

Evaluation of the Performance and Clinical Impact of a Rapid Intraoperative Parathyroid Hormone Assay in Conjunction with Preoperative Imaging and Concise Parathyroidectomy

LAWRENCE R. JOHNSON,¹ GERARD DOHERTY,² TERRY LAIRMORE,² JEFFREY F. MOLEY,²
L. MICHAEL BRUNT,² JOHN KOENIG,³ and MITCHELL G. SCOTT^{1*}

Background: ^{99m}Tc-sestamibi scans and rapid, intraoperative intact parathyroid hormone (PTH) assays allow preoperative identification of diseased glands and intraoperative confirmation of diseased gland removal, respectively. Use of these two new technologies may facilitate simpler, more concise surgery, shorter hospital stays, and decreased costs for frozen-section analysis. One major drawback to this new strategy has been the high cost of rapid point-of-care PTH assays.

Methods: We performed rapid PTH assays with the DPC Turbo PTH assay on the DPC IMMULITE automated analyzer. The number of intraoperative frozen sections, type of anesthesia, surgical approach, length of hospital stay, and pre- and postoperative calcium values were compared between a group of 49 patients undergoing parathyroidectomy where the intraoperative PTH assay was used in conjunction with preoperative imaging, and a historical control group of 55 patients before the use of these two technologies in our institution.

Results: Comparison of the Turbo PTH assay to the standard IMMULITE PTH assay gave the following: $y = 1.08x - 4.36$ ($r = 0.97$; $n = 48$). For the 49 patients, the median turnaround time for each intraoperative PTH determination was 19 min (range, 14–40 min). The median decrease in PTH values from baseline was 88% (range, 33–99%). Thirty-seven patients required two PTH determinations, 7 required three, 4 had four, and 1

required five determinations. The average laboratory cost for the rapid intraoperative PTH assays was <\$100 per patient (range, \$55 to \$113). Compared with the control group, the experimental group had significantly fewer frozen sections (1.4 vs 2.5; $P < 0.0001$), shorter hospital stays (17 discharged on the day of surgery vs none discharged on the day of surgery; $P < 0.0001$), greater use of local anesthesia (33% vs 0%; $P < 0.001$), and more unilateral, rather than bilateral neck explorations (65% vs 0%; $P < 0.001$).

Conclusions: The combination of intraoperative Turbo PTH assay and preoperative ^{99m}Tc-sestamibi scans can lead to significant decreases in laboratory and surgical pathology costs, hospital stays, and exposure to general anesthesia by facilitating concise parathyroidectomy surgery.

© 2001 American Association for Clinical Chemistry

Primary hyperparathyroidism is a common cause of hypercalcemia and has an estimated annual incidence of 1–2 per 1000 (1). In ~85% of cases, primary hyperparathyroidism is a result of a solitary adenoma, with the remainder attributable to parathyroid hyperplasia and, very rarely, parathyroid carcinoma (1). The diagnosis of primary hyperparathyroidism relies on increased serum calcium values in the presence of inappropriately high parathyroid hormone (PTH) values in addition to clinical symptoms (1). In most cases, the recommended therapy is parathyroidectomy (1). The “classic” approach to surgical treatment has been bilateral, open-neck exploration under general anesthesia with intraoperative, frozen-section histopathologic examination of the parathyroid glands. Historically, patients stayed an average of 24–48 h in the hospital postoperatively (2), and failure rates for this approach have been reported to be >10% in some institutions (3). Recent advances in surgical techniques have led

Washington University School of Medicine, ¹ Department of Pathology and Immunology and ² Department of Surgery; and ³ Department of Laboratories, Barnes-Jewish Hospital, St. Louis, MO 63110.

*Address correspondence to this author at: Department of Pathology and Immunology, Campus Box 8118, Washington University School of Medicine, Washington University Medical Center, 660 S. Euclid Ave., St. Louis, MO 63110-1093. Fax 314-362-1461; e-mail mscott@labmed.wustl.edu.

Received September 28, 2000; accepted February 1, 2001.

to the use of concise parathyroidectomy, which is performed with smaller, less invasive incisions, leading to fewer postoperative complications (4). However, even these minimal surgical approaches can require bilateral exploration, overnight stays, and the use of general anesthesia (4). Furthermore, the failure of standard intraoperative frozen-section diagnosis to agree with definitive histology in up to 10% of cases can impact intra- and postoperative management (5–7). Therefore, we sought an improved means of assessing the intraoperative success of surgery to improve on the limitations of intraoperative frozen section.

