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The Role of ^{131}I SPECT-CT as a Diagnostic Tool in Management of Patients with Differentiated Thyroid Cancer

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ABSTRACT

The purpose of the study was to estimate the value of using of 131I single photon emission tomography – computed tomography (SPECT/CT) in differentiated thyroid carcinoma (DTC) for diagnoses and follow up. **Methods:** Eighty-seven planar whole body scan (WBS) and SPECT/CT neck and chest were obtained for 77 pathologically proved DTC patients (17 males and 60 females; age range, 14 – 79 years). Fifty-two scans were 131I diagnostic (Dx) follow up studies, and 35 scans were 131I post-therapy (Rx) studies. Results: Planar scans depicted 106 foci in 45 studies (61 in the neck and 45 in distant sites); SPECT/CT scans depicted 125 foci in 51 studies (72 in the neck and 53 in distant sites), and characterized 16 indeterminate foci on planar scans in 13 /45 positive planar studies (28.9%). Both Planar and SPECT-CT scans were concurrently positive in 45 studies (51.7%), concurrently negative in 36 studies (41.4%), and discordant in 6 studies (6.9%). The incremental diagnostic value of SPECT-CT over planar imaging was obtained for approximately 30 % of detected lesions. **Conclusion:** SPECT/CT had better diagnostic information compared with planar whole body imaging. It correctly modified the risk classification defined by planar imaging and allowed for avoidance of unnecessary radioiodine (RI) treatment.

Key Words: SPECT-CT **&** Differentiated Thyroid Cancer.

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INTRODUCTION:

Thyroid cancer accounts for 95% of all endocrine cancers and approximately 2% of all cancers diagnosed all over the world [(1)]. Papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) are collectively classified as DTC, and accounts for at least 94% of thyroid carcinoma [(2)]. Although ^{131}I WBS, in association with serum thyroglobulin (TG) measurement, is considered as the main stay of the diagnostic strategy in patients with DTC, interpretation of planar images may be difficult because of the absence of anatomic information [(3)]. On the other hand, false positive findings can occur on the WBS due to benign processes, physiological radiation excretion or contamination [(4)]. The combination of functional and anatomic information provided by SPECT/CT has many advantages in different clinical settings; it allows better anatomic localization of radioactive foci, in addition to CT benefits. Hybrid SPECT/CT represents a powerful tool for assessing unexpected concentrations of ^{131}I resulting from physiological uptake, radioactive secretions or excretory products, inflammation and other mechanisms of uptake [(5.6)].

Aim of The work: To assess the value of ^{131}I SPECT-CT as a diagnostic tool in management of patients with differentiated thyroid cancer**.**

PATIENTS AND METHODS:

77 patients (17 males and 60 females; age range, 14 – 79 years) who previously underwent thyroidectomy for DTC (62 PTC and 15 FTC) were referred to Nuclear Medicine unit, South Egypt cancer Institute, Assiut University to perform Dx or Rx ^{131}I WBS and SPECT-CT imaging studies were prospectively studied, 67 patients had been underwent one study and the other 10 patients had been underwent 2 studies. A total of 87 ^{131}I WBS and SPECT-CT studies were performed; 52 scans were Dx (59.8%) and 35 scans were Rx studies. 20 scans (23%) after the 1st postsurgical therapeutic dose of ^{131}I for remnant radioiodine ablation (RRA)and 15 scans (17.2%) after repeated RI treatment (RIT) for suspected or proved persistent, recurrent or metastatic disease. All patients were examined at high TSH level (≥ 30 μIU⁄ ml); except for 3 patients their TSH level failed to be increased (TSH was <30 μIU⁄ ml). Patient preparation included a low-iodine diet and avoidance of iodide-containing medications for 7-14 days before RI administration, iodinated contrast investigations within the previous 2 months as well as pregnancy and breast feeding

Were excluded, and contraception was confirmed in all child bearing female patients. The specific ^{131}I therapeutic dose was determined according to the patient risk profile including histopathological features, stimulated TG levels, clinical parameters, and other imaging studies when available. Patients were scanned 5–10 as post therapy scan following 80 - 200 mCi or 2-3 Days following 2- 5 mCi of ^{131}I, diagnostic dose.

