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**Title:** Usefulness of SPECT/CT imaging in the management of patients with differentiated thyroid carcinoma

**Running Title:** Usefulness of SPECT/CT in differentiated thyroid carcinoma

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## Abstract

**Objective:** Whole body I-131 scanning (WBS), as a standard method in the evaluation of patients with differentiated thyroid carcinoma (DTC), has some limitations in distinguishing between physiological and pathological tracer uptake and in defining exact anatomical localization of pathological foci. The purpose of our study was to determine the additional diagnostic value of the SPECT/CT in patients with DTC.

**Methods:** One hundred and forty-two patients with previous total thyroidectomy who underwent diagnostic or post-therapeutic WB imaging were included in this retrospective study. The distinction between physiological and pathological uptake could not be clearly done and/or the localization of pathological uptake could not be clearly defined on WBS, were considered as inconclusive finding and regional SPECT/CT images of these patients were evaluated.

**Results:** The number of pathological foci detected by WBS and SPECT/CT was 64 and 59 respectively. Exact anatomical localization was determined in 85.9% of the lesions with SPECT/CT. Benign accumulations (inflammatory / physiological) were determined in 12.5% of inconclusive foci. In 14.1% of WBS detected foci, no significant tracer uptake was observed on SPECT/CT images. Four additional foci were detected on SPECT/CT (3 thyroid remnant, 1 bone).

**Conclusion:** SPECT/CT improves the specificity of I-131 scanning and contributes to the management of DTC patients.

**Keywords:** Differentiated thyroid carcinoma, 131-I,SPECT.

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## Introduction

Differentiated thyroid carcinoma (DTC) is the most widely encountered malignant endocrine disease and is related with a good prognosis depending on prognostic indicators such as stage and age at diagnosis, histological subtype and sex (1,2). Primary treatment modality is surgery; recently recommendations suggest only lobectomy in especially papillary microcarcinoma without any additional risk factor (3). In patient's with moderate-high risk, procedure contains destroying remnant thyroid tissues, locoregional or distant foci with radioiodine. American Thyroid Association Practice Guidelines for Thyroid Cancer Management recommended 131-I ablation in: grossly invasive cancer, primary tumors > 4 cm, presence of distant metastasis and in patients with 1 to 4 cm large tumors limited in the thyroid who have documented node metastasis or other high-risk features (4).

Radionuclide planar whole-body scanning (WBS) with 131-I or 123-I is a commonly performed modality with a high sensitivity in the follow-up of patients with DTC (5,6). However, low image resolution, physiological uptake sites confused with pathological foci and difficulties in determining the exact anatomical localization of foci limit the diagnostic capacity of this technic. SPECT/CT provides morphological and functional data together and has been reported to increases the sensitivity and specificity of 131-I WBS in patients with DTC (7). In our study, we evaluated retrospectively the additional diagnostic value of the SPECT/CT in patients with DTC.

## Materials and Methods

One hundred and forty two (27M,115F) with previous total thyroidectomy were evaluated retrospectively (20-79 yrs, mean age  $48 \pm 13$ ). The study was approved by the ethic committee of Ondokuz Mayıs University. Histopathological examination revealed with papillary carcinoma in 92 patients, follicular carcinoma in 43 patients and mixed type carcinoma (papillary and follicular) in 7 patient. Twenty-one patients were re-operated for residual tissue or relapse. Of 142 patients, 47 underwent diagnostic WB imaging after the administration of 185 MBq 131-I orally (all patients had previously been treated with radioiodine). Other 95 patients underwent post-therapeutic WB imaging 6-7 day after oral administration of 2775-7400 MBq 131-I. A double-head gamma camera and high energy

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collimators were used for radionuclide imaging. Table speed was 5 cm/min for WB imaging. Additional spot images were acquired for 10 minutes. SPECT parameters were: 128x128 matrix, 3° angular step and 40 seconds per frame. Immediately hereafter, a CT scan of the same region was obtained. Tracer uptake in salivary glands, gastrointestinal system and bladder was considered as physiologic on planar images. The distinction of physiological / pathological uptake could not be clearly done and/or the localization of pathological uptake could not be clearly defined on WBS, was considered as inconclusive finding and regional SPECT/CT imaging was performed. In all patients, serum thyroid stimulating hormone (TSH) levels were measured after at least 4 weeks of thyroid hormone withdrawal. At the time of imaging, all patients presented with at least 50 µU/mL of TSH levels.

