Preablation 131-I Scans With SPECT/CT in Postoperative Thyroid Cancer Patients: What Is the Impact on Staging?

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Context: The utility of preablation radioiodine scans for the management of differentiated thyroid cancer remains controversial.

Objective: To determine the contribution of preablation Iodine 131 (131-I) planar with single-photon emission computed tomography/computed tomography (SPECT/CT; diagnostic [Dx] scans) to differentiated thyroid cancer staging.

Design: Prospective sequential series at university clinic.

Methods: Using American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) staging, seventh edition 320 patients post–total thyroidectomy were initially staged based on clinical and pathology data (pTN) and then restaged after imaging (TNM). The impact of Dx scans with SPECT/CT on N and M scores, and TNM stage, was assessed in younger, age $<$45 years, n = 138 (43%), and older, age $\geq$45 years, n = 182 (57%) patients, with subgroup analysis for T1a and T1b tumors.

Results: In younger patients Dx scans detected distant metastases in 5 of 138 patients (4%), and nodal metastases in 61 of 138 patients (44%), including unsuspected nodal metastases in 24 of 63 (38%) patients initially assigned pathologic (p) N0 or pNx. In older patients distant metastases were detected in 18 of 182 patients (10%), and nodal metastases in 51 of 182 patients (28%), including unsuspected nodal metastases in 26 of 108 (24%) patients initially assigned pN0 or pNx. Dx scans detected distant metastases in 2 of 49 (4%) T1a, and 3 of 67 (4.5%) T1b patients.

Conclusions: Dx scans detected regional metastases in 35% of patients, and distant metastases in 8% of patients. Information acquired with Dx scans changed staging in 4% of younger, and 25% of older patients. Preablation scans with SPECT/CT contribute to staging of thyroid cancer. Identification of regional and distant metastases prior to radioiodine therapy has significant potential to alter patient management. **(*J Clin Endocrinol Metab* 98: 1163–1171, 2013)**

The incidence of differentiated thyroid cancer (DTC) is increasing worldwide based largely on the detection of small ($\leq$2 cm) tumors, which represent 87% of newly diagnosed cases (1). Once diagnosed, staging and risk stratification are used to individualize treatment decisions and determine surveillance strategy (2, 3). As radioactive iodine remnant ablation has not demonstrated improved outcomes in low-risk patients (4, 5), selective use of radioiodine is now reserved for patients with locally advanced and/or metastatic disease (3, 6). Radioactive iodine imaging has traditionally been used to define the extent of metastatic disease: although posttherapy scans are rou-

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Abbreviations: AJCC, American Joint Committee on Cancer; DTC, differentiated thyroid cancer; Dx, diagnostic; pN0, no nodal metastases on pathology; pNx, unknown nodal metastases on pathology, pN1, nodal metastases on pathology; pTN, pathology data; Rx, therapy; SPECT/CT, single-photon emission computed tomography/computed tomography; Tg, thyroglobulin; THW, thyroid hormone withdrawal; TNM, tumor, node, metastasis; US, ultrasound; WBS, whole-body scan.

tinely performed, the contribution of preablation scans to patient management remains controversial. Authors supporting the use of preablation scintigraphy maintain that the findings on diagnostic (Dx) scans can change clinical management and guide Iodine 131 (131-I) therapy (7–10), while others who favor posttherapy (post-Rx) scans argue that studies performed after radioactive iodine remnant ablation are more sensitive for disease detection and avoid possible stunning of thyroid tissues by the preablation radioiodine dose (11–13). Imaging technology has significantly evolved over the past 10 years, making optimal coregistration of tomographic volumes of functional data obtained by gamma cameras (single-photon emission computer tomography, SPECT) with inline computed tomography (CT) possible, both imaging modalities being acquired with the patient in the same bed position. In addition, the image quality of current SPECT/CT systems is substantially superior to earlier gamma cameras: this progress has been achieved by an improvement of spatial and contrast resolution of modern SPECT/CT cameras, and application of scatter rejection, iterative reconstruction, and CT-based attenuation correction algorithms for SPECT. In this context, revisiting the topic of preablation radioiodine scintigraphy and its impact on thyroid cancer staging is relevant.

