



Comparison of Planar Imaging Using Dual-phase Tc-99m-sestamibi Scintigraphy and Single Photon Emission Computed Tomography/Computed Tomography in Hyperparathyroidism

Hiperparatiroidizmde Çift Fazlı Tc-99m-sestamibi Planar Görüntüleme Sintigrafisi ve Tek Foton Emisyonlu Bilgisayarlı Tomografi/Bilgisayarlı Tomografi Karşılaştırılması

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Abstract

Objectives: The aim of this study was to compare Technetium-99m (Tc-99m)-sestamibi dual-phase planar imaging method and delayed phase single photon emission computed tomography/computed tomography (SPECT/CT) imaging in patients with primary hyperparathyroidism and to evaluate the accuracy of scintigraphy with histopathological results.

Methods: Thirty-six patients with a prediagnosis of hyperparathyroidism, who had not been operated on the neck region before, and were not followed up for any other malignancy, and has confirmed histopathologic and biochemical diagnosis after parathyroidectomy, were retrospectively scanned and included in the study. The images of 36 patients who underwent dual-phase Tc-99m-sestamibi planar scintigraphy at the 20th and 120th minutes in the nuclear medicine clinic and delayed phase SPECT/CT imaging immediately after the 120th minute planar imaging were evaluated visually by two nuclear medicine specialists as positive or negative lesion. Dual-phase planar and SPECT/CT images were statistically compared in terms of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

Results: Thirty-six patients with 41 lesions were evaluated. Comparing dual-phase planar imaging and delayed phase SPECT/CT revealed, sensitivity 84.21%-94.74%, specificity 66.67%-66.67%. Positive predictive value 96.97%-97.30%, negative predictive value 25%-50.0%, accuracy 82.93%-92.68% respectively. There was a statistically significant difference between planar imaging and SPECT/CT; SPECT/CT localized the lesion more accurately (p<0.05).

Conclusion: SPECT/CT is superior to planar imaging in determining the anatomical details and localization of the lesion, especially in determining the depth of the lesions in the neck and whether it is ectopic. In patients with hyperparathyroidism, SPECT/CT should be used routinely to detect parathyroid pathologies because it has a lower rate of error and higher accuracy rate.

Keywords: SPECT, SPECT/CT, hyperparathyroidism, parathyroid scintigraphy

Öz

Amaç: Bu çalışmanın amacı primer hiperparatiroidilli hastalarda Teknesyum-99m (Tc-99m)-sestamibi çift faz planar görüntüleme yöntemi ile geç faz tek foton emisyonlu bilgisayarlı tomografi/bilgisayarlı tomografi (SPECT/CT) görüntülemenin karşılaştırılması ve histopatolojik sonuçları ile sintigrafinin doğruluğunun değerlendirilmesidir.

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Yöntem: Hiperparatiroidi ön tanısı alan, daha önce boyun bölgesinden opere olmamış, 10 malignite nedeniyle takip edilmeyen, paratiroid cerrahisi uygulanarak patolojik incelemesi yapılan 36 olgu retrospektif taranarak çalışmaya dahil edildi. Nükleer tıp kliniğinde 20. ve 120. dakikada çift faz Tc-99m-sestamibi planar sintigrafisi ve 120. dakikadaki planar görüntülemenin hemen ardından geç faz SPECT/BT görüntülemesi yapılan 36 olgunun görüntüleri iki nükleer tıp uzmanı tarafından lezyon pozitif veya negatif şeklinde vizüel olarak değerlendirildi. Çift faz planar ve SPECT/BT görüntüleri duyarlılık, özgünlük, pozitif tahmin edici değer, negatif tahmin edici değer ve doğruluk açısından istatistiksel olarak karşılaştırıldı.

Bulgular: Otuz altı hastada cerrahi sonrası bulunan 41 lezyon değerlendirildiğinde çift faz planar görüntüleme ile geç faz SPECT/BT'nin karşılaştırılmasında sırayla duyarlılığı %84,21-%94,74, özgünlüğü %66,67-%66,67 Pozitif prediktif değeri %96,97-%97,30 negatif prediktif değeri %25-%50,0 doğruluk %82,93-20 %92,68 olarak bulunmuştur. Planar görüntüleme ile SPECT/BT arasında incelemede istatistiksel olarak anlamlı farklılık görülmektedir ($p<0,05$).

Sonuç: SPECT/BT, lezyonun anatomik detaylarını ve lokalizasyonunu belirlemede, özellikle lezyonun boyundaki derinliğini ve ektopik olup olmadığını belirlemede planar görüntülemeye üstündür. Hiperparatiroidizmlı hastalarda SPECT/BT'nin hata payı daha düşük, doğruluk oranı daha yüksek olduğundan paratiroid patolojilerini saptamak için rutin olarak kullanılmalıdır.

Anahtar kelimeler: SPECT, SPECT/BT, hiperparatiroidi, paratiroid sintigrafisi

Introduction

Primary hyperparathyroidism is the most common pathology of the parathyroid glands and is one of the most common endocrine disorders overall, usually resulting from solitary parathyroid adenoma, less frequently from multiple parathyroid gland disease, and rarely from parathyroid carcinoma (1). The diagnosis of primary hyperparathyroidism is diagnosed biochemically, and the only curative treatment is surgery (2).