## Results

In 47/142 patients, WBS detected 64 inconclusive tracer uptake (35 foci were in the servical region, 19 foci in the thoracic region, 9 foci in the abdomen and 1 focus in the upper extremity) and patients underwent regional SPECT/CT imaging. The total number of pathological foci detected by SPECT/CT was 59, of which 33 were located in the cervical region, 20 foci in the thoracic region, 5 foci in the abdomen and 1 focus in the upper extremity. Twenty-four of 33 servical foci were compatible with remnant thyroid tissue, 5 with lymph nodes, 1 with dental structures, 1 with nasal soft tissue and 2 were salivary activity. Of 20 foci detected at thoracic region, 7 were localized in the lung, 5 in the mediastinal lymph nodes, 6 in the bone structures and 2 in the breast tissue. There were 2 foci in pelvic soft tissue and 1 focus in the upper extremity bone structure. Numbers of pathologic foci detected on WBS and SPECT/CT images were given in table 1 and 2.

Of 35 servical inconclusive foci on WBS, 5 foci were not detected on SPECT/CT. SPECT/CT images were revealed with residual tissue in 21 foci. Five were interpreted as lymph nodes, 2 were identified as inflammatory accumulations located at dental and nasal structures, 2 foci were located at esophagus and considered as physiological salivary activity. SPECT/CT detected 3 additional low intensity thyroid remnant foci.

In 19 thoracic foci on WBS, bone and soft tissue could not be safely differentiated. On SPECT/CT images, these were described as: 5 mediastinal lymph nodes, 5 bone lesions, 7 lung

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lesions and 2 breast lesions. SPECT/CT detected 1 additional small sized radioiodine accumulating lesion in the bone.

In abdominal and pelvic areas, a total of 9 inconclusive foci were detected on WBS. SPECT/CT images were revealed with intestinal activity in 2 foci and reactive/inflammatory findings associated with IM injections in 2 foci. One focus was located on the pelvic bone. Four foci were no more seen by SPECT/CT. One upper extremity uptake was located at the bone on SPECT/CT.

Overall, SPECT/CT determined exact anatomical localization in 55/64 lesions (85.9%) described as inconclusive on WBS. Figure 1 and 2 represent I-131 WBS and SPECT/CT images of two patients. WBS showed inconclusive tracer accumulations in the thoracic and pelvic regions. SPECT/CT determined the location of pathological foci. Benign accumulations (inflammatory / physiological) were determined in 8/64 (12.5%) inconclusive foci (4 servical and 4 abdominopelvik). Nine of 64 (14.1%) detected foci on WBS (5 servical and 4 abdominal) could not be redetected with SPECT/CT. Three additional thyroid remnant foci and 1 additional bone lesion in the thoracic region were determined on SPECT/CT.

## **Discussion**

Radionuclide whole body scanning with 131-I is known as a standard method with high specificity in the evaluation of patients with DTC but has some limitations in distinguishing between physiological and pathological tracer uptake and in defining exact anatomical localization of uptake sites. These limitations and the possibility of overcoming problems with SPECT/CT have accelerated further investigation on this subject (8,9,10,11). SPECT/CT allows combining morphological and functional data, improves the accuracy of technique. Menges et al. reported the sensitivity of both 131-I SPECT/CT and WBS as 62% in the diagnosis of DTC, whereas the specificity was increased from 78% to 98% with SPECT/CT (12).

Localization of pathological foci is important in the therapy management. Computed tomography is probably the most important component of this technique, since it's very difficult to determine the location of pathological foci only with WBS or SPECT without any morphological marker. Spanu et al. mentioned that SPECT/CT had better performance than

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WBS on both classification and location of lesions and changed the therapeutic management in 21.6% of the patients (13). Additional diagnostic value rates of SPECT/CT over planar imaging has a wide variation in literature and changes between 34% and 74% (14,15,16). According to Barwick et al, this wide variation was associated with the selection of patients. They mentioned, if SPECT/CT is used routinely for every patient, incremental diagnostic value might be expected. When SPECT/CT was performed in all patients from the neck and thoracic region, reported diagnostic benefit was 34–42% (14). In our study, 85.9% of the WBS inconclusive foci were localized with SPECT/CT and this rate was higher than the literature. The highest ratio was in the cervical region. It's thought that, differentiation of residual thyroid tissue and lymph nodes was difficult because of lacking the evaluation of thyroid scintigraphy in the study and this was caused the high ratio. Assessment of WBS findings with thyroid scintigraphy will reduce the number of cervical inconclusive results on WBS.