We hypothesized that the use of preablation radioiodine scans with SPECT/CT (henceforth abbreviated as Dx scans throughout this article) provides incremental information regarding nodal and distant metastases and improves the postoperative DTC staging. SPECT/CT was routinely used in our clinic since 2007 as an integral part of the preablation imaging protocol of DTC patients after total thyroidectomy. The aim of our study was to determine the contribution of Dx scans to postoperative DTC staging, by quantifying the instances in which data acquired with preablation Dx 131-I scans changed the initial staging based on clinical and histopathologic information.

Materials and Methods

Patient information

The study was approved by the University of Michigan Institutional Review Board. We prospectively evaluated 320 consecutive patients (219 women; 101 men, mean age, 47.3 ± 16.4 y, range, 10–90) with DTC (289 papillary, 22 follicular, and 9 Hurthle cell) referred to our clinic between April 2007 and April 2011 for consideration of postoperative 131-I therapy, based on surgical pathology information revealing histopathologic risk factors indicative of possible increase in tumor biologic aggressiveness. All patients underwent preablation 131-I planar and SPECT/CT imaging per routine clinical protocol at our institution. Patient demographics are summarized in Table 1. Inclusion criteria for study were as follows: patients with DTC after total or near-total thyroidectomy, preparation with a low-iodine diet for 2 weeks, and thyroid hormone withdrawal (THW) before radioiodine imaging (after surgery patients either underwent levothyroxine deprivation for 4 weeks or were treated with triiodothyronine for 4 wk, which was subsequently discontinued for 2 wk prior to Dx scan). A group of 15 patients with TSH <30 mU/L was not excluded from the analysis because Dx scans provided information for determining management, as follows:

Table 1. Patient (n = 320) Demographics, Tumor Histology, and Laboratory Results

Characteristics	Number of Patients (%)
Age: 47 ± 16 y, 10–90[a]	
<45	138 (43)
≥45	182 (57)
Gender	
Female	219 (68)
Male	101 (32)
Tumor subtypes	
Papillary	289 (90)
Follicular	22 (7)
Hürthle cell variant	9 (3)
High-risk features	
Classic PTC	190 (59)
Follicular variant of PTC	51 (16)
Tall cell	26 (8)
Columnar	2 (1)
Cystic	7 (2)
Sclerosing	1 (<1)
Squamoid	6 (2)
Insular	4 (1)
Anaplastic component	2 (1)
Histology	
Size: 2.4 ± 1.8 cm, 0.1–12[a]	
Laterality	
Right	129 (40)
Left	95 (30)
Bilateral	84 (26)
Others[b]	12 (4)
Multifocality, yes	144 (45)
Vascular invasion, present	96 (30)
Capsular invasion, present	202 (63)
Extrathyroidal extension, yes	116 (36)
Surgical margins	
Positive	82 (26)
Negative	230 (72)
Unknown	8 (2)
Neck nodal metastases, present[c]	149 (47)
Laboratory results	
TSH	
<30 mIU/L	15 (5)
≥30 mIU/L	305 (95)
Thyroglobulin	
<0.5 ng/mL	74 (23)
0.5 to <2.0 ng/mL	47 (15)
2.0 to <10 ng/mL	102 (32)
10 to <100 ng/mL	66 (21)
100 to <1000 ng/mL	22 (7)
≥1000 ng/mL	9 (3)
Anti-Tg antibodies, present	50 (16)

[a] Presented as mean ± SD (range).

[b] No primary tumor, ectopic, isthmus, thyroglossal cyst.

[c] Before diagnostic imaging (ie, pN1).

functional metastatic disease in 5 patients, large thyroid remnant in 5 patients; 1 patient with partial pituitary insufficiency (TSH 28 mU/L) due to remote cranial radiotherapy; 4 patients prepared with recombinant human thyroid-stimulating hormone (rhTSH; Thyrogen). Exclusion criteria included positive pregnancy test and recent (<6 wk) history of stable iodine exposure (eg, radiographic contrast, kelp, amiodarone). TSH, free T_4, thyroglobulin (Tg), and antithyroglobulin antibodies were obtained in all patients and confirmation of negative serum β-human chorionic gonadotropin status was obtained for women of childbearing age.

