

Comparison of FDG-PET and Sestamibi-SPECT in Primary Hyperparathyroidism

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Preoperative localization of hyperfunctioning parathyroid tissue in patients with primary hyperparathyroidism has been a longstanding diagnostic challenge. This study directly compared FDG-PET and sestamibi-SPECT for preoperative detection of abnormal parathyroid tissue. **Methods:** Twenty-one consecutive patients with primary hyperparathyroidism were studied prospectively before surgical neck exploration. SPECT of the neck and chest was performed at 15 min and 2 hr after intravenous ^{99m}Tc -sestamibi. Regional body PET was performed 45 min after intravenous FDG. **Results:** Surgery revealed 19 solitary parathyroid adenomas, 2 parathyroid adenomas in one patient; and 3 hyperplastic parathyroid glands in one patient, and 51 normal parathyroid glands. The diagnostic sensitivities for detection of parathyroid adenomas of 43% (9 of 21) for dual-phase sestamibi-SPECT and 86% (18 of 21) for FDG-PET were significantly different ($p < 0.001$). The difference in diagnostic specificities of 78% (40 of 51) for FDG-PET and 90% (46 of 51) for dual-phase sestamibi-SPECT approached statistical significance ($p = 0.063$). **Conclusion:** This study demonstrates that FDG-PET is more sensitive than sestamibi-SPECT in the preoperative localization of parathyroid adenomas in patients with primary hyperparathyroidism.

Key Words: primary hyperparathyroidism; parathyroid; fluorine-18-FDG; technetium-99m-sestamibi

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Primary hyperparathyroidism is a relatively common endocrine disorder, with a solitary parathyroid adenoma responsible for 80%–85% of all cases (1). If conservative methods fail to prevent the complications of hyperparathyroidism, a surgical neck exploration with subtotal parathyroidectomy is indicated (2,3). A preoperative imaging procedure that could decrease the surgical time and dissection necessary for localization and excision of abnormal parathyroid tissue might have several benefits, including shorter operation and anesthesia times and decreased postoperative morbidity (4). Several imaging techniques have been used for the detection of abnormal parathyroid glands, including CT, ultrasonography, angiography, selective venous sampling and MRI (1,5,6).

Among the scintigraphic approaches to parathyroid imaging, ^{99m}Tc -sestamibi was proposed by Coakley et al. (7). Because of significant sestamibi uptake by the thyroid gland, several protocols have been proposed to discriminate thyroid from parathyroid accumulation. While some have added a second tracer as a thyroid marker, such as [^{99m}Tc]pertechnetate (8,9) or [^{123}I]sodium iodide (10–13), others have used sestamibi alone in the so-called double-phase technique (14,15). Tallifer et al. (14) used early and delayed imaging after sestamibi injection and reported a sensitivity of 90% for the detection of parathyroid adenomas.

The feasibility of using PET with 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG) to localize abnormal parathyroid tissue also has been demonstrated. In a series of 17 patients with primary hyperparathyroidism, regional body FDG-PET correctly localized 94% of the 18 parathyroid adenomas preoperatively (16).

This study directly compared, in the same patients, regional body FDG-PET and double-phase ^{99m}Tc -sestamibi-SPECT for the preoperative detection and localization of abnormal parathyroid tissue.

MATERIALS AND METHODS

Patients

To qualify for this study, patients were required to have biochemical evidence of primary hyperparathyroidism (inappropriate elevation of serum parathyroid hormones levels, combined with elevation of serum calcium concentration) and no history of previous neck surgery. Preoperative serum parathyroid hormone levels were determined using a radioimmunoassay measuring the intact parathyroid gland.

This study included 21 patients (13 women, 8 men; aged 24–85 yr; mean age 62 yr). Preoperative serum calcium levels ranged from 10.3 to 12.1 mg/dl, with a mean of 11.19 mg/dl. Preoperative intact serum parathyroid hormone levels ranged from 66 to 346 pg/ml, with a mean of 169.9 pg/ml (normal range, 10–60 pg/ml).

All patients were scheduled to undergo surgical neck exploration. These patients were prospectively studied with double-phase ^{99m}Tc -sestamibi-SPECT and regional body FDG-PET. No other preoperative localization studies were performed. Surgical and histopathologic correlation was obtained in every patient.

