

# Parathyroid scintigraphy and minimal invasive surgery in parathyroid adenomas

## Paratiroid adenomlarda paratiroid sintigrafisi ve minimal invaziv cerrahi

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### ABSTRACT

**Objectives:** This study aims to identify the diagnostic capacity of the technetium 99m sestamibi scintigraphy with single photon emission computed tomography for localizing parathyroid pathologies.

**Patients and Methods:** Data of 13 patients (4 males, 9 females; mean age 49.23 years; range 27 to 63 years) who had minimally invasive parathyroidectomy due to primary hyperparathyroidism at the Haseki Training and Research Hospital Ear-Nose-Throat clinic between January 2013 and December 2013 were retrospectively analyzed. Two patients were excluded due to incomplete documentation.

**Results:** Mean preoperative parathyroid hormone and calcium levels were 284.36 (134-1,083 pg/mL) and 11.9 (10.7-13.5 mg/dL), respectively. The operation was deemed adequate if intraoperative parathyroid hormone dropped by 50% from the preoperative level or frozen section analysis showed hypercellular gland or adenoma. Only sestamibi scintigraphy results were consistent with focal exploration findings in all patients. Focal exploration and parathyroid adenoma excision via minimally invasive parathyroidectomy were successfully carried out in 10 patients with single adenoma confirmed by sestamibi.

**Conclusion:** Technetium 99m sestamibi scintigraphy with single photon emission computed tomography and frozen section analysis may provide more meaningful information and be more advantageous compared to other preoperative localization techniques.

**Keywords:** Parathyroidectomy; primary hyperparathyroidism; technetium 99m sestamibi.

### ÖZ

**Amaç:** Bu çalışmada, paratiroid patolojileri lokalize etmede tek foton emisyon bilgisayarlı tomografi ile teknesyum 99m sestamibi sintigrafisinin diyagnostik kapasitesi tanımlandı.

**Hastalar ve Yöntemler:** Ocak 2013-Aralık 2013 tarihleri arasında Haseki Eğitim ve Araştırma Hastanesi Kulak-Burun-Boğaz Kliniğinde primer hiperparatiroidizm nedeniyle minimal invaziv paratiroidektomi yapılan 13 hastanın (4 erkek, 9 kadın; ort. yaş 49.23 yıl; dağılım 27-63 yıl) verileri retrospektif olarak incelendi. İki hasta eksik belge nedeniyle çalışma dışı bırakıldı.

**Bulgular:** Ameliyat öncesi ortalama paratiroid hormonu ve kalsiyum seviyeleri sırasıyla 284.36 (134-1083 pg/mL) ve 11.9 (10.7-13.5 mg/dL) idi. Ameliyat sırası paratiroid hormonunun ameliyat öncesi seviyenin %50 altına düşmesi veya dondurulmuş kesit incelemesinin hiperselüler bez veya adenoma göstermesi halinde ameliyat yeterli kabul edildi. Tüm hastalarda, sadece sestamibi sintigrafisi sonuçları ile fokal eksplorasyon sonuçları uyumluydu. Sestamibi ile tek adenoma tespit edilen 10 hastada minimal invaziv paratiroidektomi yoluyla fokal eksplorasyon ve paratiroid adenoma eksizeyonu başarıyla yapıldı.

**Sonuç:** Tek foton emisyon bilgisayarlı tomografi ile teknesyum 99m sestamibi sintigrafisi ve dondurulmuş kesit analizi diğer ameliyat öncesi lokalizasyon tekniklerine göre daha anlamlı bilgiler sağlayıp daha avantajlı olabilir.

**Anahtar Sözcükler:** Paratiroidektomi; primer hiperparatiroidizm; teknesyum 99m sestamibi.



Primary hyperparathyroidism (PHPT) is one of the most common endocrine diseases that occur due to single adenoma in approximately 85-90% patients.<sup>[1]</sup> The management of PHPT has dramatically advanced with increasing biochemical screening in recent decades. Most patients are asymptomatic and characterized by overproduction of parathyroid hormone (PTH) and hypercalcemia.<sup>[2]</sup> Many endocrinologists previously considered parathyroidectomy via bilateral cervical exploration (BCE) as an unnecessarily extensive and potentially dangerous operation. Over time, BCE has been modified with the introduction of modern preoperative localization procedures<sup>[3-6]</sup> and physicians are more prepared to refer patients for this minimally invasive parathyroidectomy (MIP).<sup>[3,7]</sup>

