Diagnostic Value of Recombinant Human Thyrotropin–Stimulated ^{123}I Whole-Body Scintigraphy in the Follow-Up of Patients With Differentiated Thyroid Cancer

Ali S. Alzahrani, MD, OmAlkhaire AlShaikh, MD,* Mahmoud Tuli, MD,† Abdulaziz Al-Sugair, MD,† Reem Alamawi, RN,* and Maha M. Al-Rasheed, MSc‡*

Purpose: Published data on recombinant human thyrotropin- (rhTSH-) stimulated iodine-123 (^{123}I) diagnostic whole-body scintigraphy (DxWBS) in differentiated thyroid cancer (DTC) surveillance after initial treatment are limited. We sought to evaluate this modality's diagnostic value in this setting.

Materials and Methods: We retrospectively compared rhTSH-stimulated ^{123}I DxWBS results with DTC status concurrently determined by stimulated serum thyroglobulin (Tg) measurement, neck ultrasonography, and other imaging studies. Disease was considered present based on stimulated Tg level $\geq$1 μg/L without interfering Tg autoantibodies with or without positive imaging or biopsy-proven DTC. We also compared scan positivity and disease detection rates of rhTSH-stimulated DxWBS scans obtained with ^{123}I with those acquired with iodine-131 (^{131}I) during the same period. The sample comprised 105 consecutive totally thyroidectomized patients undergoing rhTSH-aided DxWBS with I-123 (n = 67) or with ^{131}I (n = 38) for diagnostic follow-up. rhTSH, 0.9 mg/d, was injected intramuscularly on 2 consecutive days. Oral diagnostic activities of 5 to 10 mCi (185–370 MBq) ^{123}I or 3 mCi (111 MBq) ^{131}I were given on the third day. DxWBS was performed 24 hours (^{123}I) or 48 to 72 hours (^{131}I) later.

Results: rhTSH-aided ^{123}I DxWBS scans showed 35.3% sensitivity, 98.0% specificity, 85.7% positive predictive value, and 81.6% negative predictive value. rhTSH-stimulated ^{123}I and ^{131}I DxWBS did not differ in scan positivity (10.4% vs. 13.2%, $P = 0.75$) or disease detection rates (35.3% vs. 27.8%, $P = 1.00$).

Conclusions: In DTC, rhTSH-aided ^{123}I DxWBS achieves comparable results in diagnostic follow-up with those of rhTSH-aided ^{131}I DxWBS. Future studies should address the preablation setting and scan activity and timing.

Key Words: recombinant human thyrotropin (rhTSH), iodine-123 (^{123}I), whole-body scintigraphy (WBS), differentiated thyroid cancer, diagnostic follow-up, sensitivity

(*Clin Nucl Med* 2012;37: 229–234)

Differentiated thyroid cancer (DTC), the most common endocrine malignancy,[1] is in most cases treated with total thyroidectomy followed by radioiodine thyroid remnant ablation.[2] After this initial care, long-term surveillance is indicated for detection and management of persistent/recurrent local disease or metastases. In most low-risk cases, serum thyroglobulin (Tg) measurement and high-resolution ultrasonography (US) have supplanted the traditional use of radioiodine diagnostic whole-body scintigraphy (DxWBS) in this surveillance.[2–4] However, DxWBS remains an important tool in the follow-up of intermediate- to high-risk patients and in some low-risk cases, especially as a pretherapeutic diagnostic imaging study when subsequent radioiodine therapy is likely.[2]

Until last decade, DxWBS typically was performed after thyroid hormone withdrawal (THW) for 4 to 6 weeks to achieve the serum thyroid-stimulating hormone elevation (to >25 or 30 mIU/L) considered to be necessary for sensitive scanning. However, in many centers, this preparation method largely has been replaced by the use of recombinant human thyrotropin (rhTSH).[5] rhTSH was approved in the United States in 1998 and Europe in 2001 to stimulate DxWBS,[5] and in the United States in 2007 and Europe in 2005 to aid thyroid remnant ablation.[5,6]

I-131 is currently the standard radioiodine isotope for DxWBS.[5,7] However, interest in the use of ^{123}I recently has increased because although the 2 isotopes have shown comparable diagnostic performance,[8–12] I-123 seems to have a number of advantages relative to ^{131}I. For one, ^{123}I is a pure γ emitter, which provides better imaging quality. Lack of β emission by ^{123}I carries the additional advantage of absence of stunning effect on thyroid cancer tissue.[13–15] Additionally, ^{123}I has a short half-life (~13 hours), which necessitates scanning within ~24 hours after radioisotope administration.[16,17] This results in an approximately 100-fold lower radiation dose for ^{123}I DxWBS relative to ^{131}I DxWBS.[12]

