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Original scientific paper

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

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Abstract

Aim: The aim of this study was to compare the images obtained from conventional planar gamma camera and hybrid SPECT/CT triple head detectors, both present in our department and to justify the diagnostic accuracy of planar and hybrid images performing the parathyroid scintigraphy. The parathyroid scintigraphy was performed, using ^{99m}Tc-MIBI (technetium- 99m methoxyisobutylisonitrile) radiopharmaceutical. The planar scintigraphy is common procedure in most countries, but the localization of the parathyroid adenoma sometimes makes a difficult task for the surgeons. The presence of SPECT/CT with triple detectors, increased the quality and efficacy of diagnostic results, in localization of parathyroid adenoma in the neck area, especially the ectopic glands in the upper thorax.
Methods: The planar scintigraphy and SPECT/CT images were performed in 42 patients that were referred in our department from March 2024 until January 2025. The initial diagnosis was primary hyperparathyroidism. Dual phase planar scintigraphy was performed at 15, 60, 90 and 120 minutes after the injection of ^{99m}Tc-MIBI radiopharmaceutical. In the same patients SPECT/CT images were obtained 160 minutes after injection of the same ^{99m}Tc-MIBI radiopharmaceutical.
Results: The group of 42 patients were undergo the both modalities: planar scintigraphy dual phase and hybrid SPECT/CT with three detectors. SPECT /CT showed higher result and imaging clarity of adenoma lesions comparing with planar scintigraphy alone with sensitivity 98.0% vs. 89.7% and specificity 88.2% vs. 77.1 %.
Conclusion: Hybrid SPECT/CT compare with planar scintigraphy showed a high diagnostic precision in localization of the parathyroid adenoma. It was a very successful in identifying the ectopic parathyroid gland especially located in mediastinum and successful in diminishing the thyroid normal gland from parathyroid adenoma. These findings support the importance of investment in hybrid SPECT/CT where PET/CT was not available. Hybrid technology with SPECT (Single Photon Emission Computed Tomography) fused with CT (computed tomography), plays a huge role not only in anatomical and functional assessment of parathyroid adenoma, but also it plays an important role in cases when reoperation is needed.

Keywords: ^{99m}Tc-MIBI, SPECT/CT, radiopharmaceutical, primary hyperparathyroidism, dual phase scintigraphy, parathyroid adenoma, PTH

1. Introduction

Hyperparathyroidism as a disorder caused from one or more overactive hyperfunctional parathyroid glands. There are two types of hyperparathyroidism-primary and secondary. In approximately 80 % of patients, primary hyperparathyroidism is caused due to a solitary adenoma alone, while 10-15 % of cases are due to hyperplasia involving more than one gland. Only 3-4 % of cases are malignant in nature. Primary hyperparathyroidism (PHPT) remain one of the main cause of persistent hypercalcemia in outpatient practice and in routine clinical work

[1,2]. Secondary hyperparathyroidism commonly seen in patients with chronic renal failure and is a result of developing the compensatory hyperproduction of PTH hormone. adenoma; however ectopic localization and anatomic variation can be seen in minority cases The main reason of PTH high level is from single parathyroid adenoma but sometimes the reason are the ectopic gland in upper thorax [3,4]. For surgical treatment to be successful, the hyperfunctioning parathyroid gland must be precisely located and removed [5]. Therefore, precise preoperative imaging plays critical role for the success of minimally invasive parathyroidectomy. It reduces the unnecessary neck dissection, shorten the time of the surgery and lower the risk of recurrent disease [6,7]. ^{99m}Tc-MIBI dual phase planar scintigraphy has been considered the gold standard protocol for preoperative localization in PHPT [8,9]. The use of this planar modality is mainly due of its cost, wide availability, simple to handle the equipment and uncomplicated acquisition protocols for technologist [10]. Despite this, there are some limitations of planar scintigraphy that are well known. Reduced effectiveness in localization can occur in case of small adenoma, multiglandular parathyroid disease, cystic degeneration or thyroid gland nodularity. These are the reasons that some imagine results lead to false negative results and confuse the surgical decision [11]. On the other hand, hybrid SPECT/CT imaging overcomes all these limitations of planar scintigraphy by incorporating the functional and anatomical imaging into one examination [11–14]. The biggest advantages of using the hybrid SPECT/CT includes three-dimensional imaging, improved anatomical correlation and attenuation correction imaging of the radiopharmaceutical uptake. These factors are very important for detecting, imaging and localization of ectopic glands, difficult anatomy of the neck or associated thyroid pathology [15–17]. While new imaging method using ^{18}F-fluorocholine PET/CT and 4D-CT show great diagnostic sensitivity, their regular clinical application is still limited due to low availability and high cost [18,19]. Biochemical data such as PTH, total and ionized calcium, 25 –hydroxyvitamin D, plays important role in diagnosing the PHPT and can affect the pattern of radiopharmaceutical uptake [20–22]. The University Clinical Center of Kosovo (UCCK) in their daily practice provides a suitable and accurate imaging in a clinical examination using already well-established hybrid SPECT/CT.