In many centers, there are three arms involved in the surgical decision -- preoperative imaging, frozen section and intraoperative PTH (IOPTH). Some researchers and surgeons have questioned the necessity of all these measures for reaching the surgical decision.<sup>[8]</sup> It is usual practice to confirm the preoperative location of the hyperactive gland with at least two concordant imaging tools. Ultrasonography (USG) is highly dependent on the experience and skill of the operator, although the recommended localization procedures before MIP were USG and Technetium 99m (99mTc)-labelled sestamibi imaging.<sup>[2]</sup>

The aim of the present study was to identify the diagnostic capacity of the 99mTc-labelled sestamibi imaging with single photon emission computed tomography (SPECT) for localizing parathyroid pathologies.

#### PATIENTS AND METHODS

Data of 13 patients (4 males, 9 females; mean age 49.23 years; range 27 to 63 years) who had minimally invasive parathyroidectomy due to primary hyperparathyroidism at the Haseki Training and Research Hospital Ear-Nose-Throat (ENT) clinic between January 2013 and December 2013 were retrospectively analyzed. Two patients were excluded due to incomplete documentation. Included patients had biochemically proven PHPT with no previous history of surgery, familial disease, or persistent recurrent disease. Exclusion criteria included patients with missing data due to lack of documentation and patients lacking the proper workup. Patients had been

incidentally identified with high serum PTH and calcium levels or referred to our clinic for confirmed PHPT from the endocrine clinic. The data evaluated for the patients included the detailed history and physical examination performed with focus on hypercalcemic signs and symptoms. Preoperative laboratory tests including PTH assay, phosphate, calcium levels, 24-hour urine calcium to rule out familial hypocalciuric hypercalcemia and demographic data such as sex and age were also recorded (Table 1). Patients were imaged by at least two modalities, USG and 99mTc-labelled sestamibi imaging with SPECT. If the imaging modalities were not concordant, magnetic resonance imaging (MRI), IOPTH or frozen section analysis were requested.

An ENT specialist resected the parathyroid adenoma in all these patients. All patients underwent MIP under general anesthesia, with a lateral or midline 2-4 cm transverse incision made within a skin crease on the side where preoperative localizing studies had identified the hyperfunctioning parathyroid gland. The incision length often depended on patient body habitus and adenoma size.<sup>[9]</sup> We used approximately 2 cm transverse incisions, with the platysma being transected and the strap muscle retracted to expose the area bounded by the thyroid gland medially, the internal carotid artery laterally and prevertebral fascia posteriorly. We always used recurrent laryngeal nerve monitoring during parathyroidectomy.

After the patient was intubated, serum PTH level was measured prior to initiation of surgery. At 12 minutes post-excision, IOPTH was analyzed on the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 9<sup>th</sup> patients who had no concordant USG and 99mTc-labelled sestamibi imaging signs to confirm the location of the hyperactive gland. If there was concordant USG and 99mTc-labelled sestamibi imaging or IOPTH level was unrecordable for any reason, frozen section analysis was planned in these patients. The confirmation of adequate excision of the adenoma was based on the Miami criterion by IOPTH results or frozen section analysis.<sup>[10]</sup> The surgery was deemed adequate if IOPTH dropped by 50% from the pre-excision level or the frozen section analysis showed hypercellular gland or adenoma. If not, a four-gland exploration was planned. The one-hour postoperative PTH value was also measured. Various pathologists

**Table 1.** Demographic characteristics of the patients

Patient no	Age/gender	Symptom/finding	Neck USG	Scintigraphy	MRI
1	56/M	Abdominal pain	Normal	Thyroid left inferior lobe	Not done
2	41/M	Hypercalcemia	Normal	Thyroid left inferior lobe	Posterior region of the left inferior thyroid pole (6.5 mm)
3	48/F	Hypercalcemia	Normal	Inferior region of the right thyroid lobe	Not done
4	52/F	Hypercalcemia	Normal	Ectopic location at superior mediastinum (inferior pole of left thyroid lobe)	Not done
5	48/F	Hypercalcemia	Parathyroid adenoma (16x7 mm, inferioromedial region of the left inferior thyroid pole)	Inferior region of the right thyroid lobe	Not done
6	42/F	Hypercalcemia	Parathyroid adenoma (18x7 mm, posterior region of right inferior thyroid pole)	Right inferior thyroid pole	Not done
7	27/M	Abdominal pain	Normal	Left inferior thyroid pole	Inferior pole of the left lobe (9 mm)
8	63/F	Hypercalcemia	Parathyroid adenoma (14x5 mm, right inferior thyroid pole)	Right inferior thyroid pole	Not done
9	54/F	Hypercalcemia	Normal	Posterior region of the left inferior thyroid lobe	Not done
10	61/F	Hypercalcemia	Parathyroid adenoma (8.5x7 mm, left superior thyroid pole)	Left superior thyroid pole	Not done
11	60/M	Hypercalcemia	Parathyroid adenoma (2 cm, posterior region of the left thyroid lobe)	Two foci at left superior and right superior thyroid pole	Not done

