

# Surgeon-Performed Ultrasound in Primary Hyperparathyroidism: A Prospective Study of 204 Consecutive Patients

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## ABSTRACT

A prospective study was conducted to assess the value of surgeon-performed ultrasound (SUS) in primary hyperparathyroidism. A total of 204 consecutive patients were studied prospectively with surgeon performed neck ultrasound. The results were compared with sestamibi nuclear scintigraphy (SNS) and radiologist-performed ultrasound (RUS) and correlated with the operative findings. SUS was true positive in 173 of 204 (85%), false positive in two (1%), false negative in 23 (11%), and true negative in six (2.5%) in patients, where the gland was inaccessible by US (sensitivity 88%, PPV 98%). SNS was true positive in 126 of 188 (67%), false positive in 3%, and false negative in 30% (sensitivity 69%, PPV 95%). RUS was true positive in 57 of 139 (40%), false positive in 5%, false negative in 52% and true negative in 3% (sensitivity 43%, PPV 89%). Comparing correct localization with incorrect localization by the Fisher's exact test, SUS was superior to SNS ( $p < 0.0001$ ) and to RUS ( $p < 0.0001$ ). 116 patients had bilateral neck exploration and 88 had open focused minimally invasive surgery. Five percent had multigland disease and 97% were cured after one operation. SUS was the only imaging modality in 16 patients and was sufficiently convincing to allow minimally invasive parathyroidectomy in eight. Surgeons treating hyperparathyroidism should find SUS a valuable tool. In our experience, SUS was more accurate than RUS whose cost-effectiveness is questionable.

**Keywords:** Primary hyperparathyroidism, Surgeon-performed ultrasound (SUS), Sestamibi nuclear scintigraphy (SNS), Radiologist-performed ultrasound (RUS).

**How to cite this article:** Al-Askari M, Gough J, Stringer KM, Gough IR. Surgeon-Performed Ultrasound in Primary Hyperparathyroidism: A Prospective Study of 204 Consecutive Patients. *World J Endocr Surg* 2012;4(1):8-12.

**Source of support:** Nil

**Conflict of interest:** None declared

## INTRODUCTION

Parathyroidectomy is the only known effective treatment for primary hyperparathyroidism. Historically, this involved a full exploration of all four glands and removal of the enlarged gland or glands.

Accurate preoperative localization has been achieved mainly with Technetium Sestamibi scans, ultrasound scans and cross-sectional imaging. With advancements in medical imaging, preoperative localization of hyperfunctioning glands has become more successful.<sup>1-3</sup> Modern radio nucleotide imaging with Technetium (<sup>99m</sup>Tc) Sestamibi scan has improved localization with sensitivities ranging from

54 to 79%.<sup>2-6</sup> The introduction of high resolution ultrasound combined with expert knowledge of the neck anatomy has enabled sensitivities of surgeon-performed ultrasound to reach 91%.<sup>5</sup> The use of both modalities has facilitated focused minimally-invasive parathyroidectomy (MIP) over the last two decades and reduced operative time, cost and morbidity.<sup>2,6,7</sup>

We reviewed our experience at a large tertiary center and compared it with the published literature.

## MATERIALS AND METHODS

Between July 2007 and November 2011, all patients who were referred with sporadic primary hyperparathyroidism underwent an USS of the neck by the treating endocrine surgeon (IRG 171, JG 15, KMS 14, MA 4) using the SonoSite<sup>®</sup> M-Turbo<sup>™</sup> or SonoSite<sup>®</sup> MicroMaxx<sup>™</sup> ultrasound device with 13-6 MHz transducer (depth 3-6 cm). This was done as part of routine clinical management of all patients with hyperparathyroidism.

Patients were placed supine with the neck extended in a similar position to the operating position. The examination began with a transverse then longitudinal view of the neck bilaterally to identify any enlarged parathyroid, thyroid nodule or lymphadenopathy. Once an enlarged parathyroid gland was identified, color Doppler was used to confirm the characteristic vascularity and the gland measurements were documented. Enlarged parathyroid glands are typically hypoechoic and oval or rain drop shaped with clearly defined margins, and have vessels entering and leaving at one pole with variegated internal vascularity.

