more than 17.5 Gy after scanning dose administration. The corresponding amounts of ^{131}I were not detailed. In the same study, the uptake was compared after two consecutive scanning doses in seven patients with thyroid remnants (148–185 MBq then 148–166 MBq ^{131}I). The mean initial absorbed dose of 43 Gy was associated with an average 55% reduction in uptake after the second scanning dose. This latter result suggests that the impairment of the uptake after treatment is not necessarily due to a specific response to the therapeutic dose but may be related to the initial scanning dose. In another study, the uptake of ^{131}I therapeutic dose by remnants was visually compared after diagnostic whole-body scan with ^{131}I (111–370 MBq) and ^{123}I (11 MBq), a pure gamma emitter that delivers a significantly lower absorbed dose than ^{131}I, a beta emitter (*12*). The uptake was impaired in 15 of 24 foci in the neck in the ^{131}I group and in none of 16 foci in the neck in the ^{123}I group. The relationship with the initial absorbed dose was supported by the finding that the higher the scanning dose, the more reduced was the apparent uptake after therapeutic dose.

It is likely that the reduction of the uptake after therapeutic dose leads to an adverse effect on radioiodine treatment efficacy even if uptake and therapeutic outcome may not be closely related (*13,14*). This hypothesis is supported by a study in which a 370-MBq ^{131}I scanning dose increased the likelihood of unsuccessful treatment compared with 185 and 37 MBq ^{131}I (*15*). However, in the same study, treatment efficacy was not statistically different after 185 MBq compared with 37 MBq. In a more recent report, an impairment of treatment efficacy is described after 111–370 MBq ^{131}I scanning doses compared with approximately 11 MBq ^{123}I (*16*). Successful results are obtained in 60% of postoperative patients treated after ^{131}I and in 75% after ^{123}I (15 of 25 patients versus 30 of 40) but the difference is not significant ($p > 0.2$).

These results show an improvement of first ^{131}I ablative treatment efficacy after a 37 MBq ^{131}I scanning dose in patients with no known metastases. The analysis of the characteristics available in our two populations indicates no other significant difference except for sex ratio. This difference might be due to a change in the detection mode of the thyroid cancer and particularly, since a few years ago, to the more systematic clinical examination of the thyroid of male patients. At any rate, the improvement remains significant for male as well as for female subgroups after 37 MBq. Thus, these data show that a significant impairment of ^{131}I ablative treatment efficacy can occur even after a no more than 111 MBq ^{131}I scanning dose compared with 37 MBq. There is evidence that this impairment can be related to the stunning phenomenon even if we have not observed a scintigraphically apparent reduction of the uptake. The success rate of 76% after 37 MBq ^{131}I scanning dose is similar to the rate reported for patients treated after 11 MBq ^{123}I (*16*). This amount of ^{123}I probably has little effect on remnant tissues because the absorbed dose is approximately one thousand times less than that of 111 MBq ^{131}I (*16*). Series of patients are perhaps not comparable between the two studies but our results suggest that the threshold amount of ^{131}I above which stunning phenomenon begins to occur, and to have an adverse effect on treatment efficacy, could be between 37 and 111 MBq ^{131}I. The duration of the stunning phenomenon is not known: 1, 2 or 4 wk have been reported (*11,12*). This study indicates that the stunning effect persists at least 9 days after scanning dose administration. Regarding histological type of primary tumor, the response to ^{131}I ablative treatment is significantly better in P2 for follicular carcinoma as well as for papillary carcinoma (with or without follicular pattern). The success rate is also significantly higher in P2 for Stage I and Stage III patients (AJCC classification). For Stage II patients, successful treatments are also more frequent in P2 (72% versus 50%), but p value is not significant ($p = 0.14$), probably due to the low number of patients in these subgroups (24 for P1, 18 for P2). Nevertheless, we must point out that most of the thyroid remnants in this study were probably constituted of nontumoral thyroid tissue. Consequently, the improvement after 37 MBq ^{131}I does not necessarily indicate that an improvement would be found in patients with tumoral remnants and, consequently, that this improvement would be identical regarding different stages and histological types. Regarding associated histological abnormalities, the use of a 37 MBq ^{131}I scanning dose improves the results of ^{131}I ablative treatment in each subgroup. However, this improvement is not significant at a confidence limit of 95% for patients with nodular goiter, nor for patients with no associated abnormalities. Conversely, it is very significant for patients with lymphocytic thyroiditis (33% in P1 versus 83% in P2; $p < 0.001$). Additionally, we found that unsuccessful treatments were significantly more frequent in P1 in patients with lymphocytic thyroiditis compared with other subgroups of P1. This lower efficacy of radioiodine treatment in P1 patients with lymphocytic thyroiditis could be related to a less homogeneous uptake and to a shorter biological half-life of ^{131}I in thyroid tissue, as previously described (*17*). However this difference disappears in P2 in which treatment is even slightly more frequently successful in patients with lymphocytic thyroiditis (83% versus 72% (nodular goiter) and 74% (no abnormalities), not significant). These results suggest that thyroid remnants with lymphocytic thyroiditis could be more sensitive to the stunning phenomenon. Nevertheless, it appears that this adverse effect could be avoided, or widely diminished, in this particular case by reducing the scanning dose to 37 MBq ^{131}I. The size of the thyroid remnants has not been included in these data because we were unable to accurately assess it. Indeed, in our populations, the uptake at 72 hr (median 1.66% for P1 and 2.05% for P2) indicates that most of the remnants were small (i.e., <1 g), as suggested by the comparison with the average uptake of 20% found in another report of patients with >5 g remnant tissues (*14*). It is known that size measurements, and consequently dosimetric calculations, have a poor reliability when the mass of the remnants is small and especially when <1 g (*18*). Consequently, we have not routinely performed dosimetric studies and are unable to establish a relationship between absorbed dose after scanning dose, absorbed dose after therapeutic dose and subsequent treatment efficacy. The uptake 72 hr after therapeutic dose has not been routinely measured either. Previous studies have shown that the stunning effect leads to an impairment of uptake. On the other hand, it is known that ^{131}I ablative treatment efficacy is related not only to the uptake and to the total absorbed dose but also to the inital absorbed dose after therapeutic dose administration (*14*). Consequently, further complete dosimetric studies are required to determine the exact mechanism involved in the impairment of first ^{131}I ablative treatment efficacy observed after scanning dose administration.