Regional Body FDG-PET Parathyroid Imaging

Each patient fasted for at least 6 hr before imaging. Each patient was positioned in a whole-body PET camera system that generates 21 transaxial tomograms with a slice thickness of 5.1 mm. Transmission scans were obtained at three contiguous levels for the purpose of attenuation correction, using a retractable ^{68}Ge rotating rod source. Laser light guides were used for these initial transmission studies, with patient positioning marks placed on the skin. Forty-five minutes after intravenous administration of 5–10 mCi (185–370 MBq) [^{18}F]FDG, each patient was carefully repositioned within the PET camera by using the laser light guides and skin markers, and emission scans were obtained for 10 min at each of the three contiguous levels. By acquiring data from three overlapping contiguous body levels, an effective axial field of view of 280.5 mm was obtained, permitting evaluation of the neck and upper chest. After attenuation correction, data from the emission sequence were reconstructed using convolution backprojection techniques and a Butterworth filter with a critical frequency of 0.5 cycles per centimeter and order of 5.0. The series of transverse tomograms were stacked in a three-dimensional volume and linearly interpolated to isotropic voxels, allowing display of re-

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TABLE 1
Scintigraphic and Surgical/Pathologic Findings

| Patient no. | FDG-PET | Sestamibi-SPECT | | | Surgery/Pathology | | |
|-------------|---------|-----------------|------|------|-------------------|----------------|-----------|
| | | Early | Late | Dual | Location | Histopathology | Size (mg) |
| 1* | + | - | - | - | Ru | N | 310 |
| | + | - | - | - | Rl | N | |
| | + | - | - | - | Lu | A | |
| | + | - | - | - | Ll | N | |
| 2 | - | - | - | - | Ru | N | 300 |
| | + | - | - | - | Rl | A | |
| | - | - | - | - | Lu | N | |
| | + | - | - | - | Ll | N | |
| 3 | - | - | - | - | Ru | N | 350 |
| | - | - | - | - | Rl | N | |
| | - | - | + | - | Lu | N | |
| | + | - | - | - | Ll | A | |
| 4 | - | - | - | - | Ru | N | 1108 |
| | + | + | + | + | Lu | A | |
| 5 | + | + | + | + | Ru | A | 722 |
| | - | - | - | - | Rl | N | |
| | - | - | - | - | Lu | N | |
| | + | - | - | - | Ll | N | |
| 6 | - | + | - | - | Ru | N | 170 |
| | - | + | - | - | Rl | N | |
| | - | - | - | - | Lu | N | |
| | - | - | - | - | Ll | N | |
| 7 | + | - | - | - | La | A | 814 |
| | + | + | + | + | Ru | - | |
| | - | - | - | - | Rl | N | |
| | - | - | - | - | Lu | N | |
| 8 | + | - | + | + | Ra | A | 350 |
| | - | + | - | - | Ru | N | |
| | - | - | - | - | Lu | N | |
| | - | - | - | - | Ra | A | |
| 9 | - | - | - | - | Rl | N | 920 |
| | + | + | + | + | Lu | A | |
| | - | + | + | + | Ll | N | |
| 10 | + | - | - | - | Rl | A | 450 |
| | - | - | + | - | Lu | - | |
| 11 | - | - | - | - | Ll | N | 1100 |
| | - | - | - | - | Ru | N | |
| | - | - | - | - | Rl | A | |
| | + | - | + | + | Lu | N | |

*Patient had thyroiditis.

R = right; L = left; u = upper neck; l = lower neck; a = anterior mediastinum; N = normal parathyroid; A = parathyroid adenoma; H = hyperplastic parathyroid; T = thyroid adenoma.

gional body tomographic images in the transverse, sagittal and coronal planes.

Double-Phase Technetium-99m-Sestamibi Imaging Protocol

Patients were given 20 mCi (740 MBq) ^{99m}Tc-sestamibi intravenously. SPECT imaging of the neck and chest was performed using a dual-head, large field of view camera system with high-resolution, parallel-hole collimators. Three hundred and sixty degrees of projection data were acquired in a 128 × 128 matrix, pixel width of 5.28 mm, for 30 sec per projection, sampling every 4° using an elliptical orbit. Two projection sets were acquired, the initial set at 10–15 min and the second set at 2 hr after the injection of ^{99m}Tc-sestamibi. Tomographic reconstruction was performed using convolution backprojection and a Hamming filter with a cutoff frequency of 0.70 cycles per centimeter.

