Iterative reconstruction: an improvement of technetium-99m MIBI SPET for the detection of parathyroid adenomas?

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Abstract. The purpose of this study was to assess the value of technetium-99m methoxyisobutylisonitrile (MIBI) single-photon emission tomography (SPET) and an iterative reconstruction algorithm for the preoperative localisation of parathyroid adenomas (PTAs). Seventy-two patients (26 male, 46 female, mean age 58±16 years) with known primary hyperparathyroidism were examined preoperatively. First, a thyroid examination was performed to detect possible MIBI-accumulating thyroid lesions. Planar scans were then acquired 15 and 120 min and tomographic images 120 min after intravenous injection of 740 MBq ^{99m}Tc-MIBI, using a triple-head gamma camera (Picker Prism 3000). Additionally, ^{99m}Tc-MIBI/^{99m}Tc-pertechnetate subtraction scintigraphy of the early planar images was performed. The SPET data were evaluated using an iterative reconstruction (multiplicative iterative SPET reconstruction: MISR) as well as a standard algorithm (FBP: filtered back-projection with application of a 3-D low-pass postfilter). The weight of the resected PTAs ranged from 110 mg to 5 g. Using planar MIBI scans, correct localisation of the side of the PTA was possible in 81% of cases (58% for PTAs weighing less than 500 mg). Sensitivity increased to 94% using SPET and FBP, while with MISR it rose further, to 97%. Patients with PTAs weighing less than 500 mg showed a sensitivity of 88% with MISR and 81% with FBP. Furthermore, there was a clear improvement in image quality using MISR. None of the normal parathyroid glands were visualised. This study indicates that, in comparison with planar scintigraphy, ^{99m}Tc-MIBI SPET is a more sensitive and specific tool for topographical localisation of PTAs, especially those that are small. There is a further improvement in sensitivity and image quality when iterative reconstruction is used instead of FBP.

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Introduction

The therapy of choice for parathyroid adenomas (PTAs) in primary hyperparathyroidism (pHPT) is parathyroidectomy, a technically intricate operation sometimes requiring extensive bilateral dissection of the neck and mediastinum. For alternative operative strategies such as image-guided unilateral parathyroidectomy, reliable preoperative localisation of the PTA(s) is necessary. Recent studies have underlined the importance of technetium-99m methoxyisobutylisonitrile (MIBI) scintigraphy in the preoperative localisation of PTAs [1, 2, 3, 4], since no other imaging technique has a sensitivity of more than 50% for small parathyroid tumours (less than or equal to 250 mg) [5]. However, to date, the question of whether or not single-photon emission tomography (SPET) should be used prior to parathyroidectomy remains controversial [1, 6, 7, 8, 9].

For SPET evaluation, iterative reconstruction offers several advantages over filtered back-projection (FBP). FBP produces serious artefacts in the investigated organ, in the patient's body and even outside the body. Iterative approximation of the SPET data, on the other hand, provides a means of reducing artefacts, especially in small lesions [10].

In this study we aimed to assess the value of SPET and an iterative reconstruction algorithm in the preoperative diagnosis of parathyroid adenomas. To this end, ^{99m}Tc-MIBI scintigraphy was performed both with planar acquisitions and with SPET using a modern triple-head gamma camera.

Materials and methods

A total of 72 consecutive patients (26 male, 46 female, mean age 58±16 years, age range 42–74 years) with pHPT [elevated levels of serum calcium (2.92±0.36 mmol/l; normal range: 2.20–2.65 mmol/l) and parathormone (PTH; 332±152 ng/l; normal range: 12–72 ng/l)] were examined prior to a scheduled parathyroidectomy. Five patients had had previous neck operations for benign goitre. Symptomatic disease (e.g. nephrolithiasis, epigastric pain, osteoporosis) was present in 38 patients, while 34 patients were clinically asymptomatic.

Following a 2-day protocol, a thyroid examination (fT_3, fT_4, TSH, ultrasonography and ^{99m}Tc-pertechnetate scintigraphy of the thyroid) was carried out on the first day to localise any further radionuclide-accumulating thyroid adenomas or carcinomas. To guarantee a homogeneous study population, ten patients who also had to be operated on for goitre in the same session were excluded.

On day 2, parathyroid scintigraphy was performed. Patients were examined in a normal supine position without hyperextension of the neck. To guarantee sufficient resolution we used a triple-head gamma camera (Picker Prism 3000) with a high-resolution collimator in all patients.

