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Value of ^{123}I-Subtraction and Single-Photon Emission Computed Tomography in Addition to Planar ^{99m}Tc-MIBI Scintigraphy Before Parathyroid Surgery

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Abstract

Purpose. To find out if single-photon emission computed tomography (SPECT) and ^{123}I-subtraction can enhance the findings of ^{99m}Tc-methoxyisobutylisonitrile (MIBI) scintigraphy for the preoperative localization of parathyroid (PT) tumors.

Methods. Among the 111 consecutive patients who underwent preoperative planar ^{99m}Tc-MIBI scintigraphy for hyperparathyroidism (HPT), 64 underwent delayed SPECT, and 17 underwent ^{123}I-subtraction. Two independent blinded experts scored the topographical localization, diagnostic confidence, and impact of each diagnostic modality on the surgical strategy.

Results. For adenomas, ^{99m}Tc-MIBI scintigraphy had a sensitivity of 77% with a positive predictive value (PPV) of 83%. SPECT did not affect the sensitivity or PPV, but it increased the diagnostic confidence and changed the surgical strategy in 21% of the patients. ^{123}I-subtraction increased the sensitivity from 64% to 82%, but decreased the PPV from 88% to 82%. In hyperplastic glands, ^{99m}Tc-MIBI scintigraphy had a sensitivity of 47% and a PPV of 95%. When ^{99m}Tc-MIBI scintigraphy was combined with SPECT and ^{123}I-subtraction, the results were 44%/10% and 52%/92%, respectively. Both SPECT and ^{123}I-subtraction decreased the diagnostic confidence.

Conclusions. Adding SPECT to ^{99m}Tc-MIBI scintigraphy improved the surgical decision for parathyroid adenomas. The addition of ^{123}I-subtraction was of limited value. For hyperplastic glands, ^{99m}Tc-MIBI scintigraphy was relatively ineffective, even with the addition of SPECT or ^{123}I-subtraction.

Key words Hyperparathyroidism · Radionuclide imaging · Subtraction technique

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Introduction

Accurate preoperative localization of pathological parathyroid (PT) glands is important in the surgical treatment of hyperparathyroidism (HPT), to identify unusual or ectopic lesions and to provide information to determine if direct, minimally invasive surgery is appropriate.[1] Currently, dual-phase ^{99m}Tc- methoxyisobutylisonitrile (MIBI) scintigraphy is the imaging modality of choice. Identification is based on a slower washout rate of MIBI from the PT than from thyroid tissues, although some PT tumors may show a rapid tracer washout.[2] Scintigraphy has a high sensitivity (90%) in detecting solitary adenomas in primary hyperparathyroidism (pHPT).[3] In multiglandular disease, which is present in about 12% of patients with pHPT and is also found in some patients with secondary (sHPT) or tertiary hyperparathyroidism (tHPT), the sensitivity for both adenomas and hyperplastic glands tends to be much lower (44%–54%).[4–7]

To improve the diagnostic performance of ^{99m}Tc-MIBI, single photon emission computed tomography (SPECT) is sometimes added to routine planar scans. SPECT improves contrast and provides a 3-dimensional visualization.[8] This may increase diagnostic confidence and assist in the detection of ectopic localizations, possibly affecting the surgical strategy. Another method of enhancement is dual tracer subtraction scintigraphy using a thyroid specific ^{123}I tracer subtracted from ^{99m}Tc-MIBI, which is retained in both thyroid and PT tissue. This method may enhance accuracy, especially in multiglandular disease, by reducing false-positive (FP) results caused by thyroid nodules,[9,10] and false-negative (FN) results caused by early MIBI washout.[11]

We conducted this study to evaluate the surgical implications of adding SPECT and ^{123}I-subtraction to ^{99m}Tc-MIBI scintigraphy to detect PT tumors.

Methods

Patients

Between 1994 and 2005, 111 consecutive patients with HPT were referred to our institute, a tertiary referral center in the North Netherlands, where planar ^{99m}Tc-MIBI scintigraphy has been performed routinely since 1994, SPECT since 1998, and ^{123}I-subtraction since 2002. All patients underwent parathyroidectomy after ^{99m}Tc-MIBI scintigraphy.