Thus far, published data on ^{123}I use with rhTSH are limited.[11,17] At our institution, which has an in-house cyclotron, ^{123}I is routinely available for scanning, and rhTSH frequently is employed for thyroid-stimulating hormone stimulation. We therefore conducted a retrospective analysis of our experience to assess the diagnostic value of rhTSH-stimulated ^{123}I DxWBS in surveillance after initial treatment. To achieve this objective, we compared rhTSH-stimulated ^{123}I DxWBS findings with the disease status as concurrently determined by stimulated serum Tg testing, neck US, and other imaging studies. Additionally, we compared the positivity rate and the sensitivity of rhTSH-aided ^{123}I DxWBS with those of rhTSH-aided ^{131}I DxWBS performed in a different group of patients but for the same purpose, by the same nuclear medicine specialists, and during the same ~45-month period at our tertiary care referral center.

MATERIALS AND METHODS

Patients

Five patients were excluded because of positive Tg autoantibody results. The remaining study sample comprised 105 consecutive patients with DTC in whom DxWBS was aided by rhTSH (Thyrogen, Genzyme Corporation, Cambridge, MA), starting with

Received for publication April 23, 2011; revision accepted June 27, 2011.
From the Departments of *Medicine, †Medical Imaging, and ‡Research Centre, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.
Presented (portions of this work) at the 91st Annual Meeting of The Endocrine Society; June 10–13, 2009; Washington, DC.
Conflicts of interest and sources of funding: Editorial assistance on the manuscript was provided by Robert J. Marlowe, Spencer-Fontayne Corporation, Jersey City, NJ. His work was financially supported by Genzyme Corporation, the rhTSH manufacturer. Mr. Marlowe was not involved with the undertaking and writing of this article. All authors have no conflicts of interest.
Reprints: Ali S. Alzahrani, MD, Department of Medicine, MBC-46, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, Saudi Arabia. E-mail: aliz@kfshrc.edu.sa.

ISSN: 0363-9762/12/3703-0229

the drug's introduction in our institution in June 2006 and continuing through February 2010. During this period, ^{123}I was used for rhTSH-stimulated DxWBS in 67 patients. During the same interval, because of occasional ^{123}I shortages, rhTSH-stimulated DxWBS was performed with ^{131}I in 38 patients.

All 105 patients (35 male [33.3%] and 70 female [66.7%]; mean age ± standard deviation, 49.5 ± 14.7 years) were totally thyroidectomized. Table 1 provides selected additional characteristics of the ^{123}I and ^{131}I subgroups. Both subgroups were comparable with respect to all tested variables, except gender (higher percentage of female patients in the ^{123}I group) and were representative of the typical referral center DTC patient population. The study was approved by our institutional review board.

rhTSH-Stimulated DxWBS

Patients were kept on a low-iodine diet for at least 1 week before scanning. Although urinary iodine excretion at the time of scanning was not routinely measured, patients were questioned regarding diet and recent imaging procedures to exclude iodine excess before DxWBS, and scanning was postponed for at least 3 months when such excess was suspected. rhTSH, 0.9 mg daily, was given by deep intramuscular injection for 2 consecutive days. On the third day, a diagnostic activity of 5 to 10 mCi (185–370 MBq) ^{123}I or 3 mCi (111 MBq) ^{131}I was administered as an oral liquid or capsules, respectively. Planar whole-body images and dedicated static views of the neck and chest and other regions as indicated were obtained 24 hours after ^{123}I intake or 48 to 72 hours after ^{131}I intake using a large field of view, static dual-head gamma camera (E.Cam, Siemens Healthcare, Erlangen, Germany), and a medium-energy parallel-hole collimator in the case of ^{123}I or a high-energy parallel-hole collimator for ^{131}I. Image acquisition for ^{123}I was performed using a 15% energy window centered at 159 keV with a table speed of 6 cm/min for whole-body images and 5-minute acquisition for static views. For ^{131}I images, a 15% energy window centered at 364 keV was used with a table speed of 4 cm/min for whole-body images and 10-minute acquisition for static views. Whole-body images were displayed using a 1024 × 256 computer matrix, and static spot views were displayed using a 256 × 256 computer matrix.

The scans were read independently in unblinded manner as part of routine patient care by 2 nuclear medicine specialists trained North America (M.T. and A.A.). However, the readers were not aware of whether the scans were rhTSH-aided or THW aided. We opted not to include a fully blinded rereading in the present analysis because we sought to assess the diagnostic value of rhTSH-aided ^{123}I DxWBS in everyday practice.

Other Diagnostic Tests

We performed stimulated serum Tg/Tg autoantibody testing 72 hours after the second (last) rhTSH injection. Neck US was a routine follow-up examination and, consequently, was performed in almost all cases. F-18-FDG PET/CT and chest CT scans were performed as clinically indicated.

