

## ORIGINAL ARTICLE

# Preoperative localization of parathyroid adenoma by dual-phase Technetium-99m Sestamibi scintigraphy - An early experience

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### ABSTRACT

**Introduction:** Most of the patients with primary hyperparathyroidism have an associated solitary parathyroid adenoma, which for definitive cure needs surgical excision through a relatively extensive bilateral neck exploration. Availability of non-invasive and easy to perform preoperative localization imaging techniques like ultrasonography (USG), computerized axial tomography (CAT), magnetic resonance imaging (MRI) and isotope imaging has generated considerable interest in performing a limited unilateral neck dissection or minimal invasive parathyroidectomy (MIP) for excision of parathyroid adenoma.

**Objectives:** The present study was undertaken to find the usefulness of dual phase Technetium-99m Sestamibi (7-methoxy Isobutyl Isonitrile) imaging in preoperative localization of parathyroid adenoma in patients with primary hyperparathyroidism.

**Material & Methods:** This prospective study was undertaken between June 2003 to August 2005 in the Department of Nuclear Medicine at Sher-I-Kashmir Institute of Medical Sciences, Srinagar. After documenting elevated levels of serum parathormone 13 patients were subjected to a preoperative dual phase scintigraphy after intravenous injection of 20 millicuries of Tc-99m Sestamibi. Patients were imaged at 15 and 90 minutes after injection under a large field of view gamma camera fitted with a low energy high resolution parallel hole collimator. A persistent focus of increased activity in the neck or adjoining mediastinum in contrast to thyroid was interpreted as a positive scan for parathyroid adenoma localization.

**Results:** Among 13 patients studied 10 had positive preoperative Tc-99m Sestamibi localization scans with a sensitivity of 77%. All of them underwent a limited neck exploration with successful excision. 3 patients with negative preoperative scans were subjected to bilateral neck exploration.

**Conclusion:** Early results in this short study confirm the utility of dual phase Tc-99m Sestamibi scan for preoperative localization of parathyroid adenoma. It enables the surgeon to plan for a less complicated and cost effective unilateral neck dissection or minimally invasive parathyroidectomy procedure. [IJEM 2007;11(1&2):15-18]

Key words: Localization, Parathyroid adenoma, Hyperparathyroidism.

## INTRODUCTION

Among the various causes of hypercalcemia malignancy and primary hyperparathyroidism account for approximately 90% of the patients(1). Cancer of prostate, breast, lungs and multiple myeloma are the commoner malignancies associated with elevated serum calcium

levels(1). Primary hyperparathyroidism occurs in approximately 1 in 500 women and 1 in 2000 men per year, usually in their fifth or sixth decade of life(1). The primary causes as suggested in the literature are solitary adenoma (80-85 % of cases), hyperplasia involving more than one gland, usually with all 4 glands being involved (10-15% of cases) and rarely parathyroid carcinoma (1% of cases)(1). A recent review of literature suggests that these figures may be inaccurate. A review of 20,225 cases from 1995 to 2003 suggests the causes of primary hyperparathyroidism are solitary adenoma (88.9%), multiple gland hyperplasia (5.74%), double adenomas (4.14%) and parathyroid

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carcinoma (0.74%)(2). The diagnosis of primary hyperparathyroidism is established by documenting elevated levels of intact parathormone (PTH) and serum calcium(3). Patients of Hyperparathyroidism with severe hypercalcemia (15 to 18mg/dl), renal stones (even if asymptomatic), bone disease with reduction of bone mass more than 2SD below normal, any coexistent illness that would complicate management or those unlikely to attend follow up are often subjected to surgical treatment(4). Preoperatively localized solitary parathyroid adenoma the commonest lesion in patients with primary hyperparathyroidism can be conveniently excised by performing a limited neck exploration aided by an intraoperative PTH assay and frozen sections(1,2,5). This limited procedure in addition to requiring a shorter operating time has lesser complication rate and better cosmetic results(6). Various useful noninvasive techniques for preoperative localization of parathyroid adenomas are ultrasonography (USG), computed axial tomography (CAT), isotope imaging and magnetic resonance imaging (MRI)(7). Technetium-99m Sestamibi imaging (dual phase and subtraction technique) has a high sensitivity and

patients were imaged at intervals of 15 minutes and 90 minutes post injection under a large field of view gamma camera fitted with a low energy high resolution parallel hole collimator. Early phase (15 minutes) and delayed phase (90minutes) static images were acquired for 10 minutes each on a 256 by256 matrix using a preset energy of 140 Kev at 20% window. The images were analyzed for differential washout rates of thyroid and a possible parathyroid adenoma(11). A focus of increased activity in the neck or mediastinum that either increased progressively over the duration of the study or persisted on delayed imaging (90 minutes) in contrast to the decreased thyroid activity was interpreted as differential washout and therefore consistent with a parathyroid adenoma. All the 13 patients were subjected to surgery. Ten patients (Table 2, Group A) with a positive preoperative

