

# Impact of Postoperative Diagnostic <sup>131</sup>I Whole Body Scan with SPECT-CT on Staging, Risk Stratification and Radioiodine Therapy Planning in Low risk Differentiated Thyroid Cancer

Teeyasoontranan W, MD<sup>1</sup>, Kaewchur T, MD<sup>1</sup>, Namwongprom S, MD<sup>1</sup>, Ekmahachai M, MD<sup>1</sup>

<sup>1</sup> Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

**Objective:** To determine the potential use of postoperative diagnostic <sup>131</sup>I whole body scan (<sup>131</sup>I DxWBS) with single photon emission computed tomography-computed tomography (SPECT-CT) on initial staging, risk stratification and <sup>131</sup>I therapy planning in differentiated thyroid cancer (DTC) patients classified as being at low risk of recurrence based on clinical and histopathology.

**Materials and Methods:** Eighty DTC patients classified as low risk using the ATA 2009 risk stratification system based on clinical and histopathology between 2014 and 2016 were retrospectively evaluated. Initial staging using the AJCC/TNM staging system seventh edition was obtained. Initial <sup>131</sup>I treatment planning was prescribed based on the protocol agreed by the authors institution. Two nuclear medicine physicians interpreted the <sup>131</sup>I DxWBS with SPECT-CT independently and came to a consensus. Staging, risk stratification and <sup>131</sup>I treatment planning were re-evaluated based on additional <sup>131</sup>I DxWBS with SPECT-CT findings.

**Results:** Of the 36 patients aged under 45 years, <sup>131</sup>I DxWBS with SPECT-CT detected nodal metastases in 12 patients (33.3%, N1a=6, N1b=6), and bone with lung metastases in 1 patient (2.8%, M1=1), which changed the TNM staging in 1 patient (2.8%). Out of the 44 patients aged more than or equal to 45 years, nodal metastases were detected in 13 patients (29.5%, N1a=8, N1b=5) and nodal with lung metastases in 1 patient (2.3%, M1=1), leading to a change in the TNM staging in 14 patients (31.8%). Risk stratification was changed from low risk to intermediate risk in 25 of 80 patients (31.3%) and to high risk in 2 of 80 patients (2.5%). <sup>131</sup>I therapy planning was altered in 27 out of 80 patients (33.8%).

**Conclusion:** The postoperative use of <sup>131</sup>I DxWBS with SPECT-CT altered the initial staging, risk stratification and <sup>131</sup>I treatment planning based on the clinical and histopathology history alone in low risk DTC patients. Nodal and distant metastases were detected leading to changes in the overall TNM staging in 18.8%, risk stratification in 33.8% and <sup>131</sup>I treatment planning in 33.8% of the study.

**Keywords:** Diagnostic scan, Iodine-131, SPECT-CT, Staging, Risk stratification, Radioiodine therapy, Thyroid carcinoma

J Med Assoc Thai 2019;102(1):10-8

Website: <http://www.jmatonline.com>

Postoperative management of differentiated thyroid cancer (DTC) has changed significantly over the last ten years. In the past, the routine treatment of DTC was total thyroidectomy followed by an adjuvant empirical fixed dose (3.7 to 7.4 GBq) of radioactive iodine (RAI) therapy<sup>(1)</sup>. Subsequently, a

post-therapy RAI scan (post RxWBS) was performed as a standard procedure to evaluate the residual thyroid remnant and RAI avid regional or distant metastases<sup>(2)</sup>. Nowadays, there is a trend to withhold or decrease the amount of RAI activity to minimize side effects due to radiation in patients. Accurate staging and initial risk stratification are needed before RAI therapy to guide treatment decisions, level of RAI activity, prognostication, disease-specific survival rate, and long-term surveillance strategy of the individual patients. AJCC/UICC TNM staging is recommended to predict the disease mortality, while a risk stratification system is necessary to predict the risk of disease recurrence<sup>(3)</sup>.

## Correspondence to:

Ekmahachai M.

Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chiang Mai University, 110 Intawarorot Road, Sriphum, Muang Chiang Mai, Chiang Mai 50200, Thailand.

Phone: +66-53-935450, Fax: +66-53-936136

Email: [molrudee.ekm@cmu.ac.th](mailto:molrudee.ekm@cmu.ac.th)

**How to cite this article:** Teeyasoontranan W, Kaewchur T, Namwongprom S, Ekmahachai M. Impact of Postoperative Diagnostic <sup>131</sup>I Whole Body Scan with SPECT-CT on Staging, Risk Stratification and Radioiodine Therapy Planning in Low risk Differentiated Thyroid Cancer. J Med Assoc Thai 2019;102:10-8.