USG: Ultrasonography; MRI: Magnetic resonance imaging.

confirmed the parathyroid pathology in all tissue samples.

The following data were collected from every patient: demographics, preoperative PTH, preoperative imaging, intraoperative findings, IOPTH, frozen section results, final pathology, accuracy of preoperative imaging in concordance with intraoperative findings and postoperative PTH levels (Table 2).

The duration of each operation was recorded along with any complications or need for postoperative calcium. All patients were discharged either on the day of surgery or the following morning if surgery was performed in the afternoon. Serum calcium levels were measured on the first operation day and 4-6 weeks after the operation. Although calcium tablets were not administered routinely, patients were informed about how to identify the

symptoms of hypocalcemia and also when they needed to take calcium. All patients were seen in the outpatient clinic 4-6 weeks after surgery and assessed for any symptoms or complications along with a review of the histopathological findings. A further follow-up appointment was organized at 6-12 months.

## RESULTS

Despite the fact that thyroid surgeries had been performed in our clinic on about 90 patients per year, the eight patients in our study group were referred from the endocrine clinic.

The patients underwent MIP, having been referred with various symptoms of hyperparathyroidism such as decreased bone mineral density, nephrolithiasis and acute pancreatitis or subjective symptoms like depressed mood. In all patients, 99mTc-labelled

**Table 2.** Preoperative and postoperative laboratory results of the patients

Patient no	Preoperative PTH (pg/mL)	Preoperative Ca (mg/dL)	Preoperative urine Ca (mg/day)	Preoperative P (mg/dL)	Frozen	Pathology result	Localization of parathyroid pathology via MIP	Postoperative PTH (pg/mL)	Postoperative Ca (mg/dL)
1	300	11.8	346	1.8	Not done	Adenoma	On the left thyroid lobe inferior lodge	64	9.4
2	143	11.7	368	2.3	Not done	Adenoma	On the left thyroid lobe inferior lodge	23	8.6
3	190	11.5	359	2.0	Not done	Adenoma	On the right thyroid lobe inferior lodge	21	10.0
4	1,083	11.2	269	4.0	Not done	Adenoma	On the lower pole of the thyroid at the the clavicle level	67	8.7
5	175	12.6	828	3.0	Positive	Adenoma	On the lower pole of the right thyroid lobe	5	9.2
6	153	11.0	336	2.0	Positive	Adenoma	Below the lower pole of the right thyroid	70	8.9
7	140	13.5	440	1.9	Positive	Adenoma	Next to recurrent laryngeal nerve in the left thyroid lobe lower pole	27	8.6
8	134	13,4	227	2.9	Not done	Adenoma	On the lower pole of the right thyroid	8	9.2
9	284	12.6	383	2,1	Not done	Adenoma	On the lower pole of the left thyroid	15	9.8
10	223	10.7	286	2,4	Positive	Adenoma	On the left thyroid lobe superior pole	30	9.4
11	303	11.5	513	2.0	Negative	Hyperplasia	On the left thyroid pole superior pole	46	9.0

PTH: Parathyroid hormone; Ca: Calcium; P: Phosphor; MIP: Minimal invasive parathyroidectomy.

sestamibi imaging with SPECT and USG were used to indicate the likely location of parathyroid adenomas (Figure 1). Parathyroid adenoma was documented by USG only in five patients. Although neck USG was reported as within normal limits in six patients, all parathyroid pathologies were identified by <sup>99m</sup>Tc-labelled sestamibi imaging with SPECT in accordance with surgical localization of each patient.

