

## Original Research Article

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# Surgical outcome of radioguided parathyroidectomy in primary hyperparathyroidism

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## ABSTRACT

**Background:** Focused parathyroidectomy is the adequate treatment for primary hyperparathyroidism for localised disease. Adequacy of resection is confirmed by the availability of intraoperative parathormone assay (iOPTH). In the absence of availability of iOPTH assay, the radio guided surgery is an option. The aim of this study was to evaluate the feasibility of radioguided parathyroidectomy in tertiary care centre in India and to compare the overall success rate, operative time, hospital stay and postoperative outcome between focused open and radioguided parathyroidectomy.

**Methods:** This was a prospective study which included 30 primary hyperparathyroidism patients with a single gland disease localised on Tc<sup>99m</sup> Sesta MIBI scan. Patients were randomized into two equal groups, and they underwent focused open or radioguided parathyroidectomy. Patients were followed up for three months.

**Results:** All patients achieved biochemical cure as evident by the normalization of serum calcium and parathormone levels after surgery. The mean incision length, and operative time in this study was significantly better for radioguided parathyroidectomy ( $p=0.0001$ ,  $<0.0001$  respectively). There was no perioperative complications like recurrent laryngeal nerve injury, gland rupture, or bleeding in either group. However, there seems to be higher grade of pain experience by the patients who underwent open focused parathyroidectomy ( $p<0.0001$ ).

**Conclusions:** Radioguided parathyroidectomy has excellent cure rate for PHPT with an added advantage of short operative time & incision length and less post-operative pain. Radioguided parathyroidectomy seems to be a good alternative in the absence of availability of iOPTH assay and frozen section.

**Keywords:** Parathyroidectomy, Primary hyperparathyroidism, Radioguided parathyroidectomy

## INTRODUCTION

Primary hyperparathyroidism (PHPT) has a worldwide prevalence of 0.2 to 0.5 % and is characterised by hypercalcemia and increased levels of parathyroid hormone (PTH).<sup>1</sup> PHPT is mainly due to single adenoma in 85-90%, parathyroid hyperplasia in 10-15% and rarely

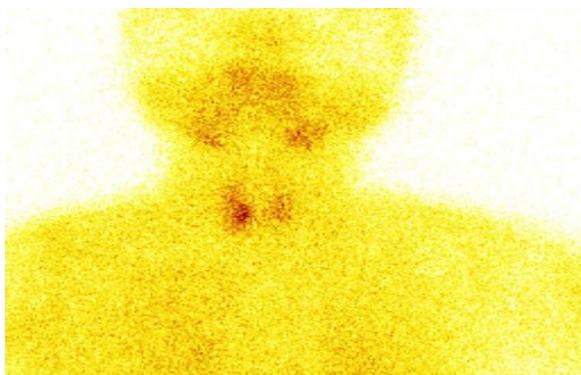
secondary to parathyroid carcinoma.<sup>2</sup> The evolution of surgical management of PHPT has been continuously changing with the development of technological advancement and better localizing investigations. The classical surgical approach for PHPT was bilateral neck exploration with excision of abnormal parathyroid gland; which was performed first by Felix Mandl in Vienna in

1925 with success rate of up to 97%.<sup>3,4</sup> Consequently in 1980s there was shift from bilateral approach to unilateral neck exploration as most of PHPT was due to single gland disease.<sup>2</sup> This approach gained universal acceptance only after the availability of <sup>99m</sup>Tc-sesta MIBI scan. The combination of USG and <sup>99m</sup>Tc scan localizes PTH adenoma in 95%.<sup>5</sup> With the advent of better pre op localization and intra-operative PTH (iOPTH) assay; focused surgical management of PHPT came into existence.<sup>6</sup> There are various prospective and retrospective studies comparing focused parathyroidectomy (PTx) with bilateral neck exploration showing comparable success rate.<sup>7,8</sup> Focused PTx has an additional advantage of avoiding recurrent laryngeal nerve injury, bleeding and also hypocalcemia secondary to handling of normal parathyroid glands in bilateral neck exploration. Focused PTx can be open, radio guided, endoscopic or robotic.

Minimally invasive radio guided parathyroidectomy (MIRP) was developed by Norman et al in 1997 and it uses gamma probe to determine the exact location of the abnormal gland with 100% cure rate. With the use of radio guided surgery, need for frozen section and iOPTH analysis is not there.<sup>9</sup> Hence this study was conducted to study the feasibility of MIRP in tertiary care centre in India and to compare the overall success rate, operative time, hospital stay and postoperative outcome between focused open and radioguided parathyroidectomy.

## METHODS

This is a prospective study conducted in the department of General Surgery and Department of Nuclear Medicine at PGIMER, Chandigarh from 1 July 2018 to 31 December 2019. All patients of PHPT with a single gland disease localised on <sup>99m</sup>Tc Sesta MIBI scan were included. Approval from the institute's ethical committee was obtained. Thirty patients were included and they were randomized in two equal groups of 15 patients. Informed written consent was taken from all the patients.