2. Materials and Methods

2.1 Study design and setting

The study was conducted at the Nuclear Medicine Department in University Clinical Center of Kosovo (UCCK). Clinical data were collected from our department electronic registry and included: patient age, sex and laboratory parameters (PTH, ionized Ca, Vitamin D) Nuclear medicine data from dual-phase planar ^{99m}Tc-MIBI scintigraphy and hybrid SPECT/CT were performed within the same diagnostic examinations [23-24] using triple-head SPECT/CT The main diagnostic advantage was coming from hybrid technology (SPECT combined with CT fusion), rather than detector numbers and configuration important only for reducing examination time.

2.2. Imaging Equipment

Hybrid SPECT/CT imaging was performed according to manufacturer protocols: Any Scan TRIO SPECT/CT system with a triple-detectors. The collimators were LEHR (low energy high resolution. The SPECT /CT system, according to manufacturer was Thera max platform with the MaX/123-15.9 detection module. Imaging protocols were standardized and remained uniform throughout the study period to ensure reproducibility and comparability. Planar scintigraphy was performed using a conventional dual-head gamma camera equipped with low-energy high-resolution collimators, providing standard two-dimensional functional imaging (Figure 1, A and B).

Figure 1. (**A**) AnyScan TRIO SPECT/CT with triple SPECT detectors

Figure 1. (**B**) Planar Gamma camera dual head

2.3. Radiopharmaceutical Preparation

Radiopharmaceutical preparation was performed using a commercially available MIBI kit and sterile sodium pertechnetate ($^{99m}TcO_4^-$) followed by gentle mixing and heating in a boiling water bath for 12 min.
After cooling at room temperature, the radiopharmaceutical preparation remained radiochemically stable for at least 6 h.
For clinical imaging, 555–740 MBq of ^{99m}Tc-MIBI was administered, with dose adjustment, according to patient body mass and institutional protocol.

2.4. Imaging Protocols

Planar imaging of the neck and upper mediastinum was performed according to a standardized dual-phase ^{99}mTc-MIBI protocol, with acquisitions at approximately 15, 60, 120, and 160 min post-injection. Anterior planar images were obtained using LEHR collimators, a 256 × 256 matrix, and a 140 keV ±10% energy window. SPECT/CT acquired at approximately 160 min without patient repositioning, using a 360° rotation, a 128 × 128 matrix, 120 projections, and 20–25 s per projection. Low-dose CT of the neck and upper mediastinum was performed immediately thereafter for anatomical localization and attenuation correction, without intravenous contrast. [23,24]

2.5. Data Analysis

All results were from obtained true-positive, false-positive, true-negative, and false-negative findings referred from diagnostic indicators, such as sensitivity, specificity and positive predictive values.
The relationship between biochemical variables and imaging positive value were assessed using Spearman's rank correlation.

2.6. Image Processing

SPECT data reconstruction was performed with iterative OS-EM (2 iterations and 10 subsets) with Gaussian post-filtering (HWHM of 8-10 mm). Attenuation correction based on CT, scatter correction and resolution recovery was employed. Multi-planar and hybrid SPECT/CT images were examined.
Quality Control of imaging equipment, both for Gamma camera and SPECT/CT are regularly tested including calibration and spatial resolution.

3. Results

Our comparative study contained 42 patients with average age of 58.0 ± 14.0 years (minimum age of 23 years and maximum age of 76 years). Due to the random availability of the patients, after collection and analyzing data, we discovered inclusion of 75% females and only around 25% of males. This indicates probability of incidence of thyroid pathology in female population (table 1)

Table 1. Population Characteristics Biochemistry

Variable	Mean ± SD	Range	Unit / n (%)
Age	58.0 ± 14.0	23–76	years
Female sex	—	—	15 (75.0%)

The biochemical profile shows markedly elevated levels of intact PTH with a wide range, consistent with significant parathyroid overactivity. Total and ionized calcium levels are elevated, indicating the presence of hypercalcemia, although some variability is noted. The 25-hydroxyvitamin D level is relatively low, suggesting frequent vitamin D insufficiency, which in turn may contribute to secondary stimulation of PTH secretion and modulation of calcium homeostasis. Overall, the pattern is compatible with calcium-PTH dysregulation (table 2).

