



Radio guided Parathyroidectomy in Oncologic Patients using Portable Gamma-Camera: a Single Centre Experience

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Abstract

Objective: The objective of this study was to evaluate the utility of portable gamma-camera at real time intraoperative imaging for assessing localization of parathyroid adenoma.

Materials and Methods: This was a retrospective analysis of patients with parathyroid adenoma and oncologic underlying condition, such as breast cancer, renal, prostate, cervix, ovarian, and melanoma; who underwent radio guided surgery at Instituto Nacional de Cáncerología (INCan, México). Planar scintigraphy was performed 15 minutes after intravenous injection of ^{99m}Tc-MIBI, 60-120 min before intervention. The portable gamma-camera was used to identify the adenoma during surgery, as well as to verify if it was removed completely. All surgical specimens were taken for intraoperative histopathological evaluation.

Results: 20 patients were diagnosed with parathyroid adenoma (17 with usual location and 3 with ectopic location). Parathyroid adenoma was localized Intraoperatively with a portable gamma-camera in all patients, reducing the time of surgery. All surgical specimens were confirmed as parathyroid adenoma in the intraoperative and definitive histopathological evaluation.

Conclusion: Parathyroid scintigraphy with portable gamma-camera in intraoperative identification of parathyroid adenoma has contributed to the development of minimally invasive parathyroidectomy. Therefore, in our opinion, in addition to the realization of preoperative scintigraphy, radio guided surgery with portable gamma-camera should always be performed, thus reducing complications, hospital stay, surgical and recovery time, with the same therapeutic effectiveness as classical treatment.

Keywords: Parathyroid adenoma; Portable gamma-camera; ^{99m}Tc-MIBI scintigraphy; Radioguided surgery; Minimally invasive parathyroidectomy

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Background

Primary hyperparathyroidism (PHPT) is a metabolic disorder It characterized by hyper secretion of parathormone parathyroid as a consequence of alterations in physiology at least one parathyroid gland; such alteration may be due to glandular hyperplasia, parathyroid adenoma, rarely parathyroid carcinoma or associated symptoms of multiple endocrine neoplastic syndromes I and II [1,2]. Parathyroid cells exhibit both increased proliferative activity (leading to enlarged glands) and decreased sensitivity to the inhibiting effect of increased calcium concentration on PTH secretion (altered set point). Parathyroid adenoma has a prevalence of 1%, with maximum incidence is in the 3rd and 5th decade of life and being more common in women (3:1). Parathyroid adenomas have an ectopic location in 5-10% of cases and the most common location is anterior mediastinum [2,3]. The conventional surgical approach is bilateral neck exploration; nevertheless the use of ^{99m}Tc-MIBI scintigraphy Intraoperatively has made minimally invasive parathyroidectomy possible [4-6].

Parathyroid adenoma assessment with ^{99m}Tc-MIBI is based on longer retention of the tracer in parathyroid compared with thyroid tissue, following injection, ^{99m}Tc-MIBI is distributed by the bloodstream and is kidnapped intracellularly by mitochondria; the large number of mitochondria cells present in most adenomas parathyroid makes a lot of radiopharmaceutical is grasped and reflects the increase in metabolic activity adenomas compared to the surrounding thyroid tissue and normal parathyroid glands [7-9].

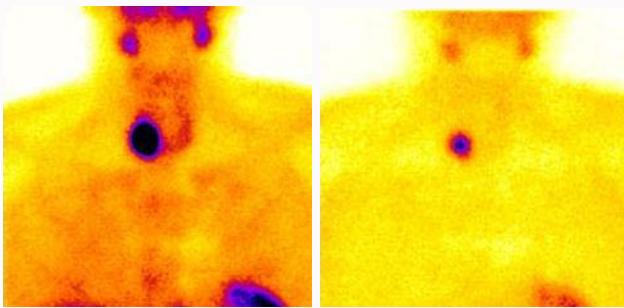


Figure 1: Static planar double-phase parathyroid scintigraphy with ^{99m}Tc -MIBI. (Left) Image at 15 min shows physiologic early uptake in thyroid gland, with clear focus of intense increased accumulation at lower pole of right thyroid lobe. (Right) Late scan shows almost complete washout of ^{99m}Tc -MIBI from thyroid gland, with obvious focal retention of radioactivity at lower pole of right thyroid lobe. Minimally invasive radio guided surgery confirmed presence of parathyroid adenoma.