Imaging Procedure: ^{131}I Whole-body scanning: ^{131}I WBSs were firstly obtained in the anterior and posterior projections using dual-head γ-camera (Siemens; Symbia T) with parallel-hole high energy collimators, using a 20 % energy window set at 364 keV. The table speed was 8 cm/min, matrix size 256x1024, anterior& posterior static views of the neck and thorax (10 min ⁄ view) were routinely obtained for all patients; static views of additional parts of the body were obtained as dictated by the WBS results.

SPECT/CT Imaging: Immediately after planar scintigraphy, SPECT/CT images of the neck and chest were routinely obtained for all subjects. In 9 studies additional SPECT/CT images were acquired on the skull, abdomen/ pelvis, and extremities because of suggestive findings were noted on planar images in 7 studies,

SPECT images were acquired in a step and-shoot mode (25 s ⁄ stop) for Dx imaging and (10 s ⁄ stop) for Rx imaging, with 64 frames⁄ head were acquired using a noncircular orbit, over 360º (180º per head); tomographic images were reconstructed into a 128 x 128 matrix using iterative reconstruction (transverse, sagittal, and coronal slices were generated). Then CT (low-dose one slice CT) scans were acquired with a tube voltage of 130 kelo Voltage and the tube current was (70 milli ambers). Reconstructed slice width was 2 mm.

Image Interpretations: Planar and SPECT/CT images were reviewed by 2 separate nuclear medicine physicians. Planar scan results were considered to be positive when one or more areas of uptake incompatible with physiologic activity were identified. Diffuse uptake in the gastrointestinal tract, urinary bladder and liver was considered physiologic.

SPECT-CT scan results were considered positive when one or more areas of uptake with or without CT correlate were identified after exclusion of physiologic uptake. Planar and SPECT/CT findings were confirmed by both clinical assessment and the main routine investigations (Neck ultrasound (NU), TG & TG-Antibodies (TG Abs).

In addition to the other confirmatory investigations that had been done in this study included: Histopathology (n = 4), Bone scan (n = 1),^{131}I Rx WBS (which confirmed the presence or absence of disease in the Dx follow up studies, n =3), contrast enhanced CT (CECT) {chest (n = 5), neck (n = 4), pelvis (n = 1), skull (n = 1)}, MRI Whole body (n = 1) and MRI neck (n = 1)

Indeterminate planar imaging findings; means that, the nature and or location of RI uptake was unclear. The incremental diagnostic value to SPECT-CT over the planar imaging was assigned with respect to better localization and characterization of focal RI activity, precise differentiation of the indeterminate findings, and detection of higher number of the RI foci which were occult on the WBS.

For each patient, focal ^{131}I uptake on planar or SPECT/CT images was analyzed for the neck (loco-regional site), and outside the neck (including both chest and other distant sites). Neck foci on planar scans, included both thyroid bed and extra-thyroid bed foci; the extra-thyroid bed foci were reclassified as lymph nodes metastasis (LNM) or indeterminate.

On SPECT-CT, neck foci were anatomically localized and characterized as thyroid bed, thyroglossal duct remnant , LNM, bone metastasis, soft tissue metastasis and physiological uptake.

Chest foci were classified on the basis of planar scan to pulmonary metastasis, mediastinal LNM and indeterminate; and reclassified after SPECT-CT imaging to pulmonary metastasis, mediastinal LNM and bone metastasis.

On planar imaging RI foci in other distant sites had been classified to bone metastasis and indeterminate; after SPECT-CT they were reclassified to bone metastasis.

The risk of recurrence according to American thyroid association (ATA) guidelines was estimated in RRA patients, considering histopathology findings. The risk of recurrence was then reassessed considering any additional findings from the I131 planar & SPECT/CT scans separately.

We addressed how often SPECT/CT findings changed the initial risk stratification, because these changes would affect the patient's follow-up.