Table 2.

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

Variable	Mean ± SD	Range	Unit / n (%)
Ionized calcium	1.32 ± 0.27	1.00– 1.98	mmol/L
25-hydroxyvitamin	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

Performance analyses were obtained in the patient population referred above. (n-42). Using planar scintigraphy, we obtained 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 results, 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. Detailed results presented in Table 3.

Table 3. Diagnostic performance of planar ^{99}mTc-MIBI and SPECT/CT (reference-standard subset).

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

Table 3 shows that hybrid SPECT/CT outperformed planar ^{99}mTc-MIBI scintigraphy, showing more correct, true -positive and true-negative classifications and fewer misclassified cases overall. Diagnostic estimates were calculated with ectopic glands classified as positive findings, and exact 95% confidence intervals obtained using the Clopper–Pearson method.
As histopathological confirmation was unavailable in all non-operated patients, specificity-related measures should be interpreted cautiously because of possible partial verification bias. Ectopic parathyroid glands were classified as positive findings. Exact 95% confidence intervals were calculated using the Clopper–Pearson method (Figure 2).

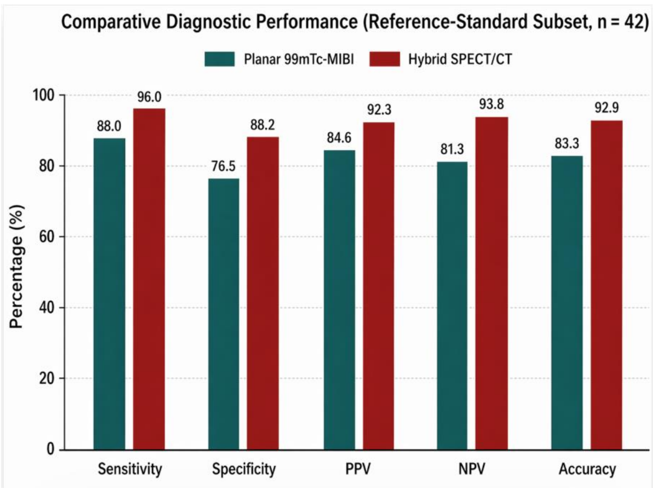

Figure 2. Diagnostic efficacy of triple-head SPECT/CT compared with planar ^{99}mTc-MIBI scintigraphy

The relevance and importance of our study and efficacy of new imaging hybrid technology (SPECT/CT), are presented following case studies.

3.2.1. Clinical Case 1

A 61-year-old female with biochemically confirmed primary hyperparathyroidism (PTH-110 pg/ml) underwent dual-phase planar ^{99m}Tc-MIBI scintigraphy, 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 better lesion imaging through improved photon-detection efficiency and angular sampling, particularly in the presence of radiopharmaceutical retention (Figure 3).

