

National Academy of Clinical Biochemistry (NACB)

Laboratory Medicine Practice Guidelines (LMPG):
Evidence-Based Practice for Point of Care Testing
2004

Intraoperative Parathyroid Hormone



Intraoperative PTH Group

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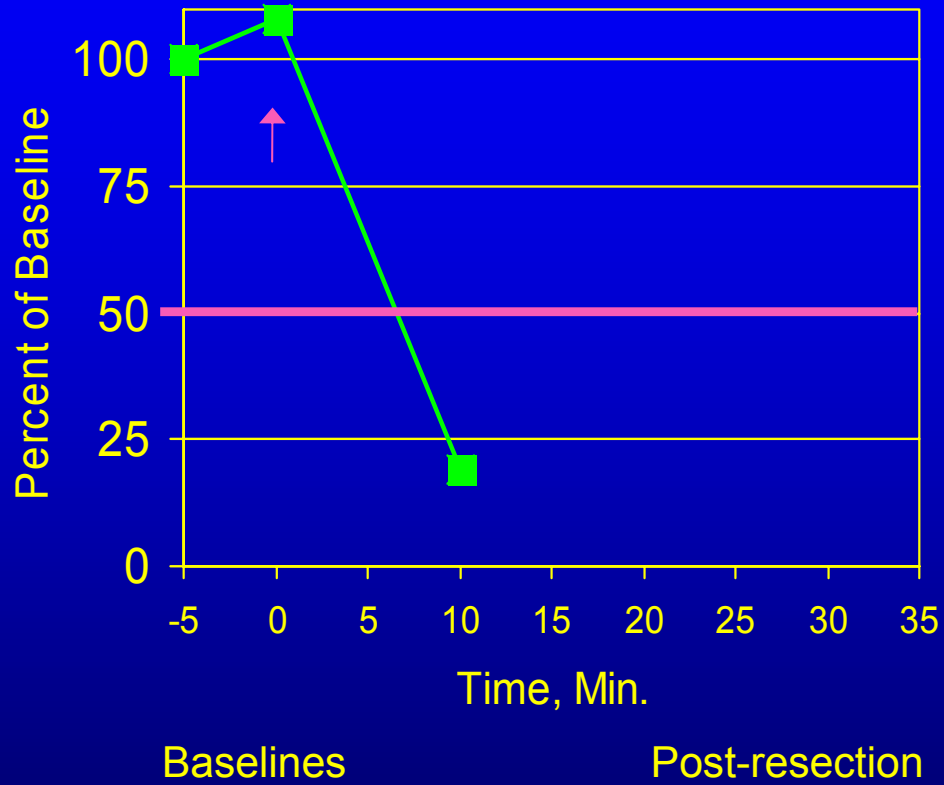


What is Intraoperative PTH (IO PTH) and Why is it Used?

