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ORIGINAL ARTICLE

Contribution of SPECT-CT to Planar Imaging in Post-Ablation Imaging in Different Thyroid Cancers, the Clinical Significance of the Differential Diagnosis of Neck and Thorax Uptakes

Diferansiye Tiroid Kanserlerinde Ablasyon Tedavisi Sonrası Görüntülemede Boyun ve Toraks Bölgesindeki Odakların Ayırıcı Tanısında SPECT-CT'nin Planar Görüntülemeye Katkısı ve Klinik Önemi

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ABSTRACT

Background: This study aims to demonstrate the superiority of Single Photon Emission Computed Tomography-Computed Tomography (SPECT-CT) over planar imaging in distinguishing benign from malignant foci and patient management after 131I ablation therapy in patients with differentiated thyroid cancer (DTC).
Material and Methods: Planar and SPECT-CT imaging findings were retrospectively analyzed in Eighty patients who received I-131 therapy for thyroid cancer. Possible foci in whole body scanning (WBS), neck, and thorax were compared with SPECT-CT. Anatomical localization of the foci and differential diagnosis of the benign and malignant lesion was made with SPECT-CT. Those without anatomical counterparts were recorded as equivocal foci. According to the 2015 American Thyroid Association (ATA) guidelines, patients were divided into three groups: High, intermediate, and low-risk groups. Interpretation changes between both scannings were recorded as downstage and upstage.
Results: A total of 80 patients, 53 female, and 27 male, were included in the study. The patients' age ranged from 21 to 88 years with a mean age of 47 ±14.2. In 80 patients, 139 foci were detected in planar images and SPECT-CT images (neck: 118, thorax: 21). SPECT-CT revealed that 50% of the lateral neck foci were compatible with pathologies of malignant nature and 50% with pathologies of benign nature. Foci in the middle part of the neck were not only thyroid remnant (56%) but also thyroglossal duct remnant (40%) foci at a significant rate. It was determined that 66% of the foci in the thorax region were lung metastases ,and 34% were bone metastases. It was proved that 33% of the foci in the mediastinal area were lymph nodes. Although only one of the remaining patients had a pathological diagnosis, it was thought that all of them might have thymus pathologies. SPECT-CT images changed the interpretation of 18 patients (22.5%), 5 of whom (6.25%) were upstage and 13 (16.25%) were downstage.
Conclusions: SPECT-CT will be very effective in, facilitating patient management and avoiding unnecessary procedures, especially in moderate/high-risk patients with suspicious focal lesions. Knowing the benign iodine uptake foci (thyroglossal duct remnant, etc.) that show iodine uptake other than the thyroid residue in the neck may be influential in deciding whether to ablate in low-risk patients.

Key words: 131I, Differentiated Thyroid Cancer, Whole Body Scanning, SPECT-CT

ÖZ

Amaç: Bu çalışmanın amacı, diferansiye tiroid kanserli (DTC) hastalarda I-131 ablasyon tedavisi sonrası odakların benign-malign ayrımını ve hasta yönetimini ayırt etmede Tek Foton Emisyonlu Bilgisayarlı Tomografi-Bilgisayarlı Tomografi'nin (SPECT-CT) planar görüntülemeye (WBS) göre üstünlüğünü göstermeyi amaçlamaktadır.
Gereç ve Yöntem: Tiroid kanseri nedeniyle I-131 tedavisi alan 80 hastanın, planar WBS ve SPECT-CT bulguları retrospektif olarak incelendi. Planar görüntülerdeki boyun ve toraksta olası odaklar SPECT-CT ile karşılaştırıldı. 2015 Amerikan Tiroid Birliği (ATA) yönergelerine göre hastalar üç gruba ayrıldı: Yüksek, orta ve düşük risk grupları. Her iki görüntüleme arasındaki yorum değişiklikleri downstage ve upstage olarak kaydedildi.
Bulgular: Çalışmaya 53 kadın ve 27 erkek olmak üzere toplam 80 hasta alındı. Hastaların yaşları 21 ile 88 arasında değişmekte olup,
ortalama yaş 47 ±14.2 idi. 80 hastada planar ve SPECT görüntülerinde (boyun: 118, toraks: 21) 139 odak tespit edildi. SPECT-CT, lateral boyun odaklarının %50'sinin malign patolojilerle, %50'sinin de benign patolojilerle uyumlu olduğunu ortaya koydu. Boyun orta kısmındaki odakların sadece tiroid kalıntısı (%56) değil, önemli oranda tiroglossal kanal kalıntısı (%40) odakları olduğu saptandı. Toraks bölgesindeki odakların %66'sının akciğer metastazı olduğu belirlendi. %34'ü ise kemik metastazıydı. Mediastinal bölgedeki odakların %33'ünün lenf düğümleri olduğu tespit edildi. Geriye kalan hastaların sadece birinde patolojik tanı olmasına rağmen diğerlerinin de timus patolojisi olabileceği düşünüldü. SPECT-CT, 5'i (%6.25) upstage ve 13'ü (%16.25) downstage olmak üzere 18 hastanın (%22.5) yorumunu değiştirdi.
Sonuç: Özellikle şüpheli fokal lezyonları olan orta/yüksek riskli hastalarda SPECT-CT kullanımı hasta yönetimini kolaylaştırmış olup gereksiz invazif işlemlerden kaçınılmasında etkili olmuştur. Boyunda tiroid kalıntısı dışında iyot tutulumu gösteren benign iyot tutulumu olan odakların (tiroglossal kanal kalıntısı vb.) bilinmesi, düşük riskli hastalarda ablasyon kararı verip-vermemede etkili olabilir.

