The Usefulness of Neck Pinhole SPECT as a Complementary Tool to Planar Scintigraphy in Primary and Secondary Hyperparathyroidism

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Pinhole SPECT (P-SPECT) has proven to be a high-resolution and sensitive method in both experimental and clinical studies. In this study, we investigated whether P-SPECT combined with conventional planar scintigraphy can give additional information in hyperfunctioning parathyroid gland detection in both primary hyperparathyroidism (pHPT) and secondary hyperparathyroidism (sHPT) since planar imaging has proved partially limited, especially in sHPT. Methods: We studied 110 consecutive patients with HPT, selecting 67 patients who underwent neck surgery and had definitive histology: 48 with pHPT and 19 with sHPT. All patients underwent planar scintigraphy, 99mTc-methoxyisobutylisonitrile (99mTc-MIBI), performed with a single tracer (double-phase scintigraphy) or with a dual-tracer technique (99mTc-pertechnetate or 123I- or 99mTc-MIBI subtraction scintigraphy), using a γ-camera with a parallel-hole collimator. P-SPECT was then performed (180°; matrix size, 128 × 128; zoom factor, 2; time per frame, 40 s) using a tilted detector equipped with a pinhole collimator (insert, 4.45 mm). Results: In the 48 pHPT patients, 49 lesions (43 adenomas, 1 carcinoma, and 5 hyperplastic glands, including 1 intrathyroidal) were found at surgery; in the 19 sHPT patients, 51 lesions (49 hyperplastic glands, including 1 in persistens thymus, and 2 adenomas) were found. P-SPECT proved to be a highly sensitive method, identifying more lesions than planar imaging in both pHPT (97.9% vs. 87.7%) and sHPT (92.1% vs. 87.8%), significantly (P < 0.05) in the latter. P-SPECT, positive in all adenomas, increased parathyroid sensitivity especially in small and light-weight ones, 30.8% of which missed on planar imaging, and also identified a significantly higher number of hyperplastic glands, irrespective of their size. P-SPECT improved image quality and resolution, offering a more correct lesion localization in eutopic and ectopic sites. Neither P-SPECT nor planar imaging had false-positive findings. Moreover, P-SPECT correctly predicted the status found at surgery in 97.9% of pHPT patients and in 82.3% of sHPT patients with multigland disease, whereas planar imaging correctly predicted the status in 89.6% and 58.8%, respectively. P-SPECT was the only positive procedure in 8.9% of all patients, also revealing more lesions in 6% of sHPT patients when both methods were positive. Conclusion: P-SPECT appears a highly sensitive, high-resolution method. We suggest its use as a preoperative complementary tool to neck planar scintigraphy, selectively in pHPT patients but extensively in sHPT patients.

Key Words: pinhole SPECT; parathyroid scintigraphy; hyperparathyroidism; parathyroid adenomas; hyperplastic parathyroid glands

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Parathyroid scintigraphy with 99mTc-methoxyisobutylisonitrile (99mTc-MIBI), performed with a single tracer (double-phase scintigraphy) or with a dual-tracer technique (99mTc-pertechnetate or 123I- or 99mTc-MIBI subtraction scintigraphy), represents at present the most widely used radioisotopic procedure for the preoperative localization of hyperfunctioning parathyroid glands (I).

99mTc-Tetrofosmin can also be used instead of 99mTc-MIBI since comparative studies have demonstrated that the 2 radiotracers give similar results (2,3). However, only the dual-tracer technique is suggested for 99mTc-Tetrofosmin given its similar washout from the thyroid and parathyroid tissue, unlike 99mTc-MIBI (3–6).

Parathyroid imaging is conventionally obtained by planar acquisition using a high-resolution large-field-of-view parallel-hole collimator, although a pinhole collimator has proven to increase the sensitivity of conventional scintigraphy in both primary hyperparathyroidism (pHPT) and secondary hyperparathyroidism (sHPT) (7). However, planar scintigraphy has proven to be limited in detection of small lesions, especially in sHPT hyperplastic gland detection (8).

