ACCURACY OF TECHNETIUM-99M SPECT-CT HYBRID IMAGES IN PREDICTING THE PRECISE INTRAOPERATIVE ANATOMICAL LOCATION OF PARATHYROID ADENOMAS

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Abstract: Background. This study evaluated the accuracy of single photon emission computed tomography (SPECT)-CT imaging for the preoperative localization of parathyroid adenomas.

Methods. This study included both a quantitative and qualitative accuracy measure. The quantitative measure was the distance between the location of the adenoma on the SPECT-CT scan and the location of the adenoma intraoperatively. Qualitatively, surgeons were asked whether or not the adenoma was in the exact location predicted by the SPECT-CT scan. The time from initial incision to identification of the parathyroid was recorded. Patients referred to London Health Sciences Centre for a suspected parathyroid adenoma were eligible for this study.

Results. Twenty-three patients participated in this study. Eighteen (78.3%) had a single adenoma, 2 (8.7%) had double adenomas, and 3 (13.0%) had multiglandular hyperplasia. SPECT-CT correctly detected and localized 16 of 18 (88.9%) cases of single parathyroid adenomas. The mean distance between the location of the adenoma on the SPECT-CT scan and the location of the adenoma intraoperatively was 16.3 mm (95% CI, 9.0–19.0 mm). For single adenomas, the median time from skin incision to identification was 14 minutes (range, 8–40 minutes). The preoperative detection and localization of a single focus of sestamibi uptake yielded a parathyroid adenoma in the specified location in 80.0% of cases (95% CI, 97.4–66.5%).

Conclusions. SPECT-CT predicted the intraoperative location of a single parathyroid adenoma within 19.0 mm with 95% confidence. The correct detection and localization of multiglandular disease remains difficult.

Keywords: SPECT-CT; parathyroid adenoma; primary hyperparathyroidism; accuracy; operative time

Primary hyperparathyroidism (PHPT), a disease of excessive parathyroid hormone secretion that leads to chronic hypercalcemia, is most commonly caused by a parathyroid adenoma. A recent meta-analysis by Ruda et al1 includes 20,225 cases of PHPT from 1995 to 2003 and reports that solitary

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adenomas, multiple gland hyperplasia disease, double adenomas, and parathyroid carcinomas occur in 88.90%, 5.74%, 4.14%, and 0.74% of cases, respectively. The success rate of parathyroidectomy reported by many authors1–6 is 95% to 98%, and changes very little with the type of parathyroidectomy offered.1,6 This has prompted many to adopt unilateral or minimally invasive approaches, and for these surgeons preoperative image guidance has become a necessity.

Scintigraphy is the most widely used localization technique, with dual-phase sestamibi Tc99m imaging as the most popular method because of its availability. Sestamibi is taken up by thyroid and parathyroid tissue but washes out of thyroid tissue more rapidly, leaving only parathyroid activity to be detected.7

Single photon emission computed tomography (SPECT) increases the sensitivity of the dual-phase sestamibi Tc99m technique.7,8 In this sense, sensitivity refers to the detection and correct lateralization of parathyroid pathology to the left or right neck. Using this definition, the sensitivity of SPECT for parathyroid adenomas ranges from 90% to 95%.8–10 However, SPECT sensitivity is still reduced in multiglandular disease.11

The best preoperative localization study should incorporate the functional imaging of SPECT into an anatomically descriptive context. This is accomplished by hybrid SPECT-CT imaging, which allows for the simultaneous acquisition of SPECT and CT images. Two studies have looked at the value of SPECT-CT over SPECT, and conclude that it has additional value for ectopic parathyroid adenomas11,12 and repeat neck explorations.12

The primary objective of this study was to determine how accurately SPECT-CT hybrid images predicted the precise intraoperative anatomical location of parathyroid adenomas. This was determined using both quantitative and qualitative outcome measures. The anatomical detail of SPECT-CT may greatly enhance preoperative planning for parathyroid surgery, and could lead to the widespread use of minimally invasive techniques for parathyroid surgery in Canada.

**PATIENTS AND METHODS**

**Eligibility Criteria.** All patients who were referred to the Department of Otolaryngology or the Division of General Surgery at the London Health Sciences Centre for a suspected parathyroid adenoma were eligible for this study.

**Consent and Ethical Approval.** Consent to participate in this study was obtained by the surgeon to whom each patient was initially referred. Permission to conduct this research study was granted by the Health Sciences Research Ethics Board of the University of Western Ontario on October 14, 2005.