Tg concentrations in serum samples were measured by chemiluminescent immunometric assay (Immulite, Siemens Healthcare, Erlangen, Germany) with a lower limit of detection of 0.2 μg/L. The same serum samples were screened for Tg autoantibodies using a solid-phase, 2-step, chemiluminescent enzyme immunometric assay (Immulite, Siemens Healthcare) with a calibration range up to 3000 IU/mL and a normal level up to 115 IU/mL. High-resolution US examinations were performed by experienced radiologists with a special expertise in thyroid US using an HDI 5000 machine (Philips Healthcare, Best, The Netherlands) with a high-frequency (10–12 MHz) flat probe. Neck lymph nodes were considered suspicious for disease if they had one or more of a round or irregular shape, a cystic component, calcifications, no hilus visibility or central hypervascularization. Suspicious findings on US were further assessed by fine-needle aspiration biopsy if feasible and followed up with serial US to ascertain their progression, stability, or regression.

For FDG PET/CT scans, dual-modality imaging was performed with a Discovery PET/CT system (GE Healthcare, Waukesha, WI). In all patients, 330 MBq of FDG was administered 30 to 60 minutes before the PET/CT examination. Blood sugar was measured before FDG injection and had to be <8 mmol/L for PET scanning to be carried out.

Interpretation of Scans and Other Diagnostic Findings

DxWBS scans were interpreted qualitatively. The scans were considered positive if they showed an abnormally located focal activity and were considered negative if only normal physiological uptake was present. Scans were defined as false positive when abnormal uptake was seen in the absence of additional evidence of disease on other diagnostic modalities according to the criteria described later in the text. Scans were defined as false negative when they showed no abnormal uptake despite evidence of disease on other diagnostic modalities.

TABLE 1. Selected Patients' Characteristics by Type of Isotope Used

Characteristics, % (n) Unless Otherwise Stated	^{123}I DxWBS (n = 67)	^{131}I DxWBS (n = 38)	*P*
Age, y	49.2 ± 13.5	49.7 ± 15.3	0.88
Gender, female	76.1% (51)	50.0% (19)	0.01
Primary tumor size, largest diameter, cm	2.6 ± 2.0	3.0 ± 2.0	0.32
Extrathyroidal extension	46.3% (31)	60.5% (23)	0.22
N1 disease at diagnosis	52.2% (35)	59.4% (19)	0.84
M1 disease at diagnosis	9.0% (6)	7.9% (3)	1.00
High tumor stage: AJCC/UICC stage III or IV	28.4% (19)	36.8% (14)	0.39
Years since DTC diagnosis, median (range)	5.7 (0.12–23.16)	7.6 (0.37–24.5)	0.74
Patients receiving additional therapeutic ^{131}I after initial ablation but before study DxWBS	23.9% (16)	34.2% (13)	0.27
Cumulative ^{131}I activity, mCi (GBq)	250.0 ± 168 (n = 16)	221.0 ± 97.5 (n = 13)	0.88

AJCC indicates American Joint Committee on Cancer; DTC, differentiated thyroid cancer; DxWBS, diagnostic whole-body scintigraphy; M1, distant metastasis-positive disease; N1, node-positive disease; UICC, Union Internationale Contre le Cancer.

TABLE 2. Sites of Pathological Uptake in 67 rhTSH-Stimulated ^{123}I DxWBS and 38 rhTSH-Stimulated ^{131}I DxWBS Scans

	^{123}I DxWBS n (%)	^{131}I DxWBS n (%)
None (negative)	60 (89.6%)	33 (86.8%)
Thyroid bed	4 (6.0%)	2 (5.3%)
Cervical lymph nodes	1 (1.5%)	0
Lungs	1 (1.5%)	0
Lungs and cervical lymph nodes	0	1 (2.6%)
Bone	1 (1.5%)	2 (5.3%)
Total	67 (100%)	38 (100%)

DxWBS indicates diagnostic whole-body scintigraphy; ^{123}I, iodine-123; ^{131}I, iodine-131; rhTSH, recombinant human thyroid-stimulating hormone.

For comparing ^{123}I DxWBS findings with DTC status according to other diagnostic modalities, disease was considered to be present based on stimulated serum Tg concentration ≥ 1 μg/L in the absence of Tg autoantibodies with or without positive FDG PET/CT or chest CT or presence of biopsy-proven DTC. Disease was otherwise considered to be absent.

Disease was classified as persistent if Tg concentration was ≥ 1 μg/L with or without imaging evidence of disease in the neck region, but not at distant sites. Disease was classified as distantly metastatic if pathologic lesions were visualized outside the neck region.

Statistical Analysis

Results are expressed as mean $\pm$ standard deviation or median and range (minimum to maximum) for numerical values and as numbers and percentages for categorical data. The *t* test and Wilcoxon rank sum test were used to compare numerical variables and the χ^2 test or the Fisher exact test was used to compare categorical variables. $P < 0.05$ was considered significant.

