UDC: 616.447-006.55-073.7(497.115)
Professional paper

THE IMPACT OF SPECT/CT HYBRID IMAGING ON ENHANCING DIAGNOSTIC ACCURACY OF PARATHYROID ADENOMA USING 99MTC-MIBI SCAN IN THE NUCLEAR MEDICINE DEPARTMENT OF KOSOVO

Ismet BAJRAMI[1,4,5,6*], Armend JASHARI[2,5], Fakir SPAHIU[1,5], Sinisa STOJANOSKI[3], Elena DRAKALSKA SERSEMOVA[1]

[1]Faculty of Medical Sciences, Goce Delcev University, Stip, Republic of North Macedonia.*
[2] Alma Mater Europeae - Campus College Rezonanca
[3] Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine,"Ss. Cyril and Methodius" University in Skopje, Republic of North Macedonia
[4] University of Business and Technology UBT, Higher Education, Kosovo
[5] Department of Nuclear Medicine, University Clinical Center of Kosovo (QKUK), Prishtina, Kosovo
[6] Medical Faculty, University of Prishtina, Prishtina, Republic of Kosovo
[*]Corresponding Author: e-mail: ismet.31171@student.ugd.edu.mk, ismet_bajrami@yahoo.com

Abstract

Aim: This study aimed to compare conventional planar 99mTc-MIBI scintigraphy with hybrid SPECT/CT imaging for the preoperative localization of parathyroid adenoma in patients with suspected primary hyperparathyroidism. The purpose of this study was to evaluate whether the addition of SPECT/CT improves diagnostic accuracy and anatomical localization, particularly in ectopic lesions and anatomically complex cases.
Methods: This retrospective observational study included 42 patients referred to the Nuclear Medicine Department of the University Clinical Center of Kosovo from March 2024 to January 2025, with suspected or biochemically confirmed primary hyperparathyroidism. All patients underwent dual-phase planar 99mTc-MIBI scintigraphy and hybrid SPECT/CT during the same diagnostic procedure. Planar images were acquired at 15, 60, 90, and 120 minutes after injection of the radiopharmaceutical 99mTc-MIBI, and SPECT/CT was obtained approximately 160 minutes after administration of the same radiopharmaceutical.
Results: All 42 patients underwent both imaging modalities. Planar scintigraphy showed 22 true-positive, 13 true-negative, 4 false-positive, and 3 false-negative findings, corresponding to a sensitivity of 88.0%, specificity of 76.5%, PPV (positive predictive value) of 84.6%, NPV (negative predictive value) of 81.3%, and accuracy of 83.3%. Hybrid SPECT/CT demonstrated 24 true-positive, 15 true-negative, 2 false-positive, and 1 false-negative finding, with higher sensitivity (96.0%), specificity (88.2%), PPV (92.3%), NPV (93.8%), and accuracy (92.9%).
Conclusion: There is improvement in the ability to localize as well as increase in diagnostic certainty by using hybrid SPECT/CT compared to plain planar scintigraphy. The most benefit from hybrid SPECT/CT has been seen in the detection of ectopic parathyroid adenoma, in cases adjacent to the thyroid gland, and in those cases that require pre-operative localization.

Keywords: 99mTc-MIBI, SPECT/CT, radiopharmaceutical, primary hyperparathyroidism, dual phase scintigraphy, parathyroid adenoma, PTH.

1. Introduction

Hyperparathyroidism is a disorder caused by one or more overactive parathyroid glands and is commonly classified as primary or secondary. In approximately 80% of patients, primary hyperparathyroidism is caused by a solitary parathyroid adenoma, while 10–15% of cases are related to multiglandular hyperplasia. Parathyroid carcinoma is rare, accounting for only 3–4% of cases. Primary hyperparathyroidism (PHPT) remains one of the main causes of persistent hypercalcemia in outpatient practice and routine clinical work [1,2]. Secondary

hyperparathyroidism is commonly seen in patients with chronic renal failure and results from compensatory overproduction of parathyroid hormone [35].
In most cases, elevated PTH (parathyroid hormone) levels are caused by a single parathyroid adenoma; however, ectopic localization and anatomical variation may occur in a minority of patients, including lesions located in the upper thorax [3,4]. For surgical treatment to be successful, the hyperfunctioning parathyroid gland must be precisely localized and removed [5]. Therefore, accurate preoperative imaging plays a critical role in the success of minimally invasive parathyroidectomy. It reduces unnecessary neck dissection, shortens operative time, and reduce the risk of persistent or recurrent disease [6,7].
99mTc-MIBI planar scintigraphy has traditionally been used as a standard imaging method for preoperative localization in PHPT [8,9,23]. This modality remains widely used because of its lower cost, broad availability, ease of use, and simple acquisition protocol [10]. Despite these advantages, planar scintigraphy has well-known limitations. Reduced localization accuracy may occur in small adenomas, multiglandular parathyroid disease, cystic degeneration, or nodular thyroid disease. For these reasons, planar imaging may produce false-negative results and complicate surgical decision-making [11].
Hybrid SPECT/CT (single photon emission computed tomography/computed tomography) imaging can overcome several limitations of planar scintigraphy by combining functional and anatomical information in a single examination [11–14]. The main advantages of hybrid SPECT/CT include three-dimensional imaging, improved anatomical correlation, attenuation correction, and more precise localization of radiopharmaceutical uptake. These factors are particularly important for detecting ectopic glands, lesions in complex neck anatomy, and parathyroid lesions associated with thyroid pathology [15–17]. Although newer imaging methods such as 18F-fluorocholine PET/CT (positron emission tomography/computed tomography) and 4D-CT show high diagnostic sensitivity, their routine clinical use remains limited by availability and cost [18,19].
Biochemical parameters such as PTH, total calcium, ionized calcium, and 25-hydroxyvitamin D play an important role in the diagnosis of PHPT and may influence the pattern of radiopharmaceutical uptake [20–22]. At the University Clinical Center of Kosovo (UCCK), hybrid SPECT/CT is used in routine clinical practice to improve diagnostic confidence and provide accurate anatomical localization.