Two foci in the left superior and right superior thyroid poles were reported in the 11<sup>th</sup> patient by <sup>99m</sup>Tc-labelled sestamibi imaging with SPECT. In this patient, USG reported a 2 cm parathyroid adenoma located in the posterior region of the left thyroid lobe. So, we scheduled MIP procedure on the left side in the 11<sup>th</sup> patient. At 12 minutes post-excision of suspected adenoma in this patient, IOPTH dropped by 50% from the pre-excision

level. Hence, the right side examination was not done. Decrease was noted in the one-hour postoperative PTH measurement too. This patient was seen in the outpatient clinic four weeks after MIP procedure and assessed for any symptoms or complications. Parathyroid hyperplasia was reported by pathologic examination, but persistent hyperparathyroidism was identified with laboratory analysis. Thus, BCE was performed as a second surgical procedure in this patient with persistent hyperparathyroidism after MIP procedure. Parathyroid hormone and calcium levels were measured within normal limits at postoperative six months later.

In other 10 patients, a single parathyroid adenoma was reported by <sup>99m</sup>Tc-labelled sestamibi imaging with SPECT. None of the 10 patients showed symptoms of

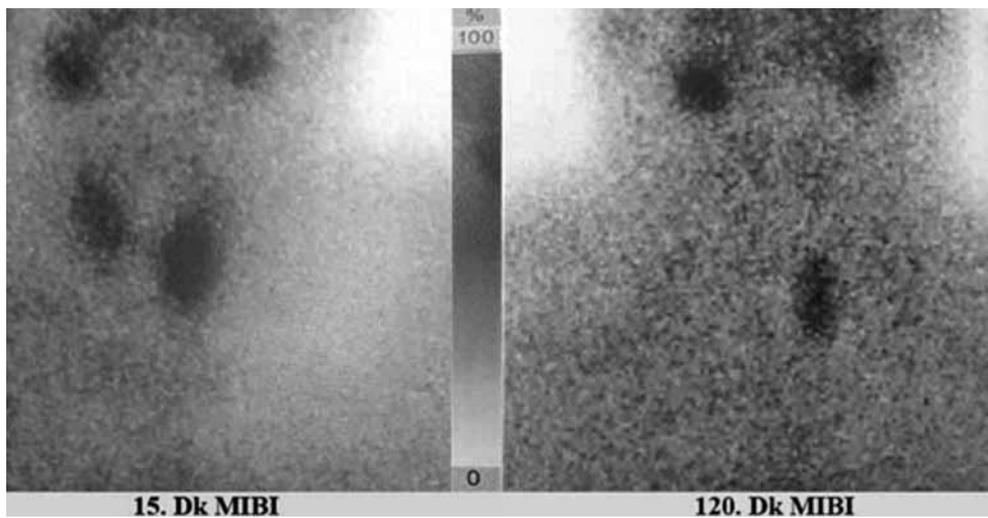


Figure 1. Technetium-99m-labelled sestamibi imaging with single photon emission computed tomography of adenoma (9<sup>th</sup> patient).

hyperparathyroidism or hypocalcemia in all postoperative examinations. Effective treatment was provided by MIP procedure as the first surgical procedure. MRI had been used in two patients whose findings were correlated with scintigraphy. On the other hand, ectopic location was detected by <sup>99m</sup>Tc-labelled sestamibi imaging in the fourth patient. Ectopic location was also confirmed by surgical findings in this patient.

The mean preoperative PTH and calcium levels were 284.36 (range 134-1,083 pg/mL) and 11.9 (range 10.7-13.5 mg/dL) respectively. After excision, PTH levels fell more than 50% from preoperative baseline levels. Intraoperative PTH measurement was done on six patients. Also, IOPTH dropped by 50% from the pre-excision level in all patients. We used frozen section analysis on five other patients in our study (Table 2).

Focal exploration and parathyroid adenoma excision was successfully carried out in 10/11 patients (90.9%) as the first surgical procedure, with the presence of adenoma being confirmed by subsequent postsurgical pathology results in all 10 patients (Figure 2). However, a postsurgical pathology result was reported as parathyroid hyperplasia in one patient who had two foci according to preoperative <sup>99m</sup>Tc-labelled sestamibi imaging. None of the patients who underwent MIP in our clinic had calcium replacement.