Recently, there has also been an increasing interest in SPECT, which seems to offer certain advantages in patients with pHPT compared with planar scintigraphy, such as a higher sensitivity (9–12), especially in the detection of small parathyroid adenomas (11–13), and a higher performance in determining the topographic localization of such adenomas deeply located in the neck and in ectopic sites (12,14) and in differentiating these from concomitant thyroid nodules (13).
SPECT data in patients with sHPT with multigland disease are more limited and also are controversial: Sensitivity values have been reported to be higher than those obtained by planar imaging (15), but these data have not been confirmed by others (9,16).

More recently, SPECT of the neck with a pinhole collimator has also been used (17–20). The results appear encouraging, but they only refer to preliminary studies performed on a few patients with HPT.

In this study, we used the neck pinhole SPECT (P-SPECT) procedure combined with conventional 99mTc-MIBI or 99mTc-tetrofosmin planar parathyroid scintigraphy with a parallel-hole collimator to further investigate whether the former high-resolution tomographic procedure can give additional information in the detection of hyperfunctioning parathyroid glands in both pHPT and sHPT.

MATERIALS AND METHODS

From May 1997 to December 2002, 110 consecutive patients with HPT underwent P-SPECT in addition to conventional planar double-phase 99mTc-MIBI or 99mTc-pertechnetate/99mTc-tetrofosmin parathyroid scintigraphy. For this study, we selected from this cohort the patients who underwent neck surgery and had definitive histologic diagnosis. The group included 67 patients (52 women, 15 men) who were 22–78 y old.

According to clinical and biochemical data—the latter referring to both serum intact parathormone (PTH; normal range, 15–65 pg/mL) and calcium (Ca; normal range, 8.4–10.2 mg/dL)—48 of the 67 patients had pHPT (PTH, 223.14 ± 154.10 pg/mL; Ca, 11.21 ± 0.63 mg/dL), including 1 patient affected by multiple endocrine neoplasia (MEN) 1a syndrome, whereas 19 had sHPT (PTH, 1,103 ± 654.69 pg/mL; Ca, 10.12 ± 1.04 mg/dL). Sixteen of the latter patients showed chronic renal failure (15 on hemodialysis and 1 on peritoneal dialysis), whereas 3 had had renal transplants. All patients with sHPT had been scheduled for surgery because of their unresponsiveness to oral calcitriol or severe osteodystrophy.

Sixty-three of the 67 patients were at their first parathyroid surgical exploration, whereas 4 patients—2 with pHPT, including the patient with MEN 1a syndrome, and 2 with sHPT—had persistent (n = 1) or recurrent (n = 3) HPT after parathyroidectomy, which was associated with total thyroidectomy in the persistent case.

Before scintigraphy, all patients submitted to a careful clinical examination to verify the presence of palpable thyroid nodules and to neck ultrasonography for evaluation of thyroid and parathyroid glands; 7 of 67 patients—5 with pHPT and 2 with sHPT—had a nodular goiter.

Bilateral surgical neck exploration was performed on each patient within 1 mo of scintigraphy by an experienced parathyroid surgeon and abnormal parathyroid glands were found in all cases at surgery. In 3 patients, parathyroidectomy was associated with total (n = 1) or partial (n = 2) thyroidectomy for benign nodular goiter and with the surgical resection of the transplanted kidney affected by chronic pyelonephritis in another case. In all 67 patients, abnormal parathyroid glands were found at surgery.

Postoperative serum PTH and Ca levels were determined in each patient, and surgical success in each patient was defined by their significant reduction postoperatively. PTH values fell to within the normal range in all 48 pHPT patients (mean value, 35 ± 9 pg/mL) and in 17 of 19 sHPT patients (mean value, 39 ± 10.2 pg/mL); Ca also decreased in the former (mean value, 8.9 ± 0.5 mg/dL) and in the latter (mean value, 9.1 ± 0.2 mg/dL) patients. In 2 sHPT patients, HPT persisted after surgery with PTH levels remaining high (835 and 342 pg/mL, respectively) and both of these patients were rechecked by scintigraphy after surgery.