Image Interpretation

Localization studies with [¹⁸F]FDG and with ^{99m}Tc-sestamibi were evaluated by one observer, with the results available to the surgeon before surgery. For the purpose of this study, four separate studies were generated for each subject: (a) FDG-PET, (b) early (15 min) sestamibi-SPECT, (c) late (2 hr) sestamibi-SPECT and (d) paired (dual) sestamibi-SPECT. All studies were read retrospectively by two observers blinded to the surgical results or histopathologic diagnosis several months after the initial interpretation session. During these reading sessions, the FDG-PET, the early, late and paired sestamibi-SPECT studies were interpreted independently of each other and in random order.

Tomograms were displayed on a computer workstation. For image interpretation, the reviewers were able to adjust window display settings and the tomographic planes and levels indepen-

TABLE 1
Continued

| Patient no. | FDG-PET | Sestamibi SPECT | | | Surgery/Pathology | | |
|-------------|---------|-----------------|------|------|-------------------|----------------|------------------|
| | | Early | Late | Dual | Location | Histopathology | Size (mg) |
| 12 | - | + | - | - | Ru | N | 1500 |
| | + | + | + | + | RI | A | |
| | - | - | - | - | Lu | N | |
| 13 | - | - | - | - | Ru | N | 880 |
| | + | + | - | + | RI | A | |
| | - | + | - | - | Lu | N | |
| 14* | - | - | - | - | U | N | 1028 |
| | + | + | + | + | Ru | A | |
| | - | - | - | - | RI | N | |
| 15 | - | - | - | - | Lu | N | 634 |
| | + | + | - | - | RI | N | |
| | + | - | + | + | Lu | A | |
| 16 | + | - | + | + | Ru | H | 1500 20 90 |
| | - | - | - | - | RI | H | |
| | - | - | - | - | Lu | H | |
| 17 | + | - | - | - | U | - | 1492 |
| | - | - | - | - | Ru | N | |
| | - | - | - | - | RI | A | |
| 18 | - | - | - | - | Lu | N | 64 |
| | + | + | + | + | U | N | |
| | - | - | - | - | Ru | N | |
| 19 | + | - | - | - | Lu | N | 65 |
| | - | - | - | - | RI | A | |
| | - | + | - | - | Lu | N | |
| 20 | + | - | - | - | U | T | 2300 320 |
| | - | - | - | - | Ru | N | |
| | + | + | + | + | U | A | |
| 21 | + | + | - | - | Ru | A | 160 |
| | - | - | - | - | RI | N | |
| | + | - | - | - | Lu | A | |
| | - | - | - | - | U | N | |

*Patient had thyroiditis.

R = right; L = left; u = upper neck; l = lower neck; a = anterior mediastinum; N = normal parathyroid; A = parathyroid adenoma; H = hyperplastic parathyroid; T = thyroid adenoma.

dently. A positive, single-phase SPECT study was defined as a focal area of increased activity. A positive, double-phase SPECT study was defined as a focal area of increased activity on the early phase that demonstrated preferential retention of activity over time on the late-phase images, in contrast to normal thyroid tissue which progressively decreased in activity over time. A positive PET study was defined as an abnormal focus of increased activity.

The observers were asked to give the exact location of any abnormality on the FDG-PET and sestamibi-SPECT studies: right or left side, upper thyroid bed, lower thyroid bed or ectopic location. A preliminary written interpretation of the location and number of abnormalities identified was rendered by each observer independently. A final interpretation was then derived by consensus.

Surgery

Each patient underwent surgical neck exploration by an experienced parathyroid surgeon. The sestamibi-SPECT and the FDG-PET findings were later correlated with the surgical and histopathologic findings for each patient.

Statistical Analysis

The results of each imaging study were judged to accurately correlate with the surgical findings only if abnormal parathyroid tissue was correctly located. Accurate lateralization alone was not considered sufficient for sensitivity determination.

For each patient, abnormal parathyroid tissue localized at imaging which was associated with a surgically-determined correct position was considered a true-positive finding. Imaging of localized abnormalities without surgically detected parathyroid abnormalities were considered false-positive findings. Normal parathyroid glands detected at surgery without imaging abnormalities were considered to be true-negative findings.