Recently, we implemented two new technologies in an attempt to further simplify parathyroidectomy surgery and simultaneously decrease costs: preoperative ^{99m}Tc -sestamibi parathyroid imaging (8–11) and a rapid intact PTH quantitative assay performed during the surgical procedure (12–15). Preoperative ^{99m}Tc -sestamibi parathyroid scanning has been shown to identify adenomatous or hyperactive glands in up to 90% of cases (9–11), thus reducing the need for routine bilateral neck exploration (2). However, this approach can miss a second diseased gland present in 2–5% of patients (11). Rapid intraoperative PTH assays may circumvent this problem by serving as “biological frozen sections” (12, 16) to confirm removal of all hyperfunctioning parathyroid tissue. The 5-min half-life of intact PTH allows it to serve as a practical intraoperative marker, and previous studies suggested that a 50% decrease in PTH values from the presurgical value after removal of the diseased gland(s) reliably predicts postoperative normocalcemia (12, 13, 15). Previous studies have clearly shown that this approach leads to successful clinical outcomes, and some suggest that it can lead to decreased costs through less exposure to anesthesia, minimized reliance on frozen-section histology, and shorter hospital stays (17). However, the initial “intraoperative” PTH assay from Nichols has a per patient cost of \$700 to \$1000 (18) because of the nature of the assay design, which necessitates the use of an entire prepackaged reagent set (up to nine patient determinations) for an individual patient (14).

In this study we examined the performance of a new, less costly automated intraoperative PTH assay. We also asked whether use of the IMMULITE Turbo rapid PTH assay, in conjunction with preoperative imaging and concise parathyroidectomy, would lead to shorter hospital stays, decrease surgical pathology costs, and afford more anesthesia options for patients. We directly examined those outcomes, which had been hypothesized to improve after the institution of a rapid intraoperative PTH assay together with preoperative imaging, by comparing them with a previously described cohort at our institution that underwent concise, minimally invasive parathyroidectomies without intraoperative PTH determination (4).

Materials and Methods

PATIENT SELECTION

Patients in the experimental and control groups were diagnosed as hyperparathyroid on the basis of serum or plasma calcium values, PTH values, and clinical symptoms. The experimental group consisted of 49 patients from July 1999 to March 2000 for whom the intraoperative rapid PTH assay and preoperative imaging were used. The control group consisted of 55 consecutive patients from a previously described series of 66 patients (4) for whom laboratory and medical records were still available. These patients underwent minimally invasive parathyroidectomy from January 1997 to June 1999 before the implementation of the rapid intraoperative PTH assay and routine preoperative imaging. In both groups, the pre- and postoperative serum or plasma calcium values, number of frozen sections, surgical approach (unilateral vs bilateral neck dissection), anesthesia (general vs local), and length of hospital stay were recorded by examination of the patients’ laboratory records, hospital charts, and surgical pathology reports. This study was approved by the Washington University Human Studies Committee.

STATISTICAL ANALYSIS

A two-tailed *t*-test assuming unequal variance was used to test the significance of difference between plasma or serum calcium and the number of frozen sections between the groups. A two-sample Wilcoxon rank-sum test was also used to test significance of difference among frozen sections. The Fisher exact test was used to calculate *P* for other outcomes examined with STATA, Ver. 6.0.

STANDARD IMMULITE INTACT PTH ASSAY

The standard PTH assay was performed using the IMMULITE automated analyzer, a solid-phase, two-site chemiluminescent immunometric assay (DPC) according to the manufacturer’s recommendations. The solid phase, a polystyrene bead enclosed within an IMMULITE Test Unit, is coated with an affinity-purified goat polyclonal anti-PTH antibody specific for residues 44–84. The soluble antibody is an affinity-purified goat anti-PTH antibody specific for residues 1–34 that is conjugated to alkaline phosphatase. The assay has a 60-min incubation and an analytical range of 5–1500 ng/L. For routine analysis, collected tubes containing no anticoagulant are placed on ice and transported immediately to the laboratory where the sample is allowed to clot for 30 min and then centrifuged at 4 °C. If not assayed immediately, serum specimens are frozen at –20 °C. Plasma from blood samples collected in potassium EDTA tubes is also suitable. The manufacturer’s stated reference range for PTH is 12–72 ng/L for both IMMULITE methods examined here.

RAPID INTRAOPERATIVE PTH ASSAY

The Turbo PTH assay was also performed on the IMMULITE automated analyzer, using the same antibodies and assay configuration. The “Turbo” mode of the IMMULITE

uses different software, allowing more rapid processing of results. When operated in the Turbo mode, standard incubation assays cannot be performed simultaneously. The Turbo IMMULITE PTH assay has an incubation time of 14 min and an analytical range of 10–1200 ng/L (data not shown).