SPECT/CT contributes to treatment approach in some patients. In a study including 365 patients, Zilioli and colleagues reported that TNM stage and treatment plan was modified in 13 patients because of exclusion of false positive accumulations with additional SPECT/CT imaging (17). In our study, 12.5% of inconclusive foci on WBS were determined as benign and pathology was ruled out in these patients. In a small number of patients, additional focus was detected with SPECT/CT in the cervical and thoracic region. Thyroid remnant compatible foci were small-sized and accumulated low radioiodine. The advantage of having higher contrast resolution with SPECT/CT may provided the detection of these foci. Focus in the bone structure of thoracic region was missed on WBS because of the location (the lateral costal area) and the low intensity.

There are some studies highlighting the limitations of SPECT/CT in the evaluation of patients with DTC. In areas that are not well delineated by CT, results may remain equivocal on SPECT/CT findings in 7-8% of cases. (10,15). Wong et al. reported that particularly in proven N1 disease, SPECT/CT is of limited value in revealing regional lymph node metastases in the presence of post-operative thyroid remnants (18). By extending the duration of the examination, SPECT/CT makes patient uncomfortable and this may cause patient movement. In this case, possible misregistration of SPECT and CT information may lead to false positive

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or negative results (9). Also, because of extra time required for SPECT/CT, some physiological activities may displace or disappear and become misleading in interpretation. In our study, 14,1% of WBS detected foci were no more detectable on SPECT/CT images. For this reason, it is necessary to obtain SPECT/CT as soon as possible after WBS. Considering the patient comfort and the risk of image misregistration, SPECT/CT should be performed in cases with equivocal / inconclusive findings on WBS.

### **Conclusion**

The possibility of overcoming the limitations of <sup>131</sup>I WBS with SPECT/CT increases the routine usage of this modality. In the recent literature, some authors reported high specificity and improved lesion location by SPECT/CT in DTC patients. Despite some minor limitations, the method clearly improves the classification and localization of <sup>131</sup>I accumulation sites in patients with DTC. Particularly in distinguishing lymph node metastases from thyroid remnants, lung metastases from mediastinal uptake or thoracic bone metastases, SPECT/CT has higher specificity than WBS. SPECT/CT has also value in detecting additional lesions compared to conventional planar imaging.

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### Figure Legends

**Figure 1:** A 46-year-old female underwent total thyroidectomy with follicular thyroid carcinoma (TSH: 100  $\mu$ IU/mL and Tg:>300 ng/mL). I-131 whole body scan showed I-131 accumulation in the left shoulder, thoracic region and left posterior pelvic area (1A). On SPECT/CT images, thoracic accumulations were localized in lytic lesions containing a soft tissue component at the anterior portion of the left 2nd - right 6th ribs and humeral head and one low intensity focus was at the posterior portion of left iliac bone (1B).

**Figure 2:** A 75-year-old male underwent total thyroidectomy with papillary thyroid carcinoma (TSH: 100  $\mu$ IU/mL and Tg: 1010 n/mL). In the I-131 whole-body scan (2A), I-131 accumulation was observed in the upper thorax at right of the medial line. On SPECT/CT images, the accumulation was localized in the right high mediastinal-paratracheal lymph nodes (2B).

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## Tables

**Table 1:** Number of inconclusive foci detected on whole body scanning and foci detected on SPECT/CT.

	Neck	Thorax	Abdomen	Extremity	TOTAL
WBS	35	19	9	1	64
SPECT/CT	33	20	5	1	59

WBS: Whole Body Scanning

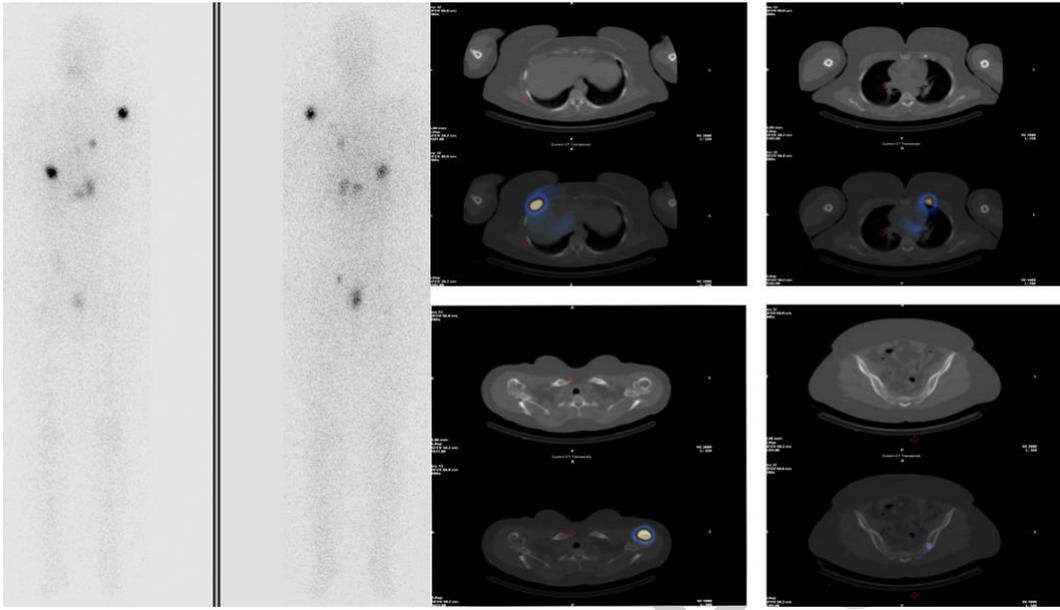
**Table 2:** Number of detected foci on SPECT/CT imaging according to the location.