Sensitivity was defined as the number of true-positive findings divided by the sum of true-positive and false-negative findings. Specificity was defined as the number of true-negative findings divided by the sum of true-negative and false-positive findings. A two-tailed exact sign test was used to analyze the differences in the sensitivity and the specificity results of the regional body FDG-PET to the double-phase sestamibi-SPECT.

TABLE 2
Diagnostic Comparison of FDG-PET and Double-Phase Sestamibi-SPECT

| | Sensitivity for detection of 21 parathyroid adenomas | | Specificity in 51 normal parathyroid glands | |
|--------------------|--|----------------|---|---------------|
| | Dual SPECT | | Dual SPECT | |
| | True-positive | False-negative | False-positive | True-negative |
| PET true-positive | 9 | 9 | PET false-positive | 4 |
| PET false-negative | 0 | 3 | PET true-negative | 7 |
| | | | | 39 |

RESULTS

Correlation Between Surgical and Scintigraphic Findings

The scintigraphic, surgical and histopathologic findings are summarized in Table 1. From the operative and histopathologic results, 19 patients had solitary parathyroid adenomas, 1 patient had 2 parathyroid adenomas and 1 patient had 3 hyperplastic parathyroid glands. At surgery, 51 normal parathyroid glands were detected.

The weights of the parathyroid adenomas varied from 64 to 2300 mg (mean 716 ± 127 mg). The weights of the three hyperplastic parathyroid glands were 20, 90 and 1500 mg.

A comparison of the diagnostic sensitivities and specificities for FDG-PET, early sestamibi-SPECT, late sestamibi-SPECT and dual-phase sestamibi-SPECT are summarized in Tables 2–7. Of the three methods for evaluating the sestamibi-SPECT studies, the dual-phase technique demonstrated the highest sensitivity and specificity values (Table 7).

Double-phase ^{99m}Tc-sestamibi-SPECT correctly detected and localized 9 of the 21 parathyroid adenomas, resulting in a sensitivity of 43%. Double-phase ^{99m}Tc-sestamibi SPECT was associated with five false-positive findings. The cause was undetermined in four and associated with focal lymphocytic thyroiditis in one. The specificity of the double-phase ^{99m}Tc-sestamibi-SPECT study was 90% (46 of 51).

Regional body FDG-PET correctly detected and localized 18 of the 21 parathyroid adenomas, resulting in a sensitivity of 86%. Regional body FDG-PET was associated with 11 false-positive findings. The etiology was focal lymphocytic thyroiditis in five instances, follicular thyroid adenoma in one and undetermined in five. The specificity of regional body FDG-PET was 78% (40 of 51).

The difference in diagnostic sensitivities of 43% and 86% for double-phase sestamibi-SPECT and FDG-PET, respectively, for the detection of parathyroid adenomas, is statistically significant (two-tailed p value = <0.001). The difference in diagnostic specificities of 78% and 90% for FDG-PET and double-phase sestamibi-SPECT, respectively, does not reach statistical significance (two-tailed p value = 0.063).

In one patient, three hyperplastic parathyroid glands were identified at surgery, weighing 20, 90 and 1500 mg. True-positive double-phase sestamibi-SPECT and FDG-PET findings were associated with the 1500-mg hyperplastic parathyroid gland. Concordant false-negative findings were associated with the remaining two hyperplastic parathyroid glands. A false-positive FDG-PET finding in the left lower neck was not associated with a surgically detected lesion at surgery. This patient had no false-positive double-phase sestamibi-SPECT results.

The weights of the 18 parathyroid adenomas associated with

TABLE 3
Diagnostic Comparison of FDG-PET and Early (15-min) Sestamibi-SPECT

| | Sensitivity for detection of 21 parathyroid adenomas | | Specificity in 51 normal parathyroid glands | |
|--------------------|--|----------------|---|---------------|
| | Early SPECT | | Early SPECT | |
| | True-positive | False-negative | False-positive | True-negative |
| PET true-positive | 8 | 10 | PET false-positive | 3 |
| PET false-negative | 0 | 3 | PET true-negative | 7 |
| | | | | 33 |