Ultimately, the exact location of the PT tumors was determined during surgery and documented accordingly. Twelve (10.8%) patients were excluded from this study because of unsuccessful surgery, defined as an elevation of both PTH (>10 pmol/l for pHPT and >20 pmol/l for sHPT) and calcium (>2.75 mmol/l) or the need for calcium lowering dialysate in case of sHPT within 6 months postoperatively. Successful parathyroidectomy was carried out in 99 patients: 29 men and 70 women with a mean age of 57 ± 14 years. Sixty-six patients had pHPT, including 11 who needed reoperations for persistent or recurrent disease; 22 patients had sHPT, including 3 who needed reoperations; 7 patients had tHPT; 3 patients had HPT as part of MEN syndrome; and 1 patient had HPT caused by long-term lithium use. Nodular thyroid disease was detected by palpation and ultrasonography in 25% of the patients. PT glands were defined as abnormal if they weighed more than 55 mg or their largest diameter exceeded 7 mm at surgical or pathologic examination.[12] If hypercellularity was seen in all excised glands, they were considered to be hyperplastic. If hypercellularity was documented in ≤2 glands found in the presence of one or more normal appearing glands, they were considered to be adenomas. If there was any doubt, the original histological slides were retrieved and re-evaluated by an experienced pathologist.

Scan Protocol

Planar scintigraphy was evaluated in all of the 99 patients, additional SPECT was evaluated in 58 of these patients, and ^{123}I-subtraction was evaluated in 16. ^{99m}Tc-MIBI scintigraphy was performed using a Siemens Multispect2 gamma camera (Hoffmann Estates, IL, USA) with a low-energy high-resolution collimator (^{99m}Tc, 140 keV, 15%). Ten minutes after the intravenous (i.v.) injection of 400 MBq ^{99m}Tc-methoxyisobutylisonitrile (MIBI), early static images were obtained with an acquisition time of 10 min. SPECT images were obtained 90 min after the i.v. injection of ^{99m}Tc-MIBI (2 × 32 views during 60 s), followed by late static images 120 min after the i.v. injection of ^{99m}Tc-MIBI with an acquisition time of 10 min. Next, a static image was taken 120 min after the patient swallowed 11 MBq ^{123}I. ^{123}I images were subtracted from the early ^{99m}Tc images using a variable multiplication factor for ^{123}I images on the basis of a visual inspection without creating imaging artifacts. Marking of the jugular notch and shoulders and careful laser-based repositioning were used to minimize subtraction artifacts caused by movement of the patient.

Image Interpretations

Images were visually evaluated by two independent experienced nuclear medicine physicians, who were blinded to the clinical outcome or results of other localization studies. A consensus was reached if there was disagreement. Early- and late-planar images were analyzed first, followed by SPECT images, and finally, ^{123}I-subtraction images, to determine the relative contributions of SPECT and ^{123}I-subtraction. A positive finding was defined as a relative increase in ^{99m}Tc-MIBI uptake in the neck area or mediastinum, which could not be attributed to normal physiologic uptake. The diagnostic confidence of each suspected lesion was categorized as high, moderate, or low, and the detected lesion was drawn on a planar anterior image of the neck (Fig. 1A). Lesions on SPECT were also drawn in the sagittal SPECT plane (Fig. 1B). Regions were chosen according to surgical relevance on the basis of the different dissection planes where parathyroid tissue is found.

The preoperative scintigraphic location of the lesions was compared with the surgically determined location. Results were considered true positive (TP) or FN when enlarged PT glands were detected correctly or incorrectly, respectively, during surgery in one of the regions, irrespective of the assigned diagnostic confidence. Scintigraphic lesions were considered FP when no abnormal glands were found in the previously indicated region. Analysis was based on individual lesions and sensitivity, defined as TP/(TP + FN). The positive predictive value (PPV), defined as TP/(TP + FP), was calculated because the PPV is important from a surgical point of view.

The effect of the scintigraphic results on the surgical strategy; namely, minimally invasive parathyroidectomy (MIP) versus conventional bilateral neck exploration, was determined only in patients with pHPT. Scoring was based on the consensus of two experienced parathyroid surgeons, after consideration of the imaging information of planar, planar + SPECT, or planar + SPECT + subtraction. MIP is a limited unilateral approach to a localized hyperfunctional parathyroid gland through a 2-cm skin incision without visualization of the remaining parathyroid glands. With MIP, there is a risk of missing an adenoma and this procedure was advised only if imaging showed a solitary adenoma with moderate to high diagnostic confidence. Conventional