## DISCUSSION

Primary hyperparathyroidism causes excessive secretion of PTH and hypercalcemia due to diseases of one or more parathyroid glands in the absence of significant renal dysfunction. Since the parathyroid glands were identified by Sir Richard Owen during an autopsy in 1849, the field of parathyroid surgery has gradually evolved over the past 160 years. Increases in the reliability of localization studies have also allowed MIP to become the initial procedure as an alternative approach to conventional BCE for patients with localized adenoma. It is now accepted that patients with PHPT caused by a solitary adenoma undergo MIP procedure in many centers.<sup>[8,11]</sup> In accordance with the

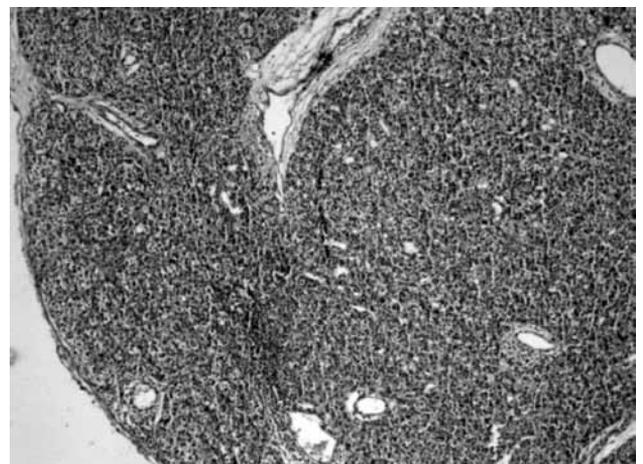


Figure 2. The histopathologic view of the adenoma (H-E x 100).

literature, we scheduled MIP as a first surgical procedure in all patients with biochemically proven PHPT where parathyroid pathologies were also identified by preoperative localization studies.

The advantages of MIP are the improved cosmetic result from the smaller incision, lower risk of recurrent laryngeal nerve injury, decreased postoperative hypocalcemia, decreased postoperative pain, shorter operating time and same-day discharge. Most importantly, surgical outcomes have been reported as over 98% cured with only 1-3% complication rates. These results indicate that MIP has comparable effectiveness levels to conventional BCE.<sup>[4,5,12]</sup> In our study, MIP was successfully carried out all patients in our clinic as a first surgical procedure. There were no complications, such as recurrent laryngeal nerve injury, hematoma, and the need to use for analgesics or calcium.

Successful surgical treatment of parathyroid diseases depends on accurate localization and identification studies of abnormal parathyroid glands. Embryological development of parathyroid glands should also be kept in mind because failure of imaging may indicate an ectopic site or an aberrant hyperfunctioning parathyroid gland.<sup>[3,13,14]</sup> So, two concordant imaging signs to confirm the location of the hyperactive gland are considered as critical for deciding to use MIP in clinical practice. The sensitivity of preoperative examination of parathyroid adenomas is increased from 94 to 99% with concordant USG and 99mTc sestamibi scintigraphy.<sup>[15]</sup> In our study, parathyroid pathologies such as multigland disease and ectopic location were correctly identified by 99mTc-labelled sestamibi imaging and confirmed by surgical localization in each patient. Single parathyroid adenoma was accurately reported by 99mTc-labelled sestamibi imaging in 10 patients and effective treatment was provided by MIP procedure as the first surgical procedure in these patients.

On the other hand, the sensitivity of USG for identifying parathyroid adenomas varies from 70 to 80%. Although USG has such advantages as noninvasive, low-cost and non-ionizing procedure, the accuracy of USG findings highly depends on the experience and skill of the operator.<sup>[2]</sup> It has poor sensitivity for locations in the substernal, retrotracheal and retroesophageal

spaces due to acoustic shadowing from overlying bone or air spaces. In addition, its sensitivity falls to 40% in patients with prior failed surgical exploration.<sup>[14]</sup> In our study, it failed to detect parathyroid pathology in six (54.5%) patients whose neck USG was reported as within normal limits. Ultrasound findings were correlated with scintigraphy findings in only three patients. Ultrasound failed to detect patients with multigland hyperplasia and ectopic location. It is acknowledged that ectopic location, double adenomas and multigland hyperplasia in patients with PHPT have been found in about 25%, 4%, and 6%, respectively.<sup>[16,17]</sup> Therefore, we recommend that any additional localization technique should be performed preoperatively or perioperatively as an alternative to USG to identify a wide range of parathyroid pathologies.