TABLE 4
Diagnostic Comparison of FDG-PET and Late (2-hr) Sestamibi-SPECT

| | Sensitivity for detection of 21 parathyroid adenomas | | Specificity in 51 normal parathyroid glands | |
|--------------------|--|----------------|---|---------------|
| | Late SPECT | | Late SPECT | |
| | True-positive | False-negative | False-positive | True-negative |
| PET true-positive | 8 | 10 | PET false-positive | 4 |
| PET false-negative | 0 | 3 | PET true-negative | 2 |
| | | | | 38 |

TABLE 5
Diagnostic Comparison of Early (15-min) and Late (2-hr) Sestamibi-SPECT

| | Sensitivity for detection of 21 parathyroid adenomas | | Specificity in 51 normal parathyroid glands | |
|----------------------|--|----------------|---|---------------|
| | Late SPECT | | Late SPECT | |
| | True-positive | False-negative | False-positive | True-negative |
| Early true-positive | 6 | 2 | Early false-positive | 3 |
| Early false-negative | 2 | 11 | Early true-negative | 3 |
| | | | | 38 |

TABLE 6
Estimated Sensitivities for 21 Parathyroid Adenomas and Specificities for 51 Normal Parathyroids

| Protocol | Sensitivity | Specificity |
|-------------|-------------|-------------|
| PET | 0.86 | 0.78 |
| Early SPECT | 0.38 | 0.80 |
| Late SPECT | 0.38 | 0.88 |
| Dual SPECT | 0.43 | 0.90 |

true-positive FDG-PET ranged from 64 to 2300 mg (mean = 669.2 ± 575 mg). The weights of the nine parathyroid adenomas associated with true-positive sestamibi-SPECT ranged from 634 to 2300 mg. (mean = 1100.7 ± 515.7 mg). A comparison of the weights of the nine adenomas positive on both tests to the weights of the nine adenomas positive on FDG-PET only indicates a significant difference ($p < 0.001$). The weights of the 12 parathyroid adenomas associated with false-negative sestamibi-SPECT ranged from 64 to 1492 mg (mean = 427.6 ± 129.9 mg) (Figs. 1, 2).

A two-sample t-test was used to test the hypothesis that the weights of the adenomas are equivalent for true-positive and false-negative test results. For FDG-PET, there is no significant difference in the weights ($p = 0.330$). For double-phase sestamibi-SPECT, the mean weight of the true-positive parathyroid adenomas is significantly greater than the mean weight of the false-negative parathyroid adenomas ($p = 0.001$).

DISCUSSION

The results in this series of patients with primary hyperparathyroidism demonstrate that FDG-PET is more sensitive than double-phase sestamibi-SPECT in preoperative detection and localization of parathyroid adenomas. In this series, there were no parathyroid adenomas undetected by FDG-PET that were detected by double-phase sestamibi-SPECT (Fig. 3). However, 9 of the 12 parathyroid adenomas undetected by double-phase sestamibi-SPECT were correctly localized by FDG-PET (Fig. 4).

A partial explanation for this discrepancy in parathyroid adenoma detection by these two methods may be related to lesion size. The weights of the nine adenomas identified by both tests were significantly greater than the nine adenomas positive on FDG-PET only (Figs. 1, 2).

The ability of regional body FDG-PET to detect smaller parathyroid adenomas may be partly related to its superior spatial resolution. Another aspect of PET that may have aided in lesion detectability was the use of attenuation correction, which was not performed on the SPECT studies. Both of these factors may have contributed to improved lesion contrast and, hence, detectability.

Differences in the mechanism of radiopharmaceutical uptake by both pathologic parathyroid glands and by adjacent normal tissues might also play an important role. In this study, dependence on the preferential retention of sestamibi activity by abnormal parathyroid glands compared to normal thyroid tissue

TABLE 7
Comparison of Estimated Sensitivities and Specificities in 21 Patients with Primary Hyperparathyroidism

| | p values | |
|----------------------|-------------|-------------|
| | Sensitivity | Specificity |
| PET vs. Early SPECT | <0.001 | 0.826 |
| PET vs. Late SPECT | <0.001 | 0.126 |
| PET vs. Dual SPECT | <0.001 | 0.063 |
| Early vs. Late SPECT | 1.0 | 0.246 |