Samples are drawn in the operating room before incision and 10–12 min after excision of the suspected diseased parathyroid gland(s). After collection into potassium EDTA anticoagulant tubes in the operating room, samples are immediately transported to the IMMULITE operator in the main laboratory, where a 1-mL aliquot of whole blood is centrifuged for 60 s and the potassium EDTA plasma is transferred to IMMULITE sample cups. To accomplish maximum efficiency, the laboratory is notified by the surgical staff the day before the procedure to allow adequate time for preoperative calibration and running of quality-control samples. During surgery, the operating room calls the laboratory as the sample is drawn, and the sample is hand-delivered to the laboratory, which is one floor below the surgical unit.

PLASMA AND SERUM CALCIUM ASSAYS

Plasma and serum calcium concentrations were determined on one of two instruments, the Dimension RxL (Dade Behring) or the Hitachi 747 (Roche Diagnostics), according to the manufacturers' recommendations. Both the Dimension RxL and Hitachi 747 calcium methods are modifications of the calcium *o*-cresolphthalein complexone reaction (19). Our reference interval for plasma and serum calcium is 86–103 mg/L.

PARATHYROID SCINTIGRAPHY

Parathyroid scintigraphy is performed by intravenous administration of 20 mCi of ^{99m}Tc-sestamibi. The equipment setup requires a gamma camera capable of single positron-emission computed tomography (SPECT) acquisition, a high-resolution collimator, and 140 keV with a 20% energy window. Ten minutes after injection of the ^{99m}Tc-sestamibi, a 10-min anterior image of the neck and upper mediastinum is begun while the patient is lying supine. After the immediate planar image, a SPECT study of the neck and upper mediastinum is acquired. Two hours after the initial injection, the SPECT images of the anterior neck and upper mediastinum are repeated. The initial uptake of ^{99m}Tc-sestamibi in parathyroid and thyroid tissue is attributable to the high blood flow to these organs. The clearance of the tracer from thyroid tissue occurs more rapidly than from parathyroid tissue (20, 21).

Results

PERFORMANCE CHARACTERISTICS OF THE TURBO PTH ASSAY

Both intrarun and total imprecision (CV) of the standard and Turbo DPC PTH assays at low and high values of PTH are shown in Table 1. Although the Turbo assay is not as precise as the standard DPC PTH assay, the Turbo

Table 1. Imprecision of standard and Turbo intact PTH assays.

Mean PTH, ng/L	CV, % (n)	
	Standard	Turbo
18.1		7.5 (10)
30.3	4.0 (10)	
38.9		6.5 (5)
75.4	5.6 (10)	
441.1		3.3 (5)
754.3	3.1 (10)	
B. Total imprecision^b		
10.8		24 (63)
23.1	10 (160)	
365		13 (59)
577	9.7 (157)	

^a Values shown are the mean and CV of a patient pool (mean = 38.9) and two concentrations of Bayer MagicLite quality-control material from a single run.

^b Values shown are the mean and total imprecision (CV) of routine quality-control material (Medical Analysis Systems) performed at Barnes-Jewish Hospital from April 1999 to July 1999 for the standard assay and from July 1999 to June 2000 for the Turbo PTH assay.

assay clearly has suitable intrarun imprecision (3.3–7.5%) for intraoperative use in detecting a >50% decrease in serum PTH values. Regression analysis of potassium EDTA plasma values from the DPC standard and Turbo PTH assays for 49 patients gave the following equation: Turbo = 1.08 × standard – 4.36 ($r = 0.97$; $S_{y/x} = 19.4$; mean $x = 60.9$; mean $y = 61.5$; Fig. 1).

PATIENT AND CONTROL GROUP CHARACTERISTICS

Characteristics of the control and experimental populations are shown in Table 2. Preoperative calcium and PTH values were not statistically different between the groups (Table 2). Both groups also had similar age, sex, and pathologic diagnoses. The pathologic diagnoses were initially made by frozen-section analysis and confirmed by examination of paraffin-embedded sections. It is important to note that the designation of “hypercellular” is

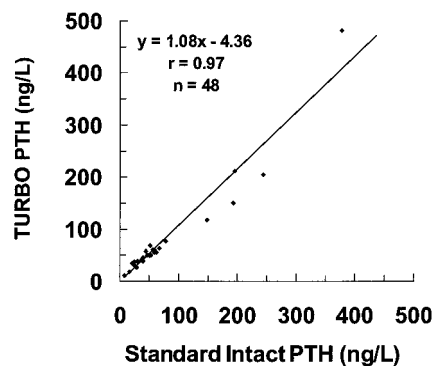


Fig. 1. Correlation plot of PTH values for potassium EDTA plasma samples from 48 patients performed on the standard IMMULITE intact PTH assay (x) and the IMMULITE Turbo intact PTH assay (y).