Ultrasound is often used in combination with other imaging tools for preoperative identification of aberrant parathyroid tissue before MIP procedure. Technetium 99m-labelled sestamibi imaging and USG are mostly preferred together.<sup>[18,19]</sup> In our study, 99mTc-labelled sestamibi imaging with SPECT and USG were used for preoperative examination in all patients. Some authors suggest that CT or MRI provides the topographical information in patients with mediastinal ectopic disease or persistent hyperparathyroidism after surgery.<sup>[3]</sup> The overall sensitivity of CT is increased to 80% by intravenous contrast enhancement when hyperplastic parathyroid glands are hypervascular. On the other hand, some authors suggest combined use of parathyroid scintigraphy and MRI for high accuracy in the preoperative identification studies.<sup>[14]</sup> In our study, MRI was used in two patients and we also found correlation between MRI and surgery findings.

The success rate of the MIP procedure was reported as 95% by many authors.<sup>[20]</sup> In our study, clinical improvement could not be achieved by MIP procedure in only one patient whose 99mTc-labelled sestamibi imaging reported foci of parathyroid pathology in both thyroid lobes. We scheduled an MIP procedure on the left side of the neck in this patient because USG reported a 2 cm parathyroid adenoma located in the posterior region of the left thyroid lobe. Although IOPTH dropped by 50% from the pre-excision level 12 minutes post-excision of the suspected adenoma, persistent hyperparathyroidism

was identified in four weeks after the MIP procedure. Also, parathyroid hyperplasia was confirmed by pathological examination in patients with multigland disease. The success of MIP procedure depends on concordance with preoperative identification studies. In the absence of concordance, we think that  $^{99m}\text{Tc}$ -labelled sestamibi imaging data should be considered more valuable than USG.

Treatment results for BCE are greater than 95% cure with a complication rate of less than 4%.<sup>[21]</sup> It remains the standard procedure for patients with multigland hyperplasia, multiple endocrine neoplasia, parathyroid cancer or failure of preoperative localization.<sup>[9]</sup> Because MIP can underestimate in patients with multigland disease, it might increase the risk of persistent or recurrent hypercalcemia.<sup>[22]</sup> In our study, whereas multigland pathology was revealed by  $^{99m}\text{Tc}$ -labelled sestamibi imaging in one patient preoperatively, BCE was performed as the second surgical procedure in this patient because of persistent hyperparathyroidism after MIP procedure.

Technetium  $^{99m}$  sestamibi is easy to perform and has proven highly sensitive and specific, able to detect 100 mg hyperfunctioning parathyroid glands. It is also considered applicable for parathyroid disease with continued increased uptake in the late phase. Technetium  $^{99m}$ -sestamibi is released from the thyroid tissue faster than parathyroid tissue. This dual-phase imaging technique operates through a simple basic procedure based on the differential washout rate of  $^{99m}\text{Tc}$  sestamibi from thyroid and parathyroid tissue. Sestamibi with SPECT provides three-dimensional information with improved contrast resolution, while SPECT offers the advantage of better discrimination of focal  $^{99m}\text{Tc}$ -sestamibi retention in thyroid nodules and parathyroid tissue. Despite its greater cost for routine use, most authors now favor the wider application of this imaging modality.<sup>[9,14,23,24]</sup> Ultrasonography provides additional information on the depth of parathyroid adenoma. However, the operator's experience is critical for the accuracy of USG. From our study's result, we conclude that sestamibi with SPECT provides more comprehensive information than other preoperative tools.<sup>[14]</sup>

In general, most experienced surgeons believe that they can distinguish normal glands from abnormal ones by perioperatively evaluating the size, shape and color of the parathyroid glands. They believe that an enlarged parathyroid gland is an adenoma if the others are visually normal. In fact, difficulties associated with parathyroidectomy for PHPT relate to variability in the number of parathyroid glands, different locations of normal and abnormal glands, and problems in distinguishing normal glands from those that are subtly diseased. Therefore, it is very important to determine if adenoma caused pathology by preoperative identification studies and to detect hyperactive glands preoperatively.<sup>[14]</sup>