2. Methods

2.1 Study design and setting: This study was performed in the Nuclear Medicine Department of the University Clinical Center of Kosovo (UCCK). Clinical and imaging information was obtained retrospectively from the department electronic database. The study included patients referred between March 2024 and January 2025 with suspected or biochemically confirmed primary hyperparathyroidism who underwent dual-phase planar scintigraphy and hybrid SPECT/CT in the same diagnostic procedure. Patients were excluded from this study if they had incomplete clinical information, incomplete imaging or unavailable follow-up data. In this study, particular attention was given to the added value of hybrid SPECT/CT which combines functional SPECT findings with low dose CT-based anatomical information of the lesion. For the patients who underwent surgery, histopathology was the reference standard, whereas for non-operated patients without positive findings in imaging, clinical and biochemical follow-up was used. This aspect needs to be taken into consideration when analyzing specificity-related values.

2.2 Imaging Equipment: Hybrid SPECT/CT three dimensional imaging was carried out on a triple-head SPECT/CT device fitted with LEHR (Low Energy High Resolution) collimators. Planar scintigraphy was performed using a double-headed gamma camera with LEHR collimators, which provided two-dimensional functional imaging. The imaging protocol was standardized and held constant throughout the study period for reproducibility and comparison across patients. Improvement in diagnosis was mainly due to the use of hybrid SPECT/CT fusion and anatomical localization rather than detector quantity alone (Figure 1).

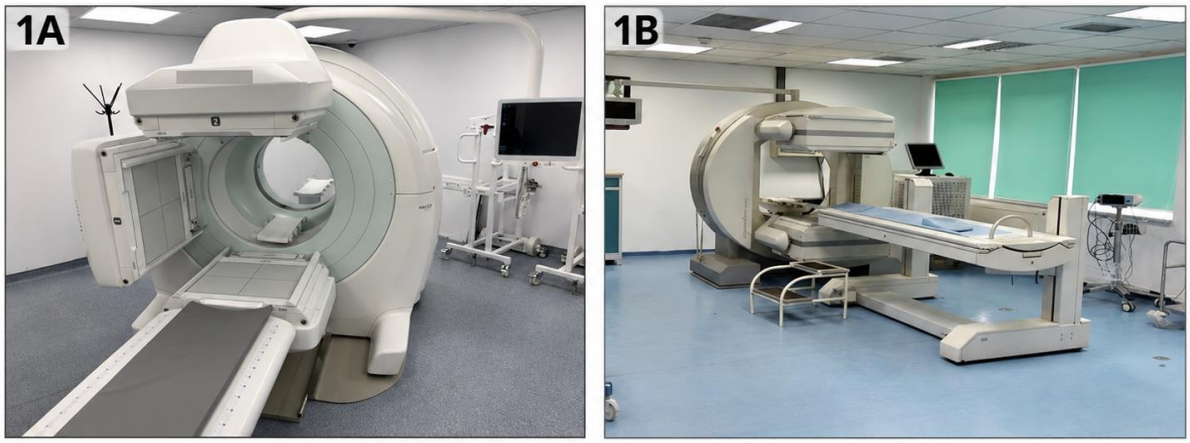


Figure 1. Imaging systems used in the study. (A) Hybrid SPECT/CT system used for tomographic functional imaging and low-dose CT anatomical localization. (B) Dual-head gamma camera used for conventional planar 99mTc-MIBI scintigraphy. The diagnostic comparison in this study was focused on the added value of hybrid SPECT/CT fusion rather than detector configuration alone.

2.3 Radiopharmaceutical Preparation*:* Radiopharmaceutical preparation was performed using a commercially available MIBI kit and sterile sodium pertechnetate ($^{99m}TcO_4^-$).
The preparation was gently mixed and heated in a boiling water bath for 12 minutes. After cooling at room temperature, the radiopharmaceutical remained radiochemically stable for at least 6 hours.
For clinical imaging, 555–740 MBq of 99mTc-MIBI was administered, with dose adjustment according to patient body weight and institutional protocol.

2.4 Imaging Protocols: Planar imaging of the neck and upper mediastinum was performed according to a standardized dual-phase 99mTc-MIBI protocol. Anterior planar images were acquired at approximately 15, 60, 90, and 120 minutes after injection using LEHR collimators, a 256 x 256 matrix, and a 140 keV ±10% energy window. SPECT/CT was acquired at approximately 160 minutes after injection without patient repositioning, using a 360° rotation, a 128 x 128 matrix, 120 projections, and 20-25 seconds per projection. Low-dose CT of the neck and upper mediastinum was performed immediately afterward for anatomical localization and attenuation correction, without intravenous contrast.

2.5 Data Analysis: Diagnostic performance was estimated by calculation of the number of true positives, false positives, true negatives, and false negatives. Sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy were calculated for both planar scintigraphy and hybrid SPECT/CT. Ectopic parathyroid adenomas were considered positive findings. The reference standard for diagnosis was histopathological examination for those patients who were treated with surgery. In patients who did not undergo surgery and imaging findings were negative, the final classification was done according to the further clinical course and follow-up, which included either persistence or normalization of biochemical parameters and treatment thereafter.

This approach was used in line with routine clinical practice; however, there is a possibility of partial verification bias as not all patients were confirmed by surgery or histopathology. Therefore, specificity, NPV, and overall diagnostic accuracy should be interpreted with caution. Correlation analysis between biochemical parameters and imaging positivity was not performed in the final analysis due to lack of complete biochemical data in some patients. Thus, the final analysis was restricted to diagnostic performance only.

***2.6 Image Processing**:* SPECT data reconstruction was performed with iterative OS-EM reconstructions with 2 iterations and 10 subsets, followed by Gaussian post-filtering with an HWHM of 8-10 mm. CT based attenuation correction, scatter correction and resolution recovery were applied. Multi-planar and hybrid SPECT/CT images were examined. Quality control of both the gamma camera and SPECT/CT systems was performed regularly, including calibration, uniformity testing, and spatial resolution assessment according to institutional protocols.