Table 2. Description of study groups.

	Control	Experimental
Dates	January 1997– June 1999	July 1999– March 2000
Age, mean (range), years	58.8 (33–87)	57.2 (15–85)
Sex		
Male	15	9
Female	40	40
Histologic diagnoses		
Adenoma	17	17
Hypercellular	33	29
Carcinoma	0	1
Equivocal	5	2
Sestamibi scan	9	44
Mean preoperative calcium, mg/L	113	117 ^a
Mean preoperative PTH, ng/L	167.2	193.9 ^b
^a <i>P</i> = 0.11.		
^b <i>P</i> = 0.47.		

often used at our institution when not all glands are available for examination. The most reliable distinction between adenoma and hyperplasia is made only after examining one or more glands in addition to an enlarged, hypercellular gland (22, 23).

Forty-four of the experimental group underwent sestamibi scans vs 9 in the control group. Of the five patients in the experimental group who did not have preoperative scans, one was a carcinoma patient who had emergency surgery because of hypercalcemia crisis, three were siblings with multiple endocrine neoplasia who had additional exploratory surgery, and one patient had renal failure with hypercellular glands. It is also important to note that the nine preoperative imaging studies in the control group were performed before the referral of the patients to the Department of Surgery. Of the patients with preoperative scans, 34 (77%) of the experimental group vs all 9 (100%) of the control group had positive scans. Four (9%) of the experimental group had negative scans, and six (14%) had an equivocal scan.

PTH VALUES

In the control group (*n* = 52), the preoperative PTH values had a mean of 167.2 ng/L, a median of 113 ng/L, and a range of 43–1300 ng/L. PTH values performed at an outside institution were not available for three patients. The mean preoperative PTH value of the experimental group was 193.9 ng/L, the median was 117 ng/L, and the range was 58–1415 ng/L (Table 2). In the one patient with “normal” PTH concentrations, disease was confirmed by clinical symptoms, plasma calcium values (calcium, 109 mg/L), and postoperative histology.

A total of 117 intraoperative PTH measurements were performed for these 49 patients. The mean number of intraoperative PTH determinations per patient in the experimental group was 2.3, with a median of 2, and a range of 2–5. The five determinations were performed in a patient who had an equivocal preoperative scan and

parathyroid glands that were difficult to locate. The mean turnaround time for PTH results from receipt of the sample in the laboratory was 19.6 min (median, 19 min; range, 14–40 min; *n* = 112). Five samples were excluded from the laboratory turnaround time analysis because they were entered into the laboratory information system after centrifugation had begun, which produced unlikely intralaboratory turnaround times of ≤15 min. An estimate of the length of surgery in this setting is the time from receipt of the first preoperative sample to the last intraoperative postresection result. In the experimental group, the mean turnaround time was 60.0 min, the median was 48 min, and the range was 27–145 min for 46 patients. The patient with parathyroid carcinoma, a patient sent to the recovery room before the last PTH result, and a patient whose pre- and postexcision samples arrived in the laboratory simultaneously were excluded from this analysis.

Of the 49 patients in the experimental group, 46 had a >50% decrease in their first postresection PTH value (Fig. 2). Twelve patients had a second postresection PTH value determined, 4 had a third postresection value, and 1 had a fourth. Of these 12 patients, only 6 actually failed to exhibit a ≥50% decrease in PTH values in the first postresection sample (Fig. 2). Three of these six exhibited a ≥50% decrease in the third sample. Of the other three, one patient had a 49% decrease, the parathyroid carcinoma patient had only a 33% decrease, whereas another patient had only a 10% decrease in the final intraoperative PTH value. Subsequent removal of additional hypercellular parathyroid glands was performed on this latter patient without the use of the intraoperative PTH assay.