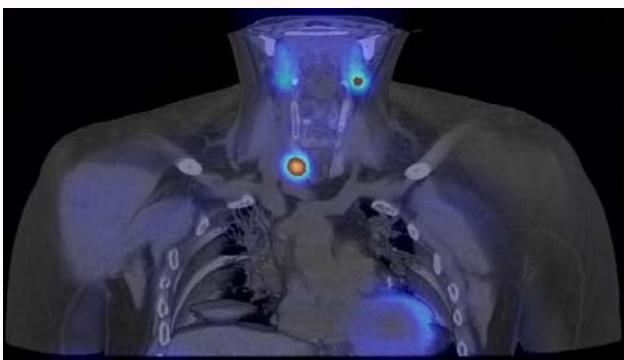


Figure 2: Image fusion of corresponding coronal slices of SPECT/CT demonstrates that lesion with focal increased uptake of ^{99m}Tc -MIBI is located in lower pole of right thyroid lobe.

The dual-phase parathyroid scintigraphy with ^{99m}Tc -MIBI has sensitivity and specificity of 91% and 98.8%, respectively, and is considered the best noninvasive study parathyroid for detection [10,11]. A portable gamma camera has recently been introduced for intra-operative visualization of radiotracer activity and can help to localize the tumor during operation. The intra-operative use of this portable device might lead to excision of additional parathyroid tissue affected. In theory, this camera can also be used to improve pre-operative adenoma or hyperplasia parathyroid visualization.

Provided that image quality and field of view are sufficient, a portable gamma camera could be used when a conventional gamma camera is unavailable, occupied or increase the specificity of the lesion based on the amount of activity in the affected tissue [12]. There are few reports in literature about the use of portable gamma-camera (pGMC) in PHPT treatment [12-14].

Parathyroid surgery allows the surgeon to identify radio guided specifically abnormal or hyper functioning parathyroid gland, without the need for a scan extensive bilateral cervical looking for abnormal tissue macroscopically it might seem parathyroid and corroborate histologically also can facilitate the realization the procedure with local anesthesia and on an outpatient basis [13-15].

The objective of this study was to evaluate the utility of portable gamma-camera at real time intraoperative imaging for assessing localization of parathyroid adenoma in patients with oncologic disease.

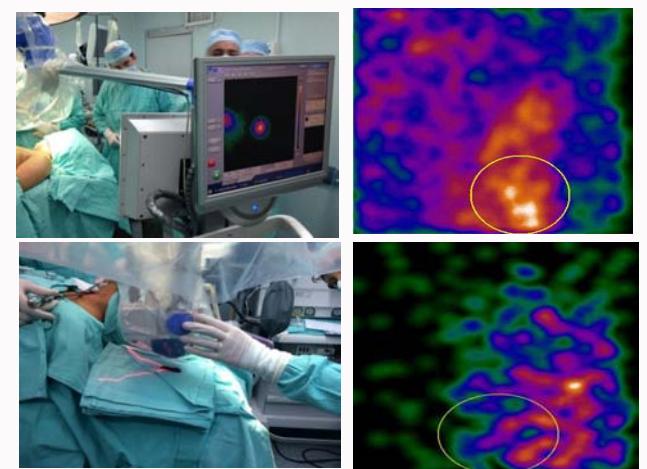


Figure 3. Surgical team making the radio guided parathyroidectomy. (Top left) Medical staff positioning the portable gamma-camera on the patient's neck 2 h after the intravenous injection of ^{99m}Tc -MIBI [approximately 740 MBq]. (Top right) Intraoperative images obtained with portable gamma-camera [Sentinella, Oncovision®] of parathyroid adenoma localized *in vivo* verified by the greater number of accounts within a ROI. (Bottom left) Images post-surgical resection of the adenoma's neck of the patient. (Bottom right) Images obtained with portable gamma-camera of *ex vivo* of parathyroid adenoma and verified by the number of accounts within the same ROI previously outlined.

Materials and Methods

This was a retrospective analysis of patients with parathyroid adenoma who underwent radio guided surgery at INCAn.

They included patients with biochemical and scintigraphy parameters of primary hyperparathyroidism.

Planar scintigraphy with the conventional gamma camera (Symbia, Siemens[®]) of the neck and thorax was performed 15 min and then 2-3 h after the intravenous injection of ^{99m}Tc -MIBI (approximately 740 MBq [20 mCi]) before intervention in all patients. The scan was considered positive for parathyroid disease when an area of increased uptake that persists on late imaging is found 60-120 min (Figure 1). Although only a marginal improvement in the overall detection rate of parathyroid adenomas is reported with SPECT(128x128 matrix, 60x25-s frames) was combined with CT (130Kv, 17 mA, B60s kernel), using hybrid camera, in this protocol each patient was carried out (Figure 2).