3. Results

***3.1 Patient and biochemical characteristics**:* The study included 42 patients with a mean age of 58.0 ± 14.0 years (range, 23-76 years). Female patients accounted for approximately three quarters of the cohort. The biochemical profile was consistent with primary hyperparathyroidism, with elevated intact PTH and calcium values and relatively low 25-hydroxyvitamin D levels. The demographic data of the study population are shown in Table 1, which include the age distribution and gender distribution.

Table 1. Population characteristics

Variable	Mean ± SD	Range	Unit / n (%)
Age	58.0 ± 14.0	23–76	years
Female Sex	-	-	32 (76.2%)

Table 2 provides biochemical data of the study population. PTH levels were greatly increased and had a wide variability, indicating high activity of the parathyroid glands. The total and ionized calcium concentrations were increased, confirming the presence of hypercalcemia. Mean levels of 25-hydroxyvitamin D were relatively low, which indicates vitamin D insufficiency.

Table 2. Biochemical data

Variable	Mean ± SD	Range	Unit / n (%)
Intact PTH*	545.4 ± 879.8	27.7–3144	pg/mL
Total calcium	2.45 ± 0.32	1.80–2.91	mmol/L
Ionized calcium	1.32 ± 0.27	1.00–1.98	mmol/L
25-hydroxyvitamin D	21.2 ± 9.6	8.1–39.1	ng/mL

* PTH data do not include qualitative results for the values that exceeded the detection limit of the test

3.2 Comparative diagnostic performance: Diagnostic performance was analyzed in the full study cohort (n = 42). Planar scintigraphy showed 22 true-positive, 13 true-negative, 4 false-positive, and 3 false-negative findings, corresponding to a sensitivity of 88.0%, specificity of 76.5%, PPV of 84.6%, NPV of 81.3%, and overall accuracy of 83.3%.

In comparison, hybrid SPECT/CT demonstrated 24 true-positive, 15 true-negative, 2 false-positive, and 1 false-negative finding, with higher sensitivity (96.0%), specificity (88.2%), PPV (92.3%), NPV (93.8%), and accuracy (92.9%). Overall, SPECT/CT reduced both false-negative and false-positive findings and showed superior diagnostic performance for preoperative lesion localization (Table 3).

Table 3. Comparative diagnostic performance of planar 99mTc-MIBI scintigraphy and hybrid SPECT/CT using the available reference standard.

Modality	TP	FP	TN	FN	Sensitivity	Specificity	PPV %	NPV %	Accuracy %
Planar	22	04	13	03	88.0	76.5	84.6	81.3	83.3
SPECT/CT	24	02	15	01	96.0	88.2	92.3	93.8	92.9

Table 3 shows that hybrid SPECT/CT outperformed planar ^{99}mTc-MIBI scintigraphy with a higher number of correct true-positive and true-negative classifications and fewer misclassified cases overall.

Because histopathological confirmation was not available for all non-operated patients, specificity-related measures should be interpreted cautiously because of possible partial verification bias. Figure 2 summarizes the comparative diagnostic performance of planar 99mTc-MIBI scintigraphy and hybrid SPECT/CT.

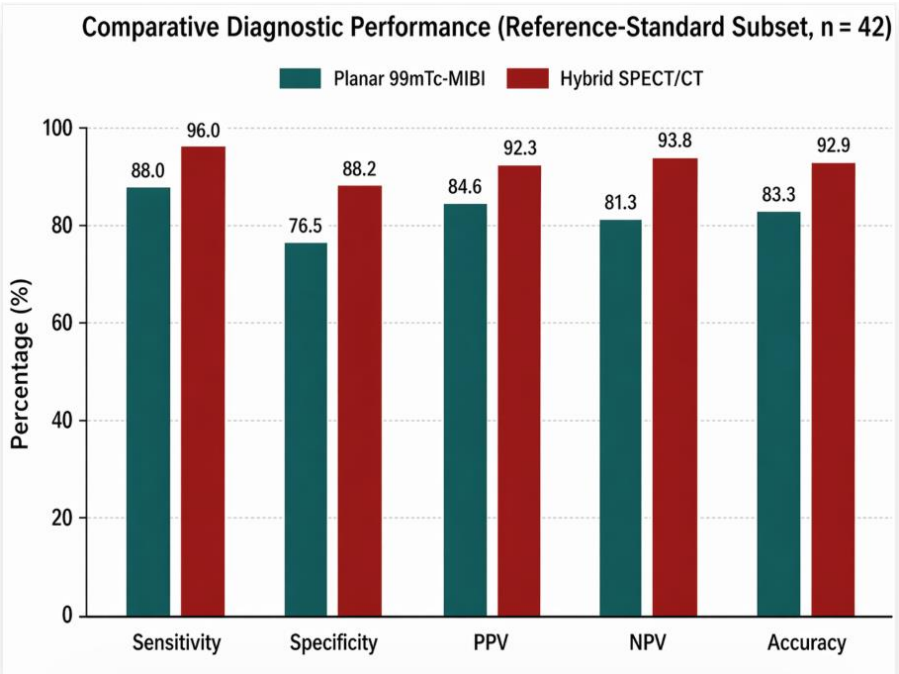


Figure 2. Diagnostic efficacy of triple-head SPECT/CT compared with planar ^{99}mTc-MIBI scintigraphy

3.2.1 Clinical study cases:

The two illustrative cases were selected for their educational value, because they demonstrate situations in which hybrid SPECT/CT provides additional anatomical information beyond planar scintigraphy, particularly in ectopic or anatomically challenging lesions.

Clinical Case 1*:* A 61-year-old female with biochemically confirmed primary hyperparathyroidism (PTH, 110 pg/ml), dual-phase planar 99mTc-MIBI scintigraphy was done, which demonstrated persistent focal tracer uptake in the lower cervical region, suspicious for

parathyroid adenoma. Subsequent hybrid SPECT/CT precisely localized the lesion in the lower neck/supraclavicular region, separate from the thyroid bed, thereby improving anatomical definition and diagnostic confidence. The triple-detector configuration enabled improved lesion visualization through higher photon-detection efficiency and enhanced angular sampling, particularly in the presence of radiopharmaceutical retention (Figure 3).