Imaging protocol

Planar whole-body scan (WBS) and static neck and chest images were acquired in anterior and posterior projections at 24 hours after oral administration of 37 MBq (1 mCi) 131-I. Our laboratory implemented a standard 1 mCi 131-I dose for preablation scintigraphy since December 1995. This was based on quantitative measurements of fractional concentrations of diagnostic and therapeutic 131-I doses in thyroid tissues performed in our clinic, demonstrating good information density with 1 mCi 131-I dose without evidence for impairment of effectiveness of subsequent 131-I treatment (11). Before the implementation of SPECT/CT, we routinely obtained dual-time (24 and 48 h) planar scans, although 48-hour images only rarely portrayed additional activity foci. Due to an increased target-to-background ratio, the 48-hour scans were used to confirm equivocal foci seen on 24-hour images, or to exclude contamination or physiologic mimics of disease. However, attenuation correction and anatomic colocalization with SPECT/CT obviated the need for 48-hour imaging.

123-I is not routinely used in our standard clinical protocol due to the higher cost, the large number of capsules required for an adequate diagnostic dose, and the short physical half-life (which increases the complexity of dosimetry calculations). In addition to these factors, the absence of evidence for stunning with low (2–5 mCi) diagnostic 131-I activities, and when 131-I therapy is administered within 72 hours of the diagnostic 131-I dose (14–17) contributed to our decision to use routinely 131-I for preablation scintigraphy.

All patients underwent routine SPECT/CT imaging with an axial field-of-view extending from the skull base to the diaphragm; the patients were imaged with their arms down without immobilizers. In addition, all foci of abnormal activity seen on planar studies outside the neck and chest were evaluated with SPECT/CT; the arms were raised for SPECT/CT of the abdomen and pelvis.

Imaging was performed on a hybrid dual-head gamma camera with an inline CT scanner (Symbia T6; Siemens Medical Solutions, Hoffman Estates, Illinois) equipped with parallel-hole, high-energy collimators, using a 20% energy window set at 364 keV. The table speed for the whole-body images was 5 cm/s. Static images were acquired for 20 minutes using a 256 × 256 matrix; this protocol produces the same information density as acquisitions for 10 minutes following 74 MBq of 131-I. SPECT images were acquired in 64 projections (20 s per stop) with a noncircular orbit greater than 360 degrees using a 128 × 128 matrix. Tomographic images were reconstructed using 3-dimensional ordered subsets expectation maximization (OSEM) iterative reconstruction (8 iterations, 4 subsets) and a CT-based attenuation correction algorithm was applied. CT imaging parameters were as follows: 130 kVp, 80 mAs, 3-mm collimation, and 0.8 pitch. CT reconstruction was performed at 5-mm slice thickness into a 512 × 512 matrix. In patients receiving 131-I treatment, post-Rx WBS and static neck and chest images were obtained at 2 days posttherapy.

In 11 patients who displayed faint uptake in the neck on planar images and received 131-I therapy due to intermediate or high histopathologic risk, SPECT/CT was performed on the post-Rx scan. This decision was based on our experience that faint foci visible on planar images may not be fully resolved on SPECT due to acquisition counting statistics: planar images are acquired for 20 minutes, whereas SPECT is acquired for 20 seconds per projection. In addition, SPECT is processed using an iterative reconstruction algorithm, which filters low counts to background level. On posttherapy scans lesions have higher count density and are resolved on SPECT.

Research plan

Before imaging, all patients were initially staged using AJCC (American Joint Committee on Cancer) TNM, seventh edition (2) based on clinical and pathology data (designated as pTN). The clinical, histopathologic, and laboratory information is summarized in Table 1. For patients who did not have central or lateral neck node dissection, the N score was designated Nx (these patients were considered clinical [c] N0 for initial staging). Distant metastatic status was based on clinical and radiologic information before surgery and noted as cM0 or cM1 for purposes of pTN staging. All patients subsequently underwent restaging incorporating the findings from Dx scans (the final staging after imaging is designated as TNM). Results of the total cohort were analyzed according to age, as follows: younger patients, age <45 years, n = 138 (43%), and older patients, age ≥45 years, n = 182 (57%). Subgroup analysis for small tumor size: T1a (size ≤1.0 cm) and T1b (size >1.0 and ≤2.0 cm), was also performed.

Dx 131-I scans were viewed by 2 experienced nuclear medicine physicians designated reader 1 (K.K.W.) and reader 2 (A.M.A.). Reader 1 was blinded, whereas reader 2 was unblinded to clinical, biochemical, and histopathology information. Both readers interpreted 131-I planar and SPECT/CT images using software that allowed side-by-side registration and display of fusion images (MedImage; MedView Pty, Canton, Michigan). Foci of radioactivity identified on planar imaging were further evaluated on SPECT/CT and classified according to their location and nature as follows: 1) remnant thyroid tissue in the surgical thyroidectomy bed or thyroglossal duct remnant; 2) local residual disease; 3) regional metastases; 4) distant metastases (with findings of diffuse pulmonary or multifocal pulmonary/osseous radioactivity considered a single focus for statistical analysis); and 5) physiologic distribution (activity seen within the nose, mouth, salivary glands, stomach, bowel, kidneys, and the urinary bladder). Consensus interpretation was obtained after review of SPECT/CT imaging by both readers when the previously blinded reader was given access to clinical, histopathology, and laboratory information.