The data were entered prospectively in a log book with the patient's details, results of scans and operative findings. Patient's details were obtained from this log book and clinical records were reviewed, including history, symptomatology, biochemistry, bone mineral density, imaging, intraoperative findings, final histopathology details and postoperative calcium and parathyroid hormone levels.

All patients who had sporadic primary hyperparathyroidism and a pathology report confirming removal of at least one parathyroid gland with adenoma or hyperplasia were included in the study. Other patients who had MEN or secondary hyperparathyroidism who were also managed during this time period were excluded from this analysis.

Statistical comparison was done using the Fisher's exact test.

## RESULTS

### Patient's Demographics

Two hundred and four patients (164 females and 40 males) undergoing parathyroidectomy for primary hyperparathyroidism had a SUS. This was done either before ( $n = 52$ ) or after ( $n = 152$ ) the sestamibi nuclear scan (SNS). The average age was 60.1 years (13-94 years old) with a median age of 59.

Preoperative corrected calcium ranged from 2.35 to 3.58 mmol/l (average = 2.79, median 2.79, normal range 2.25-2.62) and intact parathyroid hormone level (iPTH) ranged from 41 to 474 ng/l (average = 130.7, median 110, normal range 14-72).

One hundred and sixty six (81%) of patients had symptoms directly related to hypercalcemia. One hundred seven patients had bone mineral density studies with 47 showing osteopenia, 35 osteoporosis and 25 normal bone density.

Six patients were reoperative cases, four were operated on for failed surgery at other institutes and two had recurrent disease after a period of normocalcemia. Five patients had previous thyroid surgery.

### Localization Techniques

The results are summarized in Table 1.

### Surgeon-performed Ultrasound (SUS)

SUS was positive in 175 patients and correct in 173 cases. SUS was negative in 29 patients, however, six of those negative patients had adenomas in areas inaccessible by USS (deep to esophagus = 3, retrosternal = 3) and were considered 'true' negatives. The remaining 23 were false negative (sensitivity 88%, specificity 75%, PPV 98%).

SUS and SNS concordantly identified an adenoma in 109 (58%) patients; all except one case (inferior adenoma on the contralateral side) were correct (Sensitivity 100%, PPV 99%). In five patients, the SNS and SUS localized to opposite sides. These five patients had BNE and SNS was correct in two and SUS was correct in three ( $p = 1.1032$ ).

In 52 patients, SUS was performed before SNS. Eleven (21%) of those were false negative and one was a true

negative. There were no false positive SUS, when performed before SNS. SUS performed before SNS had a true positive rate of 40/52 (77%).

In 152 patients, SUS was performed after SNS. Twelve of those were false negative, five were true negative and two were false positive (one case the SNS was also FP). SUS performed after SNS had a true positive rate of 133/152 (87.5%). There was no statistically significant difference in the true positive rates, when SUS was performed before or after SNS ( $p = 0.6314$ ).

16 patients had only SUS (2 were pregnant). Only one had a negative SUS and refused SNS and requested BNE (which found a single adenoma). In the remaining 15 patients, SUS identified an adenoma correctly without any other localization study. The SUS findings were very convincing and eight of these patients had successful MIP.

In eleven patients with a negative SUS, SNS correctly identified an enlarged parathyroid gland. In contrast, 45 patients with a negative SNS, SUS correctly identified an enlarged parathyroid gland, indicating that SUS was more reliable in localization when only one imaging test was positive ( $p < 0.0001$ ).

Sestamibi was particularly useful in six cases where SUS could not access the location (three retrosternal and three retro-esophageal). These findings were confirmed in five patients with a CT ( $p = 0.0022$ ).

SUS also identified incidental thyroid pathology in 34 patients of whom five had a differentiated thyroid cancer.

