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Primary Hyperparathyroidism: MIP vs. BNE

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- Current consensus guidelines
- Surgical approaches
- Recommendations

Primary Hyperparathyroidism

- Hypercalcemia in the setting of inappropriately nonsuppressed PTH
- Normohormonal HPT
- Normocalcemic HPT

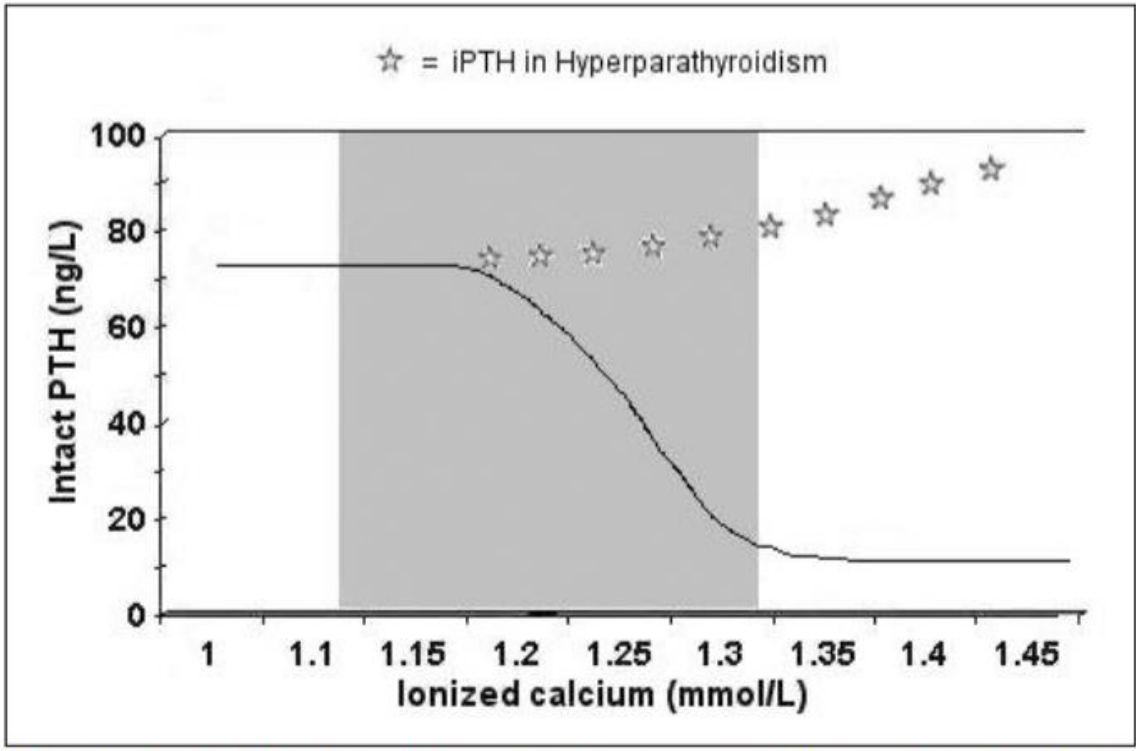

Fig. 1. Relationship between intact parathyroid hormone (*iPTH*) and ionized calcium in normal physiologic state and hyperparathyroidism. *Shaded area* = normal range for ionized calcium.

Kukora J et al. Endo Pract 2005

Primary Hyperparathyroidism

- Hypercalcemia
  - HPT, FHH, malignancy, sarcoidosis, vitamin D intoxication, thiazide diuretics, immobility
- Elevated PTH
  - 1ºHPT, 2ºHPT (vitamin D deficiency, CRF), calcium deficiency, malabsorption, hypercalciuria
- Evaluation
  - Serum Ca^{+}, iCa, 24-hour urine Ca^{+}/Cr, vitamin D, PTHrP
- Im[redacted]ng

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Table 1. Guidelines for Surgery in Asymptomatic PHPT: A Comparison of Current Recommendations With Previous Ones[a]

	1990	2002	2008	2013
Measurement[b]				
Serum calcium (>upper limit of normal)	1–1.6 mg/dL (0.25–0.4 mmol/L)	1.0 mg/dL (0.25 mmol/L)	1.0 mg/dL (0.25 mmol/L)	1.0 mg/dL (0.25 mmol/L)
Skeletal	BMD by DXA: Z-score <−2.0 (site unspecified)	BMD by DXA: T-score <−2.5 at any site[b]	BMD by DXA: T-score <−2.5 at any site[b]	A. BMD by DXA: T-score < −2.5 at lumbar spine, total hip, femoral neck, or distal 1/3 radius[b]
			Previous fragility fracture[c]	B. Vertebral fracture by x-ray, CT, MRI, or VFA
Renal	A. eGFR reduced by >30% from expected B. 24-h urine for calcium >400 mg/d (>10 mmol/d)	A. eGFR reduced by >30% from expected B. 24-h urine for calcium >400 mg/d (>10 mmol/d)	A. eGFR < 60 cc/min B. 24-h urine for calcium not recommended	A. Creatinine clearance < 60 cc/min B. 24-h urine for calcium >400 mg/d (>10 mmol/d) and increased stone risk by biochemical stone risk analysis[d] C. Presence of nephrolithiasis or nephrocalcinosis by x-ray, ultrasound, or CT
Age, y	<50	<50	<50	<50

- Prefers surgery
- Unable/unwilling to follow up

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Bilezikian et al. JCEM Oct 2014

The American Association of Endocrine Surgeons (AAES) Guidelines for Definitive Management of Primary Hyperparathyroidism

SM Wilhelm, JA Lee, DT Ruan, TS Wang, SL Asa, QY Duh, GM Doherty, MF Herrera, JL Pasieka, ND Perrier, SJ Silverberg, CC Solórzano, C Sturgeon, ME Tublin, R Udelsman, SE Carty

- Expert group of medical and surgical endocrinologists
- First guidelines which focus on surgical recommendations

RECOMMENDATION 4.1: Parathyroidectomy is indicated, and is the preferred treatment, for all patients with symptomatic pHPT.

Strong Recommendation - High quality evidence

- More effective than medical tx
- more cost-effective
- Similar recommendations to NIH guidelines

- **RECOMMENDATION 4.7:** Parathyroidectomy is the preferred