**Figure 1: Hybrid SPECT image of mibi scan used in localizing the abnormal parathyroid gland.**

All PHPT patients were subjected to preoperative localization of parathyroid adenoma by giving injection

of 740 MBq (20 mCi) MIBI and undergoing dual phase technique. Early phase image was taken at 10 minutes and delayed phase at 60 minutes. This was followed by SPECT CT scan to confirm the position of parathyroid adenoma identified by dual phase technique (Figure 1).

### **Method for focused open parathyroidectomy**

Open PTx was performed under general anaesthesia. Incision was made over the left/right side of neck as per localization preoperatively by MIBI scan. Abnormal parathyroid gland was identified and removed. Incision was closed and removed parathyroid gland was sent for frozen section. Diagnosis of parathyroid adenoma was confirmed on histopathological examination. Post-operative serum calcium and PTH hormone levels were monitored on postoperative day 1 and subsequently at one and three months after PTx.

### **Method for MIRP**

MIRP was performed under general anaesthesia. On the day of surgery, the patient was given intravenous injection of 3 mCi MIBI one hour prior to surgery and early image was taken to confirm the already identified adenoma. Handheld gamma probe EUROPORBE 3 manufacture by EURORAD SA, France (Figure 2) was used to count the highest number of radioactivity counts of parathyroid adenoma and the background in the scan room. Patient was shifted to operation theatre. The site of highest count was noted by gamma probe EUROPORBE 3 and incision site was marked. Incision was made and gamma probe EUROPORBE 3 was used intra-operatively to identify the area of higher radioactivity which corresponded to location of abnormal parathyroid adenoma (Figure 3).



**Figure 2: Gamma probe EUROPORBE 3 used in radioguided parathyroidectomy.**

The abnormal parathyroid gland was excised. If the excised tissue had the radioactivity count of more than 20% of background activity, it was considered as confirmation of parathyroid adenoma. Radioactive counts in the bed were also checked to look for any residual or

second adenoma. Incision was closed and removed parathyroid gland was sent for histopathological confirmation. Post-operative serum calcium and PTH hormone levels were monitored on postoperative day 1 and subsequently at one and three months after PTx.



**Figure 3: Intra operative use of EUROPORBE 3 to localize abnormal parathyroid gland.**

#### Statistical analysis

The statistical analysis was carried out using IBM SPSS (Statistical Package for Social Sciences) version 20. All quantitative variables were estimated using measures of central location (mean and median) and measures of dispersion (standard deviation). For normally distributed data, mean was compared with respect to independent t-test (for two groups). Pearson Correlation method was used for relationship between parameters. All statistical tests were seen at two-tailed level of significance ( $p \leq 0.01$  and  $p \leq 0.05$ ).

#### RESULTS

**Table 1: Comparison of preoperative and 3 month's postoperative biochemical parameters in PHPT patients who underwent radioguided or open parathyroidectomy.**

	Serum calcium (8.6-10.2 mg/dl)		PTH (5-65 pg/ml)	
	Preoperative (mean $\pm$ SD)	Postoperative (mean $\pm$ SD)	Preoperative (mean $\pm$ SD)	Postoperative (mean $\pm$ SD)
<b>Radioguided Parathyroidectomy</b>	11.68 $\pm$ 1.34	8.54 $\pm$ 0.7	784.27 $\pm$ 550.80	45.39 $\pm$ 28.56
<b>Open Parathyroidectomy</b>	11.84 $\pm$ 0.98	8.5 $\pm$ 0.34	732.13 $\pm$ 876.07	40.63 $\pm$ 19.04

Primary Hyperparathyroidism (PHPT), Parathormone (PTH)

The operative time for both the groups was considered from the time of skin incision to the excision of gland. The mean operative time for radioguided and open PTx was 9.33 $\pm$ 1.54 minutes and 19.33 $\pm$ 4.15 minutes respectively ( $p < 0.0001$ ). (Table 2) The incision length in radioguided PTx was 1.42 $\pm$ 0.15 cm and was 2.08 $\pm$ 0.20 cm for open PTx ( $p < 0.0001$ ) (Table 2). None of the patient had any perioperative complication in either group. The mean hospital stay for radioguided PTx was 4.80 $\pm$ 4.77 days and for open PTx was 4.93 $\pm$ 3.83 days. There was no significant difference in postoperative hospital stay between two study groups. Both modality of the PTx had higher average days of postoperative stay as we do PTx

Mean age of all patients was 46.97 years (49.8  $\pm$ 12.12), with range of 21-73 years. Average age of patients who underwent radioguided and open PTx was 48.47 years (48.47 $\pm$ 12.06) and 45.47 years (45 $\pm$ 12.18) respectively. In radioguided surgery, total number of females was 13 and males were 2 whereas in open PTx, the total number of females was 14 and there was only one male patient. Majority of PHPT patients were symptomatic for the disease except one patient who was asymptomatic. Majority of patients had nephrolithiasis (42%) followed by generalized malaise (40%), bone disease (30%), joint pain (20%), and headache (20%).