**Table 1. Sensitivities of Imaging Modalities**

	Adenoma (%)	Hyperplasia (%)	Ectopic (%)	Reoperate (%)	Specificity Adenoma (%)
USG	34-92	53-78	0	36-82	78-100
CT	41-86	0-54	47-70	47-63	92-95
MRI	57-90	0-75	50	50-78	92-95
Tc-99m MIBI	90	55	75	98-100	98

specificity of about 90% and 98% respectively in localizing solitary parathyroid adenoma (Table 1)(8). A double isotope (Tc-99m Sestamibi/I-123 or Tc-99m Sestamibi/Tc-99m) subtraction scan appears to have slight advantage over Tc-99m Sestamibi dual phase imaging(9). However this marginal advantage in my opinion is offset by stringent technical and patient preparation considerations. Tc-99m Sestamibi is primarily sequestered within the mitochondria in response to an electrical potential generated across it and the cell. Large number of mitochondria in the parathyroid adenoma may be responsible for the avid uptake of the Tc-99m Sestamibi compared to the surrounding thyroid tissue commonly referred to as differential washout(10).

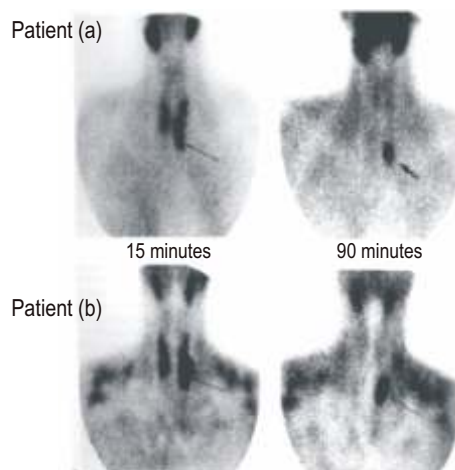
**MATERIAL AND METHODS**

Thirteen patients clinically diagnosed as having primary hyperparathyroidism with elevated levels of PTH were imaged in the department of Nuclear medicine, at Sher-i-Kashmir institute of Medical Sciences between June 2003 to August 2005. All the patients were subjected to a dual phase parathyroid scintigraphy after intravenous injection of 20 milli curies (mCi) of Tc-99m Sestamibi. The

**Table 2. Characteristics of groups on the basis of localization**

	Positive Preoperative localization (Group A)	Negative Preoperative localization (Group B)
No of patients (n=13)	10 (77%)	3 (23%)
Right Lobe	7 (70%)	-
Left Lobe	3 (30%)	-
Lower Pole	10 (100%)	-
Pre-operative PTH elevated	10	3
Mean preoperative PTH (pg/ml)*	414.46	92.62
Mean postoperative PTH	43	36
Mean preoperative Calcium (mg/dl)	13.2	11.01
Mean postoperative Calcium(mg/dl)	10.1	9.2
Sensitivity	77%	

\*PTH (Intact) Ref Range: 14.0- 72.0 pg/ml, Calcium (Total): 8.5- 10.1 mg/dl. (Harrison's principles of Internal Medicine, 15 Ed, 2001)



**Fig. 1: Patients a & b showing well localized parathyroid adenoma in relation to the lower pole of left lobe of thyroid on Tc-99m Sestamibi scans.**

localization were subjected to a limited exploration and 3 patients (Table 2, Group B) with a negative preoperative localization scans were subjected to conventional bilateral neck exploration.