RESULTS:

The study population consisted of 77 patients, age range, 14 – 79 years this group include 17 males and 60 females; 62 are papillary while only 15 patient are follicular carcinoma, the majority of patients are stage one (59.1%) ***(Table 1)***.

Table (1): Patients characteristics and demographic data of the 77 patients with cancer thyroid.

	No. (n= 77)	%
Sex:		
Male	17	22.1
Female	60	77.9
Tumor histology:		
Papillary	62	80.5
Follicular	15	19.5
Staging (TNM) at diagnosis :		
Stage 1	46	59.7
Stage 2	7	9.1
Stage 3	10	13.0
Stage 4	14	18.2

Planar scans depicted 106 foci (61 in the neck and 45 in distant sites). SPECT/CT scans depicted 125 foci (72 in the neck and 53 in distant sites). Whereas the sensitivities of SPECT/CT and planar imaging did not show statistical difference (78.8% vs. 73.9% respectively, P value > 0.05) for RI positive foci which increased to 89% for all lesion (include non-iodine avid lesion seen only in CT images), with significantly higher the SPECT/CT specificity than that of planar imaging (100% vs. 73 %, P value < 0.05)

Table (2) Distribution of ^{131}I foci according to their sites on planar and SPECT/CT imaging

Site of uptake	Planner (106)		SPECT/CT (125)	
	No	%	No	%
Neck	61	57.5 %	72	57.6 %
Chest	25	23.6 %	29	23.2 %
Distant sites outside the chest	20	18.9 %	24	19.2 %
Total	106	100 %	125	100 %

I-Localization & Characterization of ^{131}I uptake in the Neck: Planner imaging neck region: 61 radioactive neck foci detected on planar WB imaging in 34 studies were classified as thyroid bed uptake (41 foci), LN (14 foci) however (6 foci) were considered as indeterminate findings ***(Table 2)***. SPECT/CT imaging neck region: All of the 61 radioactive neck foci were detected on SPECT/CT imaging in 34 studies and were classified as thyroid bed uptake (37 foci), LN (12 foci) however (10 foci) were considered as physiological uptake (in the tracheostomy tube, thyroglossal duct remnant and salivary uptake as well as bone metastases in (2 foci) ***(Table 2)***.

Thyroid bed: SPECT-CT and planner images are concordant in 35 foci out of 41 foci considered as thyroid bed by planner images with degree of agreement of 85%.

LNM: SPECT-CT showed all 14 foci interpreted as LNM on planar imaging, confirmed 10 of them as LNM with degree of agreement nearly 71%. SPECT-CT characterized 6 indeterminate foci detected on planar imaging in 5 studies and confirmed 5 of them as physiological uptake with degree of agreement nearly 83% ***(Table 3 and Figure 1).***

Chest: In the chest, planar imaging detected 25 foci and SPECT-CT detected 29 foci.

Pulmonary metastasis: SPECT-CT showed all 14 foci classified as pulmonary metastasis on planar imaging, and confirm only 8 of them, with degree of agreement nearly 57% . ***(Figure 2).***

Mediastinal LNM: SPECT-CT also showed all 5 foci classified as mediastinal LNM on planar imaging in 5 studies, confirmed 3 of them in 3 studies with degree of agreement nearly 60%.

SPECT-CT characterized 6 foci in 5 studies that had been indeterminate on planar imaging to physiological uptake (oesophagus (2 foci), thymus (2 foci) and breast (2 foci) with degree of agreement nearly 100%.

Other distant sites outside the chest: In the skull, abdomen⁄ pelvis, and extremities SPECT-CT showed 20 foci concordantly with planar imaging in 11 studies.

Bone metastases: SPECT/CT confirmed 11 of 16 foci diagnosed as bone metastasis on planar imaging in 4 studies, but changed the diagnosis of 5 foci bone metastasis to physiological uptake (dental artificial material and orbital uptake (3 foci) in 3 studies with degree of agreement nearly 68%. Also; SPECT-CT characterized additional 4 foci interpreted as indeterminate on planar imaging, and clarified them as physiological colonic uptake and costo-vertbral metastasis.

