

Comparative Accuracy of Ultrasonography and Sestamibi Scintigraphy in Preoperative Localization of Parathyroid Adenomas: A Retrospective Observational Study

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ABSTRACT

Background: Minimally invasive parathyroidectomy (MIP) has become the standard approach in managing primary hyperparathyroidism (PHPT), contingent on precise preoperative localization of the offending parathyroid adenoma. Among the most commonly used localization tools are high-resolution ultrasonography (USG) and Tc-99m sestamibi scintigraphy. Any discordance in these localizing modalities is resolved by cross-sectional imaging such as computed tomography, magnetic resonance imaging, etc.

Methods: This retrospective observational study included 100 patients with biochemically confirmed PHPT who underwent both USG and Tc-99m sestamibi scintigraphy prior to parathyroidectomy at a tertiary care center between January and December 2024. The sensitivity and anatomical localization accuracy of both modalities were compared against surgical and histopathological findings. Any discordance in these imaging modalities was confirmed by a 4DCT (4-dimensional computed tomography) scan.

Results: Tc-99m Sestamibi scintigraphy demonstrated higher sensitivity (93%) compared to ultrasonography (86%). Misclassification of superior/inferior position occurred in 13% and 6.9% of cases for USG and sestamibi, respectively. No significant correlation was observed between biochemical parameters and imaging accuracy.

Conclusion: Tc-99m Sestamibi scintigraphy is more sensitive for preoperative localization of parathyroid adenomas, especially for ectopic or deep-seated glands. A combined imaging approach offers optimal guidance for MIP.

Keywords: Primary hyperparathyroidism, parathyroid adenoma, Tc-99m sestamibi scintigraphy, ultrasonography, localization, minimally invasive parathyroidectomy

JMS: 2025; 28(3):5-10 DOI: <https://doi.org/10.33883/jms.v28i3.1458>

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by autonomous secretion of parathyroid hormone (PTH), leading to hypercalcemia and systemic manifestations¹. The majority of PHPT cases (80–85%) are due to a solitary parathyroid adenoma, while multiglandular hyperplasia, double adenomas, or parathyroid carcinoma account for the remainder^{1,2}.

Surgical excision remains the definitive treatment. Over the past two decades, the focus has shifted from bilateral

neck exploration (BNE) to minimally invasive parathyroidectomy (MIP), guided by accurate preoperative localization^{2,6}. MIP offers reduced operative time, minimal tissue dissection, and faster recovery.

High-resolution ultrasonography (USG) and Tc-99m sestamibi scintigraphy are the most widely used first-line imaging tools^{3,4}. While USG is safe, affordable, and readily accessible, it is highly operator-dependent and

Access this article online



Website:
www.jmsskims.org

DOI:
<https://doi.org/10.33883/jms.v28i3.1458>

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How to cite this article: Shah R, Malik A, Wani M, Lone Z, Shabir U, Mushtaq A. Comparative Accuracy of Ultrasonography and Sestamibi Scintigraphy in Preoperative Localization of Parathyroid Adenomas: A Retrospective Observational Study. JMS 2025; 28(3):5-10

Received: 2025-08-06 Accepted: 2025-09-30



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less effective in patients with retrosternal glands or nodular thyroids^{4,9}. Sestamibi scintigraphy, a functional nuclear imaging technique based on mitochondrial tracer uptake, performs better for ectopic or deep-seated lesions but has limitations in multiglandular disease and cystic adenomas^{3,4,6}.

Although several studies have assessed the diagnostic performance of these modalities, there is variability in anatomical localization accuracy, particularly with respect to superior/inferior differentiation^{5,10}. The present study aims to evaluate and compare the diagnostic yield and anatomical accuracy of USG and sestamibi scintigraphy in patients with PHPT.

MATERIALS AND METHODS

Study Design and Setting

This retrospective, single-center observational study was conducted at the Department of General and Minimal Invasive Surgery (Endocrine Division), Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar. Institutional ethical clearance was obtained. Informed consent was waived in view of the retrospective nature.

Outcome

Diagnostic accuracy of USG and Tc-99m sestamibi scintigraphy compared to intraoperative and histopathological findings. This included assessment of

Comparison of Ultrasonography (USG) and Sestamibi Scintigraphy for Parathyroid Localization