This study concerns only thyroid remnants. One report (*12*) mentions that the visual impairment of the uptake described after 111–370 MBq ^{131}I in 15 of 24 cervical remnants was seen

in only 1 of 11 distant metastases, suggesting a lesser sensitivity to the stunning effect. Nevertheless, even if the sensitivity of the neoplastic tissue to the stunning effect must be confirmed and even if we have no evidence that it is comparable with that of the normal tissue, we must keep in mind this possibility and take it into account in choosing scanning doses before first treatment and for follow-up studies.

How is the stunning effect avoided? The issue is rather different if we consider first treatment or further radioiodine studies and treatments. The main goal of the scanning dose administration before first treatment is to detect extensive remnants, lymph node involvement or even distant metastases, leading to surgical treatment before radioiodine ablative therapy (2% in our experience) or to the reduction of the therapeutic dose to avoid neck pain and edema in patients with extensive remnants (6% in our experience) (*19,20*). In this particular use, we think that a scanning dose of 37 MBq is sufficient. Another solution is to use ^{123}I as suggested in a recent study (*16*), in which the accuracy of scans performed 24 hr after the administration of 11 MBq ^{123}I was similar to that of scans obtained 72 hr after administration of 111–370 MBq ^{131}I (89.5% versus 92.9%, respectively). Some false-negatives are described after both of the isotopes, especially regarding detection of distant metastases, but, because nearly all patients are treated at least one time, we know that a more accurate detection will be possible by performing a post-therapeutic scan.

For follow-up after radioiodine treatment, the minimum amount of ^{131}I recommended for scanning doses is 74–111 MBq (*10*) and, on the other hand, the accuracy of a 11 MBq ^{123}I scanning dose seems to be insufficient [70% versus 93% compared with 111–370 MBq ^{131}I (*16*)]. Higher doses of ^{123}I might be considered but are too expensive for routine use. One solution would be to use only Tg level under TSH stimulation to decide if a new radioiodine treatment is necessary, but it is known that this is a less sensitive method (*21*). Another possible solution is to postpone radiodiodine therapy some weeks or months after scanning dose administration but, further studies are warranted to know the duration of the stunning effect.

CONCLUSION

The results of this study suggest that the stunning effect can be present in postoperative patients with thyroid remnants after the relatively low scanning dose of 111 MBq ^{131}I, leading to a significant reduction of the efficacy of the first ablative treatment. A scanning dose of 37 MBq ^{131}I seems to avoid or to widely diminish this effect and could be recommended before the first treatment. Further studies are required to confirm the existence of the stunning effect in tumoral tissue, especially after the recommended follow-up scanning dose of 111 MBq ^{131}I and to know its duration to establish guidelines for follow-up scintigraphy.