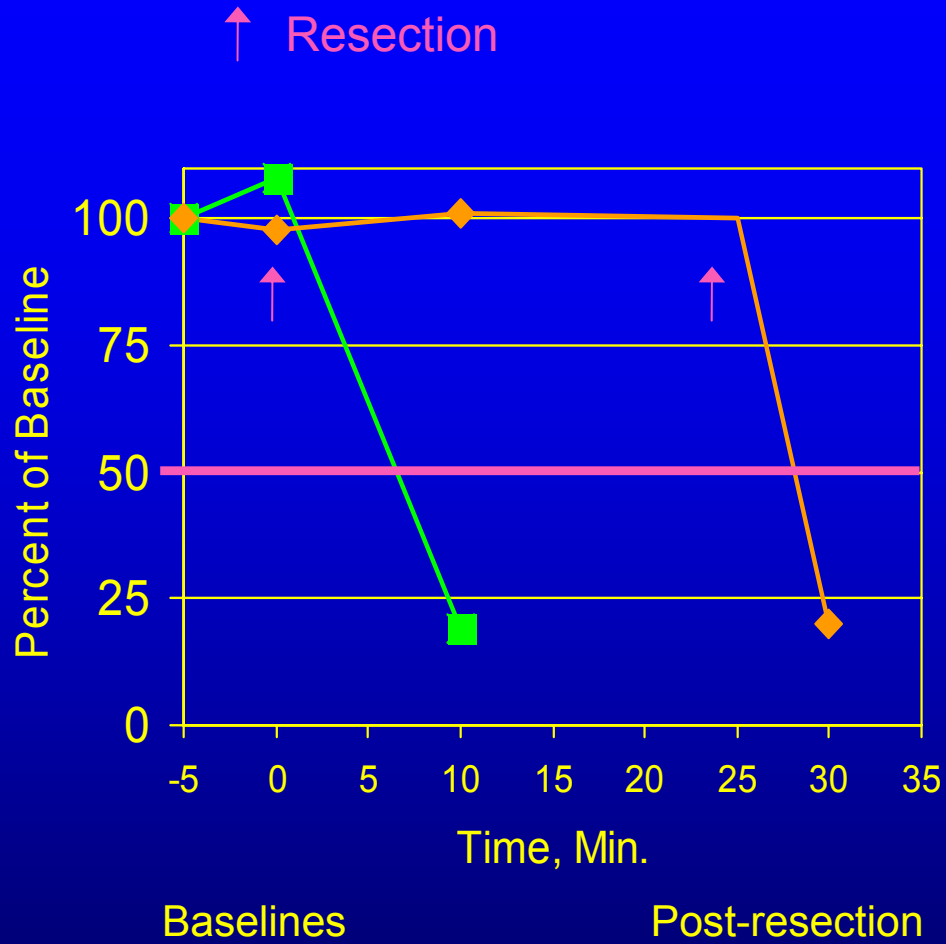
- Despite the success rate of surgical treatment for primary hyperparathyroidism of >90-95%, a troubling fraction remained hypercalcemic post-surgery
- Persistent hypercalcemia was attributable to the presence hyperfunctioning tissue
- Thus, there was a search for a biochemical measure indicative of a physiologic cure as an adjunct to surgical expertise and histologic frozen tissue sections
- PTH was proposed as an intraoperative monitor because of:
 - a half-life of the intact molecule of < 5 min which allows a rapid decrease in PTH concentrations when hyperfunctioning tissue is excised
 - the availability of a rapid assay with results available in < 15 min

↑ Resection

■ Uniglandular Disease



- Uniglandular Disease
- ◆ Multiglandular Disease



Utility of Intraoperative PTH in Primary Hyperparathyroidism

- Does the addition of intraoperative PTH measurements to surgery for parathyroid disease improve
 - the accuracy of identifying multiglandular disease compared to bilateral exploratory surgery?
 - the adequacy of resection or cure rate compared to bilateral exploratory surgery?



Evidence: Cure Rate

Study	Design	Control Group		Experimental Group with IO PTH	
		Approach	Cure Rate	Approach	Cure Rate
Bergenfelz, 2002	RCT	Bilateral (n=44)	98%	Unilateral (n=47)	96%
Miccoli, 1999	RCT	Bilateral (n=18)	100%	Video-Assisted (n=20)	100%
Carty, 1997	Cohort	Unilateral w/ palpation (n=61)	95%	Unilateral w/ Preop. Imaging (N=67)	97%
Henry, 2001	Historical Controls	Bilateral (n=68)	100%	Video-Assisted (n=68)	100%
Chen, 1999	Historical Controls	Bilateral (n=184)	97%	MIP (n=33)	100%
Udelsman, 2003	Historical Controls	Bilateral (n=401)	97%	MIP (n=255)	99%

Utility of Intraoperative PTH in Primary Hyperparathyroidism

- Does the addition of intraoperative PTH measurements to surgery for parathyroid disease improve
 - the adequacy of resection or cure rate compared to bilateral exploratory surgery alone?
 - the accuracy of identifying multiglandular disease compared to bilateral exploratory surgery?
- Does the use of intraoperative PTH measurements alone or in combination with a unilateral or minimally invasive surgical procedure improve _____ compared to a standard bilateral exploratory operation?

