The whole-body radiation delivered by ^{131}I remnant ablation can be significantly reduced by preparing patients with recombinant human thyrotropin rather than with thyroid hormone withdrawal

Remy H, Borget I, Leboulleux S, Guilabert N, Lavielle F, Garsi J, Bournaud C, Gupta S, Schlumberger M, Ricard M. ^{131}I effective half-life and dosimetry in thyroid cancer patients. J Nucl Med 2008;49:1445-50.

SUMMARY

BACKGROUND There is compelling evidence that ^{131}I treatment of thyroid cancer may induce extrathyroidal cancers and leukemias. This makes it imperative that precautionary measures be taken when using ^{131}I treatment in patients with differentiated thyroid carcinoma, especially young patients, who generally have a good prognosis and long life expectancy, leaving them at risk of second tumors over many years. One measure is to use the smallest effective amount of ^{131}I to treat the patient. The other measure is to use safeguards that lower the extent of total-body radiation derived from ^{131}I. Recent studies suggest that preparing patients by administering recombinant human thyrotropin (rhTSH) may favorably influence the effective half-life of ^{131}I and reduce the radiation doses absorbed by extrathyroidal organs. However, there still are uncertainties about the extent to which this occurs, requiring further study of this issue.

METHODS This is a prospective study of patients with differentiated thyroid carcinoma treated with ^{131}I at the Institut Gustave Roussy from December 2004 through June 2007. Some of the patients were prepared for treatment by thyroid hormone withdrawal (THW) for 5 weeks, during which triiodothyronine (T_3) was administered for 3 weeks, and total withdrawal of thyroid hormone was performed for 2 weeks. The others remained on levothyroxine and were treated with 0.9 mg of rhTSH on 2 consecutive days in preparation for treatment with 100 mCi (3700 MBq) of ^{131}I. Twenty patients with low-risk cancer were treated with 30 mCi (1110 MBq). All had abundant hydration and were treated with laxatives during hospitalization. Three types of measurement were performed: whole-body counting in 245 patients, quantitative whole-body scans with total urinary ^{131}I excretion in 30, and urine samples from 19 who had THW and 11 treated with rhTSH. Whole-body retention of ^{131}I was measured by a probe fixed on the ceiling of each hospital room. From the three sets of available data (whole-body retention, whole-body scans, and urinary excretion), it was possible to extract dosimetry data on the organs of interest. The half-life (T1/2) is the time radioiodine remains in a body target divided by a factor of 2. The effective T1/2 is determined from the combination of physical isotope decay and the biologic T1/2 of ^{131}I (retention time of ^{131}I within the target cell), which is not dependent on the administered activity of ^{131}I (100 mCi or 30 mCi (Figure 1). Data from 254 patients were pooled for analysis.

RESULTS The mean effective whole-body half-life for the 30 patients who underwent repeated whole-body scans was 10.6 hr for the 11 who received rhTSH and 16.0 hr for the 19 who underwent THW ($P = 0.0006$), which was similar to those in corresponding patients in the entire series. The ^{131}I residence times for bladder, stomach, and colon were significantly different (Figure 2). The whole-body residence time was 15.2 hr in patients treated with rhTSH and 23.0 hr in the patients who underwent THW. The residence time in the stomach was significantly shorter ($P = 0.01$) in the patients treated with rhTSH as compared with those who underwent THW; however, there was no difference for the colon ($P = 0.07$), urinary bladder ($P = 0.9$), or breast ($P = 0.53$) (Figures 2 and 3). The residence time in the remainder of the