According to the American Thyroid Association (ATA) 2009 guidelines<sup>(4)</sup>, low risk stratification of recurrence in DTC patients is defined as all of the following: no local or distant metastases, no residual macroscopic tumor, no tumor invasion of locoregional tissues or structures, no aggressive histology (e.g., tall cell, insular, columnar cell carcinoma) or vascular invasion, and no evidence of <sup>131</sup>I uptake outside the thyroid bed on the first post <sup>131</sup>I treatment WBS if RAI was given. In the present group of patients, RAI ablation is not recommended, especially in case of microcarcinoma, and either unifocal or multifocal tumors. Low dose (1.11 GBq) thyroid remnant ablation plays a role in some low risk patients, while medium to high dose (3.7 to 7.4 GBq) RAI therapy is now reserved for some of the intermediate and high risk groups to eliminate regional or distant metastases. However, lymph node and distant metastases could be found in some patients classified as initial low risk DTC based on clinical and histopathology alone<sup>(5)</sup>. Low dose (1.11 GBq) RAI activity is sufficient for thyroid remnant ablation<sup>(6)</sup>; however, elimination of lymph node or distant metastases may need higher doses of radioactivity. The radiation absorbed dose to tumor should reach 8,500 cGy to successfully treat lymph node or distant metastases<sup>(7)</sup>. Therefore, accurate initial evaluation of regional and/or distant metastasis before RAI therapy is necessary.

Either the use of diagnostic <sup>131</sup>I or <sup>123</sup>I whole body scan (DxWBS), with or without single photon emission computed tomography-computed tomography (SPECT-CT), have proved to be useful techniques in the evaluation and follow-up of the residual thyroid remnant or RAI avid regional/distant metastases after radioiodine therapy in patients with DTC<sup>(8-11)</sup>. However, accurate knowledge surrounding the use of postoperative <sup>131</sup>I DxWBS with SPECT-CT for initial staging, risk stratification and management in low risk DTC patients is still controversial.

The aim of the present study was to determine the impact of the use of postoperative <sup>131</sup>I DxWBS with SPECT-CT on initial staging, risk stratification and <sup>131</sup>I therapy planning in DTC patients identified as being low risk stratification of recurrence. The authors believe that postoperative <sup>131</sup>I DxWBS with SPECT-CT will detect and give the precise location of regional and/or distant metastases, and the findings will alter the staging, risk stratification and <sup>131</sup>I treatment planning in the present group of patients.

## Materials and Methods

### Patients

A retrospective series of 80 low risk DTC patients (73 female, 7 male, mean age 45.8 years, range 15 to 76 years) who underwent <sup>131</sup>I DxWBS with SPECT-CT imaging between January 2014 and December 2016 were retrospectively reviewed.

Patients were included if they were post near-total or total thyroidectomy and classified as low risk of recurrence based on clinical and histopathology according to the ATA 2009 guidelines.

Patients were excluded if there were incomplete medical records as regards the following data: clinical history, operative findings, histopathology, serum thyroglobulin (Tg) and thyroglobulin antibody (TgAb) levels.

In accordance to the institute protocol, the post-thyroidectomy DTC patients classified as low risk based on the ATA 2009 guidelines, had <sup>131</sup>I DxWBS with SPECT-CT of neck and chest routinely performed along with additional SPECT-CT images of the specific regions based on equivocal lesions seen on planar imaging. All patients kept on a low iodine diet for 2 weeks. Thyroid hormone was withdrawn for 4 weeks before the scan. Serum TSH level on the day of <sup>131</sup>I ingestion was more than or equal to 30  $\mu$ IU/ml. Postoperative <sup>131</sup>I DxWBS with SPECT-CT was performed using <sup>131</sup>I activity of 37 MBq.

Table 1 showed the patient characteristics. The mean tumor size was 2.0 cm, range 0.1 to 8.0 cm. The mean stimulated serum Tg was 2.2 ng/ml, range from undetectable to 8.7 ng/ml. The mean serum TSH was 78.3  $\mu$ IU/ml, range 37.8 to 298.0  $\mu$ IU/ml.

### Research plan

Clinical history, laboratory results, operative findings and histopathology of each low risk DTC patient were extracted from medical records and reviewed. Initial staging based on the AJCC/TNM staging system 7<sup>th</sup> edition<sup>(12)</sup>, risk stratification based on the ATA 2009 guidelines<sup>(4)</sup> and <sup>131</sup>I therapy planning in accordance with the authors institute protocol (Table 2) were prescribed. Two experienced nuclear medicine (NM) physicians reviewed the postoperative <sup>131</sup>I DxWBS with SPECT-CT findings independently. The first NM physician was aware of the clinical history, laboratory results, operative findings and histopathology, while the second NM physician was blinded. Any non-consensual readings were reviewed and agreement reached. Re-staging, risk stratification and <sup>131</sup>I therapy planning were altered based on the postoperative <sup>131</sup>I DxWBS findings.