### Technetium ( $^{99m}\text{Tc}$ ) Sestamibi Scan (SNS)

SNS was performed in 188 patients, an adenoma was identified in 132 patients and imaging was reported as negative in 56 patients. In 126 patients, the localization was correct and six incorrectly localized to the wrong side. However, on reviewing the images by the surgeon, six of the 56 reported as negative actually showed increased uptake and were convincing enough for the surgeon to be considered positive (sensitivity 69%, PPV 95%).

### Radiologist-performed Ultrasound (RUS)

RUS was performed in 141 patients (all being requested by the referring endocrinologist or general practitioner prior

Table 1: Summary of imaging

	SNS (N = 188)	SUS (N = 204)	RUS (N = 141)	SNS and SUS	p-value
TP	126 (67%)	173 (85%)	57 (40%)	99%	<0.0001
TN	–	6 (3%)	4 (3%)	–	1.2645
FP	6 (3%)	2 (1%)	7 (5%)	1%	0.1863
FN	56 (30%)	23 (11%)	73 (52%)	–	<0.0001
Sensitivity	69%	88%	43%	100%	–
Specificity	–	75%	36%	–	–
PPV	95%	98%	89%	99%	–

to being seen by the surgeon). Only 64 were reported as positive and seven of those were incorrect. In 77 patients, RUS failed to identify any parathyroid gland, however, three of those were retrosternal and one was retroesophageal (sensitivity 43%, specificity 36%, PPV 89%).

### Other Imaging

Thirteen patients had CT scans, two had selective venous sampling (SVS) and one had an MRI. As previously mentioned, CT identified five adenomas in areas inaccessible to US, the MRI confirmed what SNS and SUS had already demonstrated and one SVS localized an abnormality.

### Multigland Disease (MGD)

Eleven (5%) patients had MGD. SNS performed in 10 of those patients was negative in seven, identified the larger of two glands in two patients and the largest of three in one patient. SUS was negative in two patients and identified enlarged glands in two cases, the largest (and heaviest) gland in five and the smaller in two cases.

### Bilateral Neck Exploration vs Minimally Invasive Parathyroidectomy

One hundred and sixteen patients had a bilateral neck exploration (BNE) and 88 had minimally invasive parathyroidectomy (MIP). Five patients who had a negative SUS had successful MIP, localization in these cases was with SNS alone (2), SNS and CT (2), SNS and selective venous sampling (1).

Despite concordant SNS and SUS in 109 patients, 38 had BNE. The main reasons were the presence of thyroid pathology requiring thyroidectomy, older age (range 41-90, median 64), patient choice and to minimize the risk of failure. Recurrent or persistent hypercalcemia was seen in six (2.9%) of patients.

## DISCUSSION

Our study demonstrates that preoperative localization with SUS is reliable and cost-effective, and the role of radiologist ultrasound is less reliable. Our findings are similar to the data of Kiriakopoulos and Linos.<sup>8</sup>

SUS is less expensive than both RUS and SNS<sup>9</sup> in terms of capital costs of equipment and professional fees. The Australian Medicare Benefits Scheme fee for SNS is \$470.45, RUS \$109.10 and SUS \$37.85, making SUS the most cost-effective localization study.<sup>3-5</sup> Most centers utilize both SNS and SUS for preoperative localization,<sup>2,4,6,7</sup> however, more data are emerging in which SUS was the only localization modality.<sup>5,10</sup>

Intraoperative parathyroid hormone assay (IOPTH) is unavailable in most Australian centers. In the United States, intraoperative parathyroid hormone assay is commonly used with the aim of achieving higher cure rates.<sup>11-13</sup> In a large series of 1,361 patients from The Mayo Clinic, the cure rate was 97% utilizing SUS, SNS and IOPTH monitoring.<sup>13</sup> Our cure rate was identical despite not using IOPTH monitoring and performing MIP in a similar percentage of patients (43%). Solorzano et al reported a cure rate of 99%, when all three (SNS, SUS and IOPTH) were used.<sup>9</sup>

MGD disease remains a challenge to the endocrine surgeon as localization studies are usually negative; the uptake of sestamibi is often negative or limited to one gland and does not match with USS findings. Kebebew et al<sup>14</sup> proposed a scheme to predict MGD based on a series of 238 patients. They concluded that patients presenting with lower calcium, iPTH and negative imaging were more likely to have MGD. Our data does not show any difference in calcium (2.79 vs 2.69), iPTH (131 vs 114) or negative imaging rate ( $p = 0.8617$ ) between single or multigland disease patients.