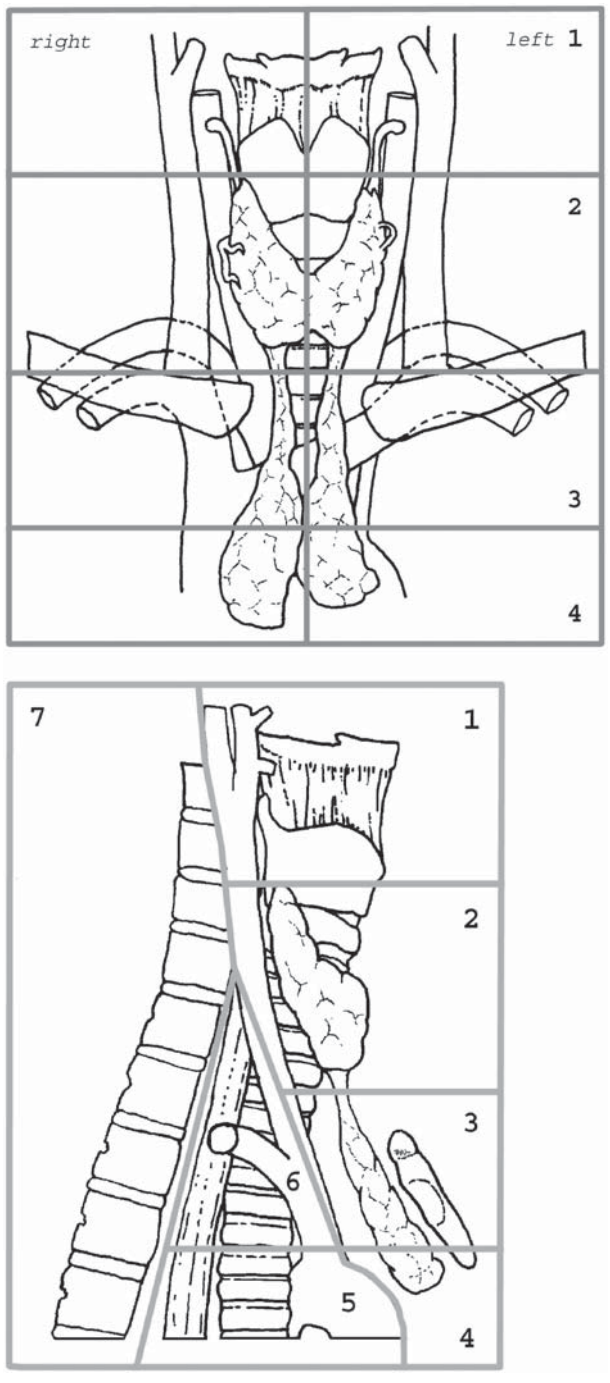

Fig. 1. Coronal (**A**) and sagittal (**B**) views of the regions used for topographical localization: *1*, retropharyngeal region; *2*, region directly lateral or posterior to the thyroid; *3*, tongue of the thymus, *4*, mediastinal thymus; *5*, mediastinal region underneath the v. brachiocephalica; *6*, dorsal or caudal tracheo-esophageal region; *7*, paravertebral region[45]

neck exploration with inspection of all parathyroid glands was performed in all other patients.

Statistical Analysis

Student's *t* test and the Chi-square test were applied and a *P* value of less than 0.05 was considered to be significant. Results are expressed as means ±2 SD throughout this study. Topographic localizations and diagnostic confidence scoring by the two readers were analyzed for interobserver agreement, and κ-statistics were computed.[13]

Results

Interobserver Agreement

The interobserver agreement for diagnostic confidence and topographic localizations ranged from 64% to 86% with a κ of 0.50–0.77 representing good agreement. Except for the localization of tumors detected after the addition of subtraction images, 77% agreement was reached with κ (0.41) representing good agreement (0.40–0.80).

Detection of Adenomas

Of the 66 patients with pHPT, 63 (95%) underwent removal of a solitary adenoma. These adenomas were detected during preoperative ^{99m}Tc-MIBI scintigraphy in 50 patients, giving a sensitivity of 79% and a PPV of 88%. Two adenomas were found in three patients, but only the largest one was detected during preoperative scintigraphy. Adenomas were also present in five of the patients with tHPT and in two of those with MEN syndrome. The total adenoma group consisted of 77 adenomas in 73 patients, 59 of which were detected during planar MIBI scintigraphy, yielding an overall sensitivity of 77% and a PPV of 83%. In the 59 correctly detected adenomas, the diagnostic confidence on planar images was categorized as low in 8%, moderate in 40%, and high in 51%. When we compared the detection of adenomas between early and late images, 11 (18.6%) adenomas were identified only on early images, 14 (23.7%) only on late images, and 34 (57.6%) on both.