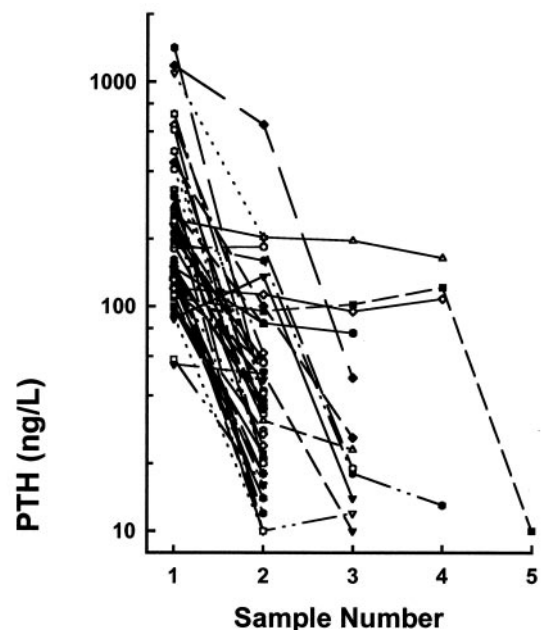


Fig. 2. Intraoperative PTH values from 49 patients.

The x axis depicts the order of PTH samples drawn during surgery with the initial sample being drawn before surgical incision. Subsequent values were drawn 10–12 min after excision of suspected diseased glands.

Table 3. Intraoperative decrease in PTH values and postoperative calcium.

Intraoperative PTH determinations	n	Intraoperative decrease in PTH, %		No. of patients with postoperative calcium:		
		Mean (range)	Median	<86 mg/L	86–103 mg/L	>103 mg/L
Two	37	85 (52–99)	88	3	34	0
Three	7	92 (85–96)	92	1	5	0
Four	3	96 (94–99)		0	2	0
Five	1	99		0	1	0
Four ^a	4	31 (10–49)	33	0	2	1 ^a

^a Includes parathyroid carcinoma patient.

These patients emphasize the usefulness of the rapid PTH assay for indicating incomplete surgery with the first postexcision value. For all patients, the final postresection PTH mean was 40.9 ng/L (84% decrease), the median was 26 ng/L, and the range was <5–231 ng/L (10–99% decrease).

Including the costs of quality-control materials, calibrators, and performing the quality-control and calibration assays, the direct cost to the laboratories was \$51.32, \$72.07, \$92.82, or \$113.57 for two, three, four, or five intraoperative PTH determinations per patient.

PLASMA AND SERUM CALCIUM CONCENTRATIONS

The mean serum or plasma calcium concentration for the experimental population was 117 mg/L vs 113 mg/L for the control group ($P = 0.11$; Table 2). Two in the experimental group and seven in the control group had preoperative serum and plasma calcium concentrations within reference values. However, hyperparathyroidism was confirmed for all nine by clinical symptoms, measurement of serum PTH, and histology. All other patients had increased calcium values. Of the 49 patients in the experimental group, 46 had a >50% decrease in their PTH values (Fig. 2), and 42 of these had postoperative calcium values within reference values 1–9 months postoperatively (Table 3). Four patients were hypocalcemic up to 7 months postoperatively (77, 82, 84, and 84 mg/L). Thus, the predictive value for a >50% decrease in intraoperative PTH value for normo- or slight hypocalcemia was 100%. Three patients exhibited a <50% decrease (Fig. 2 and Table 3). One was the parathyroid carcinoma patient (33% decrease), who remained hypercalcemic (137.0 mg/L) 9 months after surgery. The other two patients were normocalcemic postoperatively and exhibited a 49% and a 10% decrease in intraoperative PTH values. The latter was the patient mentioned previously who underwent additional neck exploration without additional intraoperative PTH values. There was no statistical difference in postoperative calcium values between the two groups ($P = 0.48$; Table 4).

FROZEN-SECTION USAGE

The experimental group showed significantly less ($P < 0.0001$, Wilcoxon rank-sum; $P < 0.002$, t -test) frozen-section usage with a mean of 1.4 per patient vs 2.5 per

patient for the control group (Table 4). The 95% confidence interval for the mean difference (1.11) in frozen sections between the groups was 0.468–1.748. Furthermore, 10 patients in the experimental group had no frozen sections of excised tissue, whereas all patients in the control group had at least one frozen section performed.

SURGICAL APPROACH AND TYPE OF ANESTHESIA

In the experimental group, 33% of the patients had only local anesthesia, whereas all patients in the control group received general anesthesia (Table 4). Furthermore, 65% of the patients in the experimental group had a unilateral neck dissection vs none in the control group.

LENGTH OF HOSPITAL STAY

Seventeen patients (35%) in the experimental group underwent same-day surgery compared with none in the control group ($P < 0.0001$). In addition, fewer patients in the experimental group than the control group had overnight hospitalizations or hospitalizations >48 h (Table 4).