Today, most patients do not have the classic symptoms or signs associated with primary hyperparathyroidism at the time of diagnosis and are diagnosed as asymptomatic or minimally symptomatic. With the introduction of routine serum calcium measurements, a significant increase in the incidence of primary hyperparathyroidism, which is mostly asymptomatic, has been observed. Parathyroid scintigraphy has proven to be a superior imaging modality for the preoperative localization of parathyroid adenomas (3,4). The main nuclear medicine method used in parathyroid imaging is dual-phase Technetium-99m-2-hexakis-methoxy-isobutyl-isonitrile (Tc-99m-sestamibi) imaging (5). Single photon emission computed tomography/computed tomography (SPECT/CT) is particularly useful for preoperative localization because it can evaluate the effectiveness of parathyroid adenoma localization in relation to adjacent anatomical structures and the depth in the neck or mediastinum.

The aim of this study was to compare Tc-99m-sestamibi dual-phase planar imaging method to delay SPECT/CT imaging in patients with primary hyperparathyroidism, to investigate whether it contributes in terms of accuracy, sensitivity, specificity, positive and negative predictive value (NPV), and to evaluate the accuracy of scintigraphy compared to histopathological results.

Materials and Methods

The images of 36 patients who applied to the Nuclear Medicine Clinic of Okmeydani Training and Research Hospital for dual-phase Tc-99m-sestamibi parathyroid scintigraphy due to primary hyperparathyroidism between March 2010 and March 2012 were evaluated retrospectively. Patients who were pre-diagnosed with hyperparathyroidism due to high parathyroid hormone (PTH) and calcium electrolyte levels in blood tests, and who underwent double-phase Tc-99m-sestamibi planar scintigraphy alongside delayed SPECT/CT examination in the Nuclear Medicine Clinic for localization, and who had a pathology report operated in the General Surgery Clinic of Okmeydani Training and Research Hospital were included in the study. Patients who had undergone previous neck surgery and were followed up for other malignancies, patients with secondary hyperparathyroidism due to chronic renal disease, patients who received parathyroidectomy more than 6 months after the scintigraphy, patients who had persistently rising intact PTH levels after surgery without compatible pathological findings of parathyroidectomy for hyperfunctioning parathyroid tissue, and patients with unavailable SPECT/CT data were excluded from the study.

Approximately 20 min after the intravenous injection of 20-25 mCi (740-925 MBq) Tc-99m-sestamibi, static images from the neck and mediastinum region, 2nd hour static images and 2nd hour SPECT/CT images were obtained in the anterior position of all patients.

Imaging Protocol

Imaging of all patients was performed using an Infinia Hawkeye 4 (General Electric Medical Systems, Milwaukee, WI) dual-headed SPECT/CT imaging system, which is a hybrid imaging technology. Planar images were recorded in a 128x128 matrix with a wide range of view, low-energy, high-resolution, parallel-hole collimator with a zoom value

of 2.5, peak energy level of 140 KeV and window spacing of 10%. With SPECT imaging, 60 images, each image for 30 seconds, was obtained at 360 degrees with a wide range of view, low energy, high resolution parallel hole collimator with peak energy level of 140 KeV, window interval of 10%, 128x128 matrix in 6 degree step and shoot mode. SPECT images were processed in Xeleris (General Electric Medical Systems, Milwaukee, WI) workstation.

After filtering with the Hann preconstruction filter, it was reconstructed with the 2-dimensional ordered-subset expectation maximization image refresh technique. Fusion images were obtained by combining SPECT images with computer attenuation correction and CT images. Areas with radiopharmaceutical involvement in SPECT/CT images on transverse, coronal, sagittal sections and 3D images were evaluated about whether they were synchronized and reported as negative or positive activity uptake.

Evaluation of Planar Imaging

Firstly, the homogeneity of the activity distribution in the early phase when the parathyroid and thyroid gland was observed together, and whether focal increased activity uptake compared to the thyroid tissue was investigated. Then, the early phase images were compared with the delayed phase images, and it was checked whether there was a persistent activity involvement that was not free from sestamibi activity. The results were recorded as negative or positive activity uptake and in terms of localization.

Evaluation of SPECT/CT Scintigraphy

Fusion images were obtained by combining SPECT images with attenuation correction by computer and CT images. Areas with radiopharmaceutical involvement in SPECT/CT images on transverse, coronal, sagittal sections and 3D images were evaluated about whether they were synchronized and reported as negative or positive activity uptake.

Evaluation of Images

Planar and SPECT/CT images were evaluated by two nuclear medicine specialists, unaware of each other. Nuclear medicine scintigraphic images of the patients were evaluated unaware of their clinical information, laboratory values and radiological imaging methods. The evaluations made by both experts were recorded as lesion positive and lesion negative. Localization of the lesions was recorded in a separate table. The images that were interpreted differently by the two experts were re-interpreted by the experts, and the positive or negative status of the lesion and the localization information were recorded.

Ethics Committee Approval

The study was approved by the Sisli Etfal Training and Research Hospital Clinical Research Ethics Committee (05/06/2012/89). All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients gave their informed consent before inclusion in the study.

Statistical Analysis

The NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, frequency, rate), Mc-Nemar test and diagnostic screening tests (sensitivity, specificity, etc.) were used to compare the qualitative data of two separate tests. The Wilcoxon Signed Rank test was used to evaluate the difference between planar imaging and SPECT/CT imaging. Statistical significance was evaluated at the $p < 0.05$ level in all comparisons. Considering all healthy and diseased parathyroid glands, true positive (TP), true negative (TN), false positive (FP), and false negative (FN) variables were used. Sensitivity, specificity, positive predictive value (PPV), NPV, and accuracy were calculated.