All patients gave their written informed consent before parathyroid scintigraphy.

Parathyroid Scintigraphy

The first 22 cases observed in our series—17 with pHPT and 5 with sHPT—were submitted to 99mTc-MIBI double-phase scintigraphy, whereas the following 45 cases—31 with pHPT and 14 with sHPT—were submitted to 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy. The labeling efficiency of both 99mTc-MIBI and 99mTc-tetrofosmin had been assessed previously by thin-layer chromatography and, in all cases, the radiochemical purity was >95% for each tracer.

99mTc-MIBI Double-Phase Scintigraphy. After a 740-MBq 99mTc-MIBI intravenous injection, both neck and chest planar images in an anterior projection were acquired (600 s each) with a 256 × 256 matrix size at 15 min (early phase) and 2 h (delayed phase), using a large-field-of-view γ-camera (SPX or SP4HR; Elscint) equipped with a low-energy, high-resolution, parallel-hole collimator. First, the neck image was acquired using a zoom factor of 2, followed by the chest image.

99mTc-Pertechnetate/99mTc-Tetrofosmin Subtraction Scintigraphy. In each patient, the acquisition protocol was as follows: 74 MBq 99mTc-pertechnetate were injected and the thyroid imaging (200 kilocounts or 5 min) was obtained 15 min after the injection using a matrix size of 256 × 256 pixels and a zoom factor of 2 with the patient in supine anterior position. Immediately afterward, and maintaining the patient in the same position, 740 MBq 99mTc-tetrofosmin were injected; the acquisition started 10 min after the injection of the radiotracer when a 600-s neck image was acquired followed by a chest planar image. The images were acquired with the same equipment and acquisition parameters as described for 99mTc-MIBI double-phase parathyroid scintigraphy; during acquisition, patient movement was prevented by fixing the mandible with a band for neck immobilization.

Neck P-SPECT Imaging. Both the early phase of 99mTc-MIBI parathyroid scintigraphy and the 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy were followed by neck P-SPECT imaging in all patients.

We used specific software, originally designed for studying the thyroid gland, implemented on an Elscint SPX computer connected to a tilted high-resolution single-head γ-camera (SP4HR) equipped with a pinhole collimator (pinhole insert, 4.45 mm). The images were acquired over 180° (from −90° to +90°) in clockwise rotation with the step-and-shoot mode.

In all cases, the distance between the center of rotation and the collimator was within 15 cm. The images were acquired using a matrix size of 128 × 128, a zoom factor of 2, an angular step of 6°, and an acquisition time per frame of 40 s.

P-SPECT projections were preprocessed by a cone-beam algorithm (21) and then processed by the backprojection filter method using a Metz filter (coefficient, 3; full width at half maximum, 14) to obtain 4-pixel-wide transaxial slices (pixel size, 0.14 cm); these slices were used to reconstruct 1-pixel-wide coronal slices that...
were used for P-SPECT analysis. High-quality images with good resolution were obtained in all cases.

**Data Analysis**

All scintigraphic studies were prospectively evaluated before surgery. The images were independently evaluated by 2 nuclear medicine physicians who were informed of the clinical and biochemical findings suggestive of pHPT or sHPT; moreover, they were also aware of the presence of thyroid nodules. Disagreement was resolved by consensus.

99mTc-MIBI double-phase scintigraphy was considered positive in the presence of a focal area of increased uptake showing either a progressive increase over time or a prolonged retention at 2 h (delayed washout vs. thyroid 99mTc-MIBI uptake) as well as in the presence of foci of radiotracer uptake in the early images even if not evident on delayed images (hyperfunctioning parathyroid glands with a rapid washout) as long as they did not correspond to thyroid nodules.