**Table 1.** Patient characteristics (n = 80)

	Number of patients	
	n	(%)
Gender		
Female	73	(91.25)
Male	7	(8.75)
Age at diagnosis		
Below 45	36	(45.00)
More than or equal to 45	44	(55.00)
Tumor subtype		
Papillary, classical variant	48	(60.00)
Papillary, follicular variant	20	(25.00)
Follicular	9	(11.25)
Hürthle cell variant	3	(3.75)
T-stage		
T1a	26	(32.5)
• Unifocal	18	(22.5)
• Multifocal	8	(10.00)
T1b	24	(30.00)
T2	21	(26.25)
T3	9	(11.25)
Laterality		
Right	40	(50.00)
Left	20	(25.00)
Isthmus	3	(3.75)
Right & left	14	(17.50)
Right & isthmus	2	(2.50)
Right & left & isthmus	1	(1.25)
Unifocal tumor	58	(72.50)
Multifocal tumor	22	(27.50)

**Postoperative <sup>131</sup>I D<sub>x</sub>WBS with SPECT-CT protocol**

Postoperative <sup>131</sup>I D<sub>x</sub>WBS with SPECT-CT was performed 2 days after <sup>131</sup>I administration, using a dual-head gamma camera equipped with 15×0.75-cm (3/8-in) NaI crystals and a multidetector (16-row) spiral CT (Symbia T16, Siemens Medical Solutions, Germany). The WBS planar images were initially acquired with parallel-hole, high-energy collimators, using a 20% energy window set at 364 keV and a scanning speed of 6 cm/minute. Static images were acquired over 5 minutes for lateral skull and anterior neck and chest, using a 256×256 matrix. The SPECT volume session included the neck and chest, with an axial field of view of 53.3×38.7 cm. For the SPECT acquisition of tomographic images, a 128×128 matrix was used, and 64 projections (45-second/stop) were acquired over 360 degrees. SPECT data were reconstructed using a 3-dimensional iterative algorithm (ordered-subsets expectation maximization

**Table 2.** Indications for RAI treatment planning (Chiang Mai University Protocol)

Radioiodine treatment	Indications
No	<ul style="list-style-type: none"> <li>• Unifocal microcarcinoma without other adverse features and stimulated Tg below 1 ng/ml</li> </ul>
1.11 GBq	<ul style="list-style-type: none"> <li>• Unifocal microcarcinoma without other adverse features and stimulated Tg more than or equal 1 ng/ml, but below 10 ng/ml</li> <li>• Multifocal microcarcinoma or tumor size 1 to 4 cm without other risk features and stimulated Tg below 10 ng/ml</li> </ul>
3.7 GBq	<ul style="list-style-type: none"> <li>• Lymphovascular, capsular, or perineural invasion</li> <li>• Tumor size more than 4 cm (tumor confined within thyroid capsule) and stimulated Tg below 10 ng/ml</li> </ul>
5.55 GBq	<ul style="list-style-type: none"> <li>• Microscopic perithyroidal soft tissue invasion</li> <li>• Aggressive histology</li> <li>• Macroscopic tumor invasion</li> </ul>
7.4 GBq	<ul style="list-style-type: none"> <li>• Incomplete tumor resection</li> <li>• Positive surgical margin</li> <li>• Cervical lymph node or distant metastases</li> <li>• Stimulated Tg more than or equal 10 ng/ml</li> </ul>
	<ul style="list-style-type: none"> <li>• Bone metastasis without lung metastasis</li> </ul>

RAI=radioactive iodine; Tg=thyroglobulin

with four iterations and eight subsets). Images were smoothed with a 3-dimensional spatial Gaussian filter. Immediately after SPECT acquisition, a CT topogram was acquired, followed by a spiral CT acquisition performed on a volume session similar to that used during the SPECT acquisition. CT scans were acquired at a tube voltage of 130 kV; the tube current was adjusted for body weight. The reconstructed slice width and spacing were 1.5 mm. CT data were used for attenuation correction and anatomical information. No contrast media were injected during the procedure. The <sup>131</sup>I D<sub>x</sub>WBS and SPECT-CT data were analyzed using Symbia.net/Esoft software (Siemens), which provided transaxial, sagittal and coronal SPECT-CT and fused SPECT-CT data slices. The additional SPECT-CT images of the specific regions based on equivocal lesions seen on planar imaging were also obtained.