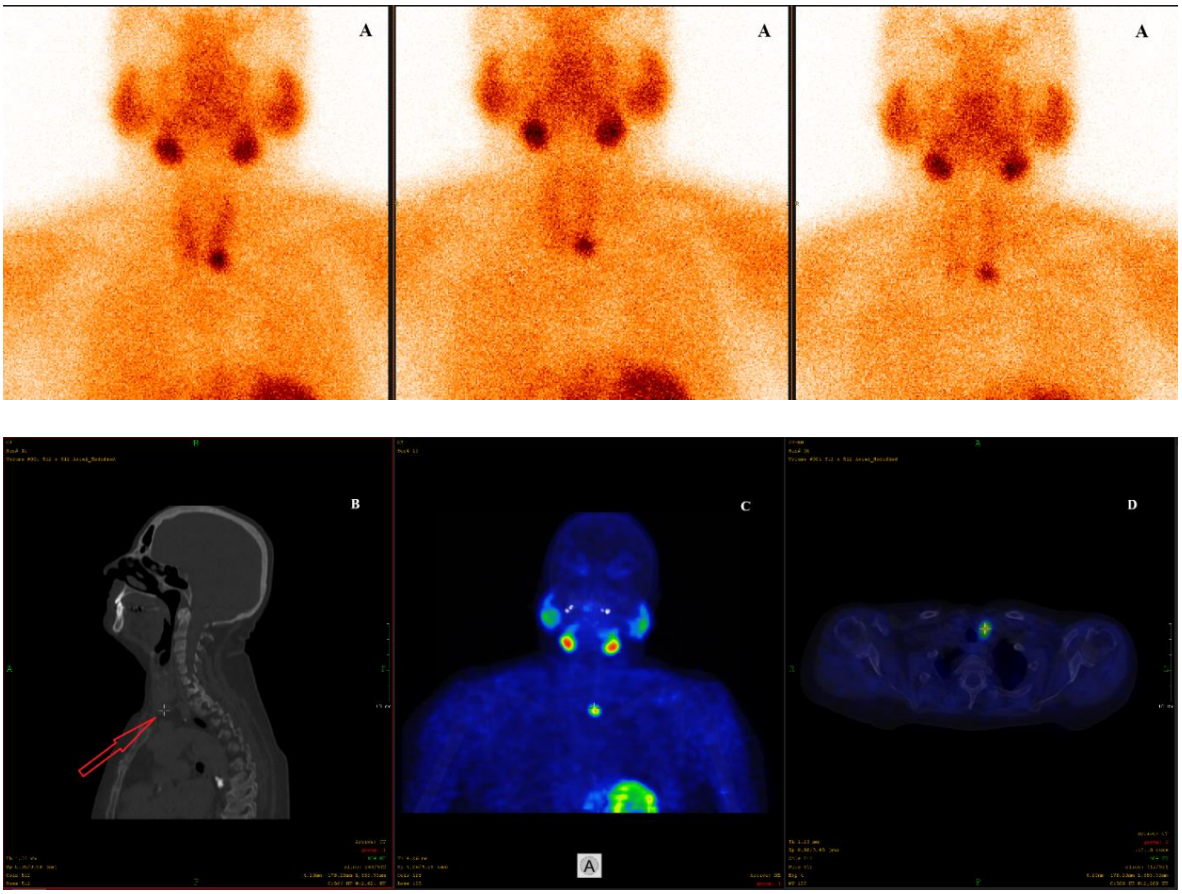


Figure 3. Combined planar and hybrid parathyroid imaging in the same patient. **(A)** Focal persistent radiopharmaceutical uptake in the lower neck/upper mediastinal region. A sagittal section of the CT scan (**B**) of the neck and thorax provides anatomy of the organs where the red arrow shows the lesion localization site. Image (**C**) shows only the fused coronal SPECT images and the localization of the lesion presented with high concentration of the radiopharmaceutical. (**D**) An axial SPECT/CT image showing exact localization of an ectopic parathyroid gland.

Clinical Case *2*: A 39-year-old female who had high levels of PTH (95 pg/mL) and hypercalcemia underwent a 99mTc-MIBI radiopharmaceutical scan. Planar dual-phase scintigraphy revealed persistent uptake of radiotracer indicating an ectopic parathyroid gland. The SPECT/CT imaging, done about 160 minutes after injection of the radiopharmaceutical, revealed the precise location of the lesion in the right lateral thorax/right axillary area, later confirmed to be an ectopic parathyroid adenoma on histopathological examination (Figure 4). This case highlights the additional diagnostic value provided by hybrid SPECT/CT for the localization of ectopic parathyroid lesions, especially those located outside the cervical or mediastinum areas where planar scintigraphy may be insufficient for accurate pre-operative localization of the lesion.