Discussion

The use of a rapid intraoperative PTH assay in conjunction with a preoperative ^{99m}Tc-sestamibi parathyroid scan

Table 4. Outcomes examined.

	Control	Experimental	P
Frozen sections, n			
Mean (range)	2.5 (1–7)	1.4 (0–6)	<0.0001
Median	2	1	
None	0	10	
Anesthesia, n (%)			
Local	0 (0%)	16 (33%)	<0.001
General	55 (100%)	33 ^a (67%)	
Surgical procedure, n (%)			
Unilateral	0 (0%)	32 (65%)	<0.001
Bilateral	55 (100%)	17 ^a (35%)	
Length of hospital stay, n (%)			
Same day surgery	0	17 (35%)	<0.0001
Overnight stay	48 (87%)	29 (59%)	
≥48 h	7 (13%)	3 ^a (6%)	
Postoperative calcium, mg/L			
Mean (range)	93 (74–122)	92 ^a (77–114)	0.48
Median	94	92	

^a Includes parathyroid carcinoma patient.

has been proposed to allow parathyroidectomy in a more concise and directed manner (16, 17). One disadvantage of the initial commercial rapid PTH assay (14) is its cost of \$700 or more per patient (18). The original rapid intraoperative PTH assay from Nichols is Food and Drug Administration approved for single-patient use although each reagent set has the capacity to perform up to nine PTH patient determinations when performed in duplicate, as recommended by the manufacturer. Considering that the median number of intraoperative PTH determinations in this cohort was two, it is extremely unlikely that nine determinations would be needed per patient. Because of the cost of this assay, we examined the performance characteristics of a new rapid PTH method with markedly lower per-patient laboratory costs. At our institution, the direct laboratory costs for the DPC Turbo PTH assay were \$55 to \$113 per patient, depending on the number of intraoperative tests performed. The Turbo method correlated well with the standard IMMULITE PTH assay, and it has adequate precision, albeit less than the standard method, to assess intraoperative decreases in plasma PTH values. We then examined the impact of implementing a rapid PTH assay in conjunction with preoperative imaging on surgical pathology costs and on other outcomes, including length of hospital stay, surgical approach, and use of general vs local anesthesia.

The use of a rapid intraoperative assay to assess successful removal of the diseased gland(s), even without preoperative imaging, has been well established (13, 24–34). A >50% decrease in PTH values from the pre-resection intraoperative value 10 min after removal of the diseased gland is a strong predictor of successful surgery (12, 13, 15). Preoperative parathyroid imaging to enable minimally invasive or unilateral parathyroidectomy has shown success rates comparable to those for bilateral dissection in selected cases when the imaging results are unequivocal (35–37). The combination of both of these technologies has thus been suggested as a means to minimize pathology costs and to allow a simple surgical procedure and the option of local anesthesia. Other studies incorporating a rapid intraoperative PTH assay with ultrasound as the imaging technique (7, 12) or various combinations of scanning and localization techniques, such as the gamma probe (29), have also shown similar success. Although prior studies comparing the classic approach with techniques using preoperative scanning and intraoperative PTH determinations showed equivalent rates of successful surgery, few directly examined the impact of these added services on reductions in hospital stay, general anesthesia usage, frozen section analysis, and overall costs. One recent study (20) concluded that intraoperative PTH assays in conjunction with preoperative imaging did lead to shorter hospital stays and lower overall costs.

When we compared two groups of patients with similar sex, age, and diagnoses, we found that 44 of 49 (90%) patients in the experimental group and 49 of 55 (89%)

patients in the control group achieved normocalcemia postoperatively. Thus, the use of minimal excision surgery with bilateral exploration and concise parathyroidectomy guided by preoperative imaging and intraoperative rapid PTH assays had identical physiologic outcomes. Confirming the hypothesis that the use of these two technologies would lead to direct cost savings in surgical pathology costs, we found that frozen-section usage of the experimental group was significantly lower than that of the control group. Furthermore, 10 of the 49 patients had no frozen sections performed. At a cost of \$203 (patient charge, \$406) per frozen section, not including the cost of analysis of permanent paraffin-embedded sections, the combination of preoperative imaging, concise surgery, and intraoperative PTH analysis led to an average savings of >\$200 per patient in surgical pathology costs alone. As surgeons become more accustomed to using the intraoperative PTH assay, we expect that frozen-section use will almost disappear when a >50% decrease in PTH values is observed. Indeed, like others (12, 13, 15, 17), we found that a $\geq 50\%$ decrease was essentially 100% predictive of curing hypercalcemia.