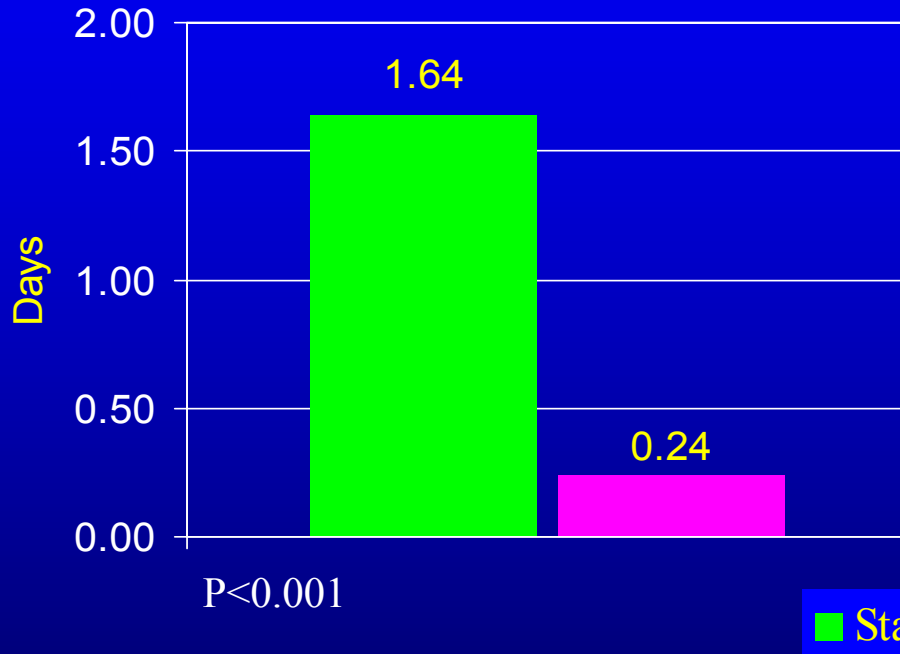


Influence of IO PTH on Patient and Economic Outcomes: Summary of Controlled Studies

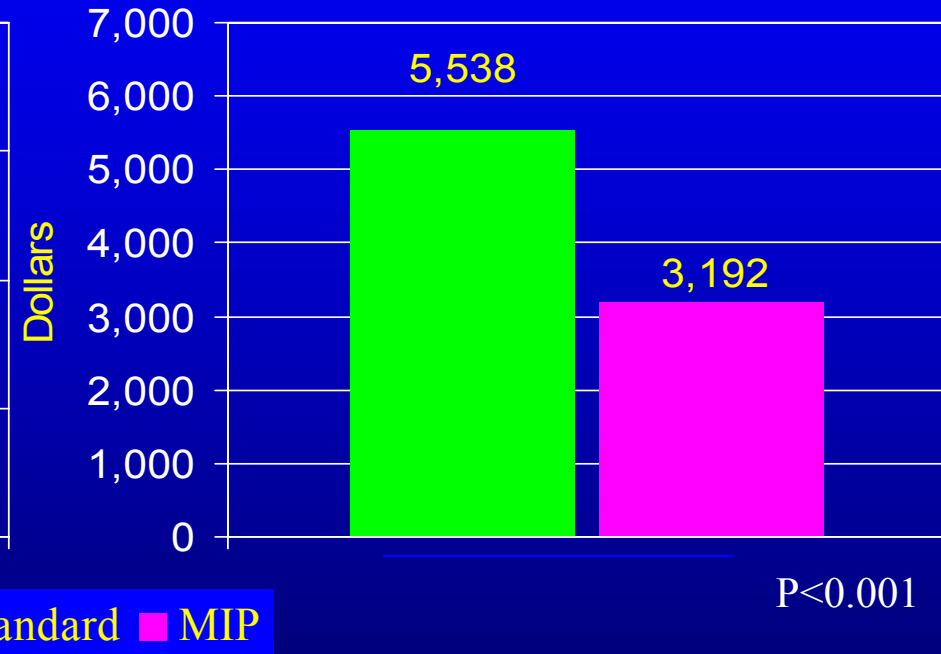
Outcome Studied	Results
Morbidity/Complications	Decrease
Use of local or regional anesthesia	Increase
Operative approach (bilateral to unilateral)	Increase
Use of frozen sections	Decrease
Cosmetic result Patient satisfaction/pain	Improved
OR time OR fees Length of stay Overall hospital costs/charges	Decrease/No Change