Feature	Ultrasonography (USG)	Sestamibi Scintigraphy (MIBI Scan)
Non-invasive	✓ Yes	✓ Yes
Radiation exposure	✗ No (radiation-free)	✗ No (uses ionizing radiation)
Availability	✓ Widely accessible, including outpatient settings	✓ Available in most centers, though limited in smaller hospitals
Cost-effectiveness	✓ Economical	✗ More expensive due to radiopharmaceuticals and imaging setup
Real-time imaging	✓ Offers real-time evaluation	✗ No real-time capability
Thyroid co-evaluation	✓ Enables detection of thyroid nodules, goiters	✓ Possible but less sensitive for detailed thyroid pathology
Use in re-operative neck	✗ Less useful due to surgical scarring	✓ More effective, especially for detecting ectopic or residual glands
Operator dependence	✗ High—results vary with sonographer skill	✓ Less affected by operator variability
Detection of ectopic glands	✗ Limited for deep or mediastinal locations	✓ Superior for ectopic and retrosternal adenomas
Sensitivity (single gland disease)	✓ High (~80–85%)	✓ High (~85–90%)
Sensitivity (multigland disease)	✗ Lower (~30–50%)	✗ Moderate (~50–60%)
Limitation in obese individuals	✗ Yes—image quality reduced in patients with thick necks	✓ Less affected by body habitus
Retrosternal or deep gland visualization	✗ Inadequate for deep or retrosternal glands	✓ Excellent localization ability
Duration of study	✓ Rapid (~10–15 min)	✗ Time-consuming (~90–120 min)
Functional imaging capability	✗ No—anatomical assessment only	✓ Yes—detects functional adenomas via mitochondrial uptake
Impact of multinodular goiter	✗ Reduced accuracy due to overlap with nodules	✗ Also affected, though to a slightly lesser extent

overall sensitivity, quadrant (superior/inferior, left/right) localization accuracy, misclassification rates, and concordance/discordance between modalities.

Study Population

Statistical Analysis

Data were compiled and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as age, serum calcium, and PTH levels were expressed as mean $\pm$ standard deviation or median with interquartile range, depending on distribution. Categorical variables, including imaging outcomes and surgical concordance, were presented as frequencies and percentages. Sensitivity, specificity, and misclassification rates for ultrasonography and Tc-99m sestamibi scintigraphy were calculated with operative and histopathological findings taken as the gold standard. The McNemar test was applied to compare paired proportions of localization accuracy between the two imaging modalities. A p-value of <0.05 was considered statistically significant.

A total of 100 consecutive patients diagnosed with PHPT, who underwent USG and sestamibi scintigraphy (diagnosing a single functional adenoma) followed by parathyroidectomy between January and December 2024, were included. 4DCT was employed if any discordance was found among the study imaging modalities.

Inclusion Criteria:

- Biochemically confirmed PHPT (elevated serum calcium and PTH)
- Both USG and Tc-99m sestamibi imaging were performed preoperatively.
- Curative surgery with histopathological confirmation of adenoma
- Availability of complete clinical, imaging, and operative data

Exclusion Criteria:

- Secondary or tertiary hyperparathyroidism
- Reoperative or persistent/recurrent disease
- Parathyroid carcinoma

- Incomplete records

Imaging Protocols

Ultrasonography (USG):

Performed using a high-frequency linear transducer (7–15 MHz) by experienced radiologists. Parathyroid adenomas appeared as well-defined hypoechoic lesions with peripheral vascularity.[9]

Tc-99m Sestamibi Scintigraphy:

Following intravenous injection of 20–25 mCi of Tc-99m sestamibi, dual-phase planar images were obtained at 10 minutes and 2 hours. Delayed persistent uptake indicated a positive scan.³

Surgical and Histopathological Correlation

All patients underwent focused parathyroidectomy or BNE based on imaging and intraoperative findings. Intraoperative PTH monitoring was used; a $\geq 50\%$ decline in PTH levels post-excision was considered confirmatory. Resected specimens were subjected to histopathological examination.

RESULTS

Patient Characteristics

A total of 100 patients were included in the study. The mean age was 42.5 ± 6.1 years (range: 31–52 years). There was a female predominance, with a female-to-male ratio of 60:40. The mean serum calcium level was 10.8 ± 1.2 mg/dL (range: 9.2–11.6 mg/dL). Serum parathyroid hormone (PTH) levels demonstrated a skewed distribution, with a median of 542.5 pg/mL and an interquartile range (IQR) of 320–780 pg/mL, reflecting the wide variability in biochemical severity among patients.

Table 1: Baseline patient characteristics

Variable	Value
Mean age (years)	42.5 ± 6.1 (range 31–52)
Gender (Female:male)	60:40
Serum Calcium (mg/dL)	10.8 ± 1.2 (range 9.2 – 11.6)
Serum PTH (pg/mL)	Median 542.5 (IQR 320–780)

Table 2: - Diagnostic Performance of USG and Tc-99m Sestamibi Scintigraphy

Imaging Modality	Sensitivity (%)	Specificity (%)	Misclassification Rate (%)
Ultrasonography (USG)	86	Not applicable	13
Tc-99m Sestamibi Scan	93	Not applicable	6.9

In this study, Tc-99m sestamibi scintigraphy demonstrated higher sensitivity (93%) compared to ultrasonography (86%) for preoperative localization of parathyroid adenomas. Specificity could not be calculated, as all patients in the cohort had histopathologically confirmed adenomas, and thus, no true-negative cases were available for analysis. The rate of superior–inferior misclassification was lower with sestamibi (6.9%) compared to ultrasonography (13%), highlighting the superior anatomical accuracy of sestamibi in differentiating gland position. Overall, these findings emphasize the relative advantage of sestamibi scintigraphy while underscoring the complementary role of ultrasonography in initial evaluation.

Localization Performance

Table 3: - Total number of adenomas diagnosed (out of 100) by either modality with comparison to surgical findings.