The combined use of imaging and intraoperative PTH assays allowed 32 (66%) of the experimental group to undergo unilateral neck dissection in contrast to all patients having bilateral dissection before implementation of these technologies. The ability to offer these patients the choice of local or general anesthesia was directly related to unilateral surgery. In the experimental group, 16 of the 32 patients undergoing unilateral neck dissection chose the local anesthesia, thereby decreasing their overall costs. Particularly significant from a cost perspective was that all of the patients with local anesthesia and one with general anesthesia had same-day surgery vs none in the control group.

In conclusion, through the use of this new rapid PTH assay, we were able to meet the turnaround-time demands of surgery, allowing removal of diseased gland(s) in a cost-efficient and clinically successful manner. The Turbo DPC PTH assay provides surgeons precise and accurate PTH results in <20 min at a reagent cost that is ~\$600 less per patient than the original rapid PTH assay and leads to a frozen-section savings of ~\$200 per patient. Taken together, this cost-effective intraoperative PTH assay, in conjunction with preoperative imaging, helps facilitate simpler surgeries, the option of local anesthesia, and shorter hospital stays when compared with minimally invasive surgery without preoperative imaging and rapid intraoperative PTH assessment.

References

1. NIH Conference. Diagnosis and management of asymptomatic primary hyperparathyroidism: consensus development conference statement. *Ann Intern Med* 1991;114:593–7.
2. Carty SE, Worsley J, Virji MA, Brown ML, Watson CG. Concise parathyroidectomy: the impact of preoperative SPECT ^{99m}Tc ses-