We found that SNS was very useful in localizing an enlarged gland in areas inaccessible by USS (retrosternal and retroesophageal) and with the addition of SPECT or CT, the localization accuracy was nearly 100%.

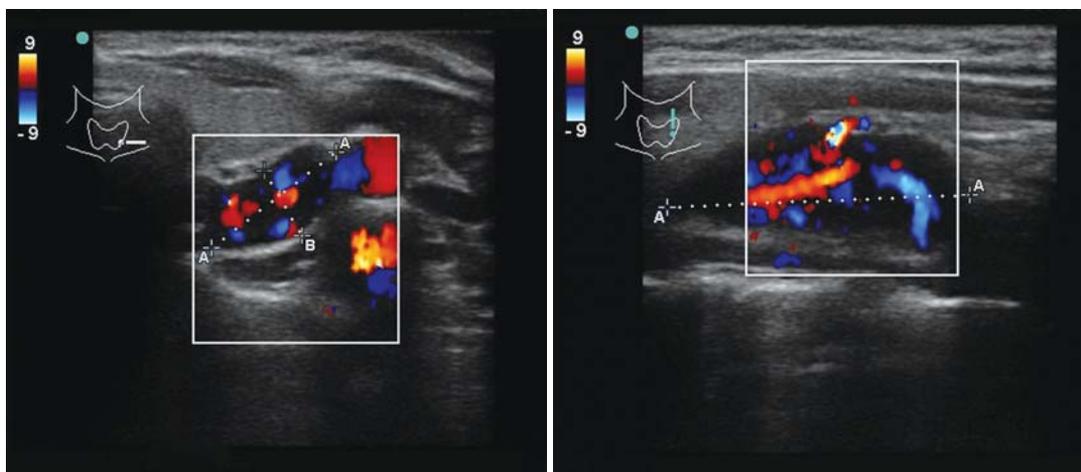
Selective venous sampling is only used in reoperative patients, when noninvasive imaging has failed to reveal the location of the enlarged gland. It has been shown to be helpful in 80 to 90% of cases.<sup>15,16</sup>

In patients who had RUS, the depth was frequently inadequate (e.g. maximum of 3.5 cm) and, in some cases on reviewing the images, the enlarged parathyroid was partially seen but not recognized or reported (Fig. 1).

In centers with no dedicated endocrine radiologist, the ultrasound scan is often performed by radiographers and only reported later by radiologists resulting in sensitivities <50%<sup>17</sup> (43% in our series). On the other hand, dedicated neck radiologists in high volume centers have similar sensitivities to experienced endocrine surgeons.<sup>7</sup> In comparison to SUS, RUS is less efficient, more expensive, and more time-consuming for the patient. In order for RUS to become more effective, it would require further education of radiographers and radiologists who undertake the investigation.

## CONCLUSION

We have found that SUS is a very cost-effective investigation for preoperative localization and recommend that it is done as part of the surgical consultation. Patients feel more confident with surgery, when an enlarged gland



**Fig. 1:** SUS (transverse and longitudinal) of large (28 x 15 x 7 mm) left superior adenoma weighing 1.9 gm. This large gland was missed on RUS as the probe settings were not deep enough and only part of the gland was seen and not recognized as a large adenoma

can be seen and demonstrated during the consultation and understand the rationale for surgery and the details of the procedure better. If SUS is positive, it facilitates the discussion regarding minimally invasive surgery and, if all imaging is negative or unconvincing, it facilitates the discussion regarding four glands exploration. Furthermore, the portable equipment we use is taken to the operating theater and the location of the gland checked with the anesthetized patient in position and the incision is planned to give optimal exposure of the gland and its blood supply. We recommend that all surgeons with an interest in parathyroid surgery should consider including neck ultrasound in their practice.

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