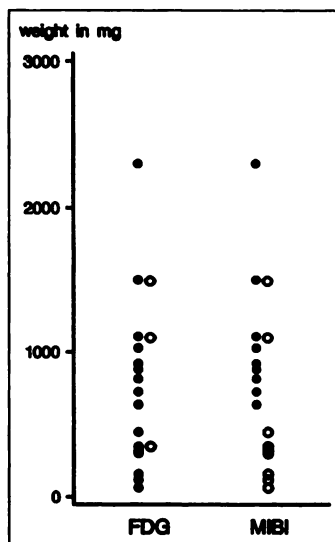


FIGURE 1. Distribution of parathyroid adenoma weights. Solid circle is true-positive. Open circle is false-negative. Each observation is plotted twice, once for FDG-PET and once for sestamibi-SPECT.

was found to be diagnostically unreliable. There was often little contrast between parathyroid and adjacent thyroid tissue on initial postinjection images, and differential washout characteristics of the two tissues was often insufficient to allow identification of the parathyroid adenomas.

Although the sensitivity of FDG-PET in the detection of parathyroid adenomas was superior to double-phase sestamibi-SPECT, there were more false-positive FDG-PET findings, with the difference in specificity approaching statistical significance ($p = 0.063$). Of the 10 false-positive FDG-PET findings, five were associated with lymphocytic thyroiditis. Only one false-positive double-phase sestamibi-SPECT was associated with thyroiditis. High accumulation of [^{18}F]FDG has been found in experimentally-induced inflammatory tissue (17). Clinical PET studies have also demonstrated high FDG uptake by abscesses (18,19) and sarcoidosis (20). The cellular uptake of FDG in these cases may be related to the presence of inflammatory cells; FDG has been found in vitro to accumulate in leukocytes, lymphocytes and macrophages (21,22).

Differential sestamibi washout characteristics may have been difficult to evaluate in this study because of the tomographic nature of the image data. Difficulty in obtaining adequate alignment of early- and late-phase tomograms due to differences in patient positioning may have contributed to this limitation. The use of reprojection SPECT, as has been demonstrated by Sfakianakis et al. (23), might prove useful as an

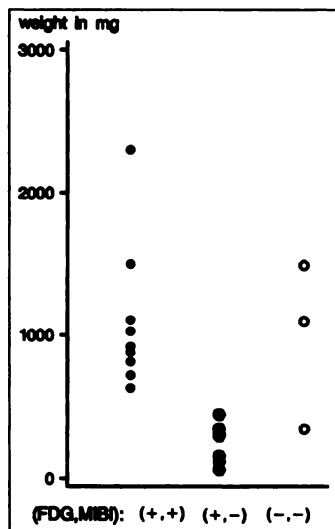


FIGURE 2. Distribution of parathyroid adenoma weights. Each observation is plotted once. +, + = true-positive FDG and true-positive sestamibi; +, - = true-positive FDG and false-negative sestamibi; -, - = false-negative FDG and false-negative sestamibi.

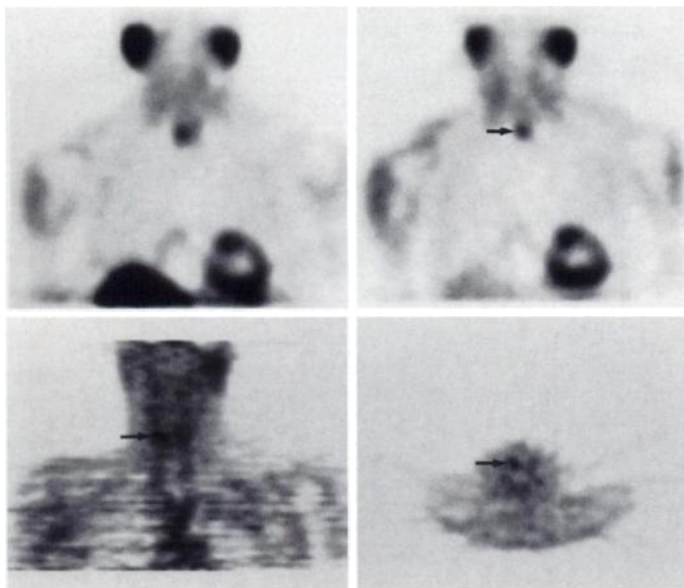


FIGURE 3. Concordant image results. A 722-mg parathyroid adenoma was found at surgery in the right lower neck. Sestamibi-SPECT shows preferential retention of activity in the right lower neck (arrows) on (A) coronal early and (B) delayed tomograms. FDG-PET shows increased uptake (arrows) in the right lower neck on (C) coronal and (D) transverse tomograms.

adjunct to the review of paired tomograms to partially avoid this potential limitation and yet retain the three-dimensional localization capabilities of SPECT imaging.