The portable gamma-camera (Sentinella, Oncovision[®]) was used to identify the adenoma during surgery with the same activity, after proper localisation, a minimally invasive parathyroidectomy with minicervicotomy was started. This portable gamma camera was equipped with a 4mm pinhole collimator and uses a CsI (Na) continuous scintillating crystal. The pinhole collimator was used to be able to visualize the whole surgical field. The was placed at a distance of 10cm over the neck of the patient. Intrinsic spatial resolution is 1.8mm, while extrinsic spatial resolution values are 7mm and 21mm for a distance of 3cm and 15cm respectively.

After removing the adenoma, the activity it was verified *in vivo* and *ex vivo*. It was taken as one whose site radioactivity counting was 20% higher than background radioactivity count, measured outside the central compartment neck (Figure 3).

All surgical specimens were taken for intraoperative histopathological evaluation.

Table 1: Clinical characteristics by patient before and after intervention.

Age	Sex	Oncologic disease	PTH before intervention (pg/ml)	PTH after intervention (pg/ml)	Calcium before intervention (mg/dl)	Calcium after intervention (mg/dl)	Location of parathyroid adenoma
47	Female	Breast cancer	165	50	11.4	8.9	Intrathyroidal
36	Female	Ovarian cancer	99	12	11.1	8.0	lower pole of right thyroid lobe
69	Male	Prostate cancer	178	19	11.8	10	Ectopic (anterior mediastinum)
41	Female	Breast cancer	70	51	11.8	9.4	lower pole of left thyroid lobe
38	Female	Breast cancer	213	36	12.1	9.0	lower pole of right thyroid lobe
50	Female	Renal cancer	185	21	10.3	9.1	Upper pole of left thyroid lobe
19	Male	Melanoma	58	19	10.9	9.8	Upper pole of left thyroid lobe
52	Female	Breast cancer	312	53	11.8	9.1	Upper pole of right thyroid lobe
30	Male	Renal cancer	104	44	8.9	9.1	lower pole of right thyroid lobe
60	Male	Prostate cancer	121	39	8.1	8.3	Upper pole of left thyroid lobe
22	Female	Breast cancer	96	16	11.9	8.9	Upper pole of right thyroid lobe
29	Female	Breast cancer	419	55	12.9	9.6	lower pole of left thyroid lobe
48	Female	Cervix cancer	189	28	10.8	9.4	Upper pole of left thyroid lobe
33	Female	Cervix cancer	57	40	10.2	10.1	Upper pole of right thyroid lobe
28	Female	Melanoma	80	33	12	8.8	lower pole of right thyroid lobe
30	Male	Renal cancer	294	27	10.8	9.4	lower pole of left thyroid lobe
39	Female	Breast cancer	169	39	11.3	9.7	lower pole of right thyroid lobe
18	Female	Melanoma	412	42	11.1	8.3	Ectopic (posterior cervico-mediastinal)
58	Male	Prostate cancer	338	53	7.7	8.9	Upper pole of left thyroid lobe
33	Female	Breast cancer	167	19	11.9	10.2	lower pole of right thyroid lobe

Results

Twenty patients were diagnosed with parathyroid adenoma (18 with usual location and 2 with ectopic location (Table 1), recruited from February 2009 to June 2015. Of 20 accrued patients, 14 (70%) were females and 6 (30%) were males. The average age was 39 years (IC 95%), with a range from 18 to 69 years.

In all cases the ^{99m}Tc -MIBI scintigraphy showed increased the concentration of the radiopharmaceutical in at least one gland parathyroid. The preoperative scintigraphy with ^{99m}Tc -MIBI showed sensitivity, specificity, diagnostic accuracy, PPV, and NPV results of 100%.

Parathyroid adenoma was localized intraoperatively with a portable gamma-camera in all patients, reducing the time of surgery. The type of radio guided surgery was: minimally invasive parathyroidectomy in 18 patients, and sternotomy in 2 patients (1 anterior mediastinal and 1 posterior cervico-mediastinal). All surgical specimens were confirmed as parathyroid adenoma in the intraoperative and definitive histopathological evaluation (Figure 4). The time from start of surgery to adenoma excision ranged from 15 to 45 min, mean 27 min (IC 95%). In all cases the radioactivity measured Intraoperatively with the gamma camera, identified the affected

gland, which coincided with the scintigraphic findings previous. The pMGC showed sensitivity, specificity, diagnostic accuracy, PPV, and NPV values of 100%.

No patient was identified disease multiglandular. All patients had normal levels of calcium postoperative serum with mean 9.5 mg / dl (IC 95%:7.65 -10.33 mg/dl), and PTH values with mean 47 pg/ml (IC95%: 10-55). At the clinical and laboratory followup after 1, 3, 6, and 12 months, no persistent or recurrent PHP was detected.