RESULTS

rhTSH-Stimulated ^{123}I DxWBS Findings

Table 2 summarizes the sites of uptake of the rhTSH-aided ^{123}I DxWBS scans. Overall, 60 of these 67 scans were negative (89.5%), and 7 scans (11.5%) showed uptake. A representative example of ^{123}I scans with distant uptake is depicted in Figure 1. Selected characteristics of the patients with positive rhTSH-aided ^{123}I DxWBS scans are noted in Table 3.

rhTSH-Aided ^{123}I DxWBS Findings Versus Disease Status by Other Diagnostic Modalities

Table 4 describes the rhTSH-aided ^{123}I DxWBS and other diagnostic findings, and Table 5 summarizes the comparison between the ^{123}I scan findings and the disease status according to the "gold standard" of concurrent stimulated serum Tg testing, and, when performed, one or more of neck US, FDG PET/CT, or chest CT. Of the 67 patients undergoing rhTSH-aided ^{123}I DxWBS, 50 (74.6%) were classified as in remission according to the "gold standard," 11 (16.4%) were classified as having persistent disease, and 6 (9.0%) were classified as having distant metastatic disease (Table 5). Among the 50 cases in remission, the scans were true negative in 49 cases (98.0%) and false positive in 1 (2.0%). Among the 11 cases with persistent disease, 8 scans (72.7%) were false negative and 3 (27.3%) were true positive. Among the 6 cases with distant metastatic disease, 3 (50.0%) were false negative and 3 (50.0%) were true positive.

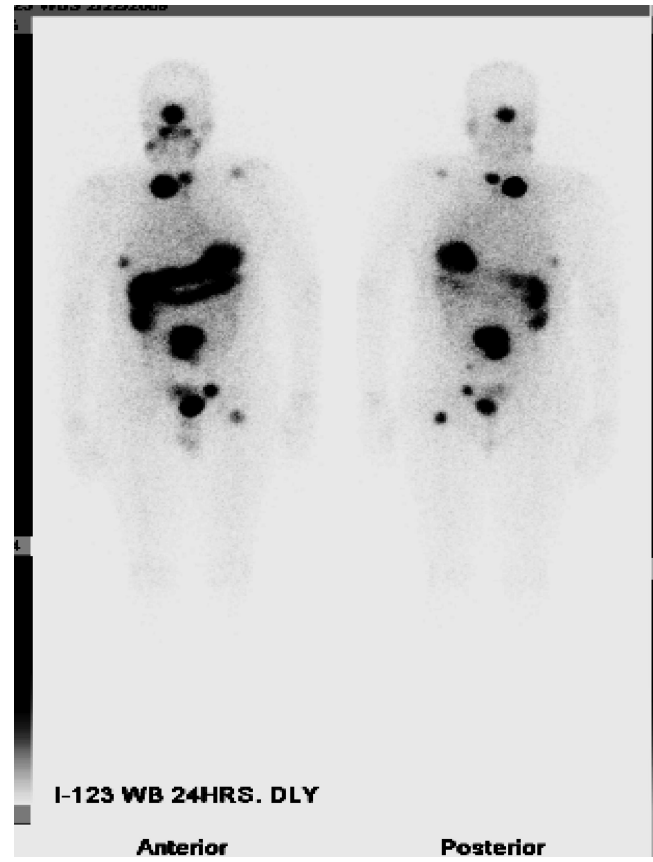

FIGURE 1. rhTSH-stimulated ^{123}I DxWBS scan in a 49-year-old man (case number 7, Table 3) showing abnormal uptake consistent with widespread skeletal metastases involving the skull, T2 vertebral pedicle, third right rib (with soft-tissue component seen on corresponding CT scan), left seventh rib, dorsal spine, left shoulder, lumbar spine, sacrum, and proximal left femur.

Overall, of 17 total patients considered to have disease, 6 (35.3%) had true-positive rhTSH-aided ^{123}I DxWBS scans. Thus, in our entire series (N = 67), rhTSH-aided ^{123}I DxWBS showed 35.3% sensitivity, 98.0% specificity, 85.7% positive predictive value, and 81.6% negative predictive value.

rhTSH-Stimulated ^{123}I DxWBS Versus rhTSH-Stimulated ^{131}I DxWBS

Table 2 reports the sites of uptake and Table 4 summarizes diagnostic findings in 38 patients who underwent rhTSH-aided ^{131}I DxWBS. As seen in Table 4, the rate of DxWBS positivity, distribution of Tg values, rate of suspicious neck US, and rates of positive PET/CT scans or chest CT scans did not statistically differ between the ^{131}I and ^{123}I subgroups. However, the ^{131}I subgroup had a significantly higher rate of detection of persistent/metastatic disease by the non-DxWBS modalities in conjunction (the overall "gold standard").