Results

The patients were between the ages of 17-76. The mean age was 50.91 ± 13.39 years. Six (16.7%) of 36 patients were male and 30 (83.3%) were female.

Table 1 shows the "positive" and "negative" distributions of the lesions in pathology, planar imaging and SPECT/CT. Of the lesions, 92.7% were found to be positive on pathology, 80.5% on planar imaging, and 90.2% on SPECT/CT (Graph 1).

The comparison of pathology results and planar imaging results revealed that, pathology identified 92.7% of the

	Lesion	n	%
Pathology	Positive	38	92.7
	Negative	3	7.3
Planar imaging	Positive	33	80.5
	Negative	8	19.5
SPECT/CT	Positive	37	90.2
	Negative	4	9.8

SPECT/CT: Single photon emission computed tomography/computed tomography

lesions, whereas the planar imaging method detected 80.5% of the lesions (Table 2). There was no significant difference between planar imaging and pathology results ($p>0.05$). Of 38 (92.7%) patients diagnosed with lesion by pathology, 32 (78%) were also diagnosed with a lesion on planar imaging. The sensitivity, specificity, PPV, NPV, and accuracy of planar imaging were 84.21%, 66.67%, 96.97%, 25%, and 82.93%, respectively.

When the distribution of the lesions in pathology and planar imaging evaluations were examined, two lesions detected in one patient were both lesion (+) in pathology, one of the two lesions was evaluated as lesions (+) and the other lesion (-) in planar imaging. Both lesions detected in one patient were lesion (+) in pathology, both were evaluated as the lesion (-) in planar imaging. Both lesions detected in the two patients were lesion (+) in pathology, both were evaluated as the lesion (-) in planar imaging. One of the two lesions detected in one patient was evaluated as lesions (+) in pathology and the other as lesions (-) in pathology, and both lesions were evaluated as lesions (-) by planar imaging. A lesion detected in one patient was evaluated as lesions (-) in both pathology and planar

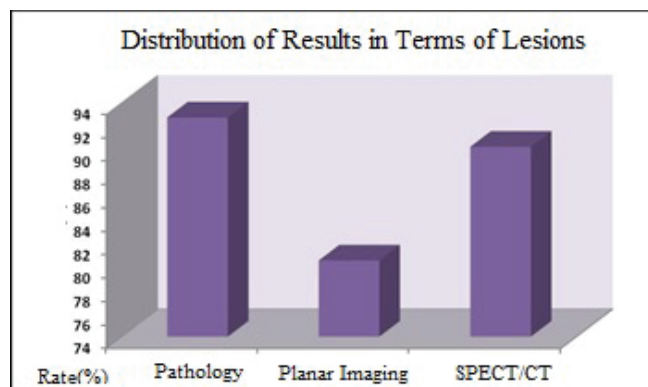
imaging. Two lesions detected in one patient were both evaluated as lesions (+) in pathology and planar imaging (Table 3) (Figures 1A, B, 2A, B).

The evaluation of the pathology results and SPECT/CT imaging results together revealed that lesions were detected in 92.7% of the patients with pathology, while lesions were detected in 90.2% of the patients with SPECT/CT (Table 4). The comparison of SPECT/CT results with the pathology results showed no significant difference between the two measurement methods ($p>0.05$). Lesions were positive in 36 (87.8%) patients in pathology and 38 (92.7%) of the patients in SPECT and were negative in the rest of the patients. The sensitivity, specificity, PPV, NPV, and accuracy of SPECT/CT was 94.74, 66.67, 97.30, 50.0, and 92.68%, respectively.

When planar imaging and SPECT/CT imaging were evaluated together on a lesion basis, 36 lesions were evaluated as TP in SPECT/CT imaging and 32 lesions in planar imaging. Four lesions were evaluated as FN only in planar imaging. Two lesions were evaluated as FN in planar imaging and SPECT/CT imaging. One lesion was evaluated as FP in planar imaging and SPECT/CT imaging. Two lesions were evaluated as TN in planar imaging and SPECT/CT imaging. SPECT/CT imaging detected four parathyroid lesions that could not be detected on planar imaging (Table 4).

There was a statistically significant difference in terms of the examination between planar imaging and SPECT/CT ($p<0.05$ Wilcoxon signed-rank test). SPECT/CT results were closer to the pathological results. The margin of error was found to be lower and the accuracy rate was higher.

When the patients were analyzed according to the surgical procedures performed, parathyroidectomy was performed together with thyroidectomy in 14 patients. In the other 22 patients, only the parathyroid gland underwent surgery.



Graph 1. Distribution of results in terms of lesions

		Pathology						p
		Lesion (+)		Lesion (-)		Total		
		n	%	n	%	n	%	
Planar imaging	Lesion (+)	32	78.0	1	2.4	33	80.5	0.125
	Lesion (-)	6	14.6	2	4.9	8	19.5	
	Total	38	92.7	3	7.3	41	100	
Sensitivity		84.21						
Specificity		66.67						
Positive predictive value		96.97						
Negative predictive value		25.00						
Accuracy		82.93						

Table 3. Distribution of planar imaging and SPECT/CT imaging results with surgical procedure and histopathology results