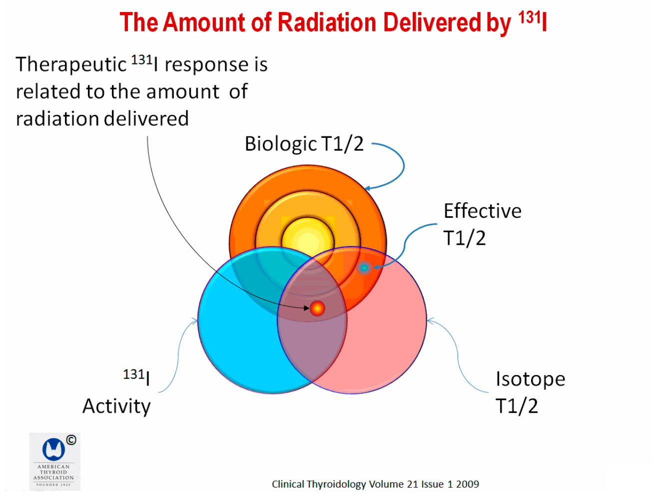

Figure 1. The effective half-life (T½) is a combination of the biologic T½ , (the residence time in the follicular cell or other body cell that concentrates ^{131}I) and the half-life of the isotope, which is approximately 8.1 days for ^{131}I. Activity is the "dose" of thyroid hormone (e.g., 30 mCi). Together, the three account for the total amount of iodine delivered to thyroid and other tissues, especially tissues that harbor sodium iodide symporters that facilitate movement of ^{131}I into a cell.

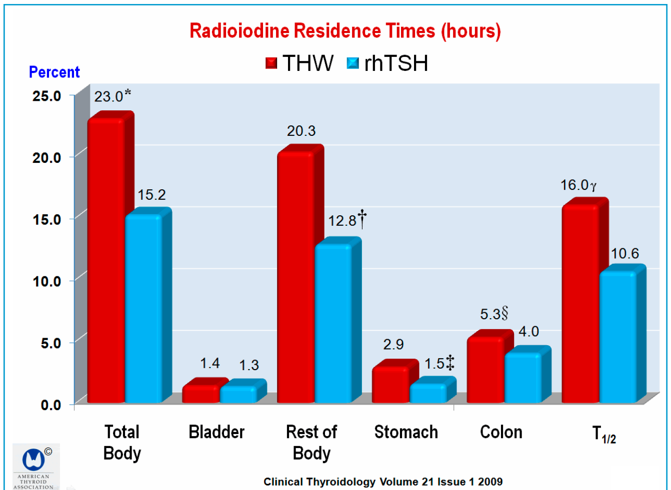

Figure 2. This depicts the residence times of ^{131}I within a cell from various tissues. THW denotes thyroid hormone withdrawal, and rhTSH recombinant human TSH. $^{*}P= 0.0006$; $†P = 0.04$; $‡P = 0.01$; $§P = 0.07$; $\gamma P = 0.0006$. All comparisons are between rhTSH and THW. Data for this graph are derived from Table 3 in Remy et al.

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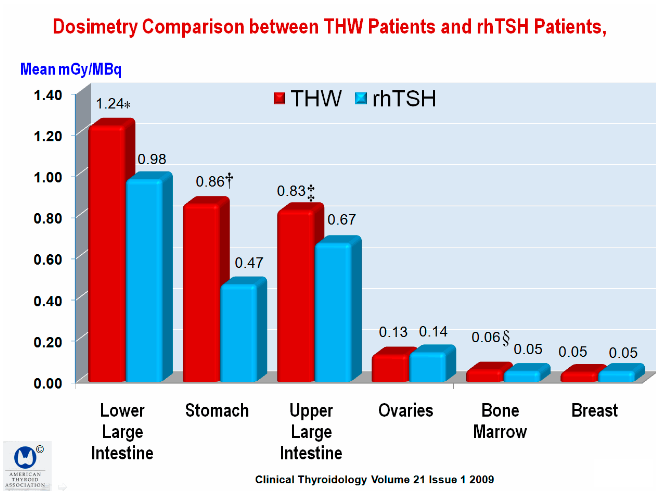

Figure 3. This figure depicts the dosimetry in terms of mean mGy of irradiation delivered to tissues per MBq of ^{131}I. *P = 0.09 †P= 0.009, ‡P = 0.05, *P = 0.05, †P = 0.009 ‡P = 0.05; §0.06. All comparisons are between rhTSH and THW. Data for this graph are derived from Table 4 in Remy et al.