Results

Interpretation of Dx 131-I scans

There were 688 neck foci seen on planar imaging (2.2 ± 1.1 foci per patient, range, 0–7). Agreement in scan interpretation between the 2 readers occurred in 268 of 320

Table 2. pTN Staging Components Using AJCC 7th Edition

	Staging Component	Number of Patients (%)
T1a	≤1.0 cm	49 (15)
T1b	>1.0 cm to ≤2.0 cm	67 (21)
T2	>2.0 cm to ≤4.0 cm	60 (19)
T3	>4.0 cm or mETE	109 (34)
T4a	Moderately advanced	29 (9)
T4b	Very advanced	3 (1)
Tx	No primary tumor	3 (1)
N0	Benign lymph nodes	65 (20)
N1a	Metastatic level VI nodes	87 (27)
N1b	Metastatic levels I-V, VII nodes	62 (20)
Nx	No surgical nodal specimen	106 (33)

Abbreviations: level VI, central neck compartment; levels I–V, lateral neck compartment; level VII, superior mediastinum; mETE, minimal extrathyroidal extension.

(84%) of 131-I SPECT/CT scans. Cohen's kappa scores were not calculated because the readers had different levels of information access at the time of image interpretation (blinded vs unblinded). Interpretation of imaging results without histopathologic information and thyroglobulin levels for the blinded reader led to diagnostic uncertainty for detection of local residual disease.

Comparison of initial (pTN) and final (TNM) staging after Dx scans

The initial pT and pN scores are summarized in Table 2. Regional nodal metastases (pN1) were present in surgical resection specimens in 149 of 320 patients (47%). The impact of the findings of Dx scans on final staging was analyzed according to patients' age.

Younger patients (age <45 y)

Table 3 summarizes the data on histopathology, imaging findings, and staging in the group of younger patients. Initial pTN staging classified all younger patients (n = 138) as stage I. Dx scans detected distant metastases in 5 of 138 patients (4%), restaging them to stage II, and nodal metastases in 61 of 138 patients (44%) as follows: residual postsurgery nodal metastases in 37 of 75 (49%) pN1 patients, and unsuspected nodal metastases in 24 of 63 (38%) patients initially assigned pN0 (no nodal metastases on pathology) or pNx (unknown nodal metastases on pathology).

Older patients (age ≥45 y)

Table 4 summarizes data on histopathology, imaging findings, and staging in the group of older patients. Dx scans detected distant metastases in 18 of 182 patients (10%), and nodal metastases in 51 of 182 patients (28%), as follows: residual postsurgery nodal metastases in 25 of 74 (34%) pN1 patients, and unsuspected nodal metastases in 26 of 108 (24%) patients initially assigned pN0 or pNx. Detection of lateral neck nodal metastases in patients with known nodal metastases in the central neck (pN1a, stage III) upstaged these patients to stage IV A, and detection of distant metastases upstaged patients to stage IV C. Incorporation of Dx imaging information led to disease upstaging in 46 (25%) older patients.

Subanalysis of T1 tumors

Table 5 summarizes data on histopathology and imaging findings in patients with T1 tumors. T1 tumors were present in 116 of 320 patients (36%): 49 patients (15%) with T1a (size ≤1.0 cm) and 67 patients (21%) with T1b (size >1.0 and ≤2.0 cm).

T1a tumors were associated with nodal metastases in 28 of 49 patients (57%). Dx scans detected distant metastases in 2 of 49 patients (4%) with T1a tumors, and nodal metastases in 11 of 49 patients (22%), as follows:

Table 3. Impact of Dx Scans in Younger Patients

	Younger Patients (Age <45, n = 138)						
	pTNcM	TNM*	M0	M1	No Nodes on SPECT/CT	Nodes on SPECT/CT	Total
Cervical nodal metastases							
pN0					12	8	20
pN1a					24	16	40
pN1b					14	21	35
pNx					27	16	43
Total					77	61	138
Distant metastases							
cM0			133	5			138
cM1			0	0			0
AJCC TNM staging							
Stage I	138 (100%)	133 (96%)					
Stage II	0	5 (4%)					

Abbreviations: cM, clinical M; M, distant metastatic status after scan; pN, pathology N; pTNcM, staging based on pathology and clinical information; TNM*, staging after preablation scan.