**Statistical analysis**

The IBM Statistical Package for Social Sciences (SPSS) 22.0 software was used for statistical calculations. The descriptive data were presented in mean and percentage. Changes of staging, risk

**Table 3.** Impact of <sup>131</sup>I DxWBS with SPECT-CT on staging

Initial staging	<sup>131</sup> I DxWBS with SPECT-CT staging						Staging changes n (%)
	I (n = 35)			II (n = 1)			
Younger patients							
I (n = 36)	35			1			1 (2.8)
II (n = 0)	-			0			0 (0.0)
Total staging changes							1 (2.8)
	I (n = 21)	II (n = 5)	III (n = 13)	IVA (n = 4)	IVB (n = 0)	IVC (n = 1)	
Older patients							
I (n = 30)	21	-	6	2	-	1	9 (30.0)
II (n = 9)	-	5	3	1	-	-	4 (44.4)
III (n = 5)	-	-	4	1	-	-	1 (20.0)
IVA (n = 0)	-	-	-	0	-	-	0 (0.0)
IVB (n = 0)	-	-	-	-	0	-	0 (0.0)
IVC (n = 0)	-	-	-	-	-	0	0 (0.0)
Total staging changes							14 (31.8)

DxWBS=whole body scan; SPECT-CT=single photon emission computed tomography-computed tomography

**Table 4.** Impact of <sup>131</sup>I DxWBS with SPECT-CT on risk stratification

Initial low risk	DxWBS risk			Risk changes n (%)
	Low (n = 53)	Intermediate (n = 25)	High (n = 2)	
Younger patients (n = 36)	23	12	1	13 (36.1)
Older patients (n = 44)	30	13	1	14 (31.8)
Total risk stratification changes				27 (33.8)

DxWBS=whole body scan; SPECT-CT=single photon emission computed tomography-computed tomography

stratification and radioiodine therapy planning were presented in percentage.

### Ethical approval

The present study was approved by the Research Ethics Committee of Faculty of Medicine, Chiang Mai University (study code: RAD-2560-04746). For the present type of study, formal consent was not required. The present article did not contain any animal experiments.

## Results

### Impact of <sup>131</sup>I DxWBS with SPECT-CT on staging

In a group of 36 patients aged below 45 years (younger patients), <sup>131</sup>I DxWBS with SPECT-CT detected nodal metastases in 12 patients (33.3%; N1a=6, N1b=6). Distant metastases to bone and lung was found in 1 patient, leading to a change of stage I to stage II in 1 patient (2.8%, M1=1).

Out of 44 patients aged more than or equal to 45 years (older patients), nodal metastases were detected in 13 patients (29.5%; N1a=8, N1b=5) and both nodal

and lung metastases were depicted in 1 patient (2.3%, N1a and lung), leading to upstaging in 14 patients (31.8%: stage I to stage III in 6 patients; stage I to stage IVA in 2 patients; stage I to stage IVC in 1 patient; stage II to stage III in 3 patients; stage II to stage IVA in 1 patient; and stage III to stage IVA in 1 patient).

The total number of stage changes in both age groups was 15 patients (18.8%). These changes were shown in Table 3.

### Impact of <sup>131</sup>I DxWBS with SPECT-CT on risk stratification

Out of the 36 younger patients, risk stratification was changed in 13 patients (36.1%: low to intermediate risk in 12 patients; and low to high risk in 1 patient).

Out of 44 older patients, risk stratification was changed in 14 patients (31.8%: low to intermediate risk in 13 patients; and low to high risk in 1 patient).

The total risk stratification changes in both age groups was 27 patients (33.8%: low to intermediate risk in 25 patients; and low to high risk in 2 patients), as shown in Table 4.

**Table 5.** Impact of <sup>131</sup>I DxWBS with SPECT-CT on RAI therapy

Initial RAI therapy	DxWBS RAI therapy					RAI therapy changes n (%)
	No (n = 13)	1.11 GBq (n = 35)	3.7 GBq (n = 4)	5.55 GBq (n = 28)	7.4 GBq (n = 0)	
<b>Younger patients</b>						
No (n = 7)	6	-	-	1	-	1 (14.3)
1.11 GBq (n = 25)	-	16	-	9	-	9 (36.0)
3.7 GBq (n = 4)	-	-	1	3	-	3 (75.0)
5.55 GBq (n = 0)	-	-	-	0	-	0 (0.0)
7.4 GBq (n = 0)	-	-	-	-	0	0 (0.0)
Total RAI therapy changes						13 (36.1)
<b>Older patients</b>						
No (n = 10)	7	-	-	3	-	3 (30.0)
1.11 GBq (n = 29)	-	19	-	10	-	10 (34.5)
3.7 GBq (n = 5)	-	-	4	1	-	1 (20.0)
5.55 GBq (n = 0)	-	-	-	0	-	0 (0.0)
7.4 GBq (n = 0)	-	-	-	-	0	0 (0.0)
Total RAI therapy changes						14 (31.8)

DxWBS=whole body scan; SPECT-CT=single photon emission computed tomography-computed tomography; RAI=radioactive iodine

### **Impact of <sup>131</sup>I DxWBS with SPECT-CT on <sup>131</sup>I therapy planning**

Of the 36 younger patients, the decision to withhold <sup>131</sup>I therapy was changed to 5.55 GBq in 1 patient. <sup>131</sup>I activities were changed from 1.11 GBq to 5.55 GBq in 9 patients, and 3.7 GBq to 5.55 GBq in 3 patients. Total <sup>131</sup>I therapy changes in this age group totaled 13 patients (36.1%).