Of the 73 patients with adenomas, 44 underwent SPECT, which did not affect the sensitivity or PPV in the detection of adenomas (Fig. 2A). SPECT resulted in the detection of two additional adenomas after planar scans, but two other adenomas were incorrectly considered to be absent after SPECT. Thus, SPECT increased the diagnostic confidence in 21% of the adenomas, but it decreased the reading confidence in 9%.

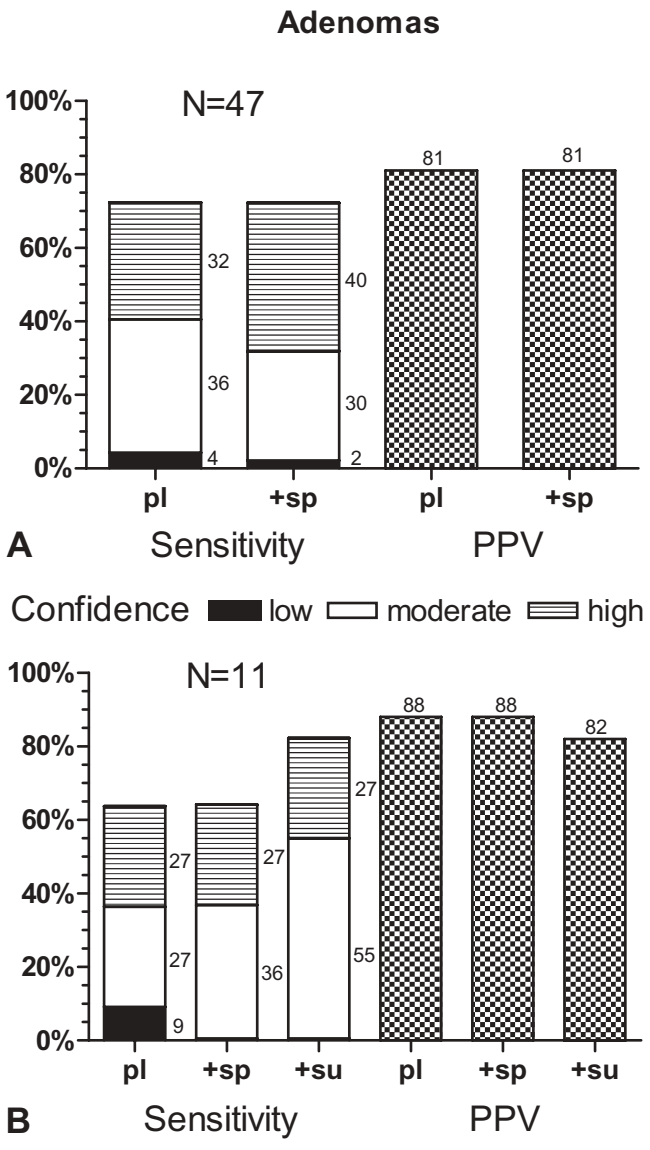

Fig. 2. Sensitivity, positive predictive value (PPV), and diagnostic confidence for adenomas after planar images with the addition of single photon emission computed tomography (SPECT) in 44 patients (**A**) and subtraction images in a subgroup of 10 of these patients (**B**). The level of diagnostic confidence is given only for correctly detected glands. *N*, number of glands; *PPV*, positive predictive value; *pl*, planar; *sp*, SPECT; *su*, ^{123}I subtraction

As SPECT provides a three-dimensional image, its contribution to the localization of ectopic parathyroid glands was analyzed separately. Of the 11 ectopic adenomas in this study, 7 were dorsocaudal of the tracheo-esophageal region, 1 was located in the paravertebral region, and 3 were located in the thymus. SPECT was performed on 8 of these 11 patients. Although SPECT provided no further information on the planar images to aid in detecting three thymic adenomas, it proved very useful in detecting three adenomas in the dorsal tracheo-esophageal region. However, one tracheo-esophageal adenoma and one paravertebral adenoma were not localized correctly in the sagittal plane.

We were able to evaluate the impact of SPECT on the surgical strategy in 38 patients with pHPT. In 11 (11/38; 29%) patients, additional topographic information or increased diagnostic confidence after SPECT changed the surgical strategy. Minimally invasive surgery was recommended for five patients, but was not advised for three, because SPECT showed an ectopic dorsal location. In three other patients decision changes were based on FP or FN SPECT results. Therefore, the change in surgical strategy on the basis of SPECT findings proved incorrect in three (3/38; 8%) and correct in eight (8/38; 21%) of these eleven (11/38; 29%) patients.