The analysis of 99mTc-MIBI subtraction scintigraphy was performed by reading both the original 99mTc-pertechnetate and 99mTc-tetrofosmin neck images and the computer-subtracted images. Scintigraphy was considered positive in the presence of a focal area of 99mTc-tetrofosmin in the neck, within or adjacent to the thyroid area or clearly separated from this, exceeding the 99mTc-pertechnetate uptake. The analysis of planar 99mTc-MIBI double-phase scintigraphy or 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy was followed by that of the neck P-SPECT coronal slices. P-SPECT imaging was considered as positive in the presence of a focal area of increased uptake of 99mTc-MIBI or 99mTc-tetrofosmin in the neck as above.

Particular care was taken in the analysis of both planar and P-SPECT images in patients with thyroid nodules to avoid misinterpretation of the radiotracer uptake.

**Statistical Analysis**

Planar scintigraphy and P-SPECT imaging were considered true-positive, false-negative, true-negative, and false-positive considering histology as the gold standard. Sensitivity and specificity were calculated on a per-parathyroid-gland basis. Sensitivity was determined by the ability to visualize and correctly localize the parathyroid hyperfunctioning lesion (adenoma, carcinoma, or hyperplasia) ascertained at surgery. Normal parathyroid glands were considered as true-negative for the calculation of specificity. Accumulation in thyroid nodules was not considered as a false-positive finding. The McNemar test was used to assess the statistical difference in sensitivity and specificity between planar imaging and P-SPECT in both pHPT and sHPT. The results were considered significant when $P < 0.05$.

**RESULTS**

**Histologic Findings**

The histologic findings obtained in the 48 patients with pHPT and the 19 patients with sHPT are reported in Table 1.

At surgery, 49 neck hyperfunctioning lesions were found in the 48 patients with pHPT; 47 of 48 patients had 1 hyperfunctioning lesion each: 1 solitary adenoma in 43 cases, 1 carcinoma in 1 case, 1 hyperplastic gland in 3 cases (intrathyroidal in 1 case), whereas 2 omolateral eutopic hyperplastic glands were found in the remaining patient. One patient with solitary adenoma and 1 with an eutopic hyperplastic gland had recurrent HPT. Nine of the 43 solitary parathyroid adenomas were <10 mm in their maximum diameter, 2 were 10 mm, and the remaining 32 were >10 mm. Moreover, 13 of 43 adenomas weighed <500 mg, whereas the remaining 30 weighed >500 mg.

Two of the 19 patients with sHPT had 1 adenoma each, 6 had 4 hyperplastic glands each (1 sited in the persistent thymus), 3 had 3, and the remaining 8 patients had 2, including 2 cases with recurrent or persistent disease. Sixteen of the 17 patients with multigland disease had bilateral disease, whereas the remaining patient with recurrent HPT had 2 omolateral hyperplastic glands. Four of the 49 hyperplastic glands were <10 mm, 18 were 10 mm, and 27 were >10 mm; moreover, 20 of 49 glands weighed <500 mg, whereas 29 weighed >500 mg.

**Scintigraphic Findings**

The results of both planar parathyroid scintigraphy and neck P-SPECT in pHPT patients are reported in Table 2.

Planar scintigraphy was positive in 43 of 48 patients, detecting 43 of 49 lesions. P-SPECT was true-positive in all 48 patients, identifying 48 of 49 lesions and missing only 1 hyperplastic gland, which was also negative on planar imaging.

The 2 pHPT patients with recurrent disease were true-positive with both procedures.

Planar scintigraphy was false-negative in 4 patients with solitary parathyroid adenomas that were <10 mm in size (range, 6.1–8 mm) and <500 mg in weight (range, 261–360 mg), whereas all of these were clearly revealed on P-SPECT (one of these cases is illustrated in Fig. 1). None of these 4 patients had concomitant thyroid nodules. A planar scan was also false-negative in the patient with 2 omolateral eutopic hyperplastic parathyroid glands without associated thyroid nodules, missing both lesions that were each 6 mm in size and 300 mg in weight; in this patient, P-SPECT revealed only 1 of the lesions sited behind the inferior pole of the thyroid left lobe, missing the lesion localized at the top of the same lobe. This was the only P-SPECT false-negative result in this group of patients.

Thus, planar scintigraphy showed a lower per-lesion sen-
sitivity than P-SPECT in pHPT patients, but the difference was not statistically significant (P > 0.05; McNemar test), as shown in Table 2. The higher sensitivity of P-SPECT with respect to planar procedures was independent of the different type of method, since it was more sensitive with respect to 99mTc-MIBI double-phase scintigraphy (94.4% vs. 77.8%) and 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy (100% vs. 93.5%); however, the difference in sensitivity was higher with respect of the former rather than the latter.

The only pHPT patient with a parathyroid carcinoma was rechecked after surgery, and no residual uptake was ascertained in the neck by either scintigraphic procedure, confirming normal clinical and hormonal data.

The results of both planar parathyroid scintigraphy and P-SPECT in the 19 sHPT patients are reported in Table 3. Planar parathyroid scintigraphy detected 40 of 51 lesions and missed 11 lesions: 1 solitary adenoma, 15 mm in size and 750 mg in weight, and 10 eutopic hyperplastic glands. Four of the latter were >10 mm in size (range, 14–20 mm), weighed >500 mg (range, 650–1,650 mg), and were sited behind the upper two thirds of the thyroid, whereas the remaining 6 were ≤10 mm in size (range, 6–10 mm), weighed ≤500 mg (range, 210–500 mg), and were sited behind the upper two thirds of the thyroid (n = 4) or behind or at the bottom of the thyroid inferior poles (n = 2).

P-SPECT was true-positive in 47 of 51 lesions and missed 4 eutopic hyperplastic glands, 3 sited behind the

### TABLE 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall (n = 49)</th>
<th>Adenoma/carcinoma (n = 44)</th>
<th>Hyperplasia (n = 5)</th>
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<tr>
<td></td>
<td>Planar</td>
<td>P-SPECT</td>
<td>Planar</td>
</tr>
<tr>
<td>TP findings</td>
<td>43</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>FN findings</td>
<td>6</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Sensitivity (%)</td>
<td>87.7</td>
<td>97.9*</td>
<td>90.9</td>
</tr>
</tbody>
</table>

*P > 0.05 when compared with corresponding planar value (McNemar test results).
TP = true-positive; FN = false-negative.

FIGURE 1. A 55-y-old female patient affected by pHPT with small parathyroid adenoma (size, 6.1 mm; weight, 261 mg) sited behind inferior pole of right thyroid lobe, negative on planar 99mTc-pertechnetate (A), 99mTc-tetrofosmin (B), and subtraction (C) scintigraphy and clearly revealed (arrow) on coronal P-SPECT (D).
upper two thirds of the thyroid and 1 behind the thyroid inferior pole, all also negative on planar scintigraphy. Three of 4 glands were 10 mm in size and ≤500 mg, whereas the fourth gland was larger (size, 20 mm; weight, 1,650 mg).

Only 1 of the sHPT patients with false-negative findings on planar imaging or P-SPECT had concomitant thyroid nodules, but these were not superimposed on the missed hyperplastic glands. The per-lesion sensitivity of P-SPECT was significantly ($P < 0.05$) higher than that of planar imaging in sHPT patients (McNemar test), as shown in Table 3. When P-SPECT was compared separately with 99mTc-MIBI double-phase scintigraphy and with 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy, we found that the difference in sensitivity was higher with respect to 99mTc-MIBI double-phase cases (93.3% vs. 73.3%) than 99mTc-pertechnetate/99mTc-tetrofosmin subtraction scintigraphy cases (91.7% vs. 80.5%).

Planar and P-SPECT were concordantly positive in 10 of 17 sHPT patients with multigland disease, including 1 with persistent HPT, whereas only P-SPECT correctly defined both the exact number of lesions and their localization in 4 of 17 cases; 1 of these latter cases is illustrated in Figure 2. The 2 procedures, both positive, underestimated the number of lesions in a further 2 of 17 patients, one of whom with recurrent HPT. In the remaining patient, both planar imaging and P-SPECT revealed 2 hot areas that did not correspond to the site of the 2 hyperplastic glands excised at surgery; these were 10 mm in size each and weighed 480 and 500 mg, respectively. Given persistently high PTH serum levels after surgery, the patient repeated scintigraphy, which confirmed the areas of increased uptake seen at the first observation.

Another sHPT patient with 2 hyperplastic glands, both true-positive on planar imaging and P-SPECT before surgery, was also rechecked after surgery because of persistently high PTH serum levels. Only P-SPECT revealed a small area of increased uptake behind the inferior pole of the right thyroid lobe; this area was contiguous with 1 of the excised glands and it had not been visualized on the first observation, probably because it was obscured by the size of the gland (size, 20 mm; weight, 1,000 mg), which had appeared highly active on scintigraphy.

Up to now, neither of the above 2 patients with persistent HPT has undergone further surgery.

We compared planar imaging and P-SPECT performance for a correct preoperative diagnosis in all 67 patients enrolled in this study. Only P-SPECT revealed hyperfunctioning glands in 6 cases (5 with pHPT, 1 with sHPT), whereas in 4 cases (all with sHPT) it revealed more lesions than planar imaging. In no case was planar imaging more sensitive than P-SPECT.

In addition, in the patients for whom both procedures were concordantly positive, P-SPECT gave a more distinct visualization of the lesions in 21 cases, 14 with pHPT adenomas, including 5 ≤10 mm (1 of these cases is illustrated in Fig. 3) and 9 >10 mm, and in 7 patients with sHPT multigland disease. In all of these cases, a sharp separation of the hyperfunctioning glands from the surrounding normal activity was observed on P-SPECT, which also precisely defined lesion depths. Moreover, neither P-SPECT nor planar imaging had false-positive results in either pHPT or sHPT patients.

Finally, to date, none of the remaining 53 of 110 patients not included in this study who underwent both planar and neck P-SPECT procedures has had neck surgical exploration; 13 of these 53 patients had pHPT and the remaining 40 had sHPT. One of the 13 pHPT patients, in whom both procedures revealed 1 area of increased tracer uptake, refused surgical treatment; 3 of 13 patients, negative for neck hyperfunctioning parathyroid lesions on both planar imaging and P-SPECT, had an adenoma in the upper mediastinum revealed on planar imaging and have undergone surgery for this; the remaining 9 patients, all positive on P-SPECT for 1 area and 8 also positive on planar imaging, have been scheduled for neck surgery.

Four of the 40 patients with sHPT were positive for 13 areas on P-SPECT and for 11 areas on planar imaging and have been scheduled for surgery; 35 of the remaining 36 patients were positive on P-SPECT for 91 areas and 30 of these were also positive on planar imaging for 72 areas; however, none of these 36 patients has had neck surgical exploration either because they were well controlled with medical treatment ($n = 32$) or because of high surgical risk ($n = 4$).

<table>
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<tr>
<th>Parameter</th>
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<th>Hyperplasia (n = 49)</th>
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<td></td>
<td>Planar</td>
<td>P-SPECT</td>
<td>Planar</td>
</tr>
<tr>
<td>TP findings</td>
<td>40</td>
<td>47</td>
<td>1</td>
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<tr>
<td>Sensitivity (%)</td>
<td>78.4</td>
<td>92.1*</td>
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*$P < 0.05$ when compared with corresponding planar value (McNemar test results).

TP = true-positive; FN = false-negative.
DISCUSSION

P-SPECT is recognized as having very high spatial resolution, superior to that achieved with conventional SPECT with a parallel-hole collimator due to the more favorable geometric properties of the cone beam collimator, as demonstrated in phantom studies (22).

The high spatial resolution of P-SPECT has also been demonstrated in small laboratory animal imaging (23–26) and confirmed in clinical studies focused on thyroid (22,27) and bone (28) diseases and, more recently, on breast cancer axillary lymph node metastasis detection (29,30), in which P-SPECT gave useful anatomic details (28) and increased the sensitivity of conventional planar imaging and SPECT imaging (22,29).

Data regarding the use of P-SPECT in the detection of hyperfunctioning parathyroid lesions have also been reported (17–20) and they are encouraging since the method showed preoperatively higher sensitivity values than conventional planar scintigraphic procedures; however, these data only refer to preliminary studies.

In this study, we used high-resolution 180° P-SPECT of the neck combined with conventional planar 99mTc-MIBI double-phase scintigraphy or 99mTc-pertechnetate/99mTc-tetrofosmin subtraction parathyroid scintigraphy, both of the latter acquired with a large-field-of-view parallel-hole collimator, in both pHPT and sHPT; in all cases, the scintigraphic findings were correlated with histology. At the beginning of the study, we used 99mTc-MIBI double-phase planar scintigraphy. However, we then chose to use the subtraction technique, since we considered it more sensitive and also time saving as it does not require delayed images and is thus better tolerated by patients, particularly sHPT patients with renal failure.

P-SPECT images were acquired with a tilted detector using a specific software originally developed for the study of thyroid diseases (22). For several years, we have also used this procedure with some personal modifications for the detection of axillary lymph node metastases from breast cancer with 99mTc-tetrofosmin as the tumor-seeking agent (29,30).
We obtained very high-quality and high-resolution P-SPECT images, also maintaining an acceptable acquisition time for the patients, using the approximate Feldkamp algorithm (21) and the backprojection filter method for image reconstruction.

In our series, P-SPECT proved to be a highly sensitive method for the detection of hyperfunctioning parathyroid glands, since it globally identified 97.9% and 92.1% of pHPT and sHPT lesions, respectively, sited in the neck in either eutopic or ectopic sites. Most of the patients were at their first surgical exploration and some were scheduled for further surgery because of persistent or recurrent disease.

P-SPECT sensitivity was higher than that of planar imaging in the identification of lesions in both pHPT and shPT patients, independent of the different type of procedure used, $99m$Tc-MIBI double-phase scintigraphy or $99m$Tc-pertechnetate/$99m$Tc-tetrofosmin subtraction scintigraphy, with a statistical difference for shPT. This finding always permitted a more distinct visualization and a more correct localization of hyperfunctioning glands than planar imaging when both were positive, with a sharp separation from the surrounding normal activity in the presence of a single adenoma or multiple hyperplastic glands, especially when small and light-weight or deeply located in the neck.

In confirmation, P-SPECT, which revealed all adenomas, increased planar sensitivity, especially in the detection of those ≤10 mm in size or ≤500 mg in weight, whereas planar scanning missed 30.8% of these. Furthermore, P-SPECT also identified more glands with hyperplasia, with respect to planar imaging, globally detecting 90.7%, whereas planar imaging was true-positive in 77.8%.

Thus, P-SPECT false-negative findings essentially referred to glands with hyperplasia that are generally more difficult to identify than adenomas, as demonstrated by several authors using conventional planar imaging or SPECT procedures, irrespective of the radiotracer and the acquisition protocol used (9,31–35), with small size generally considered the most important limiting factor (8).

However, biologic factors (8), such as low proliferative cell activity and a low quantity of mitochondria, might also be associated with a low radiotracer uptake, thus reducing the possibility of visualizing hyperplastic glands, particularly in shPT patients in whom biochemical factors may also interfere—such as normal serum Ca combined with only slightly increased PTH levels.

Moreover, the overexpression of P-glycoprotein or other multidrug-resistance proteins could also be probable causes of false-negative findings in shPT hyperplasia (36), as also demonstrated in adenomas (37,38).

In this study, the hyperplastic glands missed on P-SPECT were relatively small in diameter and weight, except in 1 case. However, it is possible that besides size, certain of the above-mentioned limiting factors could cause interference, since some hyperplastic glands smaller than those missed were detected on P-SPECT, and also on planar imaging, although the latter proved to be more affected by size than P-SPECT.

In confirmation, planar imaging was false-negative in 6 small glands, 3 of which also were missed on P-SPECT, but it was also false-negative in 4 large glands, only 1 of which was missed on P-SPECT. Thus, it could also be hypothesized that P-SPECT could partially overcome low gland uptake in large glands that were false-negative on planar imaging, most probably due to the above biologic or biochemical factors.

Our data seem to suggest that P-SPECT could represent a reliable complementary tool to conventional planar scintigraphy, also giving more information than planar imaging in some cases. In our series, only P-SPECT permitted a preoperative localization of hyperfunctioning lesions in 8.9% of all patients and revealed a higher number of hyperfunctioning shPT lesions in a further 6% of cases, whereas in no case did planar imaging give more information than P-SPECT. Furthermore, neither P-SPECT nor planar imaging had false-positive findings.
Thus, P-SPECT could represent a useful guide to the surgeon in the localization of abnormal parathyroid glands in patients with pHPT, since in our study it correctly identified all lesions found at surgery except 1 small hyperplastic gland. Planar imaging also proved highly sensitive in the detection of large, but not small, adenomas in our patients, although it did not always give a distinct visualization of the lesions or define their site and depth; thus, the addition of P-SPECT to conventional planar scintigraphy seems particularly indicated in selected patients with pHPT, both when planar imaging is negative, although suspect clinical and biochemical signs of disease are present, and when it is positive but inconclusive for the localization of gland site.

Moreover, P-SPECT correctly predicted the status found at surgery in 82.3% of patients with sHPT with multigland disease, whereas planar imaging correctly predicted the status in 58.8% of cases. These results, although limited to a small number of patients, appear extremely encouraging and suggest the addition of this new procedure as a better guide to the surgeon in sHPT patients than planar imaging alone.

At present, given the difficulty of identifying hyperplastic glands by planar scintigraphy, and also by conventional SPECT, and on the assumption that in sHPT patients 4 hyperplastic glands may be involved, all of which need to be removed, the usefulness of preoperative conventional parathyroid scintigraphy in this group of patients is markedly reduced and its use is limited to cases with recurrent or persistent disease.

However, the combination of a highly sensitive, high-resolution imaging procedure such as P-SPECT and an expert surgeon lead to a significant increase in the number of hyperplastic glands found at surgery and, thus, to the reduction of recurrences due to incomplete surgical treatment. Finally, in our experience, parathyroid P-SPECT proved to be simple, time saving, and easy to read.

CONCLUSION

P-SPECT appears a highly sensitive method in the preoperative localization of hyperfunctioning parathyroid glands sited in the neck in both pHPT and sHPT. In our cases, this procedure increased the sensitivity of conventional planar parathyroid scintigraphy, particularly in small adenomas and in hyperplastic glands, improving the quality and the resolution of images and also permitting a better topographic localization.

Thus, we suggest a more extensive clinical application of this new procedure as a complementary tool to conventional planar imaging in selected pHPT patients in whom the latter is negative or inconclusive, whereas the use of P-SPECT could be widely suggested in sHPT patients since it proved to be a more effective aid than planar imaging to surgical planning. However, these suggestions need to be confirmed by further studies in a larger number of patients.

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The Usefulness of Neck Pinhole SPECT as a Complementary Tool to Planar Scintigraphy in Primary and Secondary Hyperparathyroidism

Angela Spanu, Antonio Falchi, Alessandra Manca, Pietro Marongiu, Antonio Cossu, Nicola Pisu, Francesca Chessa, Susanna Nuvoli and Giuseppe Madeddu


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