Despite the apparently more "diagnostic target-rich environment" in the ^{131}I subgroup, the ability of the DxWBS to detect real disease was higher for ^{123}I scans compared with ^{131}I scans. The difference did not, however, reach statistical significance.

TABLE 3. Selected Characteristics at the Time of the Scan in 7 Patients With DTC With Positive rhTSH-Stimulated ^{123}I DxWBS

Number	Age, y	Sex	Ablative Activity, mCi (GBq)	Cumulative Activity, mCi (GBq)	Free T_4, pmol/L	TSH, mIU/L	Stimulated Tg, μg/L	Site(s) of Uptake
1*	68	F	151.7 (5.6)	151.7 (5.6)	16.8	229.4	0.1	Thyroid bed
2	75	M	29.7 (1.1)	29.7 (1.1)	24.5	184.3	1.8	Thyroid bed
3	49	F	145.0 (5.4)	145.0 (5.4)	20.4	117.5	14.8	Thyroid bed
4	63	F	162.0 (5.6)	162.0 (5.6)	20.5	192.7	25.8	Lungs
5	54	M	29.9 (1.1)	154.6 (5.7)	25.6	163.1	4.7	Thyroid bed
6	62	M	149.8 (5.5)	149.8 (5.5)	25.0	202.3	6.4	Cervical lymph nodes
7	49	M	252.6 (9.3)	663.3 (24.5)	39.4	145.1	853.0	Bone

*Case number 1 is an apparent false positive with no biochemical or radiological evidence of disease but a thyroid bed focus, probably indicating persistent remnant thyroid tissue.

DTC indicates differentiated thyroid cancer; DxWBS, diagnostic whole-body scan; F, female; M, male; rhTSH, recombinant human thyroid-stimulating hormone; T4, thyroxine; Tg, serum thyroglobulin; TSH, thyroid-stimulating hormone.

TABLE 4. Selected Diagnostic Findings by Diagnostic Group

Characteristics, %* (n) Unless Otherwise Stated	^{123}I DxWBS (n = 67)	^{131}I DxWBS (n = 38)	*P*, ^{123}I vs. ^{131}I
Positive rhTSH–stimulated DxWBS	10.4% (7)	13.2% (5)	0.75
rhTSH–aided Tg level			
Undetectable	52.2% (35)	42.1% (16)	0.69
0.2–1.0 μg/L	23.9% (16)	18.4% (7)	
1.1–10.0 μg/L	13.4% (9)	23.7% (9)	
10.1–100 μg/L	7.5% (5)	10.5% (4)	
>100 μg/L	3.0% (2)	5.3% (2)	
Suspicious neck US*†	58.5% (38)	42.9% (15)	0.15
Positive PET/CT scan*‡	66.7% (14)	41.2% (7)	0.19
Positive chest CT scan*§	22.4% (9)	35.7% (5)	0.27
Persistent/metastatic disease by Tg +/− other imaging	25.3% (17)	47.3% (18)	0.037
DxWBS detection of persistent/metastatic disease	35.3% (6/17)¶	27.8% (5/18)	1.00

*Percentages correspond to those of the entire isotope subgroup, except in the cases of positive US, FDG PET/CT, and CT, where the percentage of positive examinations is given.

†Neck US was a routine examination according to our follow-up protocol, but actually done in 65 cases (97.0%) in the ^{123}I group and 35 cases (92.1%) in the ^{131}I group.

‡FDG PET/CT scans were done in 21 cases (31.3%) in the ^{123}I group and 17 cases (44.7%) in the ^{131}I group.

§Chest CT was done in 15 cases (22.4%) in the ^{123}I group and 14 cases (36.8%) in the ^{131}I group.

¶Excludes 1 apparent false-positive ^{123}I DxWBS.

DxWBS indicates diagnostic whole-body scintigraphy; ^{123}I, iodine-123; ^{131}I, iodine-131; rhTSH, recombinant human thyroid-stimulating hormone; US, ultrasonography.

TABLE 5. rhTSH-Simulated ^{123}I DxWBS Findings Compared With the Disease Status as Assessed by All Other Testing (N = 67)

Status According to All Other Testing	Disease Absent Remission	Disease Present		Total
		Persistent	Metastatic	
Positive DxWBS	1	3	3	7
Negative DxWBS	49	8	3	60
Total	50	11	6	67

DxWBS indicates diagnostic whole-body scan; rhTSH, recombinant human thyroid-stimulating hormone.