^{123}I-subtraction images were added to the planar and SPECT images in a subgroup of 10 patients with adenomas. This increased sensitivity from 63% to 82% by showing two additional adenomas. Despite this increase, the PPV decreased, because there were more FPs (Fig. 2B). ^{123}I-subtraction images proved helpful in 1 of the 10 patients, and changed the surgical strategy by filtering out a FP lesion detected on planar and SPECT images. The increase in sensitivity, the decrease in PPV, and the lower interobserver agreement for topographical localization after subtraction, is largely explained by the imaging results of two patients. In both patients, planar and SPECT studies were negative, whereas subtraction revealed a TP and a FP lesion (Fig. 3).

Detection of Hyperplastic Glands

We performed subtotal parathyroidectomy for sHPT in 22 patients, 19 of whom were operated on for the first time. Preoperative MIBI scintigraphy localized 36 of the 68 hyperplastic glands removed from these patients, yielding a sensitivity of 52% and a PPV of 95%. In three patients who underwent reoperation for persistent sHPT, one or two hyperplastic glands were removed. A single gland was detected by preoperative scintigraphy in all three patients, but a second residual gland was missed in two of these patients. Hyperplastic glands were also found in two patients with tHPT, one with MEN syndrome, and the one with HPT caused by long-term lithium use. There was a total of 89 hyperplastic glands in 26 patients. Planar scintigraphy resulted in correct localization in 42 of these glands, yielding a sensitivity of 47%, with a PPV of 95%. In these 42 correctly localized glands, the examiners scored their diagnostic confidence on the basis of planar images as low in 17%, moderate in 60%, and high in 24%. On early and late images, 9 (21%) glands were detected only on early images, 15 (36%) only on late images, and 18

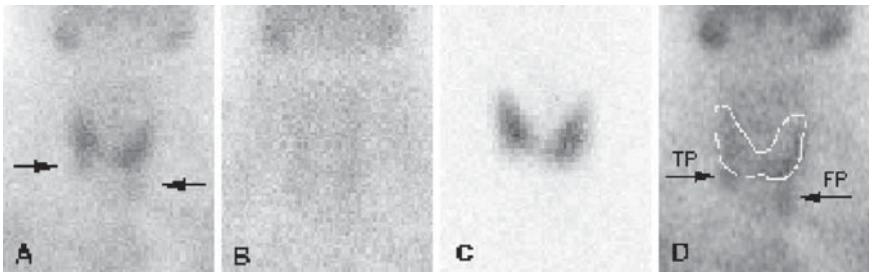

Fig. 3. Early planar (**A**), late planar (**B**), and SPECT images (not shown) were read as negative in a patient with primary hyperparathyroidism (pHPT). On retrospective evaluation, two lesions were seen on the early image (*arrows*). Subtraction of ^{123}I (**C**) from the early planar image (**D**), showed two lesions clearly. One was true positive (TP) and one was false positive (FP), illustrating the mixed effect of subtraction

(43%) on both. The early- and late-detection rates for adenomas and hyperplastic glands did not differ.

Single photon emission computed tomography, which was done for 14 of the 26 patients with hyperplastic glands, decreased rather than increased sensitivity (Fig. 4A). After the planar scans, SPECT images resulted in the identification of three (6%) extra hyperplastic glands, but at least eight (16%) were incorrectly considered absent after SPECT. Diagnostic confidence increased in 22% of the glands, but decreased in 26% after SPECT. In total, seven ectopic hyperplastic glands were found in seven patients: four in the thymus, one dorsal of the tracheo-esophageal region, and two inside the thyroid. SPECT resulted in the localization of two thymic glands, but failed to correctly localize two glands inside the thyroid. The other three glands were not detected at all.

The subsequent addition of subtraction images in a subgroup of six patients with hyperplastic glands increased the sensitivity by localizing an extra hyperplastic gland (Fig. 4B). However, diagnostic confidence decreased and one extra FP gland was detected.

Gland Weight

The mean weight of the adenomas was 1442 ± 1635 mg, whereas that of the hyperplastic glands was 784 ± 665 mg ($P < 0.05$). The weights of the correctly and incorrectly detected glands are shown in Table 1. The five glands detected on SPECT, but not on planar images, ranged in weight from 960 mg to 6000 mg, which was not different from that of the glands detected on both images.