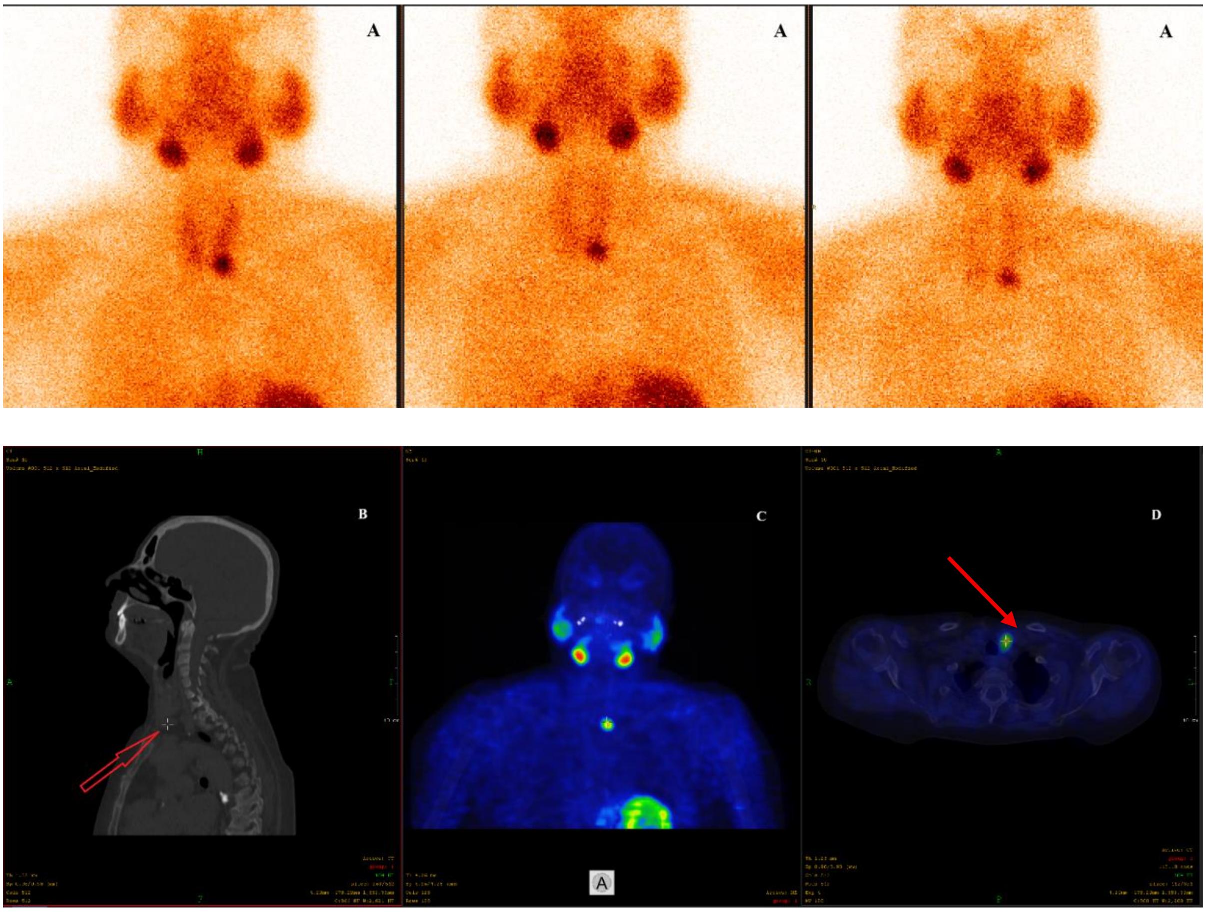

Figure 3. Combined planar and hybrid parathyroid imaging in the same patient. **(A)** Focal persistent radiopharmaceutical uptake in the lower neck/upper mediastinal region. A sagittal section of the CT scan (**B**) of the neck and thorax provides anatomy of the organs where the red arrow shows the lesion localization site. Image (**C**) shows only the fussed 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.

3.2.2. Clinical Case 2

A 39-year-old female with laboratory findings -PTH 95 pg/ml and hypercalciemia was examined using ^{99m}Tc-MIBI radiopharmaceutical. The dual phase planar scintigraphy showed persistent radiotracer accumulation that indicated the ectopic parathyroid gland. SPECT/CT performed after 160 min from the initial injected dose demonstrated the exact localization of the lesion on the right lateral of thorax, confirmed with HP for ectopic parathyroid adenoma (Figure 4). This case underscores the additional diagnostic contribution of hybrid SPECT/CT, as endorsed by EANM guidelines, in the localization of ectopic parathyroid glands, particularly in non-cervical or mediastinal positions where planar scintigraphy may be inadequate for reliable preoperative localization. Accurate lesion localization with SPECT/CT supports targeted operative planning and may assist in the performance of minimally invasive parathyroidectomy.