Neck	Thorax				Abdo men	Extre mity	TOT AL					
Thyr oid Rem nant	Ly mph Nod e	Nasal/D ental	Esoph agus	Lu ng	Medias tinal Lymph Node	Bo ne Tiss ue	Bre ast Tiss ue	Pelvic soft Tissu e	İntest ine	Bo ne		
24	5	2	2	7	5	6	2	2	2	1	1	59

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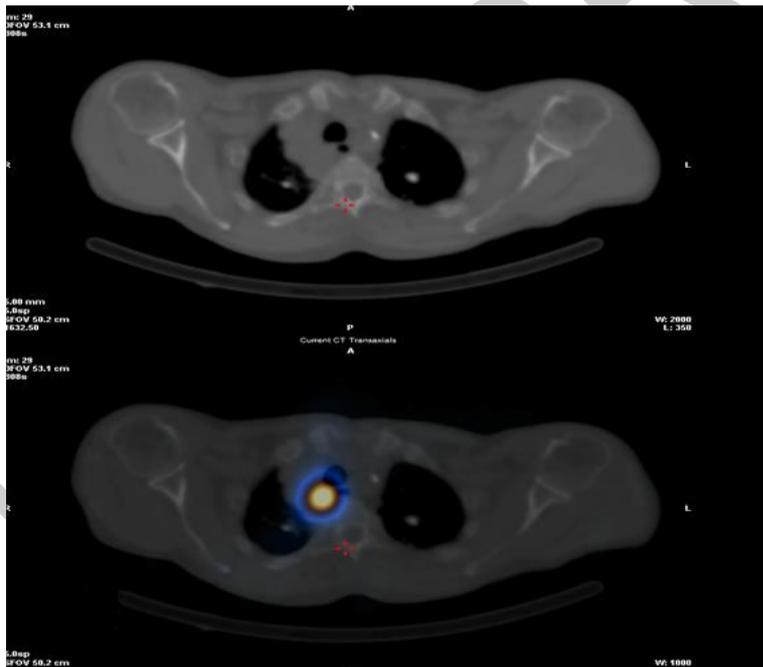
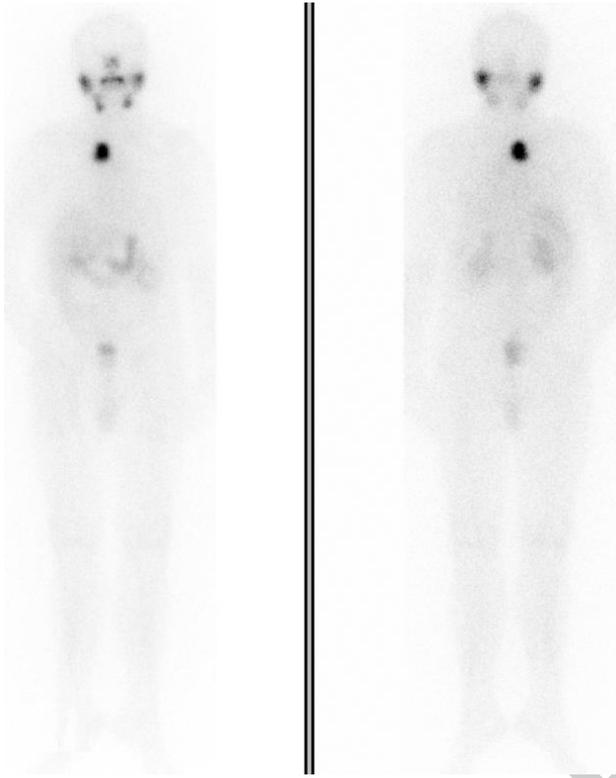
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