Discussion

About 12% of patients with pHPT have multiglandular disease.[3] The preoperative localization of abnormal parathyroid glands is important for determining if MIP is appropriate.[1] The sensitivity of 77% in the topographical localization of pHPT with dual-phase scintigraphy in our series is in accordance with the reported sensitivities of 53%–100% in a recent systematic meta-analysis.[14] Like Staudenherz et al.,[15] we found that adding delayed SPECT did not increase sensitivity. However, other investigators described an increase in sensitivity from 87% to 95%.[16] SPECT provides the surgeon with a 3-dimensional image of the location of adenomas, especially dorsal ectopic adenomas, and enhances the diagnostic interpretations by nuclear physicians.[17] On the basis of our interpretation of the SPECT images, we changed the surgical strategy for 21% of our patients with pHPT, allowing minimally invasive surgery to be performed more safely.

Delayed SPECT has lower sensitivity (55%–91%)[8,18,19] than early SPECT (91%–96%),[20,21] which was reported to be superior because a limited number of adenomas showed retention of MIBI.[20] We observed retention on late-planar images in 62% of the adenomas in this series. However, in 14% of the adenomas, retention was observed on early images 20 min after injection, but not on late images 120 min after injection. However, as 80% of these adenomas were detected on delayed SPECT, the optimal time for SPECT with the highest sensitivity and a good discrimination of the adenoma from the thyroid has yet to be determined.

The sensitivity for detecting adenomas improved by adding ^{123}I-subtraction imaging, but at the expense of PPV, and the diagnostic confidence was not improved. ^{123}I-subtraction imaging had a beneficial impact on the surgical strategy in only 10% of the patients. Moreover, there was poor interobserver agreement, as lesions with a low signal were difficult to differentiate from background noise, leading to FP or FN results. The supposed advantage of ^{123}I-subtraction imaging is that it prevents FP findings by MIBI uptake in the thyroid nodules.[1,17] ^{123}I-subtraction imaging corrected FP findings in one of our patients, but it failed in another patient with a

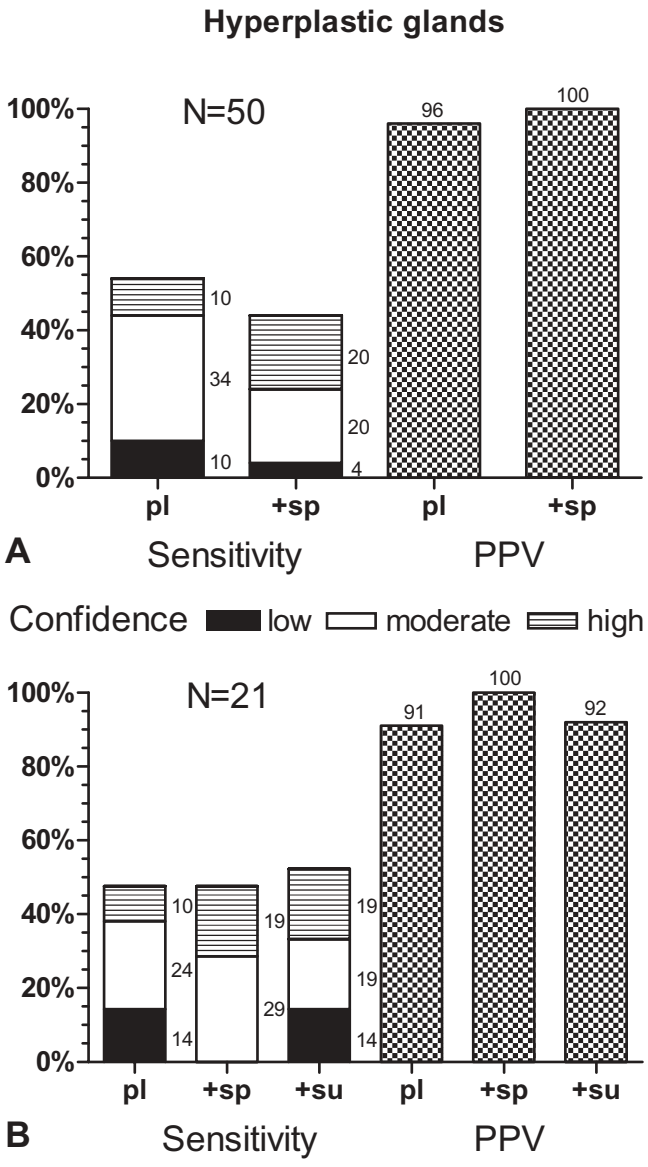

Fig. 4. Sensitivity, PPV, and diagnostic confidence for hyperplastic glands after planar images with the addition of SPECT in 14 patients (**A**) and subtraction images in a subgroup of 6 of these patients (**B**). The level of diagnostic confidence is given only for correctly detected glands. *N*, number of glands; *PPV*, positive predictive value; *pl,* planar; *sp*, SPECT; *su*, ^{123}I subtraction