Table 4. Impact of Dx Scans in Older Patients

	Older Patients (Age ≥45, n = 182)						
	pTNcM	TNM*	M0	M1	No Nodes on SPECT/CT	Nodes on SPECT/CT	Total
Cervical nodal metastases							
pN0					38	7	45
pN1a					31	16	47
pN1b					18	9	27
pNx					44	19	63
Total					131	51	182
Distant metastases							
cM0			163	18			181
cM1			0	1			1
Total			163	19			182
AJCC TNM staging							
Stage I	47 (26%)	29 (16%)					
Stage II	23 (13%)	18 (10%)					
Stage III	66 (36%)	49 (27%)					
Stage IV A/B	45 (25%)	67 (37%)					
Stage IV C	1 (0.6%)	19 (10%)					

See abbreviations for Table 3. TNM*, staging after preablation scan.

residual postsurgery nodal metastases in 7 of 24 (29%) pN1 patients, and unsuspected nodal metastases in 4 of 25 (16%) patients initially assigned pN0 or pNx.

T1b tumors were associated with nodal metastases in 35 of 67 patients (52%). Dx scans detected distant metastases in 3 of 67 patients (4.5%) with T1b tumors, and nodal metastases in 28 of 67 patients (42%), as follows: residual postsurgery nodal metastases in 11 of 18 (61%) pN1 patients, and unsuspected nodal metastases in 17 of 49 (35%) patients initially assigned pN0 or pNx.

The presence of multifocal disease appeared to increase the risk for distant metastases for both T1a and T1b tumors— however, the small number of cases with distant metastases precluded statistical analysis.

Subanalysis of thyroglobulin levels in rapport with regional and distant metastatic status

Stimulated Tg was an imperfect marker for differentiating regional vs distant metastatic disease, and at levels <10 ng/mL, there was considerable overlap between thyroid remnant tissue and N1 status. Furthermore, the presence of anti-Tg antibodies invalidated Tg measurement in 50 patients. See Supplemental Table 1 published on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org.

Correlation of imaging findings between Dx and post-Rx radioiodine scans

In 303 patients, the number and distribution of radioiodine foci on preablation scans were compared with subsequent post-Rx scans by reviewing paired datasets of planar whole-body and static views of the neck and chest images. The remaining 17 patients, who had either a negative scan or undetectable Tg and low-risk histopathology, did not receive radioiodine therapy. The imaging findings on preablation and post-Rx planar scans were concordant in 280 of 303 patients (92%). In only 4 of 303 patients (1.3%) a relative decreased uptake in the previously detected radioactivity foci was seen on the post-Rx scan as compared to the Dx scan, likely representing an initial treatment effect of the therapeutic dose (11). There were 19 of 303 patients (6%) in whom additional foci were identified on the post-Rx 131-I scan; of these, in only

Table 5. Impact of Dx Scans for Patients With T1 Tumors

T1 Tumors (n = 116)	pN1/pN1*	N1	Total N1 (%)	cM1	M1 (%)
T1a (n = 49)	24/7*	4	28 (57)	0	2 (4)
Unifocal (n = 19)	11/2*	3	14 (74)	0	0
Multifocal (n = 30)	13/5*	1	14 (47)	0	2
T1b (n = 67)	18/11*	17	35 (52)	0	3 (4.5)
Unifocal (n = 41)	10/5*	8	18 (44)	0	1
Multifocal (n = 26)	8/6*	9	17 (65)	0	2

Abbreviations: cM1, clinical M1, patients with distant metastases prior to radioiodine imaging; M1, patients with distant metastases after imaging; N1, patients with nodal metastases seen only on SPECT/CT (initial pN0 or pNx patients); pN1, nodal metastases on histopathology; T1a, tumor ≤1.0 cm; T1b, tumor >1.0 and ≤2.0 cm; pN1*, patients with residual nodal metastases seen on SPECT/CT.

4 patients (1.4%) did posttherapy scans reveal metastatic lesions that upstaged disease status.