Anahtar Kelimeler: I-131, Diferansiye Tiroid Kanseri, Tüm Vücut Taraması (Whole Body Scanning), SPECT-CT

Background

Differentiated thyroid carcinoma (DTC) is the most common type of endocrine cancer worldwide. It is classified histopathologically as papillary (80.2%), follicular (11.4%), hurthle cell (3.1%), medullary (3.5%) and anaplastic (1.7%) (1). Papillary and follicular carcinomas account for the majority of DTC, and these histological variants are characterized by radioiodine uptake. 5-year survival rates in DTC have been reported as 99.8% for early-stage tumors, 97.0% for regional metastases, and 57.3% for tumors with distant metastases (2). Age, male gender, tumor size, pathological subtypes, extrathyroidal spread, metastatic disease, and iodine uptake affect the prognosis (3).

Morphological imaging methods such as 131I Whole body scan (WBS), ultrasonography (US), computed tomography (CT), and biochemical markers such as thyroglobulin (Tg), antithyroglobulin (TgAb) are used in staging (4). Functional imaging using 123I and 131I in patients with differentiated thyroid cancer provides important information about suitability for treatment and comprehensive stage of the disease. In these patients, whole-body imaging is performed following 131I ablation therapy after total thyroidectomy as standard for disease staging(5). However, since the resolution of whole-body imaging is limited in planar 131I, abnormal and sometimes physiological 131I uptake may result in incorrect localization and characterization (6). Although single-photon emission tomography (SPECT) imaging has better resolution than planar 131I whole-body imaging, it may not be accurate enough to characterize it due to the lack of anatomical markers. SPECT-CT (hybrid imaging) provides functional and structural data together in a single session. This technique provides a significant advantage in patient management by demonstrating the localization and characterization of iodine-avid and non-avid abnormalities (7).

In this study, we aimed to investigate the contribution of hybrid imaging to patient management by making anatomical correlations with SPECT-CT of indeterminate RAI involvement in planar WBS after 131I ablation therapy in patients with thyroid cancer.

Materials and Methods

One hundred nineteen patients who underwent planar 131I WBS and SPECT-CT imaging after total thyroidectomy between 2018 and 2021 were analyzed retrospectively. 34 of these patients were not included in the study because SPECT-CT was not performed. The dose of 131I ranged from 50 to 200 mCi according to the institutional protocol, guided by the American Thyroid Association (ATA) risk classification (5). Thyroid functions were checked in all patients. Tri-iodothyronine (T3) was discontinued fortwo2 weeks, and TSH level was ensured to be >30 miU/l after discontinuation of thyroxine (T4) 4 weeks before treatment. A low-iodine diet was given for two weeks before radioiodine therapy. Histological type/grade and clinical data obtained were from multidisciplinary team meeting correspondence and an electronic patient information system. Response to treatment was based on non-stimulated Tg values <0.2 ng/mL and normal imaging findings. Patients were classified as low (L), intermediate (IM), and high (H) risk according to the 2015 ATA risk classification.