Ventral and dorsal cervico-thoracic planar scans were taken (10 min, 300,000 counts) 15 and 120 min after intravenous injection of 740 MBq ^{99m}Tc-MIBI (Cardiolite, Du Pont Pharma, FRG). For better localisation and to exclude any influence related to thyroid uptake (volume effects, nodules), ^{99m}Tc-MIBI/^{99m}Tc-pertechnetate subtraction scintigraphy of the early images was also performed. For the interpretation of the planar images we used our knowledge of the thyroid anatomy (exact volume distribution measure by ultrasound), comparison of the early and late planar images and ^{99m}Tc-MIBI/^{99m}Tc-pertechnetate subtraction scintigraphy of the early images.

Furthermore, SPET images were acquired 120 min p.i. using a 128×128 pixel matrix, obtaining 120 views over 360° at 20 s per view.

For reconstruction of the SPET data we used two algorithms available with the Odyssey computer attached to the Picker Prism 3000 camera:

1. Filtered back-projection (FBP). Raw data were reconstructed without prior processing using a ramp filter. Subsequently, a 3-D low-pass postfilter was applied with a cut-off frequency of 0.26 pixel^{-1} and an order of 4.0. Attenuation correction was not performed because the available algorithm assumes an elliptical body shape which is not given in the part of the human body imaged here.
2. Multiplicative iterative SPET reconstruction (MISR [11]). This iterative algorithm is computationally related to the ML-EM algorithm [12] but uses a geometric rather than an arithmetic mean over all projections. In this way, all pixel values outside the body are set to zero in the first iteration step, yielding a very clear delineation of the body contour. Furthermore, it takes into account: (a) the physical properties of the gamma camera and collimator, resulting in a recovery of spatial resolution [13] and (b) photon attenuation within the body for arbitrary shapes of the attenuating medium. Like ML-EM, it is a simultaneous technique and therefore does not allow for high over-relaxation. We used seven iterations with a total over-relaxation of 15, an attenuation coefficient of 0.12 cm^{-1} and default values for resolution recovery. The algorithm had previously been applied successfully to SPET of the thyroid [10].

All reconstructed SPET images (transverse, coronal and sagittal slices, 3-D display) as well as the planar images were visually interpreted by two independent observers who reached a consensus prior to surgery. In our study, an abnormal radionuclide focus somewhere in the neck region or mediastinum (below the salivary glands and above the heart) was taken to indicate an adenoma. As no control patients were examined, normal parathyroid glands in the study population were considered as true-negatives for the calculation of specificity. Histopathological correlation was obtained in every patient.

Results

All patients underwent bilateral neck exploration. In three patients a mediastinal exploration (sternotomy) was necessary. All abnormal serum parameters returned to normal values after surgery. Histopathological examination of the removed glands showed a hyperplastic gland in one patient, while in all other cases there were parathyroid adenomas, mostly with predominantly high levels of mitochondria-rich cells. No parathyroid or thyroid carcinomas were detected in any of the patients. The weight of the adenomas varied from 110 mg to 5000 mg (mean weight 910±422 mg). Three patients had two cervical adenomas, two had a solitary mediastinal adenoma and one had a cervical as well as a mediastinal adenoma.

Planar MIBI scans correctly identified and precisely localised adenomas in 50 of 62 patients (81%). Sensitivity was increased to 94% (58/62 patients) using SPET and FBP as the evaluation algorithm. Using SPET and iterative reconstruction there was a further, slight increase in sensitivity in all patients to 97% (60/62 patients). In patients with small parathyroid adenomas the differences in sensitivity were more distinct (Table 1). For the detection of adenomas weighing less than 500 mg, SPET (MISR) was the most sensitive technique [88% compared with 81% for SPET (FBP) and 58% for planar scans].

Of the patients with surgical and pathological evidence of abnormal glands, only two with iterative reconstruction and four with FBP had a false-negative result on MIBI SPET. In the first case MIBI accumulation by the adenoma was obscured by an abnormally high radionuclide uptake in the thyroid gland, which did not decrease over time (as usually occurs). The reason for this persistent MIBI accumulation in the thyroid remained unclear, as the general thyroid examination (fT_3, fT_4, TSH, ultrasonography and ^{99m}Tc thyroid scintigraphy) was inconclusive. In the second patient, who had two parathyroid adenomas, the larger PTA (340 mg) was localised correctly but a second small adenoma (120 mg) was not detected. In the other cases only SPET with standard evaluation produced false-negatives, while SPET evaluated with the iterative algorithm localised the PTAs successfully (Fig. 1).

None of the normal parathyroid glands showed persistent MIBI accumulation on either planar scans or on SPET (specificity 100%).