Out of the 44 older patients, the decision to withhold <sup>131</sup>I therapy was reversed and a dose of 5.55 GBq was planned in 3 patients. <sup>131</sup>I activities were changed from 1.11 GBq to 5.55 GBq in 10 patients, and 3.7 GBq to 5.55 GBq in 1 patient. In this age group, changes in <sup>131</sup>I therapy dose included 15 patients (34.1%).

Changes of the <sup>131</sup>I therapy dosage in both age groups were recommended in 27 patients (33.8%), as shown in Table 5.

### **Microcarcinoma**

Out of 18 patients with unifocal microcarcinoma, <sup>131</sup>I DxWBS with SPECT-CT detected nodal metastasis in 5 patients (27.8%), 4 older patients and 1 younger patient, 3 patients with N1a and 2 patients with N1b. No distant metastasis was found. Therefore, staging was changed from stage I to stage III in 3 patients (16.7%), and stage I to stage IVA in 1 patient (5.6%). Risk stratification was changed in 5 patients (27.8%). <sup>131</sup>I therapy was changed from withholding <sup>131</sup>I treatment to 5.55 GBq in 5 patients (27.8%).

Out of the 8 patients with multifocal microcarcinoma, nodal metastasis (N1a) was detected from <sup>131</sup>I DxWBS with SPECT-CT in 1 younger patient (12.5%). Then, the staging was not changed, but the risk stratification was altered to intermediate risk and <sup>131</sup>I activity was altered from 1.11 GBq to 5.55 GBq.

### **Discussion**

The efficacy of role of postoperative <sup>131</sup>I DxWBS is still controversial. Postoperative <sup>131</sup>I DxWBS (with or without SPECT-CT) is not widely performed because of concern about the possibility of stunning the thyroid remnant and metastasis<sup>(13)</sup>, especially in the case of high <sup>131</sup>I activity use (185 to 370 MBq)<sup>(14)</sup>. However, the use of lower <sup>131</sup>I activities (37 to 111 MBq)<sup>(15)</sup> or changing the radioisotope to <sup>123</sup>I<sup>(16)</sup> can avoid the stunning effect. No adverse effects on clinical outcomes were reported when using low <sup>131</sup>I activity<sup>(17)</sup>. In the present study, the authors used low <sup>131</sup>I activity of 37 MBq for postoperative <sup>131</sup>I DxWBS and found no stunning effect on the post <sup>131</sup>I RxWBS.

The utility of postoperative DxWBS planar imaging with <sup>131</sup>I or <sup>123</sup>I has been reported. Management in DTC patients was changed in up to 53% of cases after pre-ablation <sup>131</sup>I DxWBS<sup>(11)</sup>. <sup>123</sup>I pre-therapy scans provided valuable information in 25% of cases with regard to unsuspected lymph node or distant metastases, indicating the requirement for a significantly higher <sup>131</sup>I dose<sup>(18)</sup>. DxWBS after surgery in combination with serum Tg measurement



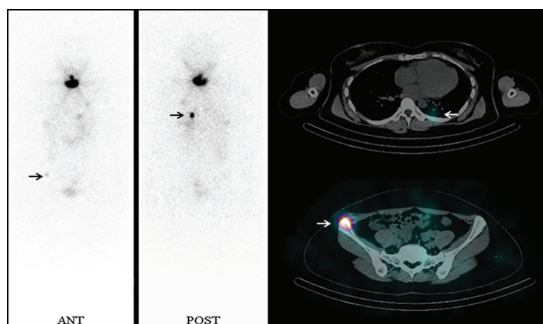
demonstrated early diagnosis of metastases from DTC in more than 80% of patients<sup>(19)</sup>.

SPECT-CT hybrid cameras are the diagnostic tools that allow fusion of functional and morphologic images in a single session. The integration of CT enables more detailed characterization of functional abnormalities identified on planar and SPECT scintigraphy by offering structural information. It thus, highly improves accuracy compared with conventional scintigraphy<sup>(20)</sup>. An incremental diagnostic value of SPECT-CT over planar imaging in 47.6% of cases was found and increased reader confidence in 70.7% of cases. SPECT-CT also changed the initial planar scan interpretation in 21% to 40% of patients by detecting regional nodal metastases and clarifying equivocal focal neck uptake<sup>(21,22)</sup>. The SPECT-CT shows additional value over planar imaging in detecting and precisely localizing postoperative residual thyroid remnant and RAI-avid metastases<sup>(23)</sup>.