Data Analysis

Informed consent was obtained from all registered patients, and the protocol was approved by the Selçuk Medical Faculty Ethics Committee (17.02.22-2022/84). Independently prepared by two nuclear medicine physicians with at least ten years of experience who are blind to clinical details. WBS and SPECT-CT images of the patients were examined sequentially.

131I WBS analysis

The foci were divided into two necks and thorax. Foci in the neck were divided as middle and lateral. Symmetrical salivary glands and breast involvement, hot nose, and contamination foci were not included in the study.

Single or multiple foci in the midline of the neck are grouped as probable thyroid remnant (TR) or thyroglossal duct remnant (TGDR). Unilateral foci on the lateral neck were differentiated as probable lymph nodes (LN). Diffuse involvement in both lung regions, possible lung metastases, and foci in the midline of the thorax (away from the neck) were grouped as possibly mediastinal LN. Each lung was taken as a single focus in diffuse metastases of the lung. Focal uptake in both lung regions was categorized as probable lung or bone metastases.

SPECT-CT analysis

Single foci located laterally in the neck were considered cervical lymph nodes (CLN). The middle part of the neck was divided into two as superior and inferior according to the lower margin of the thyroid cartilage. Foci under the lower margin of the thyroid cartilage were recorded as thyroid remnants (TR). The foci from the inferior margin of the thyroid cartilage to the level of the hyoid bone were defined as thyroglossal duct remnant (TGDR). The uptakes in this region that may be compatible with lymph nodes and pyramidal lobes were excluded. Diffuse or focal foci in the lung were evaluated as metastases. Anatomically determined foci in the mediastinum by CT were grouped as mediastinal lymph nodes, and those without it were grouped as equivocal mediastinal LN. Foci in planar images were compared with SPECT-CT, and interpretation changes were recorded as downstage and upstage.

Imaging Protocol

131I WBS was performed 5-7 days after radioiodine treatment. Additional planar images of the neck were obtained using anterior and posterior projections. A departmental imaging protocol of a dual-head gamma camera (GE Optima, NM/CT 640, 4 slices CT scanner) was used. 131I WBS images were obtained by using a high-energy, high-resolution collimator (neck: matrix 256 × 256, energy window 364 ± 10% and WBS: matrix 256 × 1,024, energy window 364 ±

20%). Scan speed was 30–80 mm/min depending upon the count rate from head to knees. SPECT-CT was performed during the same session as the whole body planar imaging. SPECT-CT images of the neck and thorax were performed in all patients. CT images were acquired using a fixed protocol (120 keV, 30mAs/ slice). All SPECT-CT images were obtained using a hybrid system (GE Healthcare, Optima NM/CT 640). SPECT data were acquired for the region of interest (matrix size, 128x128 pixels, 6° angle steps, 20 s/frame). The acquisition parameters for CT were: 120 keV, pitch 0.75, rotation time 1s, and slice thickness of 2.5 mm. SPECT images were then acquired with a high-energy, high- resolution collimator and 64 projections over 360° of the dual-head gamma camera. The energy window of 10% was centered over 364 keV.

Statistical analysis

Data were analyzed using standard statistical parameters in Microsoft Excel. The data were analyzed using percentages to examine the relationship between the variables. The mean age of the patients was calculated together with the standard deviation. The percentages of SPECT-CT and planar 131I WBS foci, stage changes, and indeterminate foci were calculated.

Results

The 80 patients consisted of 53 women and 27 men. The patients' age ranged from 21 to 88 years, with a mean age of 47 ±15.5. Seventy-three of the patients were diagnosed with papillary thyroid (%91), 5 with follicular thyroid cancer (%6), and two patients with hurtle cells cancer (%3). Ten patients were given radioiodine therapy for recurrent or metastatic disease. Two of these patients, who received high-dose 131I ablation therapy (100-200-200 mCi) three times, developed an iodine-refractory state and continued treatment with tyrosine kinase inhibitors.

One hundred forty focal uptakes were detected in 131I WBS and SPECT images: 118 necks and 21 thorax regions. There were 14 foci probable CLN in the lateral and probable TR and TGDR 104 foci in the middle part. SPECT-CT, uptakes in the probable CLN group; 3 salivary glands (21%), 4 dental prostheses (29%), 6 CLN (43%), and 1 bone metastasis (7%). In the probable TR and TGDR group; TR:58 (56%), TGDR:42 (40%), dental prosthesis:2 (2%) and parapharyngeal LN:2 (2%). It was noted that 29 single focus (28%), TR: 18 (17%), TGDR: 9 (7%), parapharyngeal LN: 2 (4%) belonged to the midline of the neck (Figure 1). Uptake was not observed in the thyroid lodge in 13 patients in 131I WBS and SPECT-CT (16.25%).