DISCUSSION

The present analysis is, to our knowledge, just the second published study to evaluate the diagnostic value of rhTSH-aided ^{123}I DxWBS, and, indeed, joins only 7 other published studies in comparing ^{123}I DxWBS and ^{131}I planar scintigraphy.[8,9,11,12,18–20] The sole previous published study assessing the diagnostic value of rhTSH-aided DxWBS, a retrospective analysis by Anderson et al,[11] used only concurrently measured stimulated serum Tg levels as the scan comparator in all patients except the small minority with discordant results. In contrast, our comparator for every patient was disease status as determined by a "gold standard" that, in addition to stimulated Tg concentrations, included results from neck US in almost all (97.0%) cases, and not infrequently, also FDG PET/CT (31.3% of cases) or chest CT (22.4% of cases) performed around the time of the DxWBS. We defined remission very strictly and in accordance with the recent American Thyroid Association guidelines[2] as stimulated Tg level <1 μg/L in the absence of Tg autoantibodies or any other radiologic, clinical, or cytologic evidence of the disease. Additionally, our rhTSH-aided ^{131}I DxWBS scans were performed during the same period as were our rhTSH-aided ^{123}I DxWBS scans, whereas Anderson et al used these modalities sequentially (^{131}I DxWBS, then ^{123}I DxWBS).

Our main finding was that rhTSH-aided ^{123}I DxWBS appeared to have at least comparable sensitivity in the follow-up of DTC with that of the more widely used rhTSH-aided ^{131}I DxWBS: 35.3% versus 27.8% in the overall series, $P = 1.00$ (Table 4); the lack of statistical significance of the difference between these rates could have been because of the small sample size but is also likely to reflect the comparability of ^{123}I DxWBS with ^{131}I DxWBS. Reinforcing this finding was the lack of intergroup statistical differences in the DxWBS positivity rates (Table 4).

Thus, using a broader and likely more clinically relevant comparator, we extend the findings of Anderson et al,[11] who noted comparable diagnostic performance of these modalities in the form of rhTSH-stimulated DxWBS versus rhTSH-stimulated serum Tg testing concordance rates of 90% with ^{123}I versus 84% with ^{131}I.[11] Our observation of comparable sensitivity for ^{123}I versus ^{131}I WBS is in line with observations in our previous study[8] as well as the studies of Mandel et al[18] and of Urhan et al.[12] These 3 studies were performed using THW and mainly evaluated ^{123}I DxWBS against subsequent post-therapy ^{131}I WBS. The results of the present analysis and the 5 other previously published comparative studies[8,11,12,18,20] discussed earlier in the text disagree with those of Sarkar et al,[9] who found that THW-aided ^{131}I DxWBS was more

sensitive than was THW-aided ^{123}I DxWBS. However, although the Sarkar et al study was a within-patient comparison, it was quite small (N = 12). In the present analysis, the sensitivity of rhTSH-aided ^{123}I DxWBS for disease detection during follow-up (n = 67 scans), 35.3%, is in accordance with the sensitivity reported in previous studies using rhTSH-aided ^{131}I DxWBS in a similar setting, ~30%.[21,22]

The present analysis has certain limitations. For one, it does not address the issues of ^{123}I DxWBS scan timing or scan activity or the possible impact of these variables on diagnostic performance when rhTSH is used. Renal clearance is faster and hence whole-body iodine retention is shorter in euthyroid patients than in hypothyroid ones.[23] These phenomena, of course, might result in different optimal ^{123}I DxWBS scanning times and activities when rhTSH is administered than when THW is used. Based on published experience,[9,11,17,18] 24 hours after ^{123}I ingestion seems to be an appropriate scanning time with THW. For example, in a study involving 99 previously treated DTC patients given an ^{123}I diagnostic activity of 1.5 mCi (56 MBq), Shankar et al noted that although 73% of ^{123}I images acquired at 5 hours and 24 hours were concordant, 24-hour scans showed more foci in 20% of cases or confirmed lesions found to be equivocal in the 5-hour scan in 5% of cases.[16] Of interest, however, using THW stimulation of activities ranging from 2.45 to ~5.4 mCi (92.5–200 MBq), Gerard and Cavalieri performed scanning 48 hours as well as 6 hours and 24 hours after ^{123}I administration in 10 cases. Of the 48-hour scans, 8 provided acceptable images with better lesion identification than was observed in the scintigraphs acquired at the earlier times.[20]

To date, only a single case report addressed rhTSH-aided ^{123}I DxWBS scan timing.[17] In that publication, involving a 34-year-old woman undergoing rhTSH-aided ^{123}I DxWBS before remnant ablation at 6 months after total thyroidectomy for multifocal papillary DTC, Yan et al noticed that a 4-hour scan was negative but a 24-hour scan revealed thyroid bed uptake. Based on this finding, these investigators suggested that 24 hours probably is also the appropriate scanning time when using ^{123}I for rhTSH-aided DxWBS. However, further studies with different scanning times are appropriate to address this issue.