The addition of a thyroid marker, such as ^{123}I , also might provide for improved parathyroid lesion detectability with sestamibi. This combination has been used successfully for parathyroid adenoma detection, with reported sensitivities ranging from 70% to 100% (10–13).

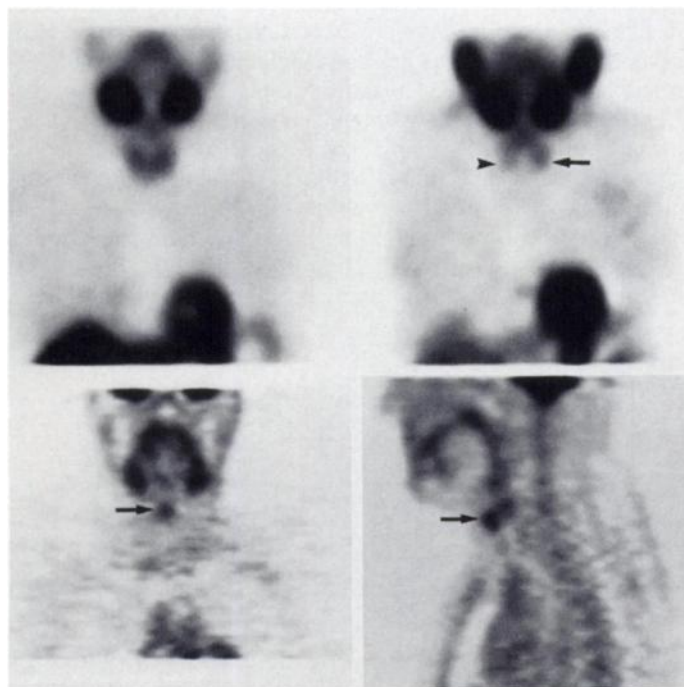


FIGURE 4. Discordant image results. A 450-mg parathyroid adenoma was found at surgery in the right upper neck. Sestamibi-SPECT shows clearance of activity from the right neck (arrowhead) but preferential retention of activity (arrow) in the left lower neck on (A) early and (B) delayed coronal tomograms. A normal left lower parathyroid gland was biopsied at surgery. FDG-PET shows increased uptake of activity in right upper neck (arrows) on (C) coronal and (D) sagittal tomograms.

Likewise, it may be possible to improve the regional body FDG-PET technique. The sensitivity and specificity of FDG-PET in the detection of parathyroid adenomas in the present study were similar to those reported in our original series of hyperparathyroid patients using this modality alone (16).

In both of our series, we relied on visual assessment of the FDG-PET images for diagnostic interpretation. The use of quantitative FDG uptake measurements, such as standardized uptake values (SUV), might prove useful as a means of improving the diagnostic accuracy of the method; the incorporation of such measurements merits further investigation.

The sensitivity of double-phase sestamibi-SPECT for detection of parathyroid adenomas was considerably lower than that of other reports of this technique. The planar double-phase technique originally described by Taillifer et al. (14) reported a sensitivity of 90% for parathyroid adenoma detection. The weights of parathyroid adenomas in that series ranged from 150 mg to 8.0 g (mean of 1.6 ± 0.9 g), which were heavier than those in the current series (716 ± 127 mg), and this difference is statistically significant (unpooled, two-sample t-test, $p < 0.0001$). The smaller sizes of the parathyroid adenomas in our series may be an important factor related to this apparent discrepancy in diagnostic accuracy.

Size alone, however, is not the sole determinant of parathyroid lesion detectability. In our series, two larger parathyroid adenomas, weighing 1100 mg and 1492 mg, were undetected by sestamibi-SPECT. This is consistent with other reports of rapid sestamibi washout from large parathyroid adenomas (24,25), making detection by dual-phase sestamibi difficult.