A B

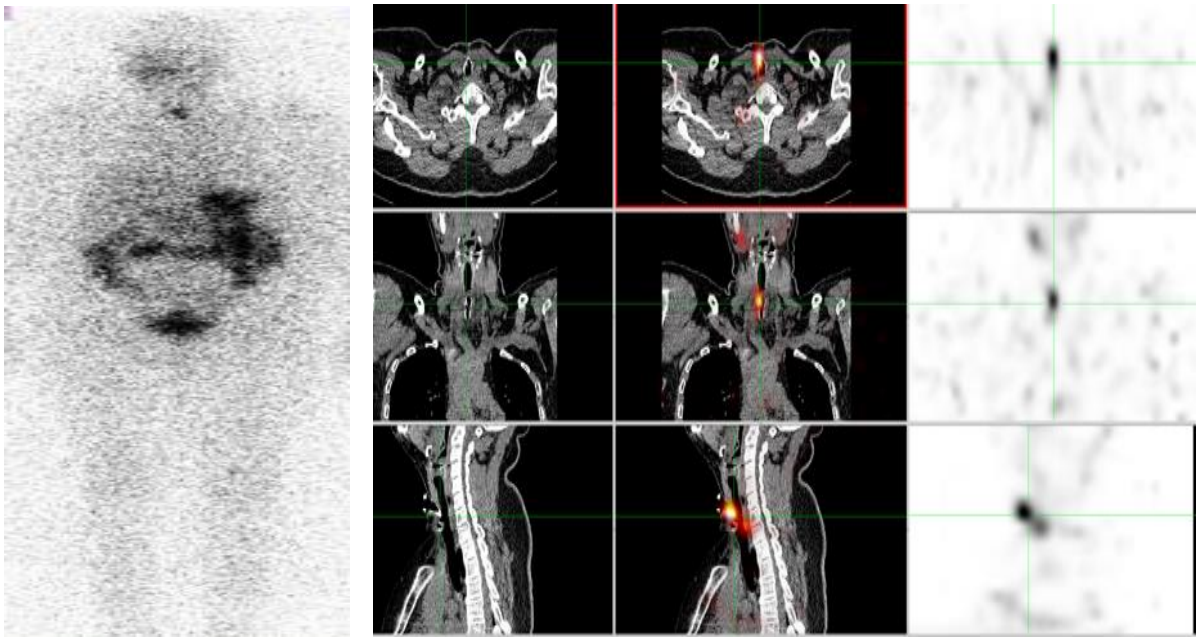

Figure (1): 48 years-old female with PTC, after surgery and radio iodine therapy. TG was 123 ng / ml, with negative anti TG-Abs. Dx follow-up WBS. (A) Planar static whole body showed a focus of RI uptake in the lower neck. (B) SPECT/CT precisely localized this activity in the tracheostomy tube at the base of the neck (false positive result).