Discussion

Considerable progress in image quality and interpretation of radioiodine scintigraphy has been achieved by the introduction of SPECT/CT systems. Technological improvements in spatial and contrast resolution of modern gamma cameras, and scatter rejection, iterative reconstruction, and CT-based attenuation correction algorithms have made high-quality diagnostic imaging possible with tracer doses of 131-I. In addition, cross-sectional functional-anatomic imaging permits precise anatomic localization of radioiodine foci minimizing equivocal interpretations, and allowing more precise characterization of the etiology (benign vs malignant) of focal radioiodine uptake seen on WBS. Accurate staging and risk stratification are important for the management of thyroid cancer as they determine the prognosis for survival and risk of recurrence, and guide therapeutic decisions and intensity of surveillance. Prior studies using SPECT/CT applied to posttherapy 131-I WBS (18–24), and to follow-up diagnostic radioiodine scans obtained after first radioablation (25, 26), showed improved characterization of nodal (N) and distant metastatic (M) status. To our knowledge, the use of SPECT/CT imaging for completion of DTC staging has been reported in only 2 prior publications; however, the investigators analyzed only the impact on nodal staging, and after therapeutic 131-I administration (20, 22). Our study presents a new paradigm, reporting the use of Dx 131-I scans with SPECT/CT for completion of initial postoperative staging (pTN) before administration of 131-I therapy, and analyzing the impact of imaging findings on characterization of both nodal and distant metastatic status in a large group of patients.

Dx preablation 131-I scans are unlikely to underestimate the extent of metastatic disease, as demonstrated by the high concordance rate (92%) between Dx and post-Rx scans. Although additional foci were identified on post-Rx scans in 6% patients, in only 1.4% did posttherapy scans reveal metastatic lesions that upstaged disease status as compared to Dx scans. When SPECT/CT is applied to preablation WBS scans, the information obtained completes initial staging before management decisions regarding 131-I therapy are made. Identification of regional and distant metastases on preablation scans has significant potential to alter patients' management: visualization of metastatic deposits on radioiodine scans confirms their capacity to concentrate 131-I (iodine-avid disease) and therefore the potential to respond to therapeutic 131-I activity. In addition, on SPECT/CT, the size of these metastatic deposits can be measured, and for localized disease this information is essential in deciding if 131-I therapy vs surgical resection is recommended: 131-I therapy is most effective for smaller (<1.0 cm) metastatic deposits (27, 28), whereas for large metastases, surgical debulking before 131-I therapy is recommended (Figure 1, Cases A and B). Identification of distant metastases will most likely alter the prescribed 131-I activity, by either adjusting empiric "ablative" 131-I doses or performing dosimetry calculations for maximizing prescribed 131-I activity (7, 10) (Figure 1, Case C). Avoidance of unnecessary 131-I therapy is equally important for patients in whom residual and/or metastatic disease has been excluded (29). SPECT/CT radioiodine studies should always be interpreted in the context of the surgical pathology report, which clarifies the presence or absence of tumor invasion into local structures and completion of surgical resection. These elements are of critical importance to interpret the significance of paratracheal central neck activity as benign thyroid remnant vs residual disease.

The results of our study demonstrate that preablation radioiodine imaging with SPECT/CT detected regional metastases in 35% and distant metastases in 8% of patients. When the patients' age at presentation was factored into analysis, these imaging findings translated into a change in AJCC staging in 4% of younger patients and 25% of older patients. In patients for whom 131-I therapy is considered based on histopathologic prognostic factors, preablation 131-I scintigraphy can detect metastases in normal-size cervical lymph nodes (which may not appear suspicious on postoperative neck ultrasonography), can identify pulmonary micrometastases (which are too small to be detected on routine chest x ray and may remain undetected on CT), and can diagnose bone metastases at an early stage before cortical disruption is identified on bone x rays. The benefits of obtaining this information at an early postoperative time point in the disease process are not negligible: because 131-I therapy is most effective for smaller metastatic deposits (27, 28), early identification of regional and distant metastases is important for successful therapy.