	Planar imaging	SPECT/CT imaging	Surgical procedure	Histopathology
1	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
2	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
3	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
4	RLQ+	RLQ (retrotracheal mediastinal area)	Thyroid lobectomy (R)+ parathyroidectomy (R)	Parathyroid hyperplasia +NG
5	LLQ+	LLQ (retrotracheal area)+	Parathyroidectomy (L)+ TT	Parathyroid adenoma +MNG
6	RLQ+	RLQ and LLQ+	Parathyroidectomy+ TT	Parathyroid adenoma (R) + Parathyroid hyperplasia (L)+ MTC
7	RQ+	RQ (posterior prevertebral area)	Parathyroidectomy (R)	Parathyroid adenoma
8	Negative	LLQ+	Parathyroidectomy	Parathyroid adenoma
9	LLQ+	LLQ+	Parathyroidectomy	Parathyroid adenoma
10	RLQ+	RLQ+	Parathyroidectomy+ TT	Parathyroid adenoma
11	RLQ+	RLQ+	Parathyroidectomy (R)+ TT	Parathyroid adenoma + MNG
12	LLQ+	LLQ+	Parathyroid mass excision	Parathyroid carcinoma
13	LUQ+	LUQ+	Parathyroidectomy (L)	Parathyroid adenoma
14	RUQ+	RUQ+	Thyroid lobectomy (R)+ parathyroidectomy (R)+	Parathyroid adenoma+ NG
15	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
16	Ectopic in midline mediastinum +	Ectopic in midline mediastinum (midclavicular area)+	Parathyroidectomy (mediastinum)	Parathyroid hyperplasia and thymus tissue
17	LLQ+	LLQ (paratracheal area)	Parathyroidectomy (L)	Parathyroid adenoma
18	RLQ+	RLQ+	Parathyroidectomy (R)+ TT	Parathyroid adenoma (R) + PTC (R+L)
19	Negative	Negative	Parathyroidectomy (L)	Parathyroid adenoma
20	Negative	LLQ and RLQ+	Parathyroidectomy (R+L)	Parathyroid hyperplasia (R+L)
21	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
22	RLQ+	RLQ+	Parathyroidectomy (R)	Parathyroid adenoma
23	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
24	Negative	Negative	Parathyroidectomy+ TT	Parathyroid hyperplasia + normal parathyroid tissue + MTC
25	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
26	Ectopic in midline mediastinum+	Ectopic in midline mediastinum (retrosternal area)+	Parathyroidectomy (mediastinum)	Parathyroid adenoma
27	RLQ+	RLQ (retrotracheal area)+	Thyroid lobectomy (R)+ parathyroidectomy	Parathyroid adenoma + NG
28	Ectopic in midline mediastinum+	Ectopic in midline mediastinum (retrosternal area)+	Parathyroidectomy (mediastinum)+ TT	Parathyroid adenoma+ PTC
29	LLQ+	LLQ (posterior paratracheal area)+	Parathyroidectomy (L)	Parathyroid adenoma
30	LLQ+	LLQ (posterior paratracheal area)+	Parathyroidectomy (L)+ TT	Parathyroid Adenoma+ PTC
31	Ectopic in midline mediastinum+	Ectopic in midline mediastinum (retrosternal area)+	Parathyroidectomy (mediastinum)	Parathyroid adenoma
32	LLQ and RUQ+	LLQ and RUQ+	Parathyroidectomy (R+L)+ TT	Parathyroid adenoma (L) + WDT-UMP (R)
33	Negative	Negative	Parathyroidectomy+ TT	Normal parathyroid tissue + MTC
34	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
35	LLQ+	LLQ+	Parathyroidectomy (L)	Parathyroid adenoma
36	LLQ and RLQ+	LLQ and RLQ+	Parathyroidectomy (R+L)+ TT	Parathyroid adenoma (R+L)+ MNG

SPECT/CT: Single photon emission computed tomography/computed tomography, RUQ: Right upper quadrant, RLQ: Right lower quadrant, LUQ: Left upper quadrant, LLQ: Left lower quadrant, +: Positive, TT: Total thyroidectomy, MTC: Medullary thyroid carcinoma, NG: Nodular goiter, PTC: Papillary thyroid carcinoma, WDT-UMP: Well differentiated thyroid tumor of uncertain malignant potential

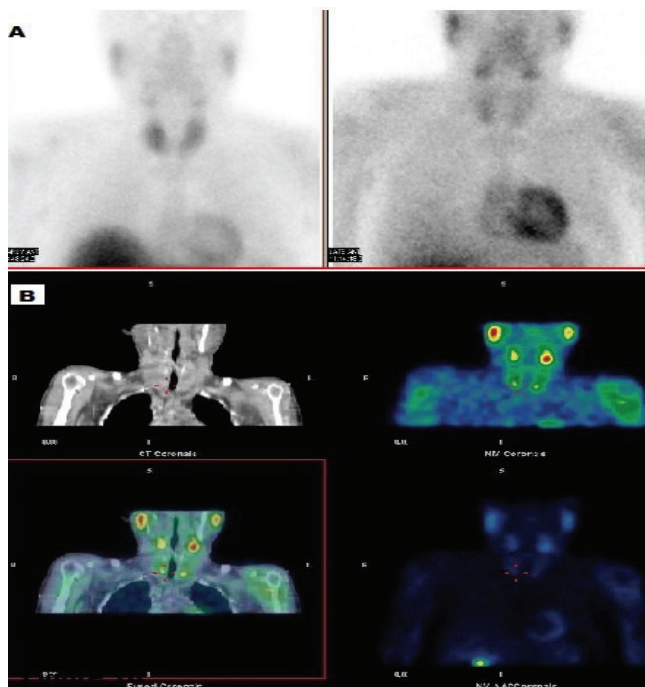


Figure 1. There was one lesion in the lower right pole in planar imaging (A), a lesion was also detected in the lower left pole in SPECT images, and the pathology report of both lesions was positive (B)
SPECT: Single photon emission computed tomography

Thyroid tumors were found in seven of 14 patients who underwent thyroid surgery, medullary carcinoma in three of them, papillary carcinoma in two, bilateral micropapillary carcinoma in one, and well-differentiated thyroid tumor in one with uncertain malignant potential. Benign thyroid pathologies were detected in the remaining seven patients. Out of 41 lesions detected in 36 patients, parathyroid hyperplasia was detected in six lesions (14.6%), parathyroid carcinoma in one lesion (2.43%), normal parathyroid tissue in two lesions (4.87%), parathyroid adenoma in 31 lesions (75.6%), and thyroid papillary carcinoma in one lesion (2.43%).