In WBS, 21 foci were detected in the thoracic region, 12 in the probable (focal/diffuse) lung or bone met group, and 9 as probable mediastinal LN. Differential diagnosis of lung metastasis:8 (66%) and bone met:4 (34%) was detected with SPECT- CT. 4 of the probable mediastinal LN group were anatomically compatible with mediastinal LN and thymus remnant. Of the 4 mediastinal LNs, 3 were in the high-risk group, and PET-CT and radiological imaging confirmed metastatic. Although the other patient (case 4) was in the low-risk group, a biopsy was performed because of the high Tg after treatment (Tg: 54 after 3 months) and the lesion diameter of 4 cm on CT, and the result was reported as residual thymus (Figure 2). However, the other 5 were recorded as equivocal mediastinal LN since their borders could not be evaluated clearly in CT. The age range of this group was 20-56, with a mean age of 40. Of these, 3 were in the IM risk group and 2 were in the H risk group. Biopsy was not performed because the foci were also not confirmed by Thorax CT and follow-up Tg one year later was <0.2 ng/mL in 5 cases. Therefore, thymus pathologies were considered first. Planar and SPECT- CT RAI foci distribution are in Table 1.

According to ATA risk classification, of 80 patients: 10 were low risk (12.5%), 39 were intermediate risk (48.75%), and 31 were high risk (38.75%). SPECT-CT images changed the interpretation of 18 patients (22.5%), 5

of whom (6.25%) were upstage and 13 (16.25%) were downstage. Data consistent with the changes were obtained in the follow-up of the patients. The clinical data of the patients with additional information provided by the 131I SPECT-CT are in Table 2.

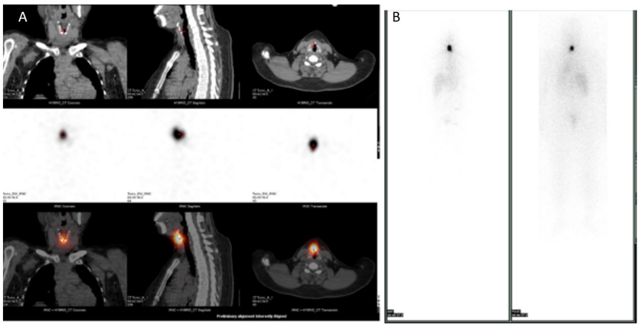

Figure 1. A 52-year-old female patient underwent surgery for thyroid papillary ca and received post-ablation 131I 100 mCi treatment. Neck midline single focus, thyroglossal duct remnant (TGDR) A: SPECT-CT image after neck ablation, B: Planar whole body scanning.

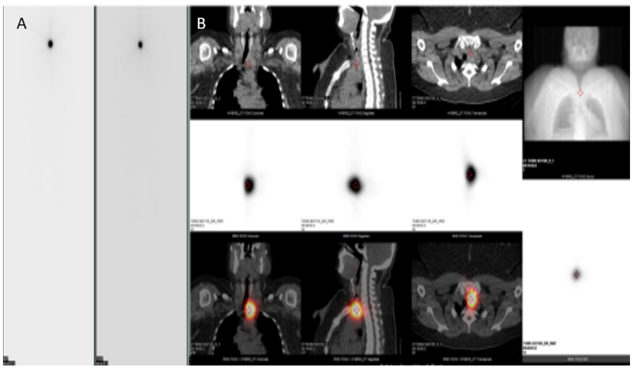

Figure 2. 48 years old female, after 50mCi 131I ablation treatment, intense focal uptake in the upper mediastinum in SPECT-CT, 3 months after Tg treatment: 54 ng/ml, 4 cm in diameter lesion in the upper mediastinum in thorax CT, biopsy: thymus remnant, post-operative Tg:0.1 ng/ml, Patient evaluated as downstage, A: Planar whole-body scanning, B: SPECT-CT image neck post-ablation.