Beyond the impact on staging, the utility of a diagnostic imaging study is defined by its impact on management. Although identification of regional metastases in younger patients does not change staging, it can impact management decisions, such as referral for resection of large residual metastatic deposits, or the decision for 131-I therapy for elimination of small metastatic foci. In our study, nodal metastases were seen on 131-I SPECT/CT in 61 of 138 younger patients (44%) and 51 of 182 older patients (28%), by either identification of unsuspected (in pN0 or

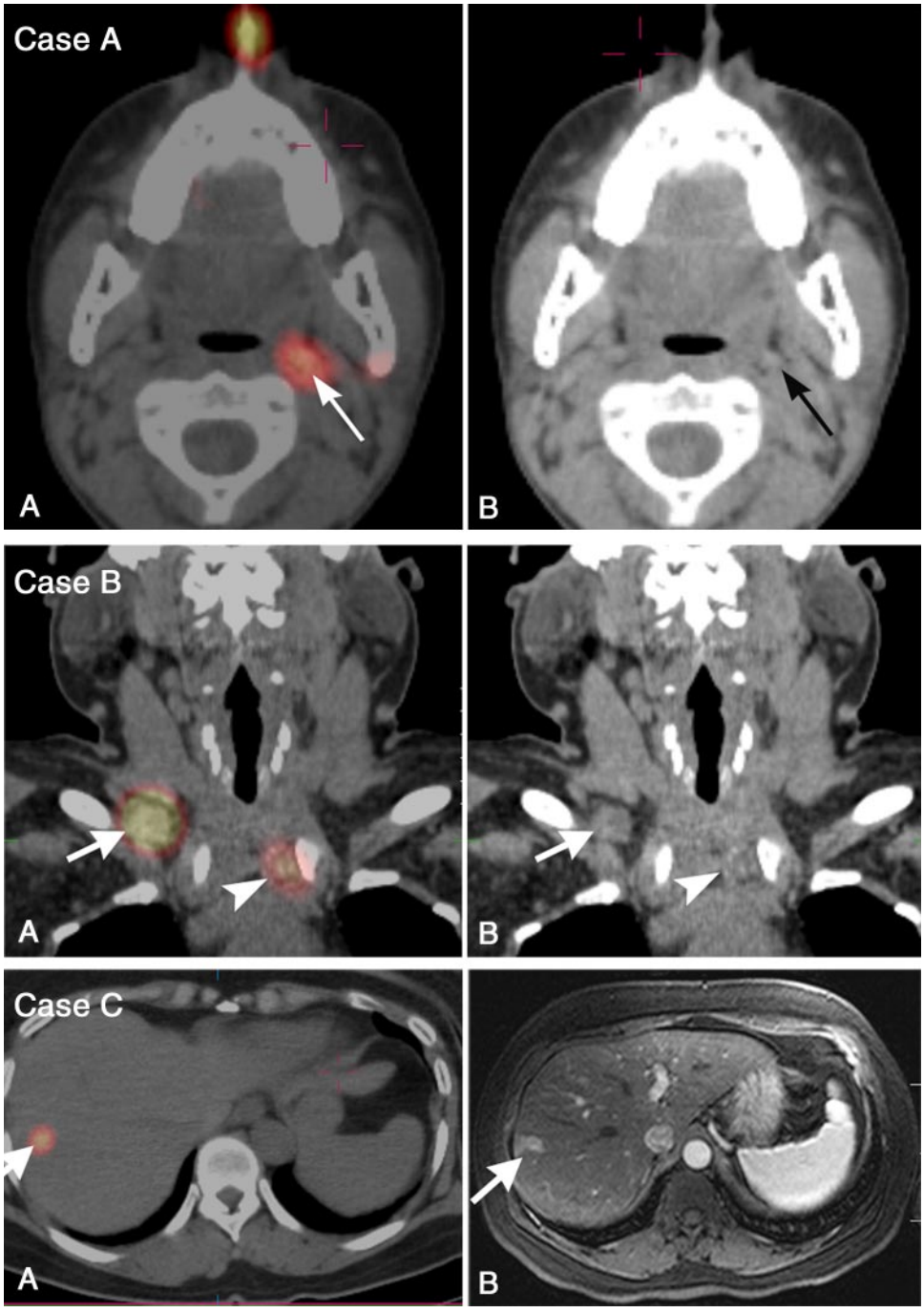

Figure 1. Case A: Diagnostic I-131 fused SPECT/CT (A) and CT (B) in a 14-year-old girl with multifocal microcarcinoma (0.8-cm and 0.4-cm papillary thyroid cancer) with extensive intrathyroidal angiolymphatic invasion, focal capsular invasion, and bilateral lymph node metastases, 13+/20 nodes resected; pT1a, N1b, M0, stage I. SPECT/CT revealed residual metastatic deposit in a 0.5-cm retropharyngeal lymph node located posterior to the left internal carotid artery (arrow). Follow-up scintigraphy at 6 months after administration of 1.85 MBq (50 mCi) 131-I demonstrated lesion resolution and no evidence of persistent or recurrent disease. Case B: Diagnostic I-131 fused SPECT/CT (A) and CT (B) in a 54-year-old woman with multifocal papillary thyroid carcinoma (largest focus 1.6 cm), confined to the thyroid, margins free; pT1b, Nx, M0, stage I. SPECT/CT revealed metastatic deposits corresponding to 1.7-cm right retroclavicular node (arrow) and 0.8-cm node at the thoracic inlet (arrowhead); pT1b, N1b, M0, stage IV A. Considering the volume of the larger metastatic deposit, the patient was referred for surgical resection prior to 131-I therapy. Case C: Diagnostic I-131 fused SPECT/CT (A) and magnetic resonance imaging (B) in a 56-year-old woman with 1.2-cm papillary thyroid cancer without capsular invasion, no extrathyroidal extension, and negative surgical margins; 0/3 central nodes resected; pT1b, N0, M0, stage I. SPECT/CT revealed focal activity in the liver (arrow) corresponding on magnetic resonance imaging to a 0.8-cm arterially enhancing lesion, consistent with hepatic metastasis; restaging: pT1b, N0, M1, stage IV C. Follow-up scintigraphy at 6 months after administration of 7.4 MBq (200 mCi) 131-I demonstrated lesion resolution and no evidence of persistent or recurrent disease.

pNx patients) or detection of residual nodal metastases after surgery (in pN1 patients). Although some studies showed that nodal status bears no effect on prognosis in younger patients (30), others have demonstrated a statistical association between nodal disease and survival for both younger and older patients (31–34). In addition, the presence of regional nodal metastases is associated with increased risk for recurrent disease (35, 36). Individualized therapy aimed at minimizing recurrence risk in both younger and older patients must be considered because statistical analysis revealed that the risk of dying from DTC significantly increases in the presence of local-regional disease recurrence (37).