REFERENCES

1. Beierwaltes WH. The treatment of thyroid carcinoma with radioactive iodine. *Semin Nucl Med* 1978;8:79–84.
2. Krishnamurthy GT, Blahd WH. Radioiodine ^{131}I therapy in the management of thyroid cancer: a prospective study. *Cancer* 1978;40:195–202.
3. Beierwaltes WH, Rabbani R, Dmuchowski C, et al. An analysis of ablation of thyroid remnants with ^{131}I in 511 patients from 1947–1984; experience at University of Michigan. *J Nucl Med* 1984;25:1287–1293.
4. Simpson WJ, Panzarella T, Carruthers JS, Gospodarowicz MK, Sutcliffe SB. Papillary and follicular thyroid cancer: impact of treatment in 1578 patients. *Int J Radiat Oncol Biol Phys* 1988;14:1063–1075.
5. DeGroot LJ, Kaplan EL, McCormick M, Straus FH. Natural history, treatment, and course of papillary thyroid carcinoma. *J Clin Endocrinol Metab* 1990;71:414–424.
6. Samaan NA, Schultz PN, Hickey RC, et al. The results of various modalities of treatment of well-differentiated thyroid carcinomas: a retrospective review of 1599 patients. *J Clin Endocrinol Metab* 1992;75:714–720.
7. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994;97:418–428.
8. Becker D, Charkes ND, Dworkin H, et al. Procedure guideline for extended scintigraphy for differentiated thyroid cancer: 1.0. *J Nucl Med* 1996;37:1269–1271.
9. Singer PA, Cooper DS, Daniels GH, et al. Treatment guidelines for patients with thyroid nodules and well-differentiated thyroid cancer. *Arch Intern Med* 1996;156: 2165–2172.
10. American Association of Clinical Endocrinologists. Clinical practice guidelines for the management of thyroid carcinoma. *Endocr Pract* 1997;31:60–71.
11. Jeevanram RK, Shah DH, Sharma SM, Ganatra RD. Influence of initial large dose on subsequent uptake of therapeutic radioiodine in thyroid cancer patients. *Nucl Med Biol* 1986;13:277–279.
12. Park HM, Perkins OW, Edmondson JW, Schnute RB, Manatunga A. Influence of diagnostic radioiodines on the uptake of ablative dose of iodine-131. *Thyroid* 1994;4:49–54.
13. Matsushita T, Toyota S, Katoh N, Nakagawa T. Iodine-131 treatment of thyroid cancer: relation between effective half-life and efficacy of treatment. *Radiat Med* 1994;12:167–170.
14. Samuel AM, Rajashekharrao B. Radioiodine therapy for well-differentiated thyroid cancer: a quantitative dosimetric evaluation for remnant thyroid ablation after surgery. *J Nucl Med* 1994;35:1944–1950.
15. Kim CK, Tse K, San Pedro E, Alavi A. Influence of various scanning doses on subsequent ^{131}I ablation of thyroid remnants [Abstract]. *J Nucl Med* 1994;35:14P.
16. Park HM, Park YA, Zhou XH. Detection of thyroid remnants/metastasis without stunning: an ongoing dilemma. *Thyroid* 1997;7:277–280.
17. Wolf J. Iodine. The active transport system. In: Leclere J, Orgiazzi J, Rousset B, Schlienger JL, Wemeau JL, eds. *La Thyroïde*. Paris: Expansion Scientifique Française; 1992:17–24.
18. Flower MA, Schlesinger T, Hinton PJ, et al. Radiation dose assessment in radioiodine therapy. 2. Practical implementation using quantitative scanning and PET, with initial results on thyroid carcinoma. *Radiother Oncol* 1989;15:345–357.
19. Burmeister LA, du Cret RP, Mariash CN. Local reactions to radioiodine in the treatment of thyroid cancer. *Am J Med* 1991;90:217–222.
20. DiRusso G, Kern KA. Comparative analysis of complications from ^{131}I radioablation for well-differentiated thyroid cancer. *Surgery* 1994;116:1024–1030.
21. Aiello DP, Manni A. Thyroglobulin measurement versus iodine-131 total-body scan for follow-up of well-differentiated thyroid cancer. *Arch Int Med* 1990;150:437–439.