With respect to the ^{123}I activity for rhTSH-aided DxWBS, in this series, we used 5 to 10 mCi (185–370 MBq), a relatively high range of activity compared with those used in most other published comparative studies of ^{123}I versus ^{131}I scintigraphy (1.3–5 mCi/46–185 MBq).[9,11,12,18,20] We chose our activities for rhTSH-aided ^{123}I DxWBS empirically, based on 2 considerations. First, in our previous study of THW-aided ^{123}I DxWBS, published some 5 years before our first rhTSH-aided DxWBS, we observed that a 5 mCi (185 MBq) activity was associated with a similar rate of concordance with post-therapy ^{131}I WBS findings as were 10 to 15 mCi (370–555 MBq) activities.[8] Second, although there is no significant difference between ^{123}I and ^{131}I kinetics after rhTSH administration, it seemed logical for at least some scans to use an activity higher than 5 mCi to mitigate the potential reduction in circulating radioiodine because of the faster iodine excretion in the euthyroid state.[23]

Although we did not perform scanning beyond 24 hours, it is worth noting that a case report and critical review of previous ^{123}I DxWBS studies by Klein et al suggests that a diagnostic activity of 10 mCi (370 MBq) ^{123}I may allow scanning at 48 hours and improve the target to nontarget count ratios.[24] These investigators' observations in a patient undergoing THW suggested the value of using higher diagnostic activities of ^{123}I, which allowed delayed and better-quality imaging. Klein et al also highlighted the shortcomings of previous studies comparing ^{123}I with ^{131}I for diagnostic imaging, including use of low diagnostic activities of ^{123}I and comparison with higher diagnostic activities of ^{131}I with delayed images and lack of technical details in many studies.[24] These authors suggested that ^{123}I is "at least as accurate" in diagnostic whole-body imaging as is ^{131}I.[24] It also should be noted, however, that where ^{123}I must be commercially obtained, acquisition cost considerations might limit the size of DxWBS activities, as might the small capacity of capsules for this isotope.[9] Indeed, the high cost of ^{123}I and unavailability of activities in the 10 mCi range likely have hindered the widespread use of DxWBS with this isotope. Nonetheless, ^{123}I activity size for rhTSH-aided DxWBS also deserves further study.

Additional limitations of the present analysis were its retrospective nature and its lack of within-patient comparison between rhTSH-aided ^{123}I and rhTSH-aided ^{131}I DxWBS scans. However, although our study was not prospective, the 2 subgroups did not statistically differ in any tested characteristic except for a higher proportion of female patients in the ^{123}I group (Table 1), a feature that is presumably unlikely to have an effect on scanning results. With respect to within-patient comparison, this analysis was based on everyday practice experience, and subjecting patients to 2 DxWBS scans within a short period would not be practical outside a clinical trial setting; moreover, given the β radiation exposure and potential stunning effect associated with ^{131}I DxWBS, such a setup could pose ethical challenges. Notwithstanding these logistical and ethical issues, there is a need for a well-designed prospective study in which the same group of patients undergoes rhTSH-aided ^{123}I DxWBS followed by rhTSH-aided ^{131}I DxWBS for comparison. Finally, the aim of any diagnostic test is to define cases with disease and rule out those without disease. Therefore, any scanning agent or technique should be evaluated against the best available tests that accurately define disease status. In DTC, these tests include stimulated Tg testing, neck US, and other imaging studies, the main comparators used in this analysis.

Also worth noting is that the present analysis addresses the diagnostic utility of rhTSH-aided ^{123}I DxWBS in follow-up after initial treatment for DTC. The utility of this modality in the pre-remnant ablation setting may be different and merits study.

In summary, in follow-up of patients with DTC who have completed initial treatment, diagnostic scanning using rhTSH preparation and ^{123}I isotope seems to offer at least comparable diagnostic performance with that of the currently commonly used technique of rhTSH-stimulated ^{131}I DxWBS. Indeed, our study and the previously published work on the use of ^{123}I in the diagnostic evaluation of patients with DTC suggest that ^{123}I is probably a better isotope for this indication, whether it is done after THW or with the aid of rhTSH. Further studies should seek to optimize the scan timing and radioiodine activity for rhTSH-aided ^{123}I DxWBS and prospectively compare rhTSH-aided ^{123}I DxWBS with rhTSH-aided ^{131}I DxWBS.

ACKNOWLEDGMENTS

Editorial assistance on the manuscript was provided by Robert J. Marlowe, Spencer-Fontayne Corporation, Jersey City, NJ, USA. His work was financially supported by Genzyme Corporation, the rhTSH manufacturer. The authors thank the patients, colleagues, and staff in the Endocrine Clinics and Nuclear Medicine Section.

REFERENCES

1. Jemal A, Siegel R, Xu J, et al. Cancer statistics, 2010. *CA Cancer J Clin*. 2010;60:277–300.
2. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167–1214.
3. Mazzaferri EL, Robbins RJ, Spencer CA, et al. A consensus report of the role of serum thyroglobulin as a monitoring method for low-risk patients with papillary thyroid carcinoma. *J Clin Endocrinol Metab*. 2003;88:1433–1441.
4. Schlumberger M, Berg G, Cohen O, et al. Follow-up of low-risk patients with differentiated thyroid carcinoma: a European perspective. *Eur J Endocrinol*. 2004;150:105–112.