The lesion was mediastinal in four of eight patients with ectopic localized lesions, posterior to the trachea in three, and anterior to the vertebra in one patient. SPECT/CT provided information about ectopic locations, location, and neighborhood in each, and planar imaging provided information about ectopic location in four of these eight ectopic lesions but provided insufficient information about the location.

Of the three patients with double lesions, the lesion on the right was adenoma and the lesion on the left was hyperplasia in one patient, two lesions were hyperplasia in one patient, and two lesions were adenoma in another.

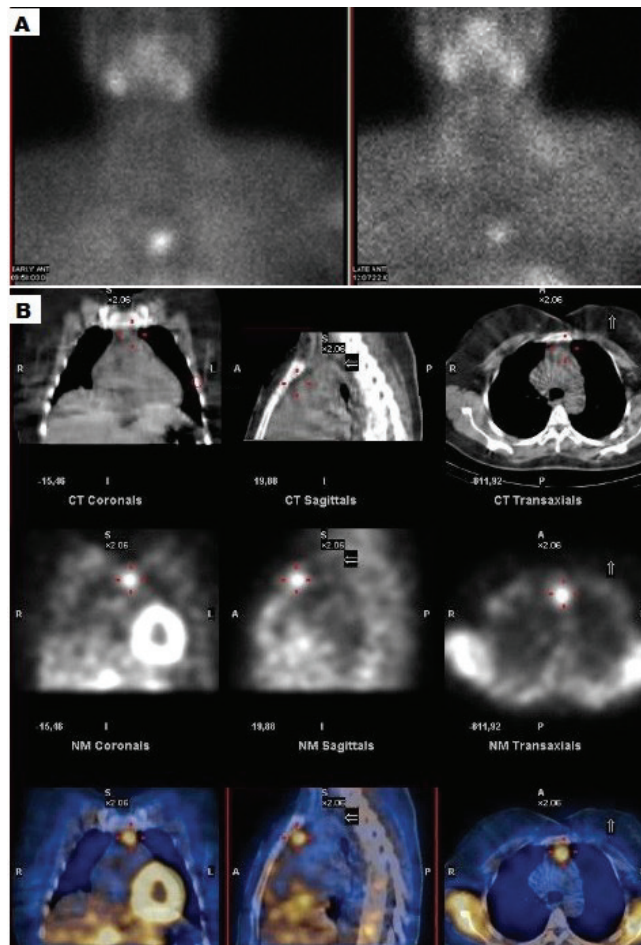


Figure 2. The lesion, which was detected intrathoracically in planar imaging (A), was localized in the anterior mediastinum in coronal, sagittal and axial SPECT/CT images (B)
SPECT/CT: Single photon emission computed tomography/computed tomography

		Pathology						p
		Lesion (+)		Lesion (-)		Total		
		n	%	n	%	n	%	
SPECT/CT	Lesion (+)	36	87.8	1	2.4	37	90.2	0.999
	Lesion (-)	2	4.9	2	4.9	4	9.8	
	Total	38	92.7	3	7.3	41	100	
Sensitivity		94.74						
Specificity		66.67						
Positive predictive value		97.30						
Negative predictive value		50.00						
Accuracy		92.68						
SPECT/CT: Single photon emission computed tomography/computed tomography								

Discussion

Pre-operative accurate localization has become extremely important in minimally invasive surgery in primary hyperparathyroidism. Preoperative imaging is important in distinguishing single-gland disease from multiglandular disease, in the differential diagnosis of co-existing thyroid pathology, and in defining ectopic parathyroid lesions (6).

Different scintigraphic methods and protocols have been defined for preoperative localization of hyperfunctioning parathyroid glands in studies conducted for many years. A wide variety of imaging protocols are available today. It explains the wide range of sensitivity reported in the literature, ranging from 70% to 95%, due to differences in protocols (7,8,9,10).

This study directly compared dual-phase Tc-99m-sestamibi planar imaging, which is frequently used in nuclear medicine clinics, and hybrid SPECT/CT imaging, one of the latest imaging methods, reporting statistical differences in terms of sensitivity, specificity, accuracy, PPV, and NPV.

Pre-operative accurate localization is required for successful minimally invasive parathyroid surgery. Because of embryological descent, the superior parathyroid glands tend to be located more posteriorly than the inferior parathyroid glands and are often located in the tracheoesophageal groove. In the ectopic infero-posterior location of superior parathyroids, surgery is often more complex because of its close relationship with the recurrent laryngeal nerve. Therefore, the use of SPECT/CT hybrid imaging in Tc-99m-sestamibi parathyroid scintigraphy is more useful in preoperative planning for minimally invasive surgery than planar and SPECT imaging. It is valuable in determining the surgical approach for the neck, particularly in ectopic glands and nodular thyroid diseases (9,10,11,12,13).