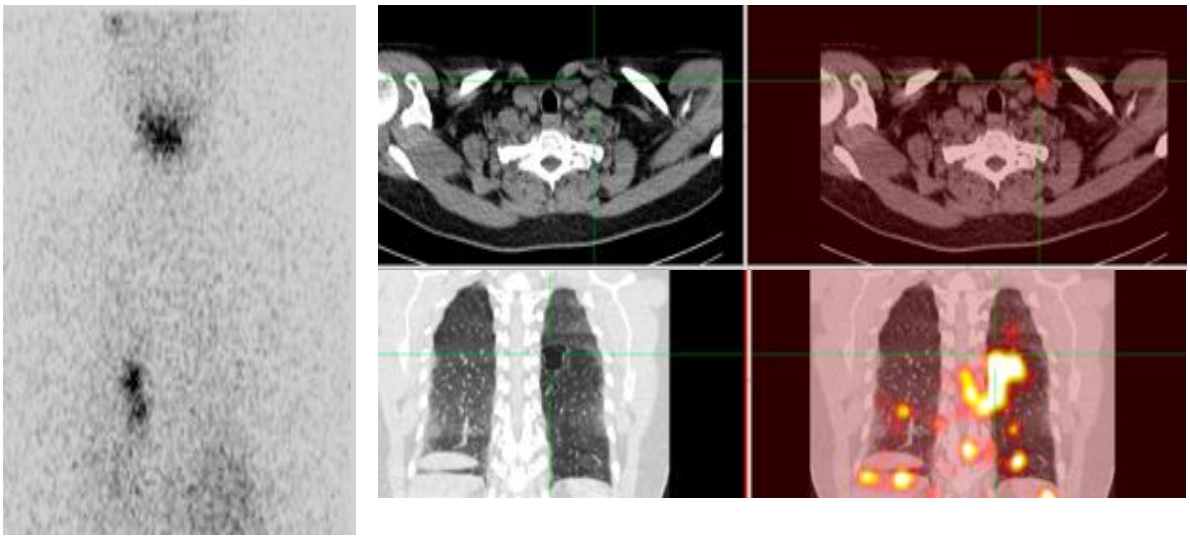

Figure (2): 47 years-old Female with PTC, after surgery and radio iodine therapy; (A) Rx WBS Planar static images showed two foci of RI activity in the left side of the chest interpreted as pulmonary metastasis. (B) SPECT/CT identified bilateral micro-nodular pulmonary metastases and left supra-clavicular LN in addition to false positive results related to the presence of bronchiectasis not seen on planar imaging.

Table (3) concordant lesions using planner and SPECT/CT.

Region	*Number of concordant lesion Between planner &SPECT/CT*	*percentage*
Neck		
Thyroid bed	(35/41)	85%
LNM	(10/14)	71%
Physiological uptake	(5/6)	83%
Lung metastasis	8/14	57%
Mediastinal LNM	3/5	60%
Bone metastasis	0	0%
Physiological uptake	6/6	100%
Other body regions	Physiological uptake 3/4	75%
	Bone metastasis 11/16	68%
Total	31/45	68%

Occult foci seen only in SPECT/CT; 19 out of 125 15.2% are seen in SPECT/CT and not seen in planner images (11 foci at the neck region, 4 foci as pulmonary, 4 foci as bone metastases.

Added value of the concomitant CT: The CT portion of the SPECT-CT provided additional information about non iodine-avid lesions in 8 ⁄87 studies (9.2%). tiny pulmonary nodules, in 6 patients and enlarged cervical LNS non avid to ^{131}I Dx scan (1 study), to radioactive and proved by US.

Impact on Management: With SPECT-CT findings, additional radiological studies were avoided in 18 ⁄45 patients with positive planar studies for whom proper diagnoses of physiological uptake; and avoidance of unnecessary RI treatment in 13⁄52 follow up studies (25%).

Impact on Risk Classification:

On the basis of the current *American Thyroid Association (*ATA), the 20 radioactive iodine remnant ablation (RRA) patients were risk-classified as follows: 9 were classified as low risk, 7 as intermediate risk, and 4 as high risk. According to planar findings; 11 were reclassified as low, 4 as intermediate, and 5 as high. While, after SPECT-CT imaging; 15 were reclassified as low, 4 as intermediate, and 1 as high.

In 8⁄ 20 patients (40%) SPECT-CT changed the risk classification: 7 patients were assigned to a lower risk category and

only patient was assigned to a higher risk category (from low to intermediate risk).

Sensitivity of SPECT/CT: in the current study, the sensitivities of SPECT/CT were 78.8 % as compared to planar imaging 73.9% with no significant statistical difference. However, if taking into account the non-iodine avid lesions which were identified by the CT component, the sensitivity of SPECT/CT increased to 89% vs. 73.9% for planner images.

DISCUSSION:

We evaluated the role of SPECT/CT in patients thyroid ectomized for DTC in both the post-therapy and diagnostic follow up radioactive scan similar date settings is agreed was reported by ***Tharp*** [(7)] ***Spanu*** [(8)] and ***Menges*** [(9)] , they assessed the role of SPECT-CT in (post-therapy and follow up) settings respectively. Whereas ***Savas*** [(10)] and ***Avram*** [(11)], who investigated the role of SPECT/CT in DTC patients after thyroidectomy but before ^{131}I therapy.