The sensitivity of double-phase sestamibi-SPECT for the detection of parathyroid adenomas (43%) was also considerably lower than that reported by other investigators using a double-phase planar techniques. Lee et al. (15) reported a sensitivity of 93% for the detection of 30 parathyroid adenomas in a mixed group of hyperparathyroid patients, which included some with prior neck surgery and severe renal osteodystrophy, as well as those without previous neck surgery. Our sensitivity, however, is more comparable with the 59% sensitivity reported by Chen et al. (12) in their report on 35 patients referred for reoperative parathyroid surgery, which again is a different population from our previously unoperated patient group.

Another factor that may partially explain the difference in parathyroid adenoma detection may again relate to our use of SPECT imaging. Planar imaging might prove to be superior to SPECT for this particular application, although this might be demonstrated best by a prospective, comparative study.

Although our preliminary, comparative results are encouraging, several aspects must be considered before advocating the use of FDG-PET rather than sestamibi-SPECT for routine preoperative imaging. First, the current availability of PET instrumentation and sites of FDG production are limited. This is in contradistinction to the availability of sestamibi-SPECT: SPECT camera systems are commonplace and $^{99\text{m}}\text{Tc}$ -sestamibi is readily available commercially. Cost is another consideration, in that radiopharmaceutical and technical fees are considerably higher for FDG-PET than for sestamibi-SPECT.

CONCLUSION

Although this study has demonstrated reasonable sensitivity of FDG-PET for the preoperative localization of parathyroid adenomas, only those patients without previous neck surgery were included in this series. Clinical preoperative parathyroid imaging, however, is not often performed routinely in these patients since the surgical success rates have been reported to exceed 95% in patients with primary hyperparathyroidism (3).

The need for parathyroid imaging in cases of persistent or recurrent postoperative hyperparathyroidism, however, is generally accepted, because the morbidity associated with neck exploration is increased by at least a factor of 10 and the surgical success rate is greatly reduced (26,27). Not only is it technically more difficult to perform subsequent operations because of the presence of scarring and obscuration of normal tissue planes, but residual abnormal parathyroid tissue is more likely to be in an aberrant or ectopic location (28).

Although postoperative hyperparathyroid patients were not evaluated in our present series, the results of this preliminary study are encouraging, and the use of both regional body FDG-PET and double-phase ^{99m}Tc-sestamibi-SPECT in patients with recurrent or persistent postoperative hyperparathyroidism deserves investigation.

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Four- to Twenty-four-Hour Uptake Ratio: An Index of Rapid Iodine-131 Turnover in Hyperthyroidism

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Rapid thyroidal iodine turnover may contribute to ¹³¹I therapy failure in patients with hyperthyroidism. The utility of a 4- to 24-hr ¹³¹I uptake ratio was evaluated as an index of thyroidal iodide retention in hyperthyroid patients. **Methods:** In 433 hyperthyroid patients, the success of ¹³¹I therapy was correlated with the following factors: gender, pretreatment with antithyroid drugs, clinical diagnosis, magnitude of early and late thyroidal ¹³¹I uptake values, and the 4- to 24-hr ¹³¹I uptake ratio. **Results:** Of the 433 patients, 362 patients (84%) had a successful outcome after a single therapeutic dose of ¹³¹I while 71 (16%) did not. Multiple linear regression analysis revealed that the highest statistically significant predictor of outcome was the 4- to 24-hr ¹³¹I uptake ratio (p-value < 0.001); all other factors showed a weaker association. An ¹³¹I uptake ratio of > 1 was found in 67 (15%) patients. Thirty-two of these 67 patients (48%) failed ¹³¹I therapy, whereas those patients with uptake ratios

of < 1.0, only 39/366 (11%) failed ¹³¹I therapy. **Conclusion:** The 4- to 24-hr ¹³¹I thyroidal uptake ratio is a practical substitute for exact determination of the effective half-life. It identifies patients who are likely to have a rapid ¹³¹I turnover without the need for extended thyroid uptake measurements. An ¹³¹I uptake ratio of ≥ 1 was found in 15% of hyperthyroid patients and was associated with a near 50% ¹³¹I therapy failure rate.

Key Words: hyperthyroidism; rapid thyroidal iodine-131 turnover; Graves' disease

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Radioactive iodine (¹³¹I) therapy is the most common modality for treatment of hyperthyroidism in the United States (1). Between 80% and 95% of patients with Graves' disease are controlled after one therapeutic dose of ¹³¹I, which is a relatively safe, simple and effective form of therapy (2-4). The success rate of ¹³¹I therapy has a high correlation with the ¹³¹I

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