Mean serum PTH, serum calcium and vitamin D levels for patients who underwent radio guided PTx were 784.27 550.80 pg/ml, 11.68 1.34 mg% and 34.56 18.33 ng/ml respectively. Mean serum PTH, serum calcium and vitamin D levels for patients who underwent open PTx was 732.13 $\pm$ 876.07 pg/ml, 11.84 $\pm$ 0.98 mg% and 26.59 $\pm$ 16.96 ng/ml respectively. All patients were monitored with serum calcium and PTH level postoperatively as well as on subsequent follow up (Table 1). Both the modality of surgery was effective in surgical management of PHPT. The parathyroid gland which was removed during surgery was confirmed to be parathyroid adenoma on histopathology in all patients.

The mean radioactivity count in scan room for the parathyroid gland was 610 $\pm$ 261 cpm (counts per minute) and for background was 242 $\pm$ 94.41 cpm. The mean radioactivity count for the parathyroid adenoma after excision was 703 $\pm$ 407.58 cpm and it was 253 $\pm$ 93.46 cpm in the thyroid bed.

after admitting patient and had protocol of discharging patient only on next OPD day.

Of 15 patients in radioguided PTx group, none developed postoperative hematoma. Pain score was assessed by VAS score. Three patients had postoperative VAS of 2 and 12 patients had VAS of 1. In the open PTx group also no patient developed any postoperative hematoma; however, 13 patients had VAS pain score of 2 and two patients had score of 3. Patients who underwent Radioguided PTx had lesser VAS pain score compared to the patient who underwent open PTx. This difference was statistical significant ( $p < 0.0001$ ) (Table 2). All patients

who underwent Radioguided PTx had better satisfaction than those who underwent open PTx due to small surgical

scar and less postoperative pain.

**Table 2: Comparison of operative time, incision length, hospital stay and visual analogue score of PHPT patient who underwent radioguided vs or open parathyroidectomy.**

Variables	Radioguided parathyroidectomy	Open parathyroidectomy	P value
<b>Operative time (minutes) mean<math>\pm</math>SD</b>	9.33 $\pm$ 1.54	19.33 $\pm$ 4.15	0.0001
<b>Incision length (cm) mean<math>\pm</math>SD</b>	1.42 $\pm$ 0.15	2.08 $\pm$ 0.20	0.0001
<b>Hospital stay (days)</b>	4.80 $\pm$ 4.77	4.77 $\pm$ 3.83	NS
<b>Visual analogue score</b>			
Score 1	0	0	
Score 2	12	3	0.0001
Score 3	3	12	

## DISCUSSION

Aim of successful parathyroidectomy is to excise the abnormal parathyroid gland and to achieve biochemical cure by normalising serum calcium and PTH levels. Focused PTx provides comparable results to conventional bilateral neck exploration if preoperative localising investigation is combined with iOPTH assay. In centres, where iOPTH assay is not available confirmation of parathyroid adenoma depends on the availability of frozen section and success of surgery depends upon the postoperative serum PTH levels. Frozen section requires a good pathologist for accurate diagnosis.

MIRP is an option in the absence of availability of iOPTH assay and frozen section facility. MIRP technique uses intra-operative localization of parathyroid adenoma with the help of gamma probe. MIRP has been proven to be a successful procedure with infrequent morbidity and success rate (97 %) comparable to the time-honoured bilateral neck exploration with lesser cost, lesser hospital stay (1.1 $\pm$ 1.0 days) and better cosmetic compliance.<sup>10</sup> The superiority of MIRP has also been shown even in patients with PHPT who have undergone previous neck exploration for parathyroid or thyroid disease; with no intra-operative complication, with average operation time of 44 minutes and average incision of 3.0 $\pm$ 0.2 cm.<sup>11</sup>

In the present study, we achieved success rate of 100% in both open focused PTx and MIRP as evident by the normalization of serum calcium and PTH levels after surgery. The mean incision length, and operative time in this study was significantly better for MIRP (p 0.0001, <0.0001). This difference in operative time among two techniques is because of precise identification of gland by gamma probe. There was no perioperative complications like recurrent laryngeal nerve injury, gland rupture, or bleeding in either group. However, there seems to be higher grade of pain experience by the patients who underwent open focused PTx (p <0.0001). Patients who underwent radioguided PTx also had better satisfaction due to lesser post-operative pain and shorter incision

length. Therefore, MIRP acts as an important surgical adjunct to confirm abnormal parathyroid tissue by using hand held gamma probe by the surgeon. Radioactivity count above 20% from the background count in the thyroid bed also confirms that there is no residual hyperfunctioning parathyroid tissue.

Despite of small sample size in this study our study has confirmed the feasibility of MIRP with good outcome. It also has replaced the need of frozen section for tissue confirmation and serum PTH analysis for biochemical confirmation by providing equal cure rate in both groups.

## CONCLUSION

Open and radioguided PTx had equally good cure rate for PHPT with an added advantage of short operative time & incision length and less post-operative pain in those who underwent radioguided parathyroidectomy. MIRP seems to be a good alternative in the absence of availability of iOPTH and frozen section.

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