**Data Acquisition.** All patients underwent a SPECT-CT scan. Patients received 700 MBq of 99mTc-sestamibi by intravenous injection. Immediate and 2-hour anterior planar images of the neck and mediastinum were obtained using a low-energy high resolution (LEHR) large field-of-view gamma camera with a high-resolution parallel hole collimator. SPECT-CT scans spanning from the angle of the mandible to the base of the heart were acquired at 2 hours. Both SPECT and CT images were obtained using the Infinia Hawkeye or the Hawkeye 4 (General Electric Medical Systems). The SPECT component was acquired on either camera in 60 projections with a 6° angular step, in a 128 × 128 matrix, at 30 seconds per view. The CT scan was acquired using 5 to 10 mm axial slicing, a 2.0 rpm velocity, a current of 2.5 mA, and a voltage of 140 kV. Scintigraphic data were corrected for attenuation and reconstructed using automatic ordered-subset expectation maximization (OSEM) iterative reconstruction and displayed with the hardware co-registered CT data. Hybrid SPECT-CT images were obtained in the axial, sagittal, and coronal planes.

If a parathyroid adenoma was present on the SPECT-CT images, the nuclear medicine physician plotted out its location using 3-dimensional Cartesian X, Y, and Z coordinates. The upper border of the ipsilateral sternoclavicular joint and the anterior midline of the trachea served as the anatomic references. The X value (lateral measure) was the distance between the anterior midline of the trachea and the midpoint of the adenoma. The Y value (vertical measure) was the distance between the upper border of the ipsilateral sternoclavicular joint and the midpoint of the adenoma. The Z value (depth measure) was the distance between the anterior border of the trachea and the midpoint of the adenoma. The coordinates determined by the nuclear medicine physician were blinded to all surgical staff.

Before and during the parathyroidectomy, the head and neck surgeon was able to view the SPECT-CT image. In the case of a negative SPECT-CT scan, a bilateral neck exploration was undertaken with the initial side of exploration.
determined at random. In the event of a scan positive for an adenoma, the positive side was explored first. Once the suspected adenoma was identified intraoperatively, the surgeon plotted out the location of the parathyroid adenoma using the same anatomic references as the nuclear medicine physician. The operative time from skin incision to adenoma identification was recorded. In addition, the surgeon responded “yes” or “no” to the following question: “Was the parathyroid adenoma in the exact location predicted by the SPECT-CT hybrid image?”

The following variables were recorded preoperatively: age, sex, calcium level at diagnosis of PHPT, parathyroid hormone level at diagnosis of PHPT, and history of previous neck surgery. Results of surgical histopathology, postoperative calcium levels, postoperative parathyroid hormone level, and complications of surgery were recorded.

The linear distance between the point in space determined by the nuclear medicine physician and the point in space determined by the surgeon represented the quantitative accuracy. Our qualitative accuracy measurement consisted of the pooled responses of surgeons to the “Yes/No” question: “Was the parathyroid adenoma in the exact location predicted by the SPECT-CT hybrid image?”

Our definition of a correct localization was based on 2 criteria: the SPECT-CT prediction of the parathyroid pathology had to be correct, and the surgeon had to find the parathyroid pathology in the exact location predicted by the scan (based on the qualitative outcome measure).

RESULTS

Twenty-three consecutive patients (14 women and 9 men) with a median age of 66 years (range, 26–80 years) participated in this study. Patients had a median corrected calcium of 2.85 mmol/L (range, 2.21–4.40 mmol/L) and a median parathyroid hormone value of 22.4 pmol/L (range, 4.7–94.4 pmol/L) preoperatively. Of the 23 patients, 18 (78.3%) had a single adenoma, 2 (8.7%) had double parathyroid adenomas, and 3 (13.0%) had multiglandular hyperplasia. After surgery, no patient had persistent hypercalcemia, nor did any patient have significant postoperative hypocalcemia.

SPECT-CT was able to correctly detect and localize 16 of 18 (88.9%; 95% CI, 103.4–74.4%) cases of single adenomas, 1 of 2 cases of double adenomas, and none of the 3 cases of multiglandular hyperplasia. Figures 1, 2 and 3 illustrate the SPECT-CT images of 3 patients participating in this study.

There were 2 cases in which the SPECT-CT scan failed to correctly localize a single parathyroid adenoma. In 1 patient, the scan showed a single focus of radiotracer uptake immediately posterior to the right lobe of the thyroid gland. At surgery, this was found to be a thyroid nodule. The opposite side was explored and a single parathyroid adenoma was found. Postoperative pathology verified the surgical findings. In a second patient, the scan showed a single focus of sestamibi uptake posterior to the left lobe of the thyroid gland. A normal parathyroid gland was found at this location and the superior ipsilateral location. An exploration of the contralateral side revealed no adenoma. However, since the patient had multiple thyroid nodules in the left lobe, a hemithyroidectomy was done. The postoperative pathology demonstrated a parathyroid adenoma embedded in the left thyroid lobe.

