Clinical role of \(^{99m}\text{TcO}_4\)/MIBI scan, ultrasound and intra-operative gamma probe in the performance of unilateral and minimally invasive surgery in primary hyperparathyroidism

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Abstract. The main purposes of this study were: (a) to investigate the efficacy of an imaging protocol based on the combination of \(^{99m}\text{TcO}_4\)/MIBI scintigraphy and neck ultrasound (US) in selecting patients with primary hyperparathyroidism (HPT) for unilateral neck exploration, and (b) to help define the role of the intraoperative MIBI gamma probe (IMGP) technique in the performance of minimally invasive radio-guided surgery (MIRS). One hundred and forty-three consecutive patients with primary HPT were enrolled in the study. We used a modified \(^{99m}\text{TcO}_4\)/MIBI scintigraphic procedure which included the oral administration of potassium perchlorate to cause rapid \(^{99m}\text{TcO}_4\) washout from the thyroid tissue, thereby permitting the acquisition of high-quality early MIBI images. A single-photon emission tomography (SPET) acquisition was also obtained in 21 patients, of whom seven had an enlarged parathyroid gland (EPG) in the mediastinum at planar scintigraphy and 14 had discordant scan/US findings for the presence of a cervical EPG. Neck US was performed in the same session as scintigraphy using a small-parts, high-resolution 10-MHz transducer. All patients were then operated on by the same surgical team. Quick PTH assay (QPTH) was used to measure PTH intraoperatively to confirm successful parathyroidectomy. In patients with scan/US evidence of a solitary EPG and a normal thyroid gland, limited, unilateral neck surgery or, more recently, MIRS was planned (\(n=91\)). In patients with scan/US evidence of multiglandular disease (MGD) (\(n=21\)) or concomitant nodular goitre (\(n=24\)) or in patients with a negative scan/US evaluation (\(n=7\)), extensive bilateral neck exploration was planned (\(n=52\)). In 87 of the 91 patients (95.6\%) in whom preoperative imaging indicated the presence of a solitary EPG and a normal thyroid gland, a single parathyroid adenoma was found at surgery, and these patients were treated by unilateral neck exploration or MIRS. In the remaining four patients of this group, conversion to bilateral neck exploration was required because parathyroid carcinoma (\(n=3\)) or MGD (\(n=1\)) was diagnosed at operation. In some cases SPET was helpful in better localising the EPG. In particular, in 5 of the 21 patients evaluated, SPET localised an EPG deep in the neck or mediastinum and at surgery a parathyroid adenoma was found in the paratracheal or para-oesophageal space. In 43 of the 46 patients (93.5\%) who were candidates for MIRS, the IMGP technique allowed parathyroidectomy to be performed through a small, 2- to 2.5-cm skin incision with a short duration of intervention (mean 34 min). We conclude that: (a) The integrated scan/US imaging protocol that we used appears to be accurate in selecting patients with primary HPT for unilateral neck exploration. (b) In our series the most prevalent cause of bilateral neck exploration was the co-existence of a nodular goitre; thus accurate preoperative evaluation of the thyroid gland by dual-tracer scintigraphy and US imaging is strongly recommended in all patients with HPT. (c) SPET can provide the surgeon with useful information when an EPG is located deep in the neck or mediastinum. (d) IMGP appears to be a useful intraoperative device in HPT patients with solitary parathyroid adenomas and a normal thyroid gland, since it permits minimally invasive and time-saving surgery.

Keywords: Primary hyperparathyroidism – \(^{99m}\text{TcO}_4\)/MIBI scintigraphy – High-resolution neck ultrasound – Intraoperative gamma probe – Minimally invasive radio-guided surgery
Introduction

Despite the fact that primary hyperparathyroidism (HPT) is caused by a solitary adenoma in the majority of cases (approximately 85%) [1], many surgeons routinely use a bilateral neck exploration with the aim of identifying and even biopsying each parathyroid gland other than the adenoma, in order to investigate the possibility of multiglandular disease (MGD) [2, 3, 4, 5]. In contrast, other authors have reported that scintigraphy, alone or in combination with neck ultrasound (US), is able to accurately predict which patients with primary HPT may be adequately explored by means of a unilateral approach [6, 7, 8, 9]. The unilateral approach is also strongly favoured by the availability of intraoperative quick parathormone (QPTH) measurement: a prompt decrease in QPTH levels after removal of the enlarged parathyroid gland (EPG) represents a sensitive indicator of successful parathyroidectomy [10]. Furthermore, an even less invasive surgical approach has recently been proposed for primary HPT patients: this approach is based on intraoperative detection of the EPG by means of insertion of a gamma probe through a small skin incision, so-called minimally invasive radio-guided surgery (MIRS) [11]. In this paper, which follows publications documenting our preliminary findings [12, 13], we report further data obtained in a large group of 143 consecutive patients with primary HPT. The main aims of this study were: (a) to evaluate the role of a single-day imaging protocol based on the combination of $^{99m}$TcO$_4$/MIBI scintigraphy and high-resolution neck US in selecting patients with primary HPT as potential candidates for a limited neck exploration, (b) to investigate the usefulness of the intraoperative MIBI gamma probe (IMGP) technique in the performance of MIRS. The potential utility of single-photon emission tomography (SPECT) imaging following planar scintigraphy was also examined.