- tamibi scanning and intraoperative quick parathormone assay. *Surgery* 1997;122:1107-14.
3. Kaplan EL, Yashiro T, Salti G. Primary hyperparathyroidism in the 1990s. *Ann Surg* 1992;215:300-17.
 4. Lowney JK, Weber B, Johnson S, Doherty GM. Minimal incision parathyroidectomy: cure, cosmesis and cost. *World J Surg* 2000;24:1442-5.
 5. Levin KE, Clark OH. The reasons for failure in parathyroid operations. *Arch Surg* 1989;124:911-5.
 6. Prey MU, Vitale T, Martin SA. Guidelines for practical utilization of intraoperative frozen sections. *Arch Surg* 1989;124:331-5.
 7. Cucumano RJ, Mahadevia P, Silver CE. Intraoperative histologic evaluation in exploration of the parathyroid glands. *Surg Gynecol Obstet* 1989;169:506-10.
 8. Malhotra A, Silver CE, Deshpande V, Freeman LM. Preoperative parathyroid localization with sestamibi. *Am J Surg* 1996;172:637-40.
 9. Bergman JA, Pallant R. Thallium/technetium subtraction scanning for primary hyperparathyroidism: scan sensitivity and effect on operative time. *Ear Nose Throat J* 1998;77:404-7.
 10. Hindie E, Melliere D, Perlemuter L, Jeanguillaume C, Galle P. Primary hyperparathyroidism: higher success rate of first surgery after preoperative Tc-99m sestamibi-I-123 subtraction scanning. *Radiology* 1997;204:221-8.
 11. Purcell GP, Dirbas FM, Jeffrey RB, Lane MJ, Desser T, McDougall R, Weigel RJ. Parathyroid localization with high resolution ultrasound and technetium Tc99m sestamibi. *Arch Surg* 1999;134:824-30.
 12. Nussbaum SR, Thompson AR, Hutcheson KA, Gas RD, Wang C. Intraoperative measurement of parathyroid hormone in the surgical management of hyperparathyroidism. *Surgery* 1988;104:1121-7.
 13. Irvin GL, Dembrow VD, Prudhomme DL. Clinical usefulness of an intraoperative "quick parathyroid hormone" assay. *Surgery* 1993;114:1019-23.
 14. Michelangeli VP, Heyma P, Colman PG, Ebeling PR. Evaluation of a new, rapid and automated immunochemiluminometric assay for the measurement of serum intact parathyroid hormone. *Ann Clin Biochem* 1997;34:97-103.
 15. Sokoll LJ, Drew H, Udelsman R. Intraoperative parathyroid hormone analysis: a study of 200 consecutive cases. *Clin Chem* 2000;46:1662-8.
 16. Irvin GL, Carneiro DM. Management changes in primary hyperparathyroidism. *JAMA* 2000;284:934-6.
 17. Chen H, Sokoll J, Udelsman R. Outpatient minimally invasive parathyroidectomy: a combination of sestamibi-SPECT localization, cervical block anesthesia, and intraoperative parathyroid hormone assay. *Surgery* 1999;126:1016-21.
 18. Wians FH, Balko JA, Hsu RM, Byrd W, Snyder WH. Intraoperative vs central laboratory PTH testing during parathyroidectomy surgery. *Lab Med* 2000;31:616-21.
 19. Connerty HV, Briggs AR. Determination of serum calcium by means of *o*-cresolphthalein complexone. *Am J Clin Pathol* 1966;45:290-6.
 20. Coakley AJ, Kettle AG, Wells CP, O'Doherty MJ, Collins REC. ⁹⁹Tcm sestamibi—a new agent for parathyroid imaging. *Nucl Med Commun* 1989;10:791-4.
 21. O'Doherty MJ, Kettle AG, Wells P, Collins REC, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: preoperative localization and tissue uptake studies. *J Nucl Med* 1992;33:313-8.
 22. Black WC, Utley JR. The differential diagnosis of parathyroid adenoma and chief cell hyperplasia. *Am J Pathol* 1968;49:761-75.
 23. Black WC, Haff RC. The surgical pathology of parathyroid chief cell hyperplasia. *Am J Clin Pathol* 1970;53:565-79.
 24. Delbridge LW, Dolan SJ, Hop TT, Robinson BG, Wilkinson MR, Reeve TS. Minimally invasive parathyroidectomy: 50 consecutive cases. *Med J Aust* 2000;172:418-22.
 25. Sofferan RA, Standage J, Tang ME. Minimal-access parathyroid surgery using intraoperative parathyroid hormone assay. *Laryngoscope* 1998;108:1497-1503.
 26. Patel PC, Pellitteri PK, Patel NM, Fleetwood MK. Use of a rapid intraoperative parathyroid hormone assay in the surgical management of parathyroid disease. *Arch Otolaryngol Head Neck Surg* 1998;124:559-62.
 27. Robertson GSM, Iqbal SJ, Bolia A, Bell PRF, Veitch PS. Intraoperative parathyroid hormone estimation: a valuable adjunct to parathyroid surgery. *Ann R Coll Surg Engl* 1992;74:19-22.
 28. Irvin GL, Molinari AS, Figueroa C, Carneiro DM. Improved success rate in reoperative parathyroidectomy with intraoperative PTH assay. *Ann Surg* 1999;229:874-8.
 29. Bergenfelz A, Isaksson A, Lindblom P, Westerdaal J, Tibblin S. Measurement of parathyroid hormone in patients with primary hyperparathyroidism undergoing first and reoperative surgery. *Br J Surg* 1998;85:1129-32.
 30. Proye CAG, Goropoulos A, Franz C, Carnaille B, Vix M, Quievreux JL, et al. Usefulness and limits of quick intraoperative measurement of intact (1-84) parathyroid hormone in the surgical management of hyperparathyroidism: sequential measurements in patients with multi-glandular disease. *Surgery* 1991;110:1035-42.
 31. Wenk RE, Efron G, Madamba L. Central laboratory analyses of intact PTH using intraoperative samples. *Lab Med* 2000;3:158-61.
 32. Dackiw APB, Sussman JJ, Fritsche HA, Delpassand ES, Stanford P, Hoff A, et al. Relative contributions of technetium Tc99m sestamibi scintigraphy, intraoperative γ probe detection, and the rapid parathyroid hormone assay to the surgical management of hyperparathyroidism. *Arch Surg* 2000;135:550-7.
 33. Gordon LL, Snyder WH, Wians F, Nwariaku F, Kim LT. The validity of quick intraoperative parathyroid hormone assay: an evaluation in seventy-two patients based on gross morphologic criteria. *Surgery* 1999;126:1030-5.
 34. Garner SC, Leight GS. Initial experience with intraoperative PTH determinations in the surgical management of 130 consecutive cases of primary hyperparathyroidism. *Surgery* 1999;126:1137-8.
 35. Miccoli P, Bendinelli C, Berti P, Vignali E, Pinchera A, Marocci C. Video-assisted versus conventional parathyroidectomy in primary hyperparathyroidism: a prospective randomized study. *Surgery* 1999;126:1117-21.
 36. Song AU, Philips TE, Edmond CV, Moore DW, Clark SK. Success of preoperative imaging and unilateral neck exploration for primary hyperparathyroidism. *Otolaryngol Head Neck Surg* 1999;121:393-7.
 37. Gauger PG, Reeve TS, Delbridge LW. Endoscopically assisted, minimally invasive parathyroidectomy. *Br J Surg* 1999;86:1563-6.