During parathyroid surgery, it can be difficult to distinguish an adenoma from hyperplasia. Some surgeons therefore attempt to confirm the presumptive diagnosis by frozen section analysis. However, multigland disease can cause enlargement of all four glands, while asymptomatic hyperplasia may appear with normal-sized glands and confuse the diagnosis, not only intraoperatively but on histopathological examination. If Miami criterion is achieved, eucalcemia and normalization of PTH values occur in 97% of patients and the use of IOPTH measurement has also been encouraged to confirm the success of parathyroidectomy at the time of MIP, given that not all four parathyroid glands are visible.<sup>[9,14]</sup> So, we preferred IOPTH measurement for our patient with multigland disease in our study. Although the patient's PTH level had fallen more than 50% from the preoperative baseline level after excision in accordance with the Miami criteria, postoperative clinical success was not achieved in this patient and further operation was required. On the other hand, we used IOPTH measurements in other five patients with one focus by  $^{99m}\text{Tc}$ -labelled sestamibi imaging. Postoperative calcium and PTH levels returned to normal value in these five patients during the follow-up period. False-positive results can be attributed to hemolysis, double adenomas or removal of asymmetrically enlarged glands in unsuspected multigland hyperplasia.<sup>[9]</sup> In our study, a false positive result was obtained in one patient with multigland hyperplasia.

Some surgeons recommend the MIP procedure without requiring IOPTH measurement if there

are concordant preoperative imaging studies. This may be appropriate in hospitals where access or financial constraints prevent the use of IOPTH monitoring.<sup>[9]</sup> In our study, IOPTH measurement was done on five patients because of the results of preoperative imaging studies were not compatible with each other.

Clerici et al.<sup>[24]</sup> studied 69 patients who underwent conventional BCE with IOPTH monitoring, and found that multiple-gland disease was missed in 75% of patients. On the other hand, Carneiro-Pla et al.<sup>[25]</sup> suggest that IOPTH should be used to guide parathyroid excision in every patient with sporadic primary hyperparathyroidism. They studied 519 consecutive patients with sporadic primary hyperparathyroidism. They found that sestamibi as a single adjunct missed 87% of patients with multiglandular disease. Including patients with negative (8%) and incorrect (12%) sestamibi, IOPTH changed the operative management in 17% of patients and led to operative success in 97%. In our study, IOPTH measurement was also unhelpful for finding the hyperactive gland in patients with multigland disease.

Probe guidance is helpful in evaluating the completeness of parathyroid tissue removal. However, although it is highly effective for the intraoperative detection of solitary parathyroid adenomas, difficulties might arise in those rare patients with multigland disease with a "dominant" parathyroid gland. In addition, the cost-effectiveness of MIP with probe guidance (PG-MIP) has been questioned. Probe guidance-MIP can also be applicable to patients with persistent or recurrent hyperparathyroidism. However, the radiation exposure dose to the surgeon and operating theater personnel should be minimized by administering the lowest dose of <sup>99m</sup>Tc-sestamibi proven to be effective for performing PG-MIP.<sup>[14,26]</sup>

In general practice, when a parathyroid adenoma has been concordantly localized with USG and <sup>99m</sup>Tc sestamibi scintigraphy, excellent results can be achieved using MIP techniques, with or without IOPTH. However, while it is cheap and easily accessible, USG is insufficient in patients with prior failed surgical exploration or ectopic adenomas. A further handicap is that its reliability depends on the operator's experience.<sup>[14]</sup> In our study, MIP procedures were

successfully performed in all patients who had one focus according to the information obtained by <sup>99m</sup>Tc sestamibi scintigraphy. The addition of SPECT imaging proved very helpful in giving additional information, such as the depth of the lesion and its topographic correlation with other anatomical structures. Thus, even though a larger series and longer follow-up studies are still required, we thought that <sup>99m</sup>Tc sestamibi scintigraphy with SPECT can provide objective topographic information about the depth of adenomas and identifies multifocal disease or ectopic pathologies even in patients with prior failed surgical exploration. Despite working with a limited number of patients but also significant number within one year for an ENT clinic, we conclude that <sup>99m</sup>Tc sestamibi scintigraphy with SPECT and frozen section analysis can provide meaningful information and advantages over other preoperative localization techniques.

### Conclusion

Our study results suggest that the reliability of preoperative evaluation may be improved by using <sup>99m</sup>Tc sestamibi scintigraphy with SPECT as the initial imaging tool for detection of hyperactive parathyroid glands that cannot be localized correctly by other imaging tools. We believe that the preoperative determination of ectopic localizations or multi-focal parathyroid pathologies are not influenced negatively by using <sup>99m</sup>Tc sestamibi scintigraphy with SPECT even in patients with prior failed surgical exploration.

### Declaration of conflicting interests

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