Discussion

Parathyroid scintigraphy with portable gamma-camera in intraoperative identification of parathyroid adenoma has contributed to the development of minimally invasive parathyroidectomy. The guidelines for Parathyroid scintigraphy can be summarized as follows: Only patients with a high probability of a solitary parathyroid adenoma and a normal thyroid gland should be considered, the most appropriate preoperative scintigraphic protocol should be selected on the basis of thyroid and parathyroid imaging information, the radiation exposure dose to the surgeon and operating theater personnel should be minimized by administering the lowest dose of ^{99m}Tc -MIBI proven to be effective for performing of Parathyroid scintigraphy, both *in vivo* or *ex vivo* γ -probe counting

and intraoperative PTH measurement should be used to evaluate the success and completeness of surgery [16-19]. Our series confirms the value of scintigraphy in the detection and localization of ectopic adenomas. Scintigraphy detected all the parathyroid adenomas in both planar and tomographic images. The use of gamma probes allows the detection of sources of radiotracers administered at the time of induction of anesthesia and well counter during the procedure. Gamma probes, however, translate focus intensity into count rate and audio signaling and as such do not guarantee the more precise localization given by imaging, and do not exclude de possibility of the more adenomas [21].

Although of pMGC in PHP treatment has been used for years in the treatment of ectopic parathyroid adenoma, no large series of patients treated with this procedure have been published in the literature.

Hypercalcemia occurring in patients with advanced breast cancer is generally due to osteolytic metastases or to the activity of circulating tumor-derived products. In these conditions, the production of endogenous PTH is reduced. The frequency of hypercalcemia due to primary hyperparathyroidism in breast cancer is unknown [20].

It is known that high levels of PTH are associated with increased bone resorption and degradation of the bone matrix. There are isolated reports of low serum calcium and high PTH levels in a number of studies involving small numbers of patients with advanced prostate cancer. The extent of these abnormalities and their pathophysiological significance is not well defined [22].

Estrems and cols. [13] evaluated the feasibility of this method in a group of 29 patients: side localization with pMGC showed a sensitivity of 86.6% and a specificity of 90.9% compared to the 79.3% and 92.5%, respectively, of preoperative investigations (ultrasound + scintigraphy) while quadrant localization showed a sensitivity of 83.3% and a specificity of 90.9%, when compared to 48.35% and 72.7%, respectively, reported in the preoperative surveys.

Casella and cols. (Casella et al. [12]) evaluated the effectively of the pMGC in a group of 20 patients properly localized all lesions by side (diagnostic accuracy 100%) with both a sensitivity and a specificity of 100%, while as far as quadrant was considered pMGC showed a diagnostic accuracy of 98.1%, a sensitivity of 95.0%, and a specificity of 98.8%.

This differentiates our protocol from other protocols described by diverse authors. Casella et al. [12] perform intraoperative image acquisition protocol, we intravenously infused 185 MBq of ^{99m}Tc -sestaMIBI immediately after the induction of general anesthesia. Casara et al. [19] and Rubello et al. [15] perform minimally invasive parathyroidectomy according to a two day protocol, also with an established dose of radionuclide (37 MBq) that is injected just before starting surgery. The absence of radiotracer uptake sources in the post excision images confirms the completeness of the parathyroidectomy, completeness that is usually confirmed by the significant fall in PTH, also.

Detect this condition can be very complicated, especially in patients with poor response to treatment, and that the first duty of the physician is to rule out the possibility of progression; however when symptomatology, especially gastrointestinal and mental, not improve despite good management, it is necessary to consider hyperparathyroidism, even when calcium levels are within normal

values, especially in prostate cancer.

Despite the limited number of patients studied, our study has confirmed the possibility of replacing the intra operative PTH measurement with the intraoperative use of the pMGC, because in all cases the images obtained after removal of the parathyroid lesions were comparable to the fall in post operative PTH levels. The pMGC may also be a possible alternative to preoperative scintigraphy with ^{99m}Tc -sestaMIBI.

Conclusion

In our opinion, in addition to the realization of preoperative scintigraphy, radio guided surgery with portable gamma-camera should always be performed, an smaller incision reduced complications, less surgical trauma, shorter length procedure is a very attractive surgical approach to treat patients with PHPT secondary to solitary parathyroid adenoma. has proven to be technically easy, safe, and with a low morbidity rate in the hands of a skilled surgeon. We suggest that serum PTH should be determined in all breast cancer patients with increased serum calcium concentration, especially in those with no evidence of metastatic disease; also in patients with other oncologic conditions with symptomatology that does not subside despite the good management, without ruling out possibility of disease progression.

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