There were three reports demonstrating the efficacy of the utilization of <sup>131</sup>I DxWBS with SPECT-CT on staging, risk stratification and management in DTC patients. Wong et al showed changes of staging in 21% of patients and alteration of therapeutic decision making in 58% of patients after postoperative <sup>131</sup>I DxWBS with SPECT-CT<sup>(24)</sup>. Avram et al demonstrated changes of staging in 4% of younger patients and 25% of older patients<sup>(25)</sup>. The postoperative use of <sup>131</sup>I DxWBS with SPECT-CT provided detection and precise localization of nodal and distant metastases, which altered risk stratification in 15% of patients and changed therapeutic decision making in 23.4% of patients<sup>(5,25)</sup>.

The results of the present study demonstrated the usefulness of postoperative <sup>131</sup>I DxWBS with SPECT-CT in DTC patients with initial low risk stratification based on clinical and histopathology alone. Postoperative <sup>131</sup>I DxWBS with SPECT-CT detects nodal metastasis in 32.5% and distant metastasis in 2.5% of patients. Therefore, the authors emphasize the clinical and histopathology alone is not enough for precise initial staging, risk stratification and <sup>131</sup>I treatment dose prescription. Even in low risk DTC patients, the impact of postoperative <sup>131</sup>I DxWBS with SPECT-CT on staging, risk stratification and <sup>131</sup>I therapy planning in the authors study was in agreement with prior publications which evaluated patients with all risk stratifications. Total staging, risk stratification and <sup>131</sup>I treatment planning were changed in 18.8%, 33.8% and 33.8% of cases, respectively.

The recommendation of treatment in low risk DTC patients is lobectomy, or total thyroidectomy



**Figure 1.** A 31-year old woman with follicular thyroid carcinoma, post-near total thyroidectomy. Pathology showed a 2.5-cm tumor without lymphovascular invasion or high risk features and all surgical margins were free. Serum TSH was 108.6  $\mu$ U/ml. Stimulated serum Tg was 2.1 ng/ml. Stimulated serum TgAb was 28.2 IU/ml. The <sup>131</sup>I DxWBS with SPECT-CT revealed left lung and right iliac bone metastases (arrow).

without <sup>131</sup>I ablation, or low dose (1.11 GBq) <sup>131</sup>I ablation<sup>(3)</sup>. However, despite the premise that <sup>131</sup>I ablation may not affect the outcome in low risk DTC patients, presence of nodal metastasis, which is a significant predictive factor of unsuccessful ablation and loco-regional recurrence, needs higher <sup>131</sup>I activity<sup>(26)</sup>.

Two patients in the present study had distant metastasis, but a low stimulated serum Tg level. One of these patients, a 31-year-old female with a unifocal papillary carcinoma, 2.5 cm in size, stimulated serum Tg 2.1 ng/ml and serum TgAb 28.2 IU/ml had lung and bone metastases (Figure 1). Another patient with a lymph node level IA and lung metastases was a 56-year-old female, unifocal papillary carcinoma with follicular variant, 2.0 cm in size, stimulated serum Tg 0.5 ng/ml and serum TgAb 17 IU/ml. These data corresponded to that described in prior reports that showed regional lymph node and distant metastases in patients with negative serum Tg levels<sup>(27)</sup>. The authors noticed that the risk of distant metastasis could not be excluded in initial low risk patients with low postoperative stimulated serum Tg. However, these two patients might have a gene mutation or other high risk features not included in the investigation.

Even though, all of patients in the present study had stimulated serum Tg level <10 ng/ml, there were 32.5% of patients with lymph node metastases. A postoperative serum Tg level <10 ng/ml may not distinguish between nodal disease and residual thyroid remnant<sup>(28)</sup>. The chance of detection of regional or distant metastases is increased if either the suppressed

or stimulated Tg values rose above 5 to 10 ng/ml (27,29,30). Some of the patients had positive serum TgAb levels, which may interfere with serum Tg levels<sup>(31)</sup>. However, to date there is no cut off value of serum TgAb level indicating regional or distant metastases. There is however a report which suggests that the TgAb level does not predict disease status in papillary thyroid carcinoma patients<sup>(32)</sup>.

The subgroup analysis of 18 patients with unifocal microcarcinoma in the present study revealed nodal metastases in 5 patients (27.8%), which were 3 N1a and 2 N1b. The involvement of the cervical lymph node can be found at the time of diagnosis in either unifocal or multifocal thyroid microcarcinoma<sup>(33,34)</sup>. Some microcarcinoma DTC patients treated with surgery alone might not have been referred for either <sup>131</sup>I treatment or postoperative <sup>131</sup>I DxWBS with SPECT-CT and these patients may receive suboptimal treatment.

The strength of the present study is that it is the publication which demonstrated the usefulness and clinical impact of postoperative <sup>131</sup>I DxWBS with SPECT-CT in low risk DTC patients. The results of the present study may encourage the physicians to routinely perform the postoperative <sup>131</sup>I DxWBS with SPECT-CT in all initial low risk DTC patients.