Table 1. Relation of PTH secretion, adenoma weight and sensitivity of MIBI scintigraphy [planar scans/SPET with filtered back-projection (FBP)/SPET with iterative reconstruction (MISR)]. Although bigger adenomas appeared to produce more PTH, the correlation between PTH concentration and adenoma weight (*r*=0.52) was not statistically significant

Adenoma weight (mg)	Patient	Mean adenoma weight (mg)	PTH (ng/l)	Sensitivity of planar MIBI scintigraphy	Sensitivity of MIBI SPET FBP	Sensitivity of MIBI SPET MISR
Total	62	910±422	332±152	81% (50/62)	93% (58/62)	97% (60/62)
0–250 mg	10	189±49	185±85	50% (5/10)	80% (8/10)	90% (9/10)
250–500 mg	14	416±82	265±85	64% (9/14)	86% (12/14)	93% (13/14)
500–1000 mg	19	832±212	365±130	89% (17/19)	100% (19/19)	100% (19/19)
1000–5000 mg	19	1710±1120	470±252	100% (19/19)	100% (19/19)	100% (19/19)

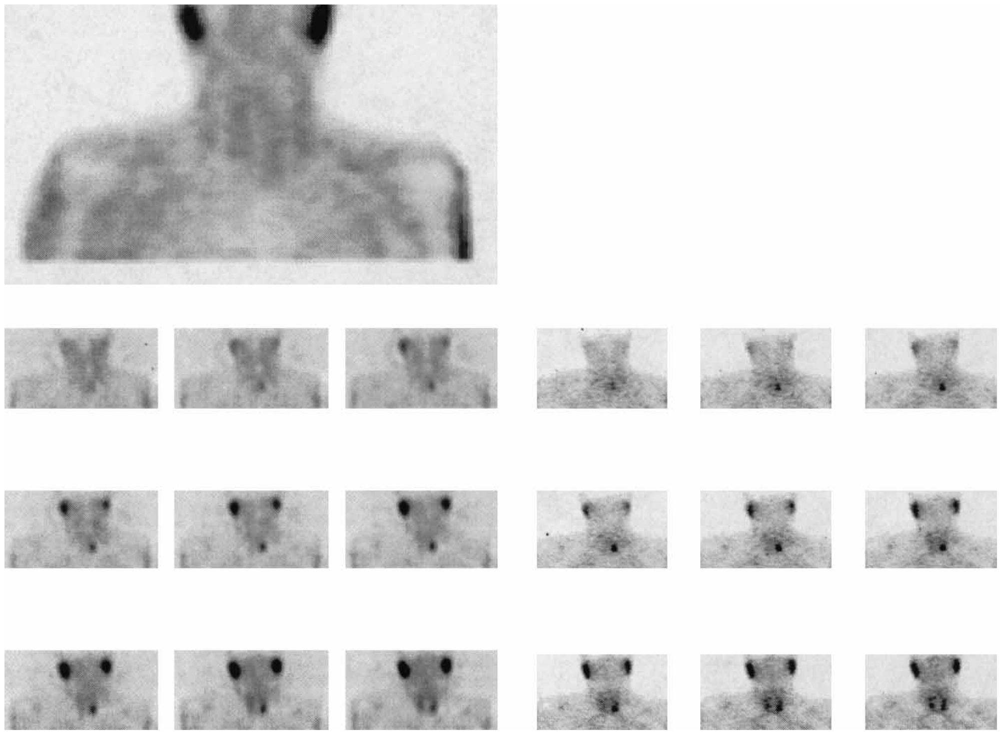

Fig. 1. ^{99m}Tc-MIBI SPET, delineating a parathyroid adenoma (250 mg) in a 64-year-old male patient with pHPT prior to surgical exploration. The focus was not detectable on planar views. The SPET images on the *left side* were analysed using FBP; the images on the *right side* were analysed using iterative reconstruction

Discussion

Parathyroidectomy with bilateral exploration exposes the patient to a greater risk of recurrent laryngeal nerve injuries [14] and increases the likelihood of hypoparathyroidism [15]. Confident localisation of PTAs facilitates successful limited neck exploration [16]. This procedure could reduce the operation time by between 30% and 60% [17, 18, 19, 20]) and also lower the operation costs [14, 21].

In the literature, whether or not SPET is really essential for the location of PTA has become a matter of controversy [1, 6, 7, 8, 9]. Our data indicate that use of SPET, especially in patients with small PTAs (<500 mg), leads to a clear increase in sensitivity. Planar scans can reliably detect only larger adenomas (>500 mg). Therefore SPET can be recommended in all patients as a means to achieve improved and reliable topographical localisation of adenomas.