A single parathyroid adenoma was the preoperative diagnosis (as shown by a single focus of sestamibi uptake on the SPECT-CT scan) in 20 cases and was the postoperative histopathological diagnosis in 18 cases. In 1 patient, the SPECT-CT scan showed a single focus of sestamibi. However, during surgery all 4 glands were enlarged. Multiglandular hyperplasia was the histopathological diagnosis. Figure 2 illustrates the SPECT-CT hybrid image of this false-positive case. In a second patient, the scan demonstrated a single focus of radiotracer uptake posterior to the trachea. At surgery, the surgeon found 4 gland hyperplasia and a firm thyroid nodule. The retrotracheal structure was thought to be a lymph node, and was removed. Pathology showed metastatic papillary thyroid carcinoma in the lymph node and multiglandular hyperplasia in the parathyroid glands. Figure 3 illustrates the SPECT-CT hybrid image of this case.

Given a single focus of sestamibi uptake, the scan was able to demonstrate a parathyroid adenoma in the specified location in 80.0% of cases (95% CI, 97.4–66.5%).

Shown in Table 1 are the distance discrepancies between the point in space determined by SPECT-CT and the point in space determined intraoperatively. Intraoperative measurements were only made if the preoperative diagnosis suggested by the SPECT-CT scan matched the postoperative histopathological diagnosis. Also shown in Table 1 are the times from incision to identification of the parathyroid adenoma.
For single adenomas that were correctly detected and localized by SPECT-CT, the mean distance between the point in space predicted by the SPECT-CT scan and the point in space determined at surgery was 16.3 mm (95% ≤ 19.0 mm).

**DISCUSSION**

The purpose of this study was to determine how accurately SPECT-CT can predict the exact intraoperative anatomic location of a parathyroid adenoma. Studies have reported specific anatomic...
localization using this imaging technology, but the accuracy of this specific anatomic localization has never been objectively quantified. The true value of this study is that it quantifies the error between the imaging localization and the intraoperative finding.

When an adenoma is identified by SPECT-CT, the anatomic accuracy may in fact be better than demonstrated by the results obtained in this study. There were definite limitations in the surgeons’ ability to take accurate intraoperative measurements. Care was taken not to interrupt
the adenoma once identified and while measurements were being taken. The head position in terms of neck extension during surgery was unlikely to be the same as during the SPECT-CT acquisition. Thus localization within 2 cm may represent not the accuracy of the imaging modality but rather the limitations of our ability to duplicate measurements intraoperatively.

Another finding that is important to clinical medicine is the positive predictive value of SPECT-CT for a single parathyroid adenoma. Given a single focus of sestamibi uptake in the set-

FIGURE 3. The preoperative single photon emission computed tomography (SPECT)-CT scan appeared to demonstrate a retrotracheal parathyroid adenoma. Intraoperatively, the surgeon discovered 4 gland hyperplasia and a thyroid nodule. The retrotracheal structure was found to be a lymph node and was removed. Pathology showed metastatic papillary thyroid carcinoma in the lymph node and multiglandular hyperplasia in the parathyroid glands. The nuclear medicine image (NM) is synonymous with the SPECT image.
ting of PHPT, there is an 80.0% (95% CI, 97.4–66.5%) chance that the focus represents a single parathyroid adenoma in the exact location specified by the SPECT-CT scan. Studies of SPECT have reported sensitivities for parathyroid adenomas ranging from 90% to 95%.8–10 A criticism of SPECT-CT might then be that new technology is not necessary when SPECT imaging is already highly sensitive. It is important to note that the definition of a true-positive event in these studies was the detection and correct assignment of the adenoma to the left or right side of the neck. Using a more rigorous definition of a true-positive result, detection and assignment to the correct anatomic quadrant, Moka et al reported a SPECT sensitivity of 88% for parathyroid adenomas. This was reduced from their 95% lateralization sensitivity.8 A study by Martin et al15 showed a similar discrepancy, demonstrating a reduction in sensitivity of 19% when using exact localization as their true positive instead of assignment to the correct side of the neck. It is difficult to compare sensitivities between SPECT and SPECT-CT when the definition of a true-positive event may differ significantly between the 2 imaging modalities.