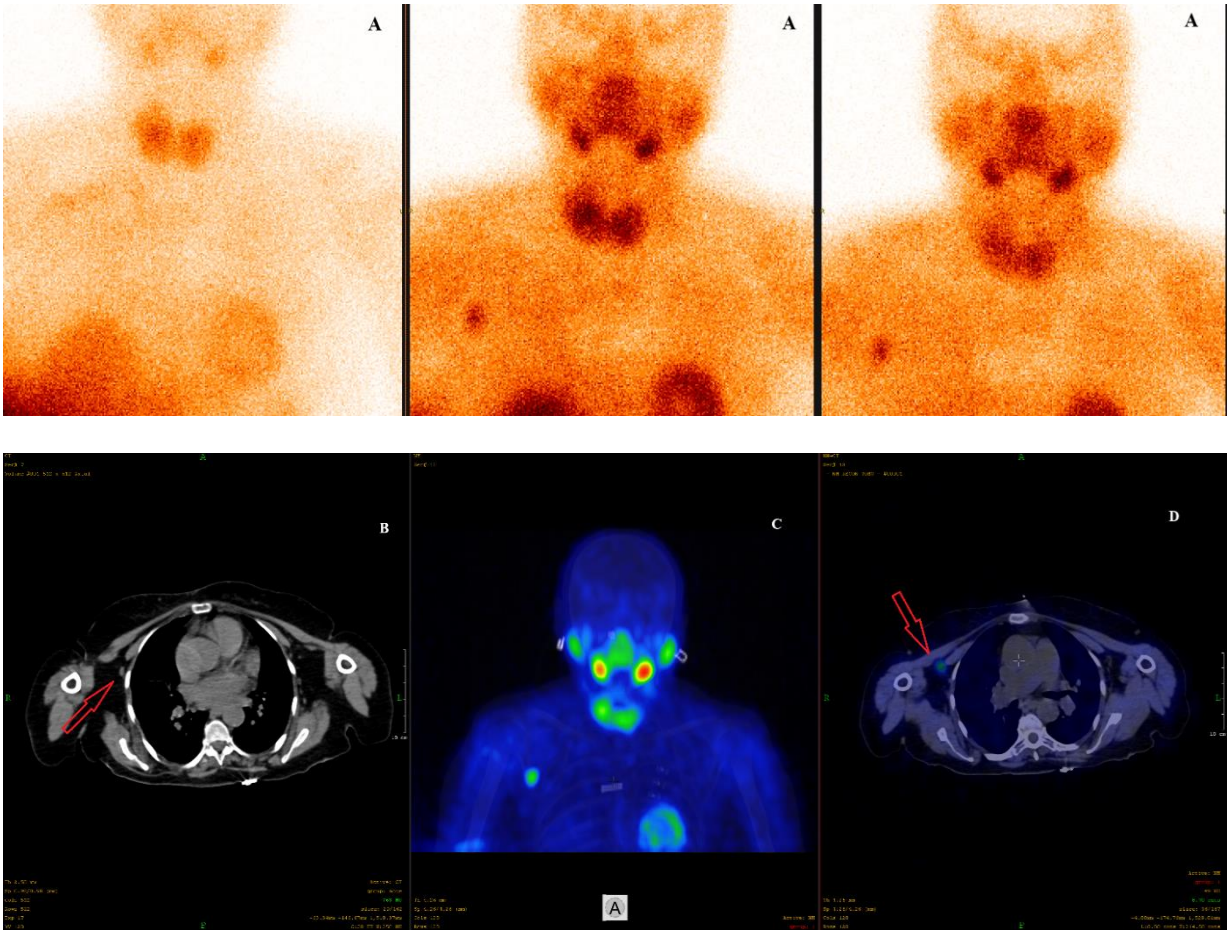


Figure 4. Combined planar and hybrid SPECT/CT parathyroid imaging in a 39-year-old woman with primary hyperparathyroidism. **A)** Early planar ^{99m}Tc-MIBI scintigraphy demonstrates uptake limited to the thyroid gland, with no definite ectopic focus identified. **(B)** Axial CT image shows the ectopic lesion in the right lateral thoracic/right axillary region (red arrow). **(C)** Coronal fused SPECT/CT image demonstrates focal tracer uptake corresponding to the lesion. **(D)** Axial fused SPECT/CT image further confirms the ectopic parathyroid adenoma

3.3 Semi-quantitative analysis for lesion-to-background ratio*:* Semi-quantitative analysis demonstrated increased radiopharmaceutical uptake in the target lesion, with a target-to-background ratio (TBR) of 3.78, calculated from the mean lesion counts relative to the average mean background counts of the adjacent reference regions (Figure 5).

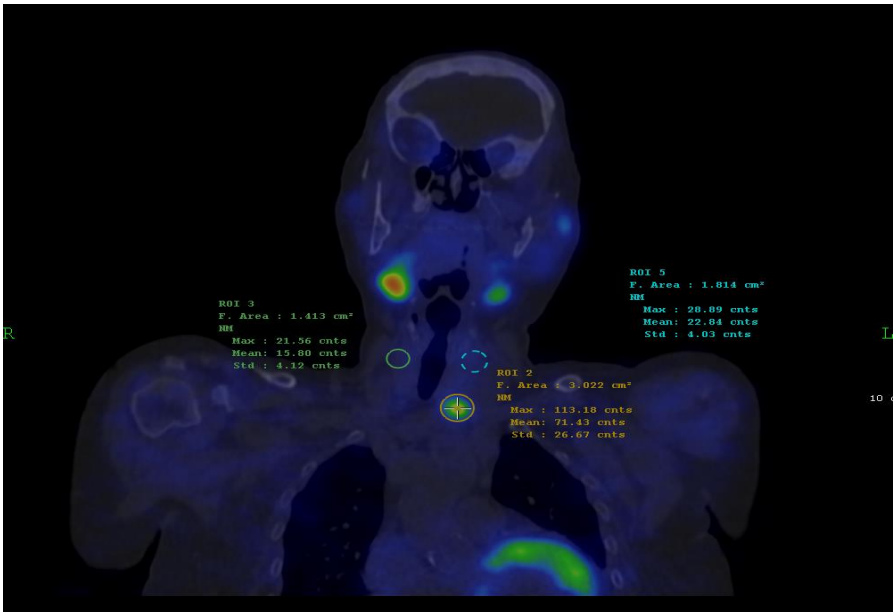


Figure 5. Fused coronal SPECT/CT showing localization of the target parathyroid lesion using 99mTc-MIBI. A semi-quantitative analysis was carried out with ROIs selected manually, in which ROI 2 is located on the lesion and ROI 1 and ROI 3 are selected in the adjacent background region. The target to background ratio (TBR) was determined by taking the mean counts of the ROI on the lesion (73.43 counts) and dividing it by the mean counts of the two background ROIs (23.04 and 15.80 counts), resulting in a TBR value of 3.78.

4. Discussion and Conclusions

Hybrid SPECT/CT using 99mTc-MIBI radiopharmaceutical, improved lesion localization compared with planar scintigraphy alone. This improvement can be explained mainly by the combination of tomographic functional imaging with low-dose CT-based anatomical correlation. In the present study, SPECT/CT increased sensitivity from 88.0% to 96.0% and specificity from 76.5% to 88.2%.