In our study we evaluate the post-surgical thyroid remnant by ^{99m}Tc Pertechnetate thyroid scintigraphy and neck ultrasound.

Kohlfuerst [(12)] and ***Blum*** [(6)] stated that SPECT/CT of the neck and chest was obtained only in the light of equivocal planar findings; in contrast, we obtained SPECT/CT of the neck and chest in one field of view routinely for all patients. Similar date was presented by ***Grewal*** [(13)] and ***Maruoka*** [(14)] thus avoiding any selection bias and addressing the most important metastatic disease sites are the neck nodes and lungs.

In the current study, the sensitivities of SPECT/CT was 89% vs. 73.9% for planner images, which is comparable with which is comparable with ***Menges et al*** [(9)]. Who studied 123 patients and reported similar sensitivities for SPECT-CT and planar scans of 62% for RI positive foci, which increased to 74% for SPECT-CT after addition of the non-iodine avid lesions.

Whereas, ***Barwick et al*** reported that SPECT/CT significantly improved the imaging sensitivity from 73% for planar to 100% for SPECT-CT (73% vs. 100%, $P< 0.05$) [(15, 16)].

In our study, the incremental value of I131 SPECT-CT over whole body scan was obtained for approximately 30 %, Similar date was presented by ***Spanu et al*** performed SPECT-CT neck and chest routinely for all patients with incremental value of 34% [(8)].

Chen found the incremental diagnostic value in 17⁄ 37 post-therapy SPECT/CT over planner imaging (46%). The reason for the higher value in such study were considered to have locally advanced or metastases after thyroidectomy and thus a igh prevalence of malignant foci. Detected

in SPECT-CT [2]. with respect to precise localization and characterization of RI foci achieved by SPECT-CT over planar imaging; in our study 16 indeterminate foci were found in 13⁄45 positive planar studies (28.9%), including 6 foci in the neck and 10 foci outside the neck, which included chest, and abdomen/pelvis. SPECT/CT revealed 11 foci due to physiologic uptake, 4 foci due to thyroid remnant tissues, and 1 focus due to bone metastasis. Similar results was noted by ***Maruoka et al*** compared post-therapy SPET–CT scans in 147 patients to the WBS and reported that SPET–CT clarified the equivocal foci in 40 ⁄147 positive planar studies (27.2%) to metastatic regional lymph nodes, thyroid remnant tissues, and physiological or benign uptake [14].

In the present study, SPECT/CT changed the risk classification for 8⁄20 postsurgical patients studied after RRA (40%); While ***Schmidt*** found that SPECT/CT altered risk stratification in 25% of patients; the lower value was due to selection of only patients with suspected or proved loco-regional disease, so that the SPECT-CT study was done for the neck only (change of risk stratification from low to intermediate and vice versa without involvement of the high risk group) [17].

Grewal, et al, performed post-therapy sans on 148 patients showed that SPECT/CT changed the risk classification for (6.5%) of patients, the significantly lower percentage of change in risk classification in this study is due to pre selection of the patients Therefore, their population only included at intermediate and high risk patients, in whom ^{131}I treatment is considered essential [13].

Also, In the present study, SPECT- CT imaging showed that radiological studies were avoided in 18 ⁄45 positive planar studies (48%) for whom they would have been considered necessary after planar scan alone, the same result (48%) was reported by (13).

Avoidance of unnecessary RI treatment was permitted in 13 of the 52 follow up studies (25%) (4 patients of them (7.7%) SPECT-CT confirmed physiological uptake. Similar date was presented by ***Tharp et al*** performed SPECT-CT and confirmed that negative WBS findings were correlated to clinical follow up and laboratory investigations [7].

CONCLUSIONS:

The current study revealed that I131 SPECT/CT significantly improved the diagnostic localization compared with planar scanning alone. It correctly modified the risk classification defined by planar imaging and allows avoidance of unnecessary RI treatment and additional imaging studies.

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