656 Consecutive Explorations for Primary Hyperparathyroidism

Length of Hospital Stay



Total Hospital Charges



Recommendation for Use of Intraoperative PTH in Primary Hyperparathyroidism

Based on evidence for improved patient/health, operational, and economic outcomes, we recommend routine use of intraoperative parathyroid hormone testing and strongly recommend routine use in minimally invasive or directed procedures.

(Grade of Evidence: I, II, III-randomized controlled trials, controlled trials, cohort study, case series, models and simulations, opinion, consensus panel)



Is There Evidence to Support a Specific Assay?



Roche Elecsys Intact PTH
E2010/E1010/Modular Analytics E170

Qui
Nic

QuiCk-IntraOperative Bio-Intact PTH (1-84)
Nichols Institute Diagnostics

STAT-IntraOperative-Intact-PTH
Future Diagnostics

Use of a Specific Assay: Evidence

- Intact PTH Assays: two small studies showing diagnostic agreement
 - Nichols QuiCk-Intraoperative Intact PTH vs. Immulite *Turbo* Intact PTH (n=10)-Wians, 2000
 - Nichols QuiCk-Intraoperative Intact PTH vs. Roche Elecsys 1010 Intact PTH (n=13)-Hermsen, 2002
- Intact PTH vs. Bio-intact PTH (1-84) Assays (standard)
 - Scantibodies CAP IRMA vs. Nichols IRMA (n=29, 1° HPT), Similar results in frozen samples
- Recommendation
 - *We do not recommend the use of a specific IO PTH assay. Additional studies comparing bio-intact or whole PTH rapid intraoperative assays to intact rapid intraoperative assays need to be performed.*



(Grade of Evidence: III-comparative studies)

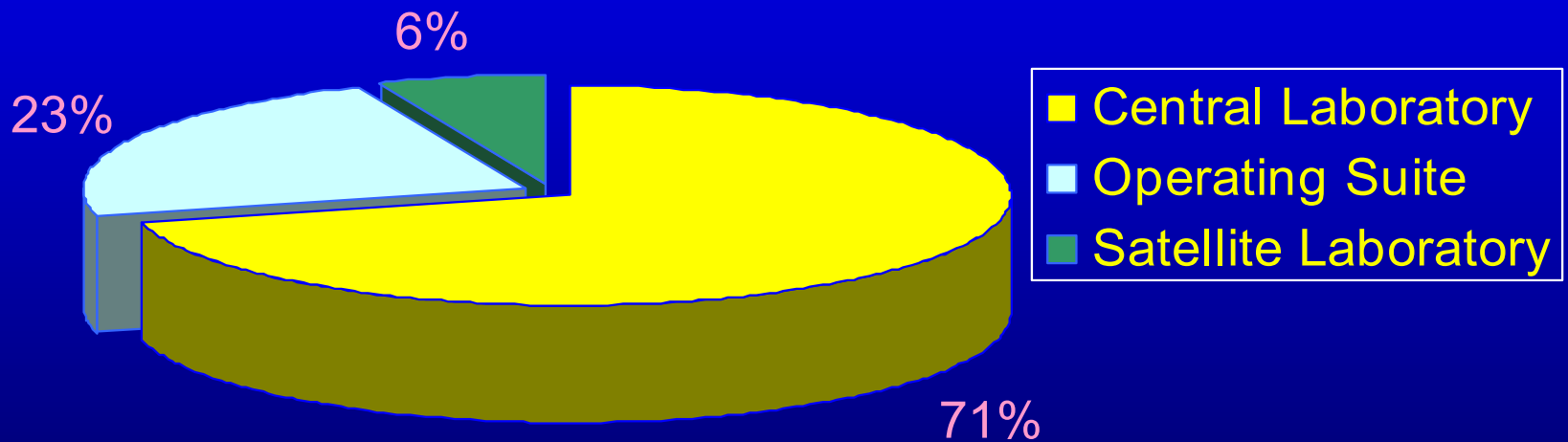
Is Intraoperative PTH a Point-of-Care Test?