Among a wide variety of radiopharmaceutical and types of scintigraphic studies, SPECT improves the ability to detect lesions by providing superior contrast resolution compared with planar imaging. For parathyroid scintigraphy, many studies have reported that SPECT has 11-18% higher sensitivity than planar imaging (14,15,16).

SPECT is obtained in a single time interval, often early or delayed. Some studies in the literature have reported high sensitivity of 96% with an early SPECT (17,18). Civelek et al. (8) reported good sensitivity of 87% with delayed SPECT. Perez-Monte et al. (18), comparing delayed and early SPECT, found that early SPECT (91%) had higher sensitivity than delayed SPECT (74%), although no statistically significant difference was reported. Another study on early and delayed SPECT also showed that early SPECT tended to have higher sensitivity than delayed SPECT in parathyroid lesion localization; however, this trend did not reach a

statistically significant value, but dual-phase SPECT results were found to be statistically significantly superior to early or delayed single-phase SPECT results (13).

Hybrid SPECT/CT has the advantage of imaging in successive slices with the patient in the same position on the same imaging table. The hybrid system 2.5 mA low-resolution four-section CT scanner, which was used in this study, provided accurate anatomic localization with limited resolution in many patients. In the literature, some researchers have investigated the statistical contribution of SPECT/CT only to the diagnostic accuracy, and others have investigated the contribution of SPECT/CT to localization and surgery. The main purpose of our study was to investigate whether delayed-phase SPECT/CT contributed to the diagnostic accuracy of dual-phase planar imaging. In a study similar to this study, Huang et al. (19) performed dual-phase Tc-99m-sestamibi planar imaging at the 20th and 120th minutes and SPECT/CT imaging at the 90th minute in 27 patients. Compared with surgery results, they found 21 TP, four FP, four TN, and four FN results with planar imaging, and 22 TP, six FP, six TN, and three FN results with SPECT/CT. The sensitivity, specificity, and accuracy for SPECT/CT were 88%, 50%, and 75.7%, and 84%, and 50%, and 75.8% for planar imaging, respectively. It was found that the diagnostic accuracy of SPECT/CT did not differ statistically significantly from planar imaging (19). In our study, dual-phase Tc-99m-sestamibi planar imaging at the 20th and 120th minutes and SPECT/CT imaging at the 120th minute was performed in 36 patients. According to the surgical results of 41 lesions in 36 patients, 32 TP, one FP, two TN, and six FN results were found with planar imaging. With SPECT/CT, 36 TP, one FP, two TN, and two FN results were found. The sensitivity, specificity, and accuracy for SPECT/CT and planar imaging were 94.74%, 66.67%, and 92.68%, and 84.21%, 66.67%, and 82.93%, respectively. In our study, it was determined that the diagnostic accuracy of SPECT/CT was statistically significantly different from planar imaging ($p < 0.005$).

In a study by Lavelly et al. (13) in which 98 patients underwent early and delayed (dual-phase) imaging with planar, SPECT, and SPECT/CT, no significant difference was found between early SPECT/CT and dual-phase planar imaging in parathyroid lesion localization. However, dual-phase SPECT/CT was found to be statistically superior to single-phase SPECT/CT, dual-phase planar imaging, and dual-phase SPECT. The combination of early SPECT/CT with delayed SPECT or delayed planar imaging was also found to be statistically superior to dual-phase planar imaging or SPECT. In the study, the sensitivity values of dual-phase planar imaging and delayed-phase SPECT/CT imaging were 56.5% and 53.5%, specificity values were 98.7%

and 98.1%, PPVs were 79.0% and 75.8%, and NPVs were 96.4% and 96.2% (13). In our study, a lesion was evaluated as FP in both planar imaging and SPECT/CT imaging, resulting in decreased specificity. Additionally, the NPV was found to be low because the other intact parathyroid glands were not affected, and TN parathyroid glands could not be determined exactly because the intervention was made for pathological parathyroid glands during surgery.

In a meta-analysis in which 18 studies were evaluated, the sensitivity and PPV were 63% and 90% in planar scintigraphy, 66%, and 82% in SPECT, 84%, and 95% in SPECT/CT, respectively. SPECT/CT was found to be superior to the other two methods (20).

In the study by McCoy et al. (21), in which 1,388 patients were evaluated, 755 SPECT/CT and 633 SPECT examinations were compared. In 1,186 patients with solitary gland disease, SPECT/CT had higher sensitivity (96% vs. 91%), accuracy (83% vs. 77%), and PPV (90% vs. 85%) than SPECT. Although the rates of negative imaging in multigland disease were similar in both methods, the accuracy of SPECT/CT was found to be better than SPECT in predicting 202 patients with preoperative multigland disease (36% vs. 22%). Additionally, for multigland disease, the sensitivity (68% vs. 49%) and PPV (53% vs. 37%) of SPECT/CT were higher than in SPECT. They also stated that SPECT/CT provided a more reliable surgical guide in both single-gland and multi-gland disease (21).

A 48-patient study with hybrid SPECT/CT showed that the combination of dual-phase planar imaging and early SPECT with or without CT fusion confirmed 89% of the localization of parathyroid adenomas removed with surgery. The researchers concluded that the addition of CT fusion alone did not add value to SPECT. In another study of 36 patients, early SPECT/CT was performed only on patients whose planar imaging results were negative or diagnostically uncertain. It was shown that early SPECT/CT contributes to localization and surgical planning in 39% of patients (22).