Although hybrid SPECT/CT showed better diagnostic performance than planar scintigraphy, these findings should be interpreted in the context of several methodological and clinical factors. The improvement was mainly related to better anatomical localization and reduction of equivocal findings, rather than to functional information alone. False-negative findings may occur in small adenomas, multiglandular disease, cystic or poorly functioning adenomas, intrathyroidal lesions, multinodular goiter, and lesions with rapid 99mTc-MIBI radiopharmaceutical washout [33,34,42]. False-positive findings may be caused by thyroid nodules, multinodular goiter, thyroid adenomas, lymph nodes, or other cervical lesions with increased radiopharmaceutical uptake [33,39,40,42]. Therefore, SPECT/CT should be interpreted together with biochemical findings, ultrasound, surgical assessment, and follow-up data.

The improvement was particularly relevant in patients with ectopic glands, thyroid nodules, or complex cervical anatomy, where planar images may be limited by overlapping structures and non-specific thyroid uptake [27–29].

These findings are consistent with published literature and current EANM recommendations, which support the use of 99mTc-MIBI SPECT/CT for accurate detection and localization of hyperfunctioning parathyroid tissue in primary hyperparathyroidism [24].

The diagnostic values observed in the present study are generally in agreement with previous reports showing that SPECT/CT improves localization accuracy compared with planar 99mTc-MIBI scintigraphy [8,11,28,29]. Earlier studies and meta-analyses have reported that the main advantage of SPECT/CT is its ability to combine functional uptake with anatomical CT information, especially in ectopic glands, posteriorly located adenomas, lesions near the thyroid

gland, and patients with complex cervical anatomy [28–30]. In our study, the increase in sensitivity from 88.0% to 96.0% and specificity from 76.5% to 88.2% supports this concept. However, the relatively small sample size and incomplete histopathological verification in non-operated patients may have influenced the estimated specificity and negative predictive value. Therefore, our results should be considered supportive rather than definitive and should be confirmed in larger prospective studies.

Previous studies have also shown that SPECT/CT improves diagnostic confidence compared with planar imaging, mainly because it combines functional radiopharmaceutical uptake with anatomical localization in a single examination [8,11,25,28]. Low-dose CT is crucial for defining lesion localization, reducing interpretive uncertainty, and supporting accurate preoperative mapping [31,32]. This may support targeted minimally invasive parathyroidectomy, reduce unnecessary bilateral neck exploration, shorten operative time, and lower the risk of persistent or recurrent disease [5–7,36–38]. Patients with associated thyroid nodules and ectopic parathyroid glands may show a more pronounced benefit from SPECT/CT imaging [28–30].

Recent studies have reported excellent diagnostic performance for newer imaging modalities, particularly 18F-fluorocholine PET/CT, 11C-methionine PET/CT and 4D-CT. In particular, 11C-methionine has been reported as a useful option for detecting parathyroid lesions, especially in selected cases where conventional imaging or other radiopharmaceuticals are negative or inconclusive [26]. 18F-fluorocholine PET/CT may provide higher sensitivity in selected difficult cases, especially when conventional imaging is negative or discordant, while 4D-CT can provide detailed anatomical information in complex or re-operative cases [9,18,19,41]. Nevertheless, these methods may be limited by availability, cost, PET radiopharmaceutical access, and, in the case of 4D-CT, radiation exposure. In this context, 99mTc-MIBI SPECT/CT remains a practical and clinically valuable method, especially in centers where advanced PET-based parathyroid imaging is not routinely available.

Accurate localization of ectopic parathyroid tissue remains one of the strongest clinical indications for hybrid SPECT/CT [27–29,36–38]. The triple-head SPECT/CT system may provide practical advantages related to photon-detection efficiency and acquisition time; however, the main diagnostic benefit in this study was attributed to hybrid SPECT/CT fusion and anatomical localization rather than detector configuration alone [43,44].

Overall, our findings support the routine use of 99mTc-MIBI SPECT/CT as an important adjunct to planar scintigraphy and ultrasound for preoperative localization of parathyroid adenomas, particularly in ectopic, anatomically complex, or surgically challenging cases.

In conclusion, 99mTc-MIBI SPECT/CT demonstrated higher diagnostic performance than planar scintigraphy in this study and improved preoperative localization of parathyroid adenomas. The method provides clinically useful functional and anatomical information, supports minimally invasive surgical planning, and remains especially important in healthcare settings where 18F-fluorocholine PET/CT is not routinely available. Further multicenter studies with larger patient populations and complete histopathological verification are needed to confirm these findings and to better define the optimal imaging algorithm for primary hyperparathyroidism.

Author Contributions

I.B. and A.J. conceived and designed the study. I.B. collected the data and performed the statistical analysis. A.J. contributed to the study framework and manuscript preparation. S.F., S.S., and E.D.S. contributed to data interpretation and provided critical revisions of the manuscript. All authors reviewed and approved the final manuscript.

Funding: This study did not receive any external funding.

Acknowledgement: All images are provided by the courtesy of Department of Nuclear Medicine, Prishtina, Kosovo.

Conflict of interest: The authors declare no conflict of interest.

References

[1]. Palermo, A.; Tabacco, G.; Makras, P.; Zavatta, G.; Trimboli, P.; Castellano, E.; Anastasilakis, A.D. Primary Hyperparathyroidism: From Guidelines to Outpatient Clinic. Rev. Endocr. Metab. Disord. 2024, 25, 875–896. https://doi.org/10.1007/s11154-024-09899-5.

[2]. Bilezikian, J.P.; Cusano, N.E.; Khan, A.A.; Liu, J.M.; Marcocci, C.; Bandeira, F. Primary Hyperparathyroidism. Nat. Rev. Dis. Primers 2016, 2, 16033. https://doi.org/10.1038/nrdp.2016.33

[3]. DeLellis, R.A.; Mazzaglia, P.; Mangray, S. Primary Hyperparathyroidism: A Current Perspective. Arch. Pathol. Lab. Med. 2008, 132, 1251–1262.