In our study the initial staging was based on clinical and histopathology information available after surgery and did not include postoperative neck ultrasound (US) performed at the same time with Dx scans. Referral to our clinic for radioiodine imaging and therapy was based on intermediate-risk and high-risk histologic features. The iodine avidity of metastatic deposits was determined on SPECT, whereas the CT component of SPECT/CT was used to determine the location and size of metastatic lesions. Therefore, proceeding with a preablation scan with SPECT/CT may lead to cost savings and streamlined management decisions in this patient population. Neck US is very sensitive, yet nonspecific, for identification of metastatic lesions, and detection of enlarged or suspicious cervical lymph nodes is followed by US-guided biopsy and thyroglobulin measurement in the fluid aspirate for definitive diagnosis.

In our study only 4 patients underwent preparation by rhTSH, and in view of reported differences in metastatic lesion detection with stimulation by rhTSH vs THW (38–40), the results of our study cannot be extrapolated to diagnostic radioiodine imaging obtained after rhTSH preparation. At the time of this investigation, rhTSH has not been approved for the treatment of residual and/or metastatic thyroid cancer, and the use of THW stimulation protocol for the majority of patients in our study was based on the higher perceived risk of residual or metastatic thyroid cancer in the patients referred to our clinic, based on histologic prognostic factors.

Our study has several limitations. A referral bias inherent in our study may influence detection rates of metastatic disease with radioiodine SPECT/CT; most importantly for patients with small tumors, patients with higher perceived histopathologic risk (as reflected by higher rates of capsular invasion, multifocality, and extrathyroidal extension in our study group) have been preferentially referred for radioiodine imaging and therapy. The other potential limitation is that although information obtained with diagnostic 131-I SPECT/CT led to changes in staging and management, this may not directly translate to a more favorable outcome. In a slowly growing malignancy such as DTC, assessing the outcome of therapeutic interventions requires prolonged follow-up.

Conclusions

In our series of 320 consecutive postthyroidectomy patients, diagnostic preablation 131-I SPECT/CT detected regional metastases in 35% and distant metastases in 8% of patients, leading to upstaging of disease in 4% of younger and 25% of older patients. Diagnostic radioiodine imaging with SPECT/CT provides an important contribution to staging. Identification of regional and distant metastases prior to radioiodine therapy has significant potential to alter patient management. Our results support the view that integration of clinical, pathologic, and imaging information can be used to create an individualized treatment plan for DTC patients.

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