5. Haugen BR, Cooper DS, Emerson CH, et al. Expanding indications for recombinant human TSH in thyroid cancer. *Thyroid*. 2008;18:687–694.
6. Ladenson PW, Braverman LE, Mazzaferri EL, et al. Comparison of administration of recombinant human thyrotropin with withdrawal of thyroid hormone for radioactive iodine scanning in patients with thyroid carcinoma. *N Engl J Med*. 1997;337:888–896.
7. Haugen BR, Pacini F, Reiners C, et al. A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab*. 1999;84:3877–3885.
8. Alzahrani AS, Bakheet S, Al Mandil M, et al. 123I isotope as a diagnostic agent in the follow-up of patients with differentiated thyroid cancer: comparison with post 131I therapy whole body scanning. *J Clin Endocrinol Metab*. 2001;86:5294–5300.
9. Sarkar SD, Kalapparambath TP, Palestro CJ. Comparison of (123)I and (131)I for whole-body imaging in thyroid cancer. *J Nucl Med*. 2002;43:632–634.
10. Siddiqi A, Foley RR, Britton KE, et al. The role of 123I-diagnostic imaging in the follow-up of patients with differentiated thyroid carcinoma as compared to 131I-scanning: avoidance of negative therapeutic uptake due to stunning. *Clin Endocrinol (Oxf)*. 2001;55:515–521.
11. Anderson GS, Fish S, Nakhoda K, et al. Comparison of I-123 and I-131 for whole-body imaging after stimulation by recombinant human thyrotropin: a preliminary report. *Clin Nucl Med*. 2003;28:93–96.
12. Urhan M, Dadparvar S, Mavi A, et al. Iodine-123 as a diagnostic imaging agent in differentiated thyroid carcinoma: a comparison with iodine-131 post-treatment scanning and serum thyroglobulin measurement. *Eur J Nucl Med Mol Imaging*. 2007;34:1012–1017.
13. Medvedec M. Thyroid stunning in vivo and in vitro. *Nucl Med Commun*. 2005;26:731–735.
14. Lassmann M, Luster M, Hanscheid H, et al. Impact of 131I diagnostic activities on the biokinetics of thyroid remnants. *J Nucl Med*. 2004;45:619–625.
15. Verburg FA, Verkooijen RB, Stokkel MP, et al. The success of 131I ablation in thyroid cancer patients is significantly reduced after a diagnostic activity of 40 MBq 131I. *Nuklearmedizin*. 2009;48:138–142; quiz N119–N120.
16. Shankar LK, Yamamoto AJ, Alavi MD, et al. Comparison of 123I scintigraphy at 5 and 24 hours in patients with differentiated thyroid cancer. *J Nucl Med*. 2002;43:72–76.
17. Yan W, Roach PJ, Bautovich GJ, et al. Timing of iodine-123 scintigraphy following use of recombinant human thyrotropin in differentiated thyroid carcinoma. *Clin Nucl Med*. 2007;32:375–377.
18. Mandel SJ, Shankar LK, Benard F, et al. Superiority of iodine-123 compared with iodine-131 scanning for thyroid remnants in patients with differentiated thyroid cancer. *Clin Nucl Med*. 2001;26:6–9.
19. Thomas DL, Menda Y, Bushnell D. A comparison between diagnostic I-123 and posttherapy I-131 scans in the detection of remnant and locoregional thyroid disease. *Clin Nucl Med*. 2009;34:745–748.
20. Gerard SK, Cavalieri RR. I-123 diagnostic thyroid tumor whole-body scanning with imaging at 6, 24, and 48 hours. *Clin Nucl Med*. 2002;27:1–8.
21. Pacini F, Molinaro E, Castagna MG, et al. Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in monitoring differentiated thyroid carcinoma. *J Clin Endocrinol Metab*. 2003;88:3668–3673.
22. Torlontano M, Crocetti U, Augello G, et al. Comparative evaluation of recombinant human thyrotropin-stimulated thyroglobulin levels, 131I whole-body scintigraphy, and neck ultrasonography in the follow-up of patients with papillary thyroid microcarcinoma who have not undergone radioiodine therapy. *J Clin Endocrinol Metab*. 2006;91:60–63.
23. Taieb D, Sebag F, Farman-Ara B, et al. Iodine biokinetics and radioiodine exposure after recombinant human thyrotropin-assisted remnant ablation in comparison with thyroid hormone withdrawal. *J Clin Endocrinol Metab*. 2010;95:3283–3290.
24. Klein HA, DiSibio KJ, Sims D, et al. I-123 whole body scanning: case report and discussion. *Clin Nucl Med*. 2005;30:312–316.