Does performing intraoperative PTH measurements in or adjacent to the operating suite improve turnaround and operative times compared to performing intraoperative PTH measurements in the central laboratory with specimens transported via pneumatic tube or messenger?



Evidence: No comparative studies

Location of IO PTH Testing: CAP Survey of 92 Labs



Recommendation for Testing Location: On-site vs. Central Lab

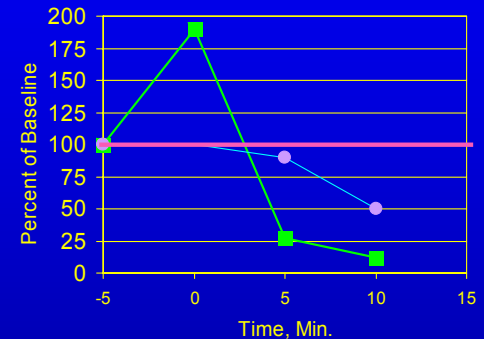
Evidence is lacking to recommend the site of intraoperative PTH testing. Important considerations such as interaction with the surgical team must be weighed in concert with costs and staffing issues. Studies to evaluate turnaround and operative times related to different sites have not been explicitly performed.

(Grade of Evidence: III-case reports and series, opinion)



Is There Evidence to Support Sampling and Interpretation Criteria?

- *We recommend:*
 - *Baseline samples drawn pre-operation/exploration and pre-excision of the affected gland**
 - *Post-resection samples drawn at 5 and 10 minutes**
Additional samples may be necessary
 - *A 50% reduction in PTH concentrations from the highest baseline for interpretation**
 - *Also, kinetic analyses appear promising, however more work needs to be done to confirm their utility*



(Grade of Evidence: III-comparative studies, opinion)

**Accuracy=97%, false positives=0.9%, false negatives=2.6%
Carneiro M, et al. Surgery 134:973-81, 2003*

Summary of Recommendations for Intraoperative PTH (1)

Disease	A Strongly Recommend	B Recommend	C No Rec.	D Recommend Against	I Insufficient Evidence
1° HPT	✓	✓			
2°/3° HPT			✓		
Reoperative		✓			
MEN I			✓		
Parathyroid Carcinoma					✓

Summary of Recommendations for Intraoperative PTH (2)

Venous/Tumor Localization	A Strongly Recommend	B Recommend	C No Rec.	D Recommend Against	I Insufficient Evidence
Pre-surgery Angiography Suite (Reoperative Cases)		✓			
Operating Suite			✓		

Summary of Recommendations for Intraoperative PTH (3)

	Recommendation
Use of a Specific Assay	No recommendation
Testing Site	No recommendation
Sampling and Interpretation Criteria	<p>In 1° HPT:</p> <p>Baseline samples: pre-operation/exploration and pre-excision.</p> <p>Post-resection specimens: 5 and 10 minutes. Additional samples may be necessary.</p> <p>Criterion: 50% reduction in PTH concentrations from the highest baseline as a criterion.</p>

Summary

- In the less than 10 years since introduction of commercially available intraoperative PTH assays there has been considerable interest and use of the assay by endocrine and other surgeons
- George Irvin, MD commented that all surgeons performing parathyroidectomies can relate to the saying, “When you know you’ve got it, you can stop looking”
- Based on strong impressions from relatively few controlled studies we recommend intraoperative PTH be routinely provided in primary hyperparathyroidism, particularly in directed surgical approaches
- Further studies are needed in other settings and to refine current use with respect to specific assays and interpretation of PTH values

