

diagnosed with thyroid cancer at age 45 y or younger; 287 of these reported cycle abnormalities before the diagnosis, and 767 had no cycle abnormalities before the diagnosis. Of these 767 women, 326 received at least 1 radioiodine treatment with 3.7 GBq, and 441 did not. The majority of women were interviewed more than 2 y after radioiodine treatment. The proportion of women who reported cycle abnormalities after thyroid cancer was not significantly higher among women who were treated with ^{131}I ($n = 34$, 10%) than among those who were not treated with ^{131}I ($n = 41$, 9%). In a multivariate logistic regression taking into account year and age at menarche, at diagnosis, and at interview; weight; and smoking habit, we did not observe any increased risk of cycle abnormalities after thyroid cancer among women who had received ^{131}I therapy (odds ratio, 1.2 [95% confidence interval, 0.7–1.2]).

As a final note, we were not able to confirm the results of Souza Rosário et al. (3), who reported transient abnormalities after ^{131}I therapy. However, our inability to confirm those results may be related to the long delay between treatment and interview in our patients, most of whom were not interviewed until more than 2 y after radioiodine treatment.

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A Proposition for the Use of Radioiodine in WDTC Management

TO THE EDITOR: Today, individualized treatments are increasingly at the forefront. Treatments tailored to tumor type and patient sensitivity are now possible. For example, breast cancer management is based mainly on menopausal status, histology, hormone receptor status, Neu status, histologic grade, and Ki67 expression rather than on TNM classification and stage. Therefore, the concept of one treatment for all (e.g., systematic radioiodine remnant ablation in patients with well-differentiated thyroid carcinoma [WDTC]) may be questioned because, as Hay et al. (1) maintain, the majority of patients are exposed to the risk from radiation for the theoretic benefit of a small minority. Thus, the viewpoint of Hay et al. is consistent with the current fashion. However, their perspective seems somewhat limited to me.

They state 3 goals of radioiodine remnant ablation: to increase the specificity of follow-up imaging using radioiodine, to attain undetectable thyroglobulin levels, and to decrease recurrence and increase disease-free survival by eliminating microfoci of carcinoma in the remaining tissue.

With regard to the first of these goals, increasing the specificity of follow-up radioiodine imaging, the future does not seem to lie in remnant ablation (which has other purposes) but in the use of SPECT/CT (2) or, especially and most recently with ^{124}I , PET/CT (3). These techniques may differentiate remnants from lymph nodes, and the sensitivity will increase substantially with the positron emitter isotope. In so doing, I agree that ablation of the remnant might be avoided, but postoperative metabolic imaging of the remnants and other iodine-avid metastatic foci must be applied and refined.

I do not completely agree with the authors when they report that “the administration of therapeutic ^{131}I without preceding scintigraphy to identify the target” is a “refinement in patient management.” Although omitting scintigraphy before therapy may simplify management, in my opinion it does not represent progress. Postoperative and pretherapeutic imaging (as well as posttherapeutic imaging) also identify locoregional iodine-avid lesions (lesions in the nodes, indicating the need for repeated surgery) or distant iodine-avid lesions (metastatic lesions, which can be treated other than by radioiodine). When properly applied, pretherapeutic imagings also allow one to calculate the amount of activity required to destroy the remnants—an amount that is lower than the 3,700 MBq classically proposed—and fewer individuals are exposed to unnecessarily high doses of irradiation (4). In Europe, the administration of high activities requires one hospitalization of variable duration, with both financial and social implications.

Paradoxically, the second of these goals, undetectable thyroglobulin levels, is seen in up to 30% of patients undergoing surgery for thyroid carcinoma as a result of circulating antithyroglobulin antibodies. When these antibodies are present, remnant ablation is needed to destroy the normal thyroid tissue, eliminating any further source of antigenic stimulation and antibody production.

For the third goal of remnant ablation, eliminating microfoci, the most important prognostic factor for a patient with thyroid carcinoma is widely believed to be the surgeon (i.e., his or her ability to perform a complete or near-complete surgery and his or her willingness to operate again to remove lymph nodes). Unfortunately, what constitutes a remnant varies from surgeon to surgeon. Furthermore, some do not remove cervical nodes if the tumor is small, and some base pN status on an insufficient number of nodes. Kuffner et al. (5) recently found neck lymph node metastases for 6% of nanopapillary tumors 1 mm or smaller and 10% of micropapillary tumors 1 cm or smaller. These reported rates of metastasis are less than the 31% observed with larger papillary thyroid carcinomas (>1 cm). However, these findings suggest that patients older than 45 y and with small lesions but with pathologically positive nodes will be undertreated in the Hay et al. perspective (1).

In fact, before raising the question of remnant ablation, I would ask whether any thyroglobulin-producing normal remnants or thyroglobulin-producing tumor tissues are present. That question can be addressed by determining whether thyroglobulin is present after the operation or increases under thyroid hormone withdrawal or after treatment with recombinant human thyroid-stimulating hormone. The question can also be addressed by performing optimized scintigraphic imaging under endogenous or exogenous thyroid-stimulating hormone stimulation as part of the patient's postsurgical management.