Takami et al. (23) showed that localization of Tc-99m-sestamibi was impossible in delayed-phase images due to rapid excretion from parathyroid adenomas in 7% of patients with hyperparathyroidism in their study using Tc-99m-sestamibi dual-phase parathyroid scintigraphy. In another study, it was reported that Tc-99m-sestamibi caused false negativity in the delayed phase due to its early excretion from the parathyroid gland, particularly due to degeneration in hemorrhagic or large-hyperplastic parathyroid glands (24). Another factor thought to affect sestamibi uptake in parathyroid adenomas is the presence of P-glycoprotein or protein associated with multi-drug resistance in adenomas. There is insufficient sestamibi

uptake in adenomas with P-glycoprotein and this leads to FN results (25). In one patient in our study, a solitary parathyroid adenoma found in surgery could not be detected in either planar imaging or SPECT/CT imaging. This is a limitation of Tc-99m-sestamibi imaging methods with a single radionuclide.

MIBI uptake is related to cell function. Hence, some parathyroid lesions do not retain MIBI, whereas thyroid disease, lymphoma, lymph node diseases (lymph node metastatic disease, inflammation, and sarcoidosis) can lead to FP results. In our study, Thyroid tumors were found in seven of 14 patients who underwent thyroid surgery, medullary carcinoma in three of them, papillary carcinoma in two, bilateral micropapillary carcinoma in one, and well-differentiated thyroid tumor in one with uncertain malignant potential. Benign thyroid pathologies were detected in the remaining seven patients. SPECT/CT may decrease FP results attributable to thyroid nodules and FN results attributed to adenoma of a cystic nature or associated with concomitant thyroid nodules, which may go unidentified by scintigraphy (26). The failure of SPECT/CT to identify thyroid lesions may be associated with several factors, such as lesion size, resolution of the system, and amount of tracer uptake by thyroid tissue (27).

Study Limitations

Although SPECT/CT plays an important role in the diagnosis and location of parathyroid adenoma, evaluation together with ultrasonography would be more suitable for choosing an appropriate therapeutic regimen for identifying concomitant thyroid pathologies. Other limitations of our study were that: Our study was retrospective, USG findings were excluded from the study as they were evaluated by different physicians.

Conclusion

Hybrid SPECT/CT imaging is superior to planar imaging in terms of anatomic detail and localization of lesions, especially in determining the depth of lesions in the neck and in determining whether lesions are ectopic. Its margin of error is lower, and its sensitivity and accuracy are higher. Additionally, it increases PPV and NPV and the determination of the exact location of lesions in minimally invasive surgery. Therefore, it should be used routinely to detect parathyroid pathologies in patients with hyperparathyroidism.

Ethics

Ethics Committee Approval: The study was approved by the Sisli Etfal Training and Research Hospital Clinical Research Ethics Committee (05/06/2012/89).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.Ö., M.Ö.T., M.M., Concept: H.Ö., M.Ö.T., M.M., Design: H.Ö., M.Ö.T., M.M., M.T.T., Data Collection or Processing: H.Ö., M.Ö.T., M.T.T., Analysis or Interpretation: H.Ö., M.Ö.T., M.T.T., Literature Search: H.Ö., M.Ö.T., M.T.T., Writing: H.Ö., M.Ö.T., M.M.