The idea of co-registering SPECT with CT showed promise in 2 case reports of ectopic mediastinal parathyroid adenomas.16,17 In both cases, SPECT-CT predicted the precise anatomical location of the ectopic adenoma and helped in the planning of curative surgery.16,17 In a small prospective study of 4 patients with parathyroid hyperactivity in the mediastinum, Kaczirek et al13 used SPECT-CT to localize ectopic parathyroid adenomas. The 4 patients showed no signs of recurrence at 16 months’ follow-up. Profanter et al,14 in a small prospective study of 6 patients with PHPT, also reported promising results. The study used planar SPECT-CT fusion images. In the 5 patients with solitary adenomas, fusion images were able to exactly predict the location and dimension of each adenoma. The remaining patient had multiglandular disease.

SPECT-CT is useful in localizing malignant or ectopic lesions but its clinical value in localizing normally located parathyroid adenomas has been contested.

### Table 1. Distance discrepancy between SPECT-CT and intraoperative measurements, and time from incision to identification of adenoma.

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Abbreviations: PA, parathyroid adenoma; MGH, multiglandular hyperplasia; DPA, double parathyroid adenoma; TN, thyroid nodule; PTCa, papillary thyroid carcinoma.
A retrospective study by Gayed et al\textsuperscript{11} included 48 patients and evaluated the value of SPECT-CT over SPECT in diagnosing and locating both parathyroid adenomas and parathyroid hyperplasia. The study’s SPECT-CT images were acquired with the same imaging system used in this study. In that study, 2 nuclear medicine physicians each read all 48 SPECT and SPECT-CT scans. For each patient, the SPECT scan was read first, and then the SPECT-CT scan. SPECT-CT augmented SPECT parathyroid adenoma localization for both readers in 4 of 48 patients (8\%). However, when used after SPECT, SPECT-CT altered only 1 diagnosis for 1 of the readers. Gayed et al concluded that SPECT-CT offered no added clinically significant value when compared with conventional SPECT, except in locating ectopic glands; these were better located by SPECT-CT in 2 of 4 patients with ectopic disease.

Krausz et al,\textsuperscript{12} in their retrospective study of 36 patients with PHPT (33 of which had a positive sestamibi scintigraphic study) reported that SPECT-CT facilitated parathyroid surgery, particularly in patients with ectopic adenomas or patients who had previously undergone failed explorations. In the study, both planar and SPECT images were used in addition to SPECT-CT. The sensitivity of planar imaging was 92\% for adenomas, and both SPECT and SPECT-CT did not improve the sensitivity by detecting any additional adenomas. The benefit of SPECT-CT was the enhanced precision of the anatomic localization, which helped focus the surgical exploration in 14 of 33 (42\%) patients with positive planar scans. SPECT-CT predicted the exact proximity of the adenoma to neighboring anatomical structures in all 10 patients with ectopic adenomas and 4 of 23 patients with cervical adenomas. Of the latter 4 patients, 3 were undergoing a second exploration following an initial failed operation. SPECT-CT was helpful for ectopic glands and cases of distorted anatomy resulting from previous neck surgery but was of limited additional value for cervical adenomas in patients undergoing initial surgery.

It was the opinion of Krausz et al that the true value of SPECT-CT was the improvement in surgical planning. Surgeons involved in the study reported the ability to perform a shorter, more directed procedure. This was reflected by smaller incisions and decreased time in the operating room. Unfortunately, objective endpoints investigating these parameters were not included in their study; however, they do comment that 6 patients with adenomas localized at the level of the suprasternal notch and manubrium were able to avoid sternotomy because of the anatomical precision of SPECT-CT imaging.\textsuperscript{12} We too found that the real value of this new technology is its ability to specifically localize parathyroid adenomas in an anatomically descriptive context. This is of importance to surgeons, especially those who perform minimally invasive parathyroid surgery. Surgeons also anecdotally noted a decrease in surgical time, although this study did not compare operations done with and without preoperative SPECT-CT scans for ethical reasons.

Although current technology may not significantly alter diagnoses with respect to SPECT, it is possible that this will change in the future. As the resolution of the CT component increases and the capsule of the thyroid gland is more readily visualized, SPECT-CT may significantly reduce the false-positive rate by reducing the number of thyroid nodules diagnosed as parathyroid adenomas. Our series included 1 such false-positive.

CONCLUSIONS
SPECT-CT is a very accurate imaging modality that was able to predict the intraoperative location of a single parathyroid adenoma within 19.0 mm with 95\% confidence. For single adenomas found at surgery, the median time from incision to identification of the adenoma was 14 minutes (range, 8–40 minutes). Given a single focus of sestamibi uptake in the setting of PHPT, there is an 80.0\% (95\% CI, 97.4–66.5\%) chance that the focus represents a single parathyroid adenoma in the exact location specified by the SPECT-CT scan. The correct detection and localization of multiglandular disease (double adenomas and multiglandular hyperplasia) remains very difficult.

REFERENCES