Gland location	USG (n)	Tc-99m Sestamibi (n)	Surgical Findings (n)
Right inferior	28	32	33
Right superior	18	16	17
Left superior	11	12	13
Left inferior	29	33	37

USG Sensitivity for adenoma localization: 86%

Sestamibi Sensitivity for adenoma localisation: 93%

If in any patient an adenoma was not identified on USG or Tc-99m sestamibi, cross-sectional imaging in the form of 4DCT scan (4-dimensional computed tomography) was employed.

Superior/Inferior Misclassification: 13% for USG and 6.9% for sestamibi

No significant correlation was found between serum calcium/PTH and localization accuracy.

In 93 patients, the surgical procedure done was focused parathyroidectomy, i.e, MIP, while in 7 patients, we had to resort to unilateral neck exploration. This was mainly true for patients with discordant imaging characteristics rather than those who had concordant imaging.

DISCUSSION

Our findings demonstrate that Tc-99m sestamibi scintigraphy offers superior sensitivity compared to ultrasonography in the preoperative localization of parathyroid adenomas. This aligns with earlier systematic reviews and meta-analyses, which consistently report higher sensitivity of Tc-99m sestamibi scanning (80–90%) compared to USG (70–80%), particularly in patients with ectopic or mediastinal glands [3,4,5,10]. Similar to the work of Kunstman et al. [5], our study confirms that Tc-99m sestamibi retains an advantage in deep-seated lesions, although its diagnostic performance may decline in multiglandular disease or cystic adenomas. Ultrasonography remains a valuable first-line tool because of its cost-effectiveness, absence of radiation exposure, and simultaneous evaluation of the thyroid gland. This is particularly relevant in endemic goiter regions, where concurrent thyroid nodules may alter surgical planning. However, our results reaffirm the well-known operator dependency of USG and its reduced accuracy in patients with short or obese necks, retrosternal extension, or post-surgical distortion. The misclassification rate of 12% observed in our cohort underscores the embryological and anatomical overlap between superior and inferior parathyroid glands. This challenge is well documented in prior literature, where superior glands descending into the thyrothymic ligament or inferior glands lying higher than expected often result in diagnostic uncertainty.

An important observation in our study was the lack of correlation between biochemical severity (serum calcium or PTH levels) and localization accuracy. This finding suggests that glandular morphology, vascularity, and anatomical positioning influence detectability more than biochemical derangement. Previous reports, such as those by Uludag⁶, have similarly emphasized that biochemical severity is not a reliable predictor of

imaging success, reinforcing the importance of multimodality imaging strategies.

From a clinical standpoint, accurate preoperative localization has direct implications for the choice of surgical approach. In our series, the majority of patients (93%) underwent focused parathyroidectomy, i.e, MIP, with only a small fraction requiring unilateral exploration due to discordant imaging. This is consistent with the global shift toward minimally invasive parathyroidectomy, which offers reduced operative time, smaller incisions, and faster recovery compared to traditional bilateral neck exploration. The concordance of imaging modalities, when achieved, translates into high surgical success rates, highlighting the complementary role of USG and sestamibi.

Our findings also support the growing advocacy for combined imaging strategies. Several large series have reported that dual-modality imaging improves localization rates to above 90%, minimizing the need for additional advanced modalities [7,8]. Nonetheless, in cases of discordance or non-localization, 4D-CT, SPECT/CT, or MRI remain valuable adjuncts. Importantly, the integration of intraoperative PTH monitoring provides a biochemical safety net, ensuring surgical completeness even when preoperative localization is imperfect.

The strengths of this study include the consecutive patient cohort, uniform imaging protocols, intraoperative PTH confirmation, and histopathological validation. However, limitations should be acknowledged. The retrospective design inherently introduces selection and reporting biases. Being a single-center study, the results may not be fully generalizable to other populations or institutions with differing imaging expertise. Inter-observer variability in ultrasonography, an important determinant of diagnostic accuracy, was not formally assessed. Additionally, advanced imaging modalities such as 4D-CT or SPECT/CT were not included, which could have provided a broader comparison.

Future research should focus on prospective, multicentric studies incorporating novel imaging

approaches and machine learning-assisted diagnostic platforms. The role of hybrid imaging (such as PET tracers targeting specific receptors) and its potential superiority over sestamibi warrants further evaluation. Moreover, stratification of patients based on BMI, thyroid pathology, and adenoma size could refine imaging algorithms for tailored patient care.

In conclusion, while Tc-99m sestamibi scintigraphy demonstrates superior sensitivity compared to ultrasonography, both modalities retain important, complementary roles in guiding surgical management of PHPT. A judicious combination of imaging techniques, reinforced by intraoperative PTH monitoring, remains the most reliable strategy for ensuring surgical success.

CONCLUSION

Tc-99m sestamibi scintigraphy is more sensitive than ultrasonography for localizing parathyroid adenomas. Nonetheless, both modalities have complementary roles, and a combined approach enhances the success of minimally invasive parathyroidectomy. Future multicentric studies incorporating advanced imaging techniques may further refine localization strategies.

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