Table 2. Clinical data of patients with additional information provided by 131I SPECT-CT (Tg: thyroglobulin, TgAb: Thyroglobulin auto-antibody, TSH: thyroid-stimulating hormone, CLN: Cervical lymph node, met: metastasis, med: mediastinal, TR: thyroid remnant, TGDR: thyroglossal duct remnant, SM SG: submandibular salivary gland, UPS: Upstage, DWS: Downstage, H: high, IM.intermediate, L: low)

	Age	Sex	TSH (mU/L)	Tg (ng/mL)	TgAb IU/ml	Histology	I-131 mCi	ATA Risk	WBS Uptakes	SPECT-CT Uptakes	Interpretation change
1	49	F	25	12	16.3	Papillary	150	H	Probably med LN	Equivocal med LN	DWS
2	56	F	48	0.4	10	Papillary	100	IM	Probably TR TGDR	TR TGDR CLN	UPS
3	53	F	100	0.1	10	Hurtle h	100	IM	Probably TRTGDR CLN	TR SM SG	DWS
4	44	F	35	0.6	13	Papillary	100	IM	Probably TRTGDR CLN	TR TGDR Dental Pros.	DWS
5	35	M	95	2.7	12	Papillary	200	H	Probably CLN	SM SG	DWS
6	61	M	40	0.4	0.9	Papillary	200	H	-	Lung met	UPS
7	61	M	50	5.2	0.9	Papillary	150	H	Probably TR TGDR	TR TGDR CLN	UPS
8	34	F	46	0.5	0.9	Papillary	100	IM	Probably TR TGDR med LN	TR Equivocal med LN	DWS
9	49	M	62	0.5	0.9	Papillary	50	L	Probably TR TGDR CLN	TR TGDR Dental Pros.	DWS
10	27	M	50	2.1	0.9	Papillary	100	IM	Probably TRTGDR CLN	TR TGDR Dental Pros	DWS
11	65	M	28	500	155	Papillary	200	H	Probably CLN Lung met	Bone Lung met	UPS
12	56	M	100	0.4	33	Papillary	100	IM	Probably CLN	TR Dental Pros.	DWS
13	20	M	50	31.8	0.9	Papillary	150	H	Probably CLN med LN	CLN Equivocal med LN	DWS
14	56	F	46	1.4	0.9	Papillary	100	IM	Probably TR TGDR med LN	TR TGDR Equivocal med LN	DWS
15	65	M	50	38.6	0.9	Papillary	200	H	Probably CLN	CLN Lung met	UPS
16	48	F	13	1.5	94	Papillary	50	L	Probably med LN	med LN (Thymus remnant)	DWS
17	41	M	100	4.9	10	Papillary	100	IM	Probably TR TGDR med LN	TR TGDR Equivocal med LN	DWS
18	71	F	30	0.04	63	Papillary	100	IM	Probably CLN	SM SG	DWS

Table 1. Planar and SPECT-CT 131I foci distribution (WBS: Whole body scanning TR: Thyroid Remnant TGDR: thyroglossal duct remnant LN: lymph node met: metastasis, CLN: Cervical lymph node)

^{131}I WBS (neck) foci	SPECT-CT (neck)
Probably CLN:14	Cervical LN:6 (43%) Bone met:1 (7%) Salivary gland:3 (21%) Dental prosthesis:4 (29%)
Probably TR and TGDR:104	TR:58 (56%) TGDR:42 (40%) Dental :2 (2%) Parapharyngeal LN:2 (2%)
Total Foci:118	**Total Foci:118**
^{131}I WBS (thorax) foci	**SPECT-CT (thorax)**
Probably (focal/diffuse) lung or bone Metastasis:12	Lung met:8 (66%) Bone met:4 (34%)
Probably mediastinal LN:9	Mediastinal LN:3 (33%) Thymus Remnant:1 (%11) Equivocal Mediastinal LN:5 (56%)
Total Foci:139	**Total Foci:139**