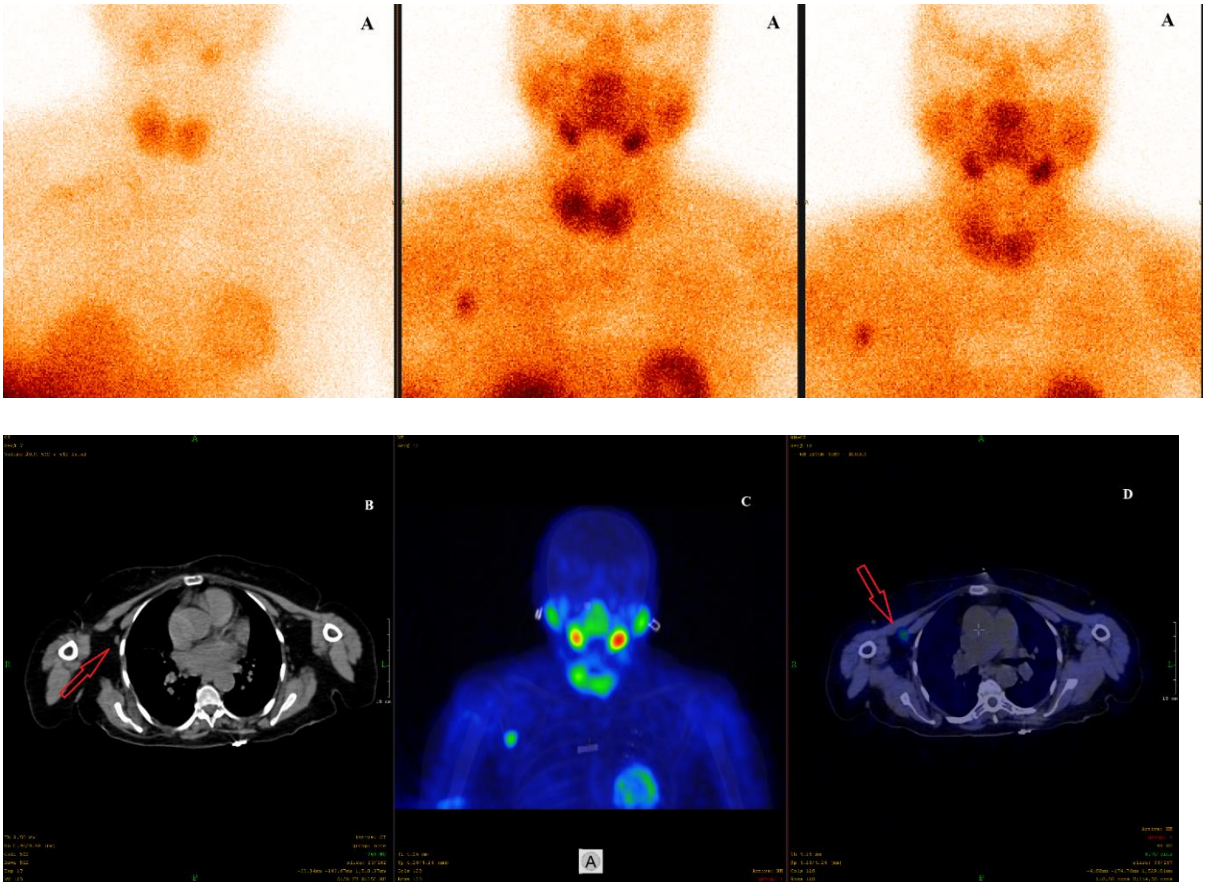

Figure 4. Combined planar and hybrid SPECT/CT parathyroid imaging in a 39-year-old woman with primary hyperparathyroidism. **A)** Early planar ^{99m}Tc-MIBI scintigraphy demonstrates uptake limited to the thyroid gland, with no definite ectopic focus identified. **(B)** Axial CT image shows the ectopic 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.

3.2.3. 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).

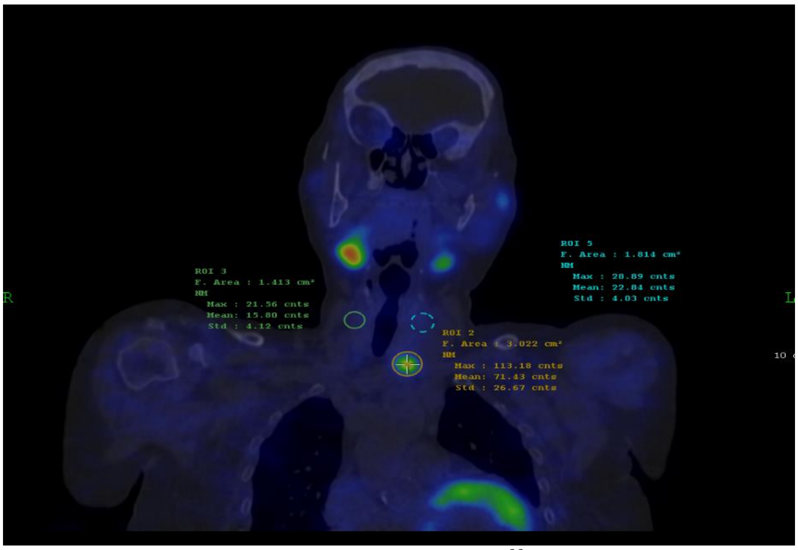

Figure 5. Coronal fused SPECT/CT image demonstrating focal ^{99m}Tc-MIBI uptake in the target parathyroid lesion. Semi-quantitative analysis was performed using manually defined regions of interest (ROIs), with **ROI 2** placed over the lesion and **ROI 1** and **ROI 3** positioned in adjacent background tissue. The target-to-background ratio (TBR) was calculated by dividing the mean counts of the lesion ROI (**73.43 counts**) by the average mean counts of the two background ROIs (**23.04** and **15.80 counts**), yielding a **TBR of 3.78**. This demonstrate that there is an increase in the tracer concentration in the lesion compared to other surrounding tissue.