[4]. Kowalski, G.J.; Buła, G.; Żądło, D.; Gawrychowska, A.; Gawrychowski, J. Primary Hyperparathyroidism. Endokrynol. Pol. 2020, 71, 260–270. 10.5603/EP.a2020.0028.

[5]. Hindié, E.; Schwartz, P.; Avram, A.M.; Imperiale, A.; Sebag, F.; Taïeb, D. Primary Hyperparathyroidism: Defining the Appropriate Preoperative Imaging Algorithm. J. Nucl. Med. 2021, 62(Suppl. 2), 3S–12S. https://doi.org/10.2967/jnumed.120.245993.

[6]. Mariani, G.; Gulec, S.A.; Rubello, D.; Boni, G.; Puccini, M.; Pelizzo, M.R.; Giuliano, A.E. Preoperative Localization and Radioguided Parathyroid Surgery. J. Nucl. Med. 2003, 44, 1443–1458.

[7]. Kunstman, J.W.; Kirsch, J.D.; Mahajan, A.; Udelsman, R. Parathyroid Localization and Implications for Clinical Management. J. Clin. Endocrinol. Metab. 2013, 98, 902–912. https://doi.org/10.1210/jc.2012-3168.

[8]. Özçevik, H.; Tamam, M.Ö.; Tatoğlu, M.T.; Mülazımoğlu, M. Comparison of Dual-Phase Tc-99m-MIBI Planar Imaging and SPECT/CT in Hyperparathyroidism. Mol. Imaging Radionucl. Ther. 2022, 31, 191–197. 10.4274/mirt.galenos.2022.60565.

[9]. Yang, J.; Lu, X.; Zhou, P.; Gao, Z.; Ding, C.; Weng, W.; Su, X. Comparison of Four-Dimensional CT and MIBI SPECT/CT in the Localization Management of Primary Hyperparathyroidism. Cancer Imaging 2025, 25, 90. https://doi.org/10.1186/s40644-025-00897-7.

[10]. Wang, Y.; Liu, Y.; Li, N.; Xu, K.; Zhang, W. Quantitative Application of Dual-Phase 99mTc-MIBI SPECT/CT for Parathyroid Lesions: Identification of Optimal Timing in Secondary Hyperparathyroidism. EJNMMI Phys. 2023, 10, 29. https://doi.org/10.1186/s40658-023-00548-5

[11]. Lavely, W.C.; Goetze, S.; Friedman, K.P.; Leal, J.P.; Zhang, Z.; Garret-Mayer, E.; Ziessman, H.A. Comparison of SPECT/CT, SPECT, and Planar Imaging Using 99mTc-MIBI. J. Nucl. Med. 2007, 48, 1084–1089. https://doi.org/10.2967/jnumed.107.040428

[12]. Papathanassiou, D.; Bruna-Muraille, C.; Jouannaud, C.; Gagneux-Lemoussu, L.; Eschard, J.P.; Liehn, J.C. SPECT/CT in Bone Diseases. Joint Bone Spine 2009, 76, 474–480. https://doi.org/10.1016/j.jbspin.2009.01.016

[13]. El Yaman, A.; Alwan, M.; El Ghazawi, A.; Al-Mallah, M.H.; Al Rifai, M. Advances in Nuclear Hybrid Imaging in Cardiovascular Diseases. Prog. Cardiovasc. Dis. 2025, in press

[14]. Prakash, D.; Kotian, R.P. Hybrid Imaging: Physics, Principles, and Quality Control. In Fundamentals of X-ray Imaging, 2nd ed.; Springer Nature Singapore: Singapore, 2025; pp. 417–506. https://doi.org/10.1007/978-981-96-7328-5_7

[15]. Even-Sapir, E.; Keidar, Z.; Bar-Shalom, R. Hybrid Imaging Improving Diagnostic Accuracy. In Semin. Nucl. Med.; WB Saunders: July 2009; Vol. 39, pp. 264–275.

[16]. Mariani, G.; Bruselli, L.; Kuwert, T.; Kim, E.E.; Flotats, A.; Israel, O.; Watanabe, N. Clinical Uses of SPECT/CT—A Review. Eur. J. Nucl. Med. Mol. Imaging 2010, 37, 1959–1985

[17]. Spanu, A.; Schillaci, O.; Piras, B.; Madeddu, G. SPECT/CT in Hyperparathyroidism. Clin. Transl. Imaging 2014, 2, 537–555

[18]. Scerrino, G.; Paladino, N.C.; Graceffa, G.; Melfa, G.; Orlando, G.; Di Vuolo, R.; Lo Casto, A. 18F-Fluorocholine PET/CT vs 4D-CT for Parathyroid Identification. J. Clin. Med. 2025, 14, 5468. https://doi.org/10.3390/jcm14155468

[19]. Latge, A.; Riehm, S.; Vix, M.; Bani, J.; Ignat, M.; Pretet, V.; Imperiale, A. 18F-Fluorocholine PET and 4D-CT in Persistent Primary Hyperparathyroidism. Diagnostics 2021, 11, 2384. https://doi.org/10.3390/diagnostics11122384