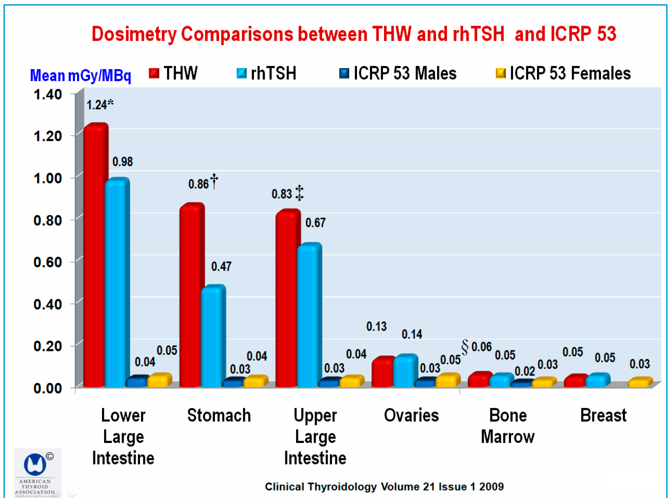

Figure 4. This is the same graph as shown in Figure 3, with the addition of data from the Commission on Radiological Protection (ICRP) that can be used for safe dose estimates in healthy subjects.*P = 0.09 †P= 0.009, ‡P = 0.05, *P = 0.05, †P = 0.009 ‡P = 0.05; §0.06; all comparisons are between rhTSH and THW. Data for this graph are derived from Table 4 in Remy et al.

body was shorter in patients treated with rhTSH as compared with those who underwent THW (P = 0.04) (Figure 3). The dose estimates were lower for the stomach (P = 0.009) and were of borderline significance for the upper large intestine (P = 0.05) and the bone marrow (P = 0.05) (Figures 3 and 4).

CONCLUSION The mean effective half-life of ^{131}I is shorter by 31% in euthyroid patients treated with rhTSH as compared with that in hypothyroid patients undergoing THW, which significantly decreases the radiation doses delivered to extrathyroidal tissues. Combined with smaller amounts of ^{131}I, the amount of whole-body radiation delivered by ^{131}I remnant ablation can be substantially reduced.

COMMENTARY

This study is of major importance. It confirms and extends the previous report by Hänscheid et al. (1) on body retention of ^{131}I and elaborates on the radiation doses to blood and bone marrow and whole-body radiation following preparation with rhTSH and THW. The side effects of ^{131}I therapy are well known and are directly related to the amount of tissue radiation. As a consequence, patients can sustain considerable nonthyroidal tissue injury from ^{131}I, making them susceptible to a significantly higher risk of second nonthyroidal cancers as compared with the general population (2). There is a linear relationship between the amount of administered ^{131}I and the rate of second cancers (3) and tissue damage. Retrospective studies suggest that empiric ^{131}I dosing regimens, the most common approach used, frequently exceed the maximum tolerated radiation levels, especially in elderly patients (4, 5). One way to decrease these adverse effects is to substantially reduce the amount of ^{131}I for remnant ablation. The ATA guidelines suggest that the minimum ^{131}I activity (30 to 100 mCi) necessary to achieve successful remnant ablation should be used, particularly for patients at low risk (6). This recommendation is based on the fact that ^{131}I activities between 30 and 100 mCi generally show similar rates of successful remnant ablation (7-12) and recurrence (11), suggesting that 30 mCi is the preferred amount of ^{131}I for patients at low risk of adverse tumor outcomes.

The Remy study confirms that using rhTSH reduces the amount of radiation exposure by about one-third (13). It confirms previous reports on body ^{131}I retention (1) and on estimated doses to the blood and bone marrow, and that whole-body residence time is shorter in patients treated with rhTSH than in those who undergo THW, in whom residence time was longer than the 11.1 hr reported in the International Commission on Radiological Protection (ICRP) report 53. Although the ICRP data are usually considered the standard in the field of internal dosimetry, it does not provide powerful information when residence times are needed for calculations after the administration of therapeutic ^{131}I. In the Remy and Hänscheid (1) studies, the mean whole-body residence time was shorter in patients pretreated with rhTSH (17.3±3.9 hr and 15.2±3.1 hr, respectively) than in patients who had THW (24.1±7.8 hr and 23.0±7.7 hr).

In summary, these studies collectively provide robust evidence that the use of rhTSH in euthyroid patients significantly reduces the amount of whole-body radiation and radiation to tissues such as the lacrimal glands, stomach, breast, salivary glands and other organs that contain sodium iodine symporters and thus concentrate ^{131}I more avidly than other tissues. Taken together, these data suggest that ^{131}I for remnant ablation should routinely be administered with the smallest amount of ^{131}I that is effective, in the range of 30 mCi in patients at low risk, and that patients should be prepared with rhTSH for remnant ablation.

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