Discussion

Thyroid cancers are the most common endocrine cancer with a rate of 1% among all cancers each year (8). Due to the presence of sodium-iodine symporter in cancer cells in DTC, most cancer cells show iodine uptake (9). Planar 131I WBS is the standard method to identify thyroid remnants or metastatic disease with high sensitivity and specificity, but it is insufficient to distinguish neoplastic tissue from normal iodinated tissue(10). High radioiodine uptake in residual thyroid tissue prevents detection of nearby metastatic lymph nodes. In 2 of our patients, RAI foci in the middle of the neck could not be distinguished from thyroid remnant or TGDR in WBS, and parapharyngeal LN was found in SPECT-CT (2,5%). Many publications in the literature are most useful in differential diagnosis of lymph nodes (11-15). In our study, there was a change in the cervical lymph node interpretation of 43% of the patients. These changes were consistent with the Tg values and structural evaluations of the patients during their follow-up. Moreover, it provides clearer localization and characterization compared to SPECT-CT and planar imaging and plays a significant role in patient follow-up and treatment management (16). In 2 of the study patients, iodine refractory development and progression were more easily understood with SPECT-CT, and tyrosine kinase inhibitors were started without additional imaging. In a comprehensive study conducted in 2012, Avram emphasized that pathological classification alone would be insufficient in staging patients with thyroid cancer, and hybrid systems should be recommended in guidelines for determining regional and distant metastases (17). Barwick et al. compared 123I SPECT-CT and showed that hybrid systems contributed 42% of additional information to patient diagnosis and treatment management (18). In a study involving 41 patients, Kohlfuerst et al. with SPECT-CT, showed 36.4% in N status, 21.1% in M status, and 24.4% in treatment change (19). Hassan et al., in their study involving 67 patients, reported that SPECT-CT provided treatment management and vital clinical information to standard planar imaging in these patients (20). In our study, interpretation changes that could affect the staging and risk assessment were made with SPECT- CT in 18 (22.5%) patients, including 7 high, 9 intermediate, and 2 low-risk groups.

Radioactive iodine isotopes such as 131I are selectively taken into the cell through the sodium/ iodide symporter (NIS) in the thyroid cell membrane. NIS is also found in non-thyroid tissues (salivary and lacrimal glands, ectopic thyroid tissue, nasal mucosa, lactating breast, etc.), and the primary mechanism of false-positive interpretation is the expression of NIS in these tissues and the retention of excreted iodine. In our study, we found TGDR in 42 patients (52.5%) in the midline of the neck. A study including 179 patients identified 86 (48%) patients with TGDR (+) and found that TGDR persisted in 15% of the patients in 131I SPECT-CT images at the 7th-month follow-up, and Tg values were slightly elevated secondary to this. They reported that this situation might lead to pitfalls in patient management (21). We also detected TGDR (+) in 2 (20%) of 10 patients who received more than one 131I due to recurrence. This result may partially support the theory of Lee et al. Barber et al. detected TGDR at a rate of 47% in the neck and suggested that it covered a significant proportion of the total radioactivity of the neck and that planar scanning was not suitable for post-ablation evaluation (22). In our study, the rate of occurrence of TGDR together with TR was 38.75%, and 7% as a single focus when TR was not observed, and we think that not only TR but also TGDR should be considered among the tissues to be ablated in the neck, especially in low-risk patients.

The mechanism of radioiodine uptake by the thymus is not fully understood. Vermiglio et al. associated iodine uptake in the thymus with Hassall bodies in epithelial cells and suggested that they had structural similarities with thyroid follicles (23). Arce et al. examined 5 patients diagnosed with thyroid cancer who received high-dose 131I treatment and did not detect metastasis in any of them after biopsy, and they found that the findings were compatible with thymic tissue, therefore, they suggested that 131I treatment should be considered as a subgroup that may develop after stress in the classification of thymic hyperplasia (24). In another case report, 5 patients were evaluated after treatment and found that they were compatible with residual thymus histopathologically and radiologically. They emphasized the importance of knowing this situation in terms of protecting patients from unnecessary invasive procedures and treatment

(25). In our study, out of 80 focal involvements, 9 were in the mediastinal region, 3 were mediastinal LN, and 1 was thymus remnants. Since 5 of them (6.25%) could not be determined anatomically in SPECT- CT, no invasive procedure was performed for the diagnosis. The fact that the 5 equivocal mediastinal LN cases wereyounge, and the structural and biochemical normality in their 1-year follow-up period may suggest primarily thymus pathologies (residue, hyperplasia).

The limitations of our study are low-resolution CT, a small number of patients, and a single-center design.

As a result, the use of SPECT-CT will be very effective in, facilitating patient management and avoiding unnecessary procedures, especially in moderate/ high-risk patients with suspicious focal lesions. The presence of benign iodine avid foci (thyroglossal duct residue, etc.) in the neck showing iodine uptake other than the thyroid remnant may be effective in making ablation decisions in low-risk patients. In addition, it provides an important contribution to the physician in the differential diagnosis of foci that are equivocal in planar images.

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