The limitation of the present study is that it was the retrospective study. There were some patients excluded from the study due to missing necessary data. Some low risk DTC patients treated with surgery alone might not have been referred for the postoperative <sup>131</sup>I DxWBS with SPECT-CT. If the present study was the prospective study and all low risk DTC patients after surgery were included, the study may show more promising results.

## Conclusion

The present study showed that postoperative <sup>131</sup>I DxWBS with SPECT-CT altered the initial staging, risk stratification and <sup>131</sup>I treatment planning based on the clinical and histopathology alone in low risk DTC patients. Nodal and distant metastases were detected leading to changing the overall TNM staging in 18.8%, risk stratification in 33.8% and <sup>131</sup>I treatment planning in 33.8%.

## What is already known on this topic?

The use of <sup>131</sup>I DxWBS with or without SPECT-CT has proved to be useful techniques in the evaluation and follow-up after radioiodine therapy in DTC patients. However, accurate knowledge concerning the use of postoperative <sup>131</sup>I DxWBS with SPECT-CT for

initial staging, risk stratification and management in low risk DTC patients is still controversial.

## What this study adds?

The present study demonstrates the utility of postoperative <sup>131</sup>I DxWBS with SPECT-CT in low risk DTC patients. Nodal and distant metastases were detected in some of these patients, leading to changing of the overall TNM staging, risk stratification and <sup>131</sup>I treatment planning.

The present study emphasized the usefulness of the postoperative <sup>131</sup>I DxWBS with SPECT-CT for appropriated management of DTC patients with initial low risk stratification.

## Acknowledgement

The present research would have been impossible without the support of the authors colleagues from the Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chiang Mai University, and Professor Satawat Thongsawat who provided insight and expertise that greatly assisted the research.

## Conflicts of interest

The authors declare no conflict of interest.

## References

1. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:109-42.
2. Souza Rosario PW, Barroso AL, Rezende LL, Padrao EL, Fagundes TA, Penna GC, et al. Post I-131 therapy scanning in patients with thyroid carcinoma metastases: an unnecessary cost or a relevant contribution? *Clin Nucl Med* 2004;29:795-8.
3. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid* 2016;26:1-133.
4. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167-214.
5. Avram AM, Esfandiari NH, Wong KK. Preablation 131-I scans with SPECT/CT contribute to thyroid cancer risk stratification and 131-I therapy planning. *J Clin Endocrinol Metab* 2015;100:1895-902.
6. Bal CS, Kumar A, Pant GS. Radioiodine dose for remnant ablation in differentiated thyroid carcinoma:

- a randomized clinical trial in 509 patients. *J Clin Endocrinol Metab* 2004;89:1666-73.
7. Maxon HR, III, Englaro EE, Thomas SR, Hertzberg VS, Hinnefeld JD, Chen LS, et al. Radioiodine-131 therapy for well-differentiated thyroid cancer—a quantitative radiation dosimetric approach: outcome and validation in 85 patients. *J Nucl Med* 1992;33:1132-6.
  8. Tharp K, Israel O, Hausmann J, Bettman L, Martin WH, Daitzchman M, et al. Impact of 131I-SPECT/CT images obtained with an integrated system in the follow-up of patients with thyroid carcinoma. *Eur J Nucl Med Mol Imaging* 2004;31:1435-42.
  9. Avram AM. Radioiodine scintigraphy with SPECT/CT: an important diagnostic tool for thyroid cancer staging and risk stratification. *J Nucl Med Technol* 2014;42:170-80.
  10. Barwick T, Murray I, Megadmi H, Drake WM, Plowman PN, Akker SA, et al. Single photon emission computed tomography (SPECT)/computed tomography using Iodine-123 in patients with differentiated thyroid cancer: additional value over whole body planar imaging and SPECT. *Eur J Endocrinol* 2010;162:1131-9.
  11. Van Nostrand D, Aiken M, Atkins F, Moreau S, Garcia C, Acio E, et al. The utility of radioiodine scans prior to iodine 131 ablation in patients with well-differentiated thyroid cancer. *Thyroid* 2009;19:849-55.
  12. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010;17:1471-4.
  13. Hu YH, Wang PW, Wang ST, Lee CH, Chen HY, Chou FF, et al. Influence of 131I diagnostic dose on subsequent ablation in patients with differentiated thyroid carcinoma: discrepancy between the presence of visually apparent stunning and the impairment of successful ablation. *Nucl Med Commun* 2004;25:793-7.
  14. 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.
  15. Morris LF, Waxman AD, Braunstein GD. The nonimpact of thyroid stunning: remnant ablation rates in 131I-scanned and non-scanned individuals. *J Clin Endocrinol Metab* 2001;86:3507-11.
  16. Silberstein EB. Comparison of outcomes after (123)I versus (131)I pre-ablation imaging before radioiodine ablation in differentiated thyroid carcinoma. *J Nucl Med* 2007;48:1043-6.
  17. Yap BK, Murby B. No adverse affect in clinical outcome using low preablation diagnostic (131) I activity in differentiated thyroid cancer: refuting thyroid-stunning effect. *J Clin Endocrinol Metab* 2014;99:2433-40.
  18. Chen MK, Yasrebi M, Samii J, Staib LH, Doddamane I, Cheng DW. The utility of I-123 pretherapy scan in I-131 radioiodine therapy for thyroid cancer. *Thyroid* 2012;22:304-9.
  19. Filesi M, Signore A, Ventroni G, Melacrinis FF, Ronga G. Role of initial iodine-131 whole-body scan and serum thyroglobulin in differentiated thyroid carcinoma metastases. *J Nucl Med* 1998;39:1542-6.
  20. Toubert ME, Vija L, Vercellino L, Banayan S, Faugeron I, Berenger N, et al. Additional diagnostic value of hybrid SPECT-CT systems imaging in patients with differentiated thyroid cancer. *Am J Clin Oncol* 2014;37:305-13.
  21. Wong KK, Zarzhevsky N, Cahill JM, Frey KA, Avram AM. Incremental value of diagnostic 131I SPECT/CT fusion imaging in the evaluation of differentiated thyroid carcinoma. *AJR Am J Roentgenol* 2008;191:1785-94.
  22. Wang H, Fu HL, Li JN, Zou RJ, Gu ZH, Wu JC. The role of single-photon emission computed tomography/computed tomography for precise localization of metastases in patients with differentiated thyroid cancer. *Clin Imaging* 2009;33:49-54.
  23. Barwick TD, Dhawan RT, Lewington V. Role of SPECT/CT in differentiated thyroid cancer. *Nucl Med Commun* 2012;33:787-98.
  24. Wong KK, Sisson JC, Koral KF, Frey KA, Avram AM. Staging of differentiated thyroid carcinoma using diagnostic 131I SPECT/CT. *AJR Am J Roentgenol* 2010;195:730-6.
  25. Avram AM, Fig LM, Frey KA, Gross MD, Wong KK. Preablation 131-I scans with SPECT/CT in postoperative thyroid cancer patients: what is the impact on staging? *J Clin Endocrinol Metab* 2013;98:1163-71.
  26. Seo M, Kim YS, Lee JC, Han MW, Kim ES, Kim KB, et al. Low-dose radioactive iodine ablation is sufficient in patients with small papillary thyroid cancer having minor extrathyroidal extension and central lymph node metastasis (T3 N1a). *Clin Nucl Med* 2017;42:842-6.
  27. Park EK, Chung JK, Lim IH, Park DJ, Lee DS, Lee MC, et al. Recurrent/metastatic thyroid carcinomas false negative for serum thyroglobulin but positive by posttherapy I-131 whole body scans. *Eur J Nucl Med Mol Imaging* 2009;36:172-9.
  28. de Rosário PW, Guimarães VC, Maia FF, Fagundes TA, Purisch S, Padrao EL, et al. Thyroglobulin before ablation and correlation with posttreatment scanning. *Laryngoscope* 2005;115:264-7.
  29. Piccardo A, Arecco F, Puntoni M, Foppiani L, Cabria M, Corvisieri S, et al. Focus on high risk DTC patients: high postoperative serum thyroglobulin level is a strong predictor of disease persistence and is associated to progression-free survival and overall survival. *Clin Nucl Med* 2013;38:18-24.
  30. Robenshtok E, Grewal RK, Fish S, Sabra M, Tuttle RM. A low postoperative nonstimulated serum thyroglobulin level does not exclude the presence of radioactive iodine avid metastatic foci in intermediate-risk differentiated thyroid cancer patients. *Thyroid* 2013;23:436-42.



31. Ringel MD, Nabhan F. Approach to follow-up of the patient with differentiated thyroid cancer and positive anti-thyroglobulin antibodies. *J Clin Endocrinol Metab* 2013;98:3104-10.
32. Smooke-Prav S, Ro K, Levin O, Ituarte PH, Harari A, Yeh MW. Thyroglobulin antibody levels do not predict disease status in papillary thyroid cancer. *Clin Endocrinol (Oxf)* 2014;81:271-5.
33. Anastasilakis AD, Polyzos SA, Makras P, Kampas L, Valeri RM, Kyriakoulis D, et al. Papillary thyroid microcarcinoma presenting as lymph node metastasis- a diagnostic challenge: case report and systematic review of literature. *Hormones (Athens)* 2012;11: 419-27.
34. Kaliszewski K, Zubkiewicz-Kucharska A, Wojtczak B, Strutynska-Karpinska M. Multi- and unifocal thyroid microcarcinoma: Are there any differences? *Adv Clin Exp Med* 2016;25:485-92.