Apart from making what might be considered a plea for the systematic use of optimized postoperative metabolic imaging in patients with thyroid carcinoma, I would also raise the problem of the frequent simplification and overgeneralization of WDTC histology. Follicular carcinomas are WDTCs, but their prognosis is different from that of papillary carcinomas, and their hematogenous route of dissemination differs from the lymphogenous route of papillary carcinomas (how do Hay et al. classify follicular carcinomas with histologically demonstrated vascular invasion?). Pure papillary carcinomas (and the so-called macrofollicular variant) are WDTCs with a good prognosis, but when familial their prognosis is reported to be worse, although these carcinomas are usually then small. Furthermore, in the papillary carcinoma family, some variants are more aggressive than others, including the follicular variants, the papillary carcinomas with an insular growth pattern, the tall cell variants (4%–12% of papillary carcinomas), the diffuse sclerosing cases (up to 3% of papillary carcinomas), and the trabecular or solid papillary variants (up to 3% of papillary carcinomas). These aggressive variants represent a substantial group but, unfortunately, in the literature are frequently not distinguished clearly from their pure parents (except for the Hürthle cell cases, which are known to be non-iodine-avid).

Thus, the management of thyroid carcinoma should be based on histologic characteristics as well as, or even instead of, TNM staging. With the introduction of ^{18}F -deoxyglucose and ^{124}I metabolic PET/CT, and new drugs that target precise metastatic pathways (6–8), we must shift from a macroscopic definition of thyroid cancers toward their microscopic, metabolic, histologic, and genetic characterization. With regard to this last point, we would stress that most cases of thyroid cancer express the sodium iodide symporter (9). As with other membranous receptors in other cancers, it would be logical to take into account immunohistologically assessed sodium iodide symporter expression in managing thyroid carcinoma and in deciding on treatment with high-activity ^{131}I .

As a conclusion and in response to the perspective of Hay et al. (1), I would propose the following approach (the cost-effectiveness of which needs to be evaluated). As a first step, patients with stage I pure papillary carcinomas using the TNM system and without antithyroglobulin antibodies (especially postsurgical patients in whom thyroglobulin does not become undetectable on thyroid hormone substitution) would be investigated by ^{123}I or ^{131}I SPECT/CT or by ^{124}I PET/CT if the tumor is sodium iodide symporter-positive, or by ^{18}F -deoxyglucose PET/CT (either after recombinant human thyroid-stimulating hormone stimulation or after thyroid hormone withdrawal) if the tumor is sodium iodide symporter-negative. Whether the patients are treated and the method of treatment would be determined by the results of these investigations.

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REPLY: We appreciate Professor Bourgeois’ thoughtful letter. Our perspective (1) was limited to making major points to indict ablation in the management of thyroid carcinomas, and Professor Bourgeois’ questions offer an opportunity to expand on our thesis.

We agree with Professor Bourgeois that refinements in scintigraphic imaging will more accurately define the anatomic sites of residual functioning thyroid tissues. The sensitivity of imaging is also likely to improve over time. We further agree that diagnostic scintigraphic imaging may help to locate residual carcinomas and thereby aid in decisions about therapy (surgical or ^{131}I). Although images made after ablation therapy may be more sensitive than pretherapeutic scans, we do not believe that this observation justifies such management of patients who have stage I carcinomas. If, from data available, there is concern about carcinoma not seen on the diagnostic images, consideration may be given to treatment, not ablation, with ^{131}I . However, long-term benefits from this approach have not been shown. We also agree that if ^{131}I treatments are to be given for carcinomas, the administered dose should be optimal, a goal that often requires dosimetry.

Whereas thyroglobulin antibodies often disappear over time after ^{131}I ablation (2), it is possible that this immune interference may also disappear without radiation treatment. In any case, such antibodies may serve as a surrogate for circulating tumor thyroglobulin (3).

Because papillary microcarcinomas are so frequently present, the numbers of patients are difficult to grasp. From autopsy evidence, such tumors have been found in 1.4%–36% of populations around the world (4–6). In addition, of those afflicted, multifocality was found in 20%–47% and micrometastases to cervical lymph nodes in 3%–18% (4), yet cause-specific mortality was 0%–1% (6). Nevertheless, after surgical therapy, recurrences have been documented. For patients with primary tumors smaller than 5 mm, recurrences appear in about 1% (7). In follow-up, cervical metastases were discovered more frequently if, at the time of the original operation, the lymph nodes contained carcinoma (8,9). Hay et al. found that postoperative ^{131}I treatments were not followed by statistically fewer nodal recurrences (8), but Chow et al. reported that, after ablation, new cervical disease was statistically less common (9). However, overall, recurrences in the absence of ablation therapy were seen in few patients: only 11 (8) and 4 (9).

Some patients with microcarcinomas may require therapy after surgical removal of the tumors; depending on ancillary findings,