Materials and methods

From September 1998 to June 2000, 143 consecutive patients with primary HPT were operated on at the general surgery department of Padova Hospital. Diagnosis of primary HPT was made on the basis of clinical and biochemical findings. There were 84 females and 59 males, aged 23–76 years (mean 47.3 years). Four patients had previously undergone partial thyroidectomy for a nodular goitre; 15 other patients had previously undergone unsuccessful parathyroid surgery in other hospitals. Four patients were affected by MEN syndrome, and two by familial HPT. When referred to our centre, all patients were investigated preoperatively by means of a dual-tracer subtraction scintigraphy and high-resolution neck US, as previously described [12].

Preoperative imaging procedures. The scintigraphic procedure we used [12] consisted of the following steps (a–e = acquisition, f–h = processing): (a) $^{99m}$TcO$_4$ (150 MBq) was injected intravenously, (b) 20 min later, potassium perchlorate (KClO$_4$) (400 mg) was administered orally, (c) immediately after this, the patient’s neck was immobilised under the gamma camera and a 5-min $^{99m}$TcO$_4$ thyroid scan was acquired, (d) MIBI (500 MBq) was injected intravenously, followed by a flush of saline (30 ml) to avoid venous tracer stagnation, (e) dynamic acquisition of seven MIBI frames, each lasting 5 min, was obtained, (f) background activity was subtracted from the $^{99m}$TcO$_4$ and MIBI frames, (g) MIBI images were normalised to the maximum pixel count activity of the $^{99m}$TcO$_4$ scan, (h) the $^{99m}$TcO$_4$ scan was subtracted from the MIBI images. The interpretative criteria for scintigraphy, in the absence of a nodular goitre, were as follows: (1) a scan showing a single focus of MIBI uptake was considered indicative of a solitary parathyroid adenoma, (2) a scan showing two or more foci of MIBI uptake was considered to be indicative of MGD. In patients with concomitant nodular goitre, the $^{99m}$TcO$_4$ scan and neck US were used to differentiate EPG(s) from thyroid nodule(s). The KClO$_4$ was administered with the aim of inducing $^{99m}$TcO$_4$ thyroid washout. In a previous investigation [12] performed on five euthyroid and US-normal subjects only injected with $^{99m}$TcO$_4$ (150 MBq), we noted that KClO$_4$ (400 mg given orally) was able to induce a rapid and significant decrease in thyroid activity (average decrease of 78% over 40 min). On the basis of these findings, we devised the $^{99m}$TcO$_4$ and KClO$_4$/MIBI procedure used in the present study. This scintigraphic technique allows us to obtain high-quality early MIBI scans with clear delineation of EPGs even if they are located behind the thyroid gland (an example is shown in Fig. 1). Another interesting aspect of this scintigraphic method is that, following the oral administration of KClO$_4$, there is a 10-min latency interval before the thyroid $^{99m}$TcO$_4$ washout begins; this time is sufficient to allow positioning of the patient under the gamma camera and acquisition of a $^{99m}$TcO$_4$ thyroid scan; subsequently, MIBI can be injected without moving the patient.

For scintigraphic examinations, a large-field-of-view (LFOV) gamma camera (Orbiter 7,500, Siemens, Hoffman Estates, Ill.) equipped with a parallel-hole low-energy, high-resolution collimator was used. Images were stored in a 128x128 matrix and processed using a dedicated computer (ICON workstation; Siemens, Hoffman Estates, Ill.).

In some patients with a $^{99m}$TcO$_4$/MIBI scan revealing an ectopic EGP focus in the mediastinum (n=7) or with scintigraphic/US findings discordant for the presence of a cervical EPG (scan positive, US negative or doubtful) (n=14), a tomographic (SPECT) acquisition was also obtained. A dual-head gamma camera (Axis, Picker International, Cleveland, Ohio) equipped with a parallel-hole low-energy ultra-high-resolution collimator was used, adopting the following parameters: elliptical orbit, 120 steps, 30 s per step, 64x64 matrix. Tomographic images were reconstructed using a low-pass filter, cut-off 0.2, order 5.0–6.0, and processed using a dedicated computer (Odyssey 830 Digital, Maynard, Mass.). Three-dimensional analysis was also performed.

Two nuclear medicine physicians independently interpreted the scintigraphic images. In the event of discrepancy, the final diagnosis was reached by consensus.

Neck US was performed in the same session as the scintigraphy, using a small-parts, high-resolution 10-MHz transducer (Diasonic, Les-Vlis, France). Longitudinal and transverse neck US scans were obtained from the level of the angle of the mandible to the sternal notch. EPG was identified on grey-scale imaging by the characteristic appearance of a hypoechoic nodule distinct from the thyroid tissue. The US interpretative criteria were as follows: (1) a US examination showing a single hypoechoic nodule distinct from the thyroid gland was considered indicative of a solitary parathyroid adenoma, (2) a US examination showing two or more hypo-