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References

1. Heath H, Hodgson SF, Kennedy MA. Primary hyperparathyroidism. Incidence, morbidity, and potential economic impact in a community. *N Engl J Med* 1980;302:189-193.
2. Schell SR, Dudley NE. Clinical outcomes and fiscal consequences of bilateral neck exploration for primary idiopathic hyperparathyroidism without preoperative radionuclide imaging or minimally invasive techniques. *Surgery* 2003;133:32-39.
3. Ishibashi M, Nishida H, Hiromatsu Y, Kojima K, Tabuchi E, Hayabuchi N. Comparison of technetium-99m-MIBI, technetium-99m-tetrofosmin, ultrasound and MRI for localization of abnormal parathyroid glands. *J Nucl Med* 1998;39:320-324.
4. Anderson SR, Vaughn A, Karakla D, Wadsworth JT. Effectiveness of surgeon interpretation of technetium tc 99m sestamibi scans in localizing parathyroid adenomas. *Arch Otolaryngol Head Neck Surg* 2008;134:953-957.
5. Hindié E, Ugur O, Fuster D, O'Doherty M, Grassetto G, Ureña P, Kettle A, Gulec SA, Pons F, Rubello D; Parathyroid Task Group of the EANM. 2009 EANM parathyroid guidelines. *Eur J Nucl Med Mol Imaging* 2009;36:1201-1216.
6. Sharma J, Mazzaglia P, Milas M, Berber E, Schuster DM, Halkar R, Siperstein A, Weber CJ. Radionuclide imaging for hyperparathyroidism (HPT): which is the best technetium-99m sestamibi modality? *Surgery* 2006;140:856-863; discussion 863-865.
7. Geatti O, Shapiro B, Orsolon PG, Proto G, Guerra UP, Antonucci F, Gasparini D. Localization of parathyroid enlargement: experience with technetium-99m methoxyisobutylisonitrite and thallium-201 scintigraphy, ultrasonography and computed tomography. *Eur J Nucl Med* 1994;21:17-22.
8. Civelek AC, Ozalp E, Donovan P, Udelsman R. Prospective evaluation of delayed technetium-99m sestamibi SPECT scintigraphy for preoperative localization of primary hyperparathyroidism. *Surgery* 2002;131:149-157.
9. Cheng JL, Hsu CC, Wang PW, Sung KC, Chiu NT, Chiu LY, Huang YC. The feasibility of anterior 180° 99m Tc-sestamibi parathyroid SPECT/CT. *Ann Nucl Med* 2021;35:203-210.
10. Tawfik AI, Kamr WH, Mahmoud W, Abo Shady IA, Mohamed MH. Added value of ultrasonography and Tc-99m MIBI SPECT/CT combined protocol in preoperative evaluation of parathyroid adenoma. *Eur J Radiol Open* 2019;6:336-342. Erratum in: *Eur J Radiol Open* 2020;8:100308.
11. Wong KK, Fig LM, Gross MD, Dwamena BA. Parathyroid adenoma localization with 99mTc-sestamibi SPECT/CT: a meta-analysis. *Nucl Med Commun* 2015;36:363-375.
12. Assante R, Zampella E, Nicolai E, Acampa W, Vergara E, Nappi C, Gaudieri V, Fiumara G, Klain M, Petretta M, Cuocolo A. Incremental value of sestamibi SPECT/CT over dual-phase planar scintigraphy in patients with primary hyperparathyroidism and inconclusive ultrasound. *Front Med (Lausanne)* 2019;6:164.
13. Lavelly WC, Goetze S, Friedman KP, Leal JP, Zhang Z, Garret-Mayer E, Dackiw AP, Tufano RP, Zeiger MA, Ziessman HA. Comparison of SPECT/CT, SPECT, and planar imaging with single- and dual-phase (99m)Tc-sestamibi parathyroid scintigraphy. *J Nucl Med* 2007;48:1084-1089. Erratum in: *J Nucl Med* 2007;48:1430.
14. Moka D, Voth E, Dietlein M, Larena-Avellaneda A, Schicha H. Technetium 99m-MIBI-SPECT: a highly sensitive diagnostic tool for localization of parathyroid adenomas. *Surgery* 2000;128:29-35.
15. Lorberboym M, Minski I, Macadziob S, Nikolov G, Schachter P. Incremental diagnostic value of preoperative 99mTc-MIBI SPECT in patients with a parathyroid adenoma. *J Nucl Med* 2003;44:904-908.
16. Slater A, Gleeson FV. Increased sensitivity and confidence of SPECT over planar imaging in dual-phase sestamibi for parathyroid adenoma detection. *Clin Nucl Med* 2005;30:1-3.
17. Chen CC, Holder LE, Scovill WA, Tehan AM, Gann DS. Comparison of parathyroid imaging with technetium-99m-pertechnetate/sestamibi subtraction, double-phase technetium-99m-sestamibi and technetium-99m-sestamibi SPECT. *J Nucl Med* 1997;38:834-839.
18. Perez-Monte JE, Brown ML, Shah AN, Ranger NT, Watson CG, Carty SE, Clarke MR. Parathyroid adenomas: accurate detection and localization with Tc-99m sestamibi SPECT. *Radiology* 1996;201:85-91.
19. Huang J, Cheng M, Tzen K. The diagnostic effectiveness of 99mTc-sestamibi SPECT/CT in primary hyperparathyroidism. *Eur J Nucl Med Mol Imaging* 2012;39(Suppl 2):384-497. doi.org/10.1007/s00259-012-2224-7
20. Wei WJ, Shen CT, Song HJ, Qiu ZL, Luo QY. Comparison of SPET/CT, SPET and planar imaging using 99mTc-MIBI as independent techniques to support minimally invasive parathyroidectomy in primary hyperparathyroidism: a meta-analysis. *Hell J Nucl Med* 2015;18:127-135.
21. McCoy KL, Ghodadra AG, Hiremath TG, Albarano A, Joyce JM, Yip L, Carty SE, Muthukrishnan A. Sestamibi SPECT/CT versus SPECT only for preoperative localization in primary hyperparathyroidism: a single institution 8-year analysis. *Surgery* 2018;163:643-647.
22. Pata G, Casella C, Magri GC, Lucchini S, Panarotto MB, Crea N, Giubbini R, Salerni B. Financial and clinical implications of low-energy CT combined with 99m Technetium-sestamibi SPECT for primary hyperparathyroidism. *Ann Surg Oncol* 2011;18:2555-2563.
23. Takami H, Oshima M, Sugawara I, Satake S, Ikeda Y, Nakamura K, Kubo A. Pre-operative localization and tissue uptake study in parathyroid imaging with technetium-99m-sestamibi. *Aust N Z J Surg* 1999;69:629-631.
24. Chen EM, Mishkin FS. Parathyroid hyperplasia may be missed by double-phase Tc-99m sestamibi scintigraphy alone. *Clin Nucl Med* 1997;22:222-226.
25. Palestro CJ, Tomas MB, Tronco GG. Radionuclide imaging of the parathyroid glands. *Semin Nucl Med* 2005;35:266-276.
26. Shafiei B, Hoseinzadeh S, Fotouhi F, Malek H, Azizi F, Jahed A, Hadaegh F, Salehian M, Parsa H, Javadi H, Assadi M. Preoperative ^{99m}Tc-sestamibi scintigraphy in patients with primary hyperparathyroidism and concomitant nodular goiter: comparison of SPECT-CT, SPECT, and planar imaging. *Nucl Med Commun* 2012;33:1070-1076.
27. Guo R, Wang J, Zhang M, Zhang M, Meng H, Zhang Y, Li B. Value of 99mTc-MIBI SPECT/CT parathyroid imaging and ultrasonography for concomitant thyroid carcinoma. *Nucl Med Commun* 2017;38:676-682.