It is known that FBP produces serious artefacts in the organ under investigation, in the patient's body and even outside the body. In contrast, iterative approximation of SPET provides a means of diminishing artefacts, especially in patients with small PTAs: the two PTAs missed by FBP but detected by iterative reconstruction weighed 200 and 270 mg. Furthermore, our study confirmed that iterative reconstruction produces markedly better image quality (Fig. 2), making the data more reliable, especially for the purpose of presenting findings to surgeons. However, iterative reconstruction resulted in only a slight improvement in sensitivity over FBP. The reason for this less-than-significant increase is that the sensitivi-

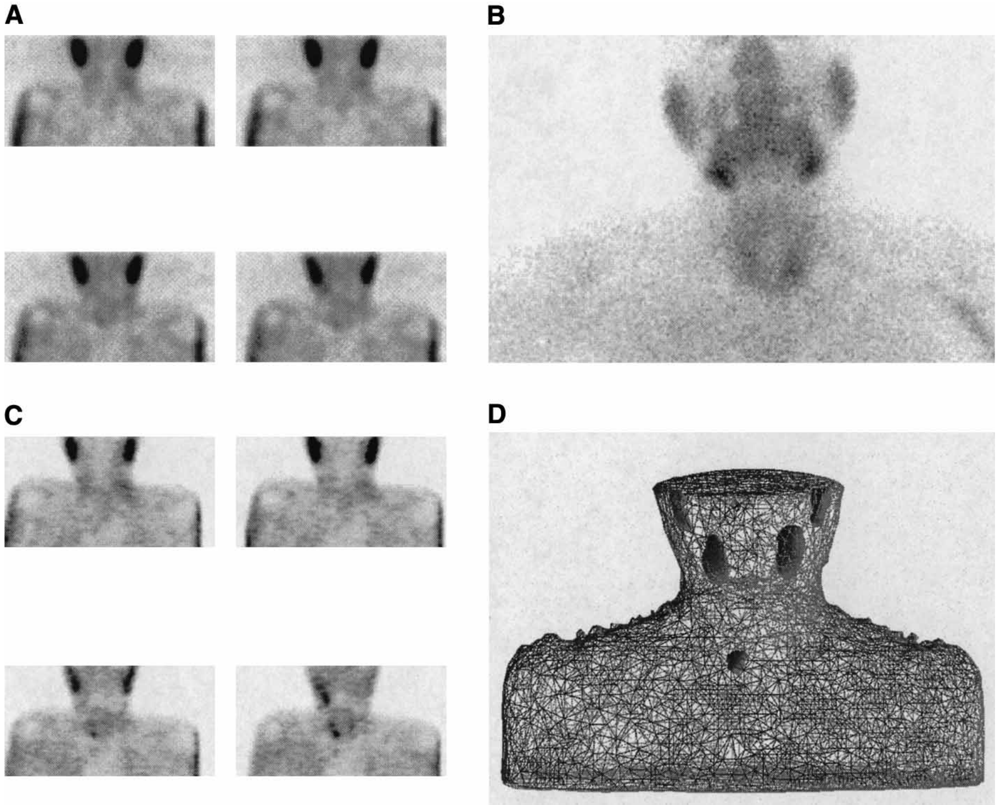

Fig. 2. Planar MIBI scan (**B**) and ^{99m}Tc-MIBI SPET [FBP (**A**), iterative reconstruction (**C**) and 3-D display (**D**)], delineating a parathyroid adenoma (200 mg) in a 64-year-old male patient with pHPT prior to surgical exploration. The focus was detectable on images analysed using iterative reconstruction, but not on the planar scan or on images analysed using FBP

ty of SPET and FBP for detecting adenoma was already high, at 94%. SPET and iterative reconstruction should therefore be the combined method of choice.

Fortunately, iterative reconstruction is no longer a time-consuming method. The extra computational expense of MISR (10 min for seven iterations compared with 3 min for FBP) is marginal in relation to the total time needed for data preparation and evaluation.

The program performing MISR (ISA v 4.4) is part of the standard software package supplied with a Picker Odyssey computer in Germany. Most of the algorithms for iterative reconstruction are closely related [22], so results similar to those presented here could be obtained with any other iterative technique assuming that the technique accounts for attenuation and limited detector resolution in a similar manner.

For routine diagnosis, FBP may be judged sufficient. Nevertheless, iterative reconstruction is necessary in patients with a confirmed diagnosis of HPT and negative MIBI SPET using FBP.

In conclusion: In the preoperative diagnosis of hyperparathyroidism, MIBI SPET is more sensitive for adenoma detection than planar MIBI scans, especially in the case of small parathyroid adenomas (<500 mg). The use of an iterative reconstruction algorithm for data analysis produces a further, slight increase in sensitivity and better image quality by diminishing the known artefacts encountered with the standard FBP algorithm.

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