4. Discussion

Hybrid SPECT/CT scan using radiopharmaceutical ^{99m}Tc-MIBI, provided significantly better localization of pathologic lesions compared to planar scintigraphy [25-27]. This improved diagnostic capability can be largely explained by the tomographic data from the SPECT/CT, which have reliably been reported to prove better results than planar scintigraphy despite any changes in detector technology. Patients with associated thyroid nodules and ectopic parathyroid glands shows more pronounced benefit from SPECT/CT scan [28-30]. In most cases the results between ultrasonography and SPECT/CT are accurate. However, in patients with multinodular thyroid disease or when the ultrasonography failed to identify the anatomical localization, SPECT/CT helped to detect the additional lesions in 35.5 % of these patients.

The above results agree with the current literature and recommendations from EANM according to which ultrasound examination is considered as a first-choice examination of the PHPT, while a hybrid technique using SPECT/CT is useful in cases when the ultrasound examination shows no lesions or there was an ectopic gland. In the case of our sample population the rate of detection by ultrasound examination was 55.7 % while the use of the SPECT/CT the detection rate was 71.4 %.

As mentioned above, CT low dose is a crucial for defining the localization, decreasing interpretation difficulties and enabling accurate preoperative localization [31]. This is very important, because can help the surgeons to find the exact location of the adenoma, and removed it with minimally cut and without need of neck dissection. There is lower risk of returning the disease. The time is shorter in operation room. SPECT/CT helps to overcome several limitations associated with conventional planar scintigraphy, including overlapping anatomical structures and different thyroid radiopharmaceutical uptake [32,33]. Sensitivity of primary hyperparathyroidism using dual-phase planar ^{99m}Tc-MIBI imaging was about 60-70 % based on size of adenoma, multiendocrine glandular disease, intra thyroid localization of the lesions, multinodular goiter, the presence of the oxyphilic cells and the rapid tracer washout [34-36]. In our study, sensitivity rate was higher-89.7 % due to combined SPECT with CT acquisition protocols achieving better results in localization of the adenoma, especially in complex anatomical cases.

The exact ectopic gland localization is still a key reason to use the SPECT/CT to help mapping out anatomically and makes minimally invasive surgery procedure possible. When identified abnormal parathyroid tissue from normal the surgeons reduce the neck exploring [37–39]. False positive results usually are present when patient has a multinodular goiter or undefined thyroid lesions. Always when examined the parathyroid gland, we have to closer look for any associated thyroid disease [40–41].
^{18}F-flurocholine PET/CT is a very good method/gold method in some difficult situation when many imagine results do not agree. In our study SPECT/CT shows high negative predictive value and this is a good and useful clinical information that when SPECT/CT image show no uptake of radiopharmaceutical ^{99m} Tc-MIBI there is no hyperactive parathyroid gland - adenoma.
Hybrid triple detector SPECT/CT system provides practical advantage in spatial resolution and shorter acquisition time [45–46],

5. Conclusion

SPECT /CT as imaging tool using radiopharmaceutical ^{99m}Tc-MIBI offered a better preoperative localization of hyperfunctioning parathyroid tissue, adenoma, than traditional planar scintigraphy. This is especially helpful for patient with ectopic lesions or concurrent thyroid nodules, combining functional and anatomical information with higher sensitivity and negative predictive value. This improved surgical targeting, reduced unnecessary neck exploration and made minimally parathyroidectomy.
Our results make a strong case of using the SPECT/CT as the go-to method to find the parathyroid problems before surgery in PHPT.
For future work, multicenter studies and cost effectiveness analyses are needed to demonstrate how these imaging approaches should be adopted in every day clinical practice.

Author Contributions

I.B. and A.J. conceived and designed the study. I.B. collected the data and carried out the statistical analysis. A.J. contributed to maintain the framework and helped prepared the manuscript. S.F., S.S. and E.D.S, contributed of interpretation of data and provided critical revisions of the manuscript. All author reviewed and approved the final manuscript.

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