thyroid adenoma. Gallowitsch et al.[22] reported more FP findings of adenomas with subtraction scintigraphy, without any difference in sensitivity (87%), than with SPECT. Three other studies compared dual-phase with subtraction scintigraphy, and although the sensitivities for dual phase (62%–79%) and subtraction (72%–94%) ranged widely, subtraction was found to be superior to dual-phase scintigraphy in all the three studies.[17,23,24] Hindie et al.[24] used the subtraction technique with simultaneous double-window acquisition and found that subtraction had higher sensitivity and a lower FP rate (3%) than the dual-phase technique. Simultaneous double-window acquisition prevents motion artifacts, which may result in FP findings, and it also takes less time. Thus, it may be a good alternative, although the problems created by the cross-talk of radioisotopes should be solved.[25] Careful reading of the images in this series showed that motion artifacts were not the cause of our two FP findings. We found that the subtraction technique is not contributory in general, but it can be helpful, particularly for patients with negative planar and SPECT studies.

Multiglandular disease in patients with pHPT, as diagnosed in three of our patients who had double adenomas, was not recognized by any of the techniques. Only the largest of the double adenomas was detected by scintigraphy. A wide range (8%–80%) of sensitivities using several techniques for the detection of multiglandular disease in pHPT has been reported.[8,26–29] Hindie et al.[30] even reported 100% (9/9) sensitivity using the subtraction technique, but they achieved a PPV of only 50% (9/18). Differentiating multi- from uniglandular disease is important to determine if minimally invasive surgery can be performed safely. As yet, there seems to be no reliable imaging technique that can identify multiglandular disease in patients with pHPT. Other methods, including intraoperative PTH measurements, are necessary to exclude multiglandular disease.[31]

Patients with sHPT usually present with hyperplasia of all glands and preoperative localization remains questionable because of the low sensitivity of most imaging modalities and the need for bilateral exposure. The main reason for unsuccessful surgery, as seen in 10%–30% of these patients, is incomplete localization of all glands.[32] Therefore, we must evaluate all the available imaging modalities thoroughly. According to previous studies, dual-phase scintigraphy yielded a low sensitivity for hyperplastic glands.[4,6,7,33] However, SPECT did not improve the sensitivity and delayed SPECT even reduced the sensitivity (54% vs. 44%), which may be attributed to the spatial resolution limits of SPECT and the low signal in some glands against background noise. Gallowitsch et al.[22] reported lower sensitivity (38%) with dual-phase scintigraphy, but higher sensitivity with SPECT (62%). SPECT increased the diagnostic confidence of some hyperplastic glands detected on both planar and SPECT images. This may be important in high-risk patients, but it has no impact on the initial surgical treatment. In hyperplastic parathyroid glands, good results have been reported with subtraction techniques using double-window acquisition for planar or SPECT imaging, leading to high sensitivities ranging from 77%–91% in small groups.[9,10,25] However, the subtraction images in our series did not increase sensitivity remarkably. Conversely, the images were more confus-

Table 1. Weight of the glands according to true positivity or false negativity

		TP	FN	*P*
Planar	WA	1295 ± 795[a]	531 ± 659[a]	<0.01[a]
	WH	990 ± 666	474 ± 543	<0.01
Planar + SPECT	WA	1853 ± 2068	356 ± 236	<0.01
	WH	1338 ± 629	359 ± 182	<0.01
Planar + SPECT + ^{123}I subtraction	WA	1100 ± 710	350 ± 354	0.19
	WH	1085 ± 640	393 ± 101	0.11

FN, false-negative glands; P, P value; TP, true positive glands; WA, weight of adenomas; WH, weight of hyperplastic glands; SPECT, single-photon emission computed tomography
[a] Analysis was done after the exclusion of outliers

ing than helpful, considering the lower confidence scores and interobserver agreement after the addition of subtraction images. This was not surprising because many of these glands have a low signal near the limit of detection.