## RESULTS

The patients were in the age range of 16-52 years and included 10 females and 3 males. The mean pre operative PTH levels among the 10 patients with positive preoperative localization scans (Table 2, Group A) who underwent limited neck exploration were 414.46 picograms/mm (pg/ml) (Normal range 14.0 –72.0pg/ml). Their mean preoperative calcium was 13.2 mg/dl (Normal 8.5-10.1 mg/dl). At surgery all of them had parathyroid lesion consistent in position as shown in their preoperative Tc-99m Sestamibi scans. Their lesions were confirmed to be parathyroid adenomas on histopathology. Their mean postoperative PTH and calcium levels done at one week dropped to 43 pg/ml and 10.1 mg/dl respectively. The 3 patients with negative preoperative localization scan (Table: 2, Group B) who underwent a bilateral neck exploration had mean preoperative PTH and calcium levels of 92.62 pg/ml and 11.01 mg/dl respectively. Among these patients at surgery one had a solitary adenoma in relation to the right lobe of thyroid, which was removed. One patient had multi glandular disease and in one patient no lesion was found. The two patients with parathyroid lesions were confirmed on histopathology. In the third patient a rescans was done and he had an unconfirmed ectopic parathyroid lesion in mediastinum awaiting exploration. Their mean postoperative PTH and calcium levels were 36 pg/ml and 9.2 mg/dl respectively. The average operating time of the patients with positive localization scans who underwent limited neck exploration was 58 minutes and those undergoing bilateral neck explorations was 124 minutes. Patients undergoing limited neck dissection had an average recovery time of 35 minutes and were discharged from the hospital the next day. In contrast patients undergoing bilateral neck exploration had a recovery time of 85 minutes and were discharged after 5 days. The sensitivity of Tc-99m Sestamibi dual phase imaging for localizing parathyroid adenoma in this study using operative findings and histopathology as gold standard was 77%.

## DISCUSSION

Hypercalcemia due to parathyroid adenoma needs surgical excision for its definitive cure. Conventionally an experienced and dedicated parathyroid surgeon is capable of localizing and removing 95% of abnormal parathyroid glands without preoperative imaging assistance(12). However due to availability of highly sensitive and specific non invasive localization imaging modalities a considerable interest has grown in performing a limited

neck dissection or minimally invasive surgery for excision of parathyroid adenoma which in majority of the patients is solitary. Not only does this reduce the operating time but also is associated with lesser morbidity and quick recovery. The procedure is also cost effective. A relatively lower sensitivity of 77% in the present study as compared to approximately 90% sensitivity reported in the literature is attributable to a small number of patients (12,13,14). In the present study though based on relatively smaller number of patients, the positive localization was more in patients with higher PTH levels probably reflecting a higher mitochondrial content in the adenoma cells. This assumption needs a scientific validation. The reasons for negative preoperative localization with Tc-99m Sestamibi scan in this study can be a lower sensitivity (44.46%) for multi gland hyperplasia or other reasons like the size of the adenoma, the cell type (oxyphil cells rather than chief cells), p-glycoprotein expression and mitochondrial structure that may influence the uptake of Tc-99m Sestamibi(1,15). Patients with a negative preoperative Tc-99m Sestamibi localization scan may be subjected to other localization modalities like MRI, CT and USG. The role of intraoperative PTH assay for judging adequacy of surgical excision is debatable(16). Perhaps a prospective multi-institutional study based on a large number of patients will eventually clarify the optimum policy regarding the surgical algorithm to be followed in patients of primary hyperparathyroidism. The use of limited neck exploration or a minimally invasive procedure with or without use of intraoperative PTH assay, frozen sections or aids such as radionuclide probe, operative endoscope should be a standard procedure rather than exception. This would be justified if the latest suggested incidence of solitary parathyroid adenomas is 88.9%(1).

## CONCLUSION

The present study reinforces the observations and recommendations made in the recent summary report by a consensus panel on primary hyperparathyroidism which states that a preoperative localization is mandatory when a minimally invasive parathyroidectomy procedure is used(1). A preoperative localization imaging is not recommended to make, confirm or exclude the diagnosis of primary hyperparathyroidism. An accurate preoperative localization reduces operation time, the recovery time is short, the complications are lesser and it is cost effective. Tc-99m Sestamibi dual phase imaging is safe, sensitive and specific. It is easy to perform and simple to interpret. A high resolution USG is a very valuable corroborative tool though it has doubtful utility in ectopic sites like mediastinum and among patients requiring re-exploration. Expensive and lesser sensitive modalities like CT and MRI may be used in patients with negative Tc-99m Sestamibi scans.

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