[20]. Al-Hraishawi, H.K. Comparison of Metabolic and Characteristic Features of PHPT Patients with Different PTH Levels; Master's Thesis, Rutgers University, USA, 2016
[21]. Bhan, A.; Athimulam, S.; Kumari, P.; Pal, R.; Bhadada, S.K.; Cook, B.C.; Rao, S.D. Large Parathyroid Adenomas: Reconciling Adenoma Size and Phenotype. Front. Endocrinol. 2023, 14, 1009516. https://doi.org/10.3389/fendo.2023.1009516
[22]. Kazakou, P.; Vrachnis, D.; Paschou, S.A.; Nastos, K.; Sarlani, H.; Kantreva, K.; Saltiki, K. Giant Parathyroid Adenoma with Carcinoma-like Presentation: Case Report. Hormones 2025, 1–6. https://doi.org/10.1007/s42000-025-00627-5
[23]. Lee, S.H.; Shin, E.; Ha, S.; Oh, J.S.; Song, D.E.; Ryu, J.S. Dual- vs. Single-Phase SPECT/CT for Parathyroid Lesion Localization. Medicine 2020, 99, e19989. 10.1097/MD.0000000000019989
[24]. Giovanella, L.; Hindie, E.; Huellner, M.W.; Talbot, J.N.; Verburg, F.A. Summary of the New EANM Guidelines for Parathyroid Imaging. Q. J. Nucl. Med. Mol. Imaging 2022, 66, 93–103.
[25]. Jacene, H.A.; Goetze, S.; Patel, H.; Wahl, R.L.; Ziessman, H.A. Advantages of Hybrid SPECT/CT. Open Med. Imaging J. 2008, 2, 67–79
[26]. Durma, A.D.; Saracyn, M.; Kołodziej, M.; Jóźwik-Plebanek, K.; Kamiński, G. Use of [11C]C-Methionine in Endocrine Diagnostics. Pharmaceuticals 2025, 18, 229. https://doi.org/10.3390/ph18020229
[27]. Wong, K.K.; Fig, L.M.; Gross, M.D.; Dwamena, B.A. Parathyroid Adenoma Localization with MIBI SPECT/CT: Meta-analysis. Nucl. Med. Commun. 2015, 36, 363–375. 10.1097/MNM.0000000000000262
[28]. Gayed, I.W.; Kim, E.E.; Broussard, W.F.; Evans, D.; Lee, J.; Broemeling, L.D.; Podoloff, D.A. Value of SPECT/CT Over SPECT in Parathyroid Imaging. J. Nucl. Med. 2005, 46, 248–252.
[29]. Morris, M.A.; Saboury, B.; Ahlman, M.; Malayeri, A.A.; Jones, E.C.; Chen, C.C.; Millo, C. Parathyroid Imaging: Past, Present, and Future. Front. Endocrinol. 2022, 12, 760419. https://doi.org/10.3389/fendo.2021.760419
[30]. Leitha, T.; Staudenherz, A. Hybrid PET/CT and SPECT/CT Imaging. In Computed Tomography—Clinical Applications; InTech: 2012; pp. 269–294
[31]. Israel, O.; Goldsmith, S.J. (Eds.). Hybrid SPECT/CT Imaging in Clinical Practice; CRC Press: Boca Raton, FL, USA, 2016
[32]. Pata, G.; Casella, C.; Magri, G.C.; Lucchini, S.; Panarotto, M.B.; Crea, N.; Salerni, B. Financial and Clinical Implications of Low-Energy CT with 99mTc-MIBI SPECT. Ann. Surg. Oncol. 2011, 18, 2555–2563. https://doi.org/10.1245/s10434-011-1641-3
[33]. Tay, D.; Das, J.P.; Yeh, R. Preoperative Localization for PHPT: A Clinical Review. Biomedicines 2021, 9, 390. https://doi.org/10.3390/biomedicines9040390
[34]. Sandqvist, P. Preoperative Localisation of Parathyroid Adenoma Using Tc-99m-MIBI SPECT/CT; Thesis, Karolinska Institutet, Sweden, 2022
[35]. Hindie, E.; Ureña-Torres, P.A.; Taïeb, D. Parathyroid Imaging in Renal Hyperparathyroidism. In Parathyroid Glands in Chronic Kidney Disease; Springer: Cham, Switzerland, 2020; pp. 35–49. https://doi.org/10.1007/978-3-030-43769-5_3
[36]. Krausz, Y.; Bettman, L.; Guralnik, L.; Yosilevsky, G.; Keidar, Z.; Bar-Shalom, R.; Israel, O. Tc-99m MIBI SPECT/CT in Primary Hyperparathyroidism. World J. Surg. 2006, 30, 76–83. https://doi.org/10.1007/s00268-005-7849-2
[37]. Taubman, M.L.; Goldfarb, M.; Lew, J.I. Role of SPECT and SPECT/CT in Parathyroid Surgery. Int. J. Mol. Imaging 2011, 2011, 141593. https://doi.org/10.1155/2011/141593
[38]. Patel, S.G.; Saunders, N.D.; Jamshed, S.; Weber, C.J.; Sharma, J. Multimodal Localization Improves Reoperative Parathyroidectomy Outcomes. Am. Surg. 2019, 85, 939–943. https://doi.org/10.1177/000313481908500932
[39]. Nandedkar, S.S.; Dixit, M.; Malukani, K.; Varma, A.V.; Gambhir, S. Evaluation of Thyroid Lesions with FNAC Using Bethesda System. Int. J. Appl. Basic Med. Res. 2018, 8, 76–82. 10.4103/ijabmr.IJABMR_169_17
[40]. Nockel, P.; Millo, C.; Keutgen, X.; Klubo-Gwiezdzinska, J.; Shell, J.; Patel, D.; Kebebew, E. Incidental Thyroid Uptake on 68Ga-DOTATATE PET/CT. Thyroid 2016, 26, 831–835. https://doi.org/10.1089/thy.2016.0174
[41]. Garnier, S.; Mahéo, C.; Potard, G.; Cavarec, M.B.; Roudaut, N.; Thuillier, P.; Leclere, J.C. Value of 18F-Fluorocholine PET-CT in Localizing Parathyroid Adenoma. Sci. Rep. 2025, 15, 10018. https://doi.org/10.1038/s41598-025-94735-2
[42]. Smith, J.R.; Oates, M.E. Radionuclide imaging of the parathyroid glands: Patterns, pearls, and pitfalls. Radiographics 2004, 24, 1101–1115. https://doi.org/10.1148/rg.244035718
[43]. Krizsan, A.K.; Kukuts, K.; Al-Muhanna, W.; Szoboszlai, Z.; Balazs, L.; Szabo, B.; Forgacs, A.; et al. Performance evaluation of a novel multipinhole collimator on a triple–NaI-detector SPECT/CT

system for dedicated myocardial imaging. EJNMMI Physics 2023, 10, 24. https://doi.org/10.1186/s40658-023-00541-y
[44]. Willowson, K.P.; Bailey, D.L. Evolving SPECT/CT technology. Br. J. Radiol. 2024, tqae200. https://doi.org/10.1093/bjr/tqae200