It is unknown why hyperplastic glands trigger weaker signals and lower sensitivities than adenomas, but several mechanisms have been proposed. First, the uptake might be limited by the size of the tumor. In the present series, hyperplastic glands were smaller than adenomas and our data confirm the association between size and the detection of parathyroid tumors by 99mTc-MIBI scintigraphy.[10,23] Second, the difference in uptake of MIBI is related to the distribution of chief and oxyphil cells in parathyroid tumors. Oxyphil cells are richer in mitochondria that accumulate MIBI. Third, the difference may be related to the expression of P-glycoprotein on the membrane of parathyroid cells responsible for the fast washout of MIBI by pumping it out of the cell.[34] Hyperplastic glands are reported to have a faster washout than adenomas, although the number of hyperplastic glands detected solely on early scan in the present study was 9%, which was not remarkably different from that of adenomas. Subtraction techniques are recommended to detect glands with a fast washout of activity.[11] However, a higher rate of detection of hyperplastic glands after the addition of subtraction images was not observed in this study. Although fast washout might have occurred before early static imaging, it is more likely that the smaller size of the hyperplastic glands and their lower uptake of MIBI were responsible for their low sensitivity.

Neither SPECT nor ^{123}I-subtraction technique improved the low sensitivity of planar ^{99m}Tc-MIBI scintigraphy in detecting hyperplastic glands, which raises the question: Is there any use for preoperative scintigraphy in patients undergoing initial surgery for sHPT? As stated earlier, bilateral neck exploration should be done in all patients undergoing initial surgery. Preoperative scintigraphy can have surgical implications if ectopic or supernumerary glands are detected.[9] In our series, the only ectopic glands detected were localized in the thymus. As this is a common location for ectopic or supernumerary glands in patients with secondary disease, it is advisable to perform transcervical thymectomy in all these patients.[35] A second surgical benefit of preoperative scintigraphy is that it may supply functional information. MIBI uptake reflects the degree of suppressibility and autonomy.[36] Therefore, glands with low uptake may have low probability of recurrence and should be chosen for autoimplantation.[9] Because size is associated with MIBI uptake, a gland with the lowest probability of recurrence should probably be selected for reimplantation. With the techniques currently available, preoperative MIBI scintigraphy is of limited value for localizing parathyroid glands in patients undergoing initial surgery for sHPT. However, in patients with persistent or recurrent sHPT it remains useful to detect residual and often ectopic glands.[6,32]

Recently, it was suggested that patients with tHPT could be treated by excising one or two enlarged glands if the remaining glands were not enlarged.[37] We found adenomas in five of seven patients with tHPT, four of whom had a solitary adenoma, which was correctly localized as such. In one patient, scintigraphy showed a solitary lesion, but four enlarged glands were found during surgery. Therefore, the value of scintigraphy in selecting candidates for limited resection of tHPT remains questionable.

Methoxyisobutylisonitrile scintigraphy is generally recommended as the initial imaging modality for patients with HPT. It is especially useful to detect a solitary adenoma in patients with pHPT, with high sensitivity, and to detect ectopic hyperplasia in patients with sHPT or tHPT. Other imaging modalities used to detect parathyroid tumors include ultrasonography, CT, and MRI. Ultrasound is operator-dependent and a wide range of sensitivities have been reported (44%–87%).[38] Moreover, it is relatively ineffective for localizing ectopic glands with dorsal or mediastinal localization. A few studies have reported that CT has 40%–88% sensitivity, with good anatomic information.[39] MRI has

an overall sensitivity of 50%–88%, and is especially sensitive for demonstrating mediastinal and intrathymic ectopic glands.[40–42] New techniques such as CT-MIBI image fusion are currently being evaluated and appear to be superior, especially for locating ectopic glands.[43,44] However, scintigraphy is readily available and reliable. For patients with pHPT, we recommend MIBI planar scintigraphy in combination with SPECT to determine if minimally invasive surgery is indicated. Institutions with excellent ultrasound equipment might consider performing additional SPECT only when the ultrasound findings are negative. For patients with sHPT, scintigraphy is not recommended before initial surgery, although it can be valuable before revision surgery. For both pHPT and sHPT, other imaging modalities are recommended when the scintigraphic findings are negative, especially in patients with residual HPT.

In conclusion, our findings show that SPECT can be valuable in addition to planar ^{99m}Tc-MIBI scintigraphy for detecting parathyroid adenomas in pHPT, by localizing ectopic glands, thereby improving diagnostic confidence and the surgical strategy. We found ^{99m}Tc-MIBI/^{123}I-subtraction to be of no additional value in pHPT, although it might be useful if the planar and SPECT findings are negative. For hyperplastic glands in patients with sHPT or tHPT, planar ^{99m}Tc-MIBI scintigraphy before the initial surgery is of limited value with minimal surgical implications, and it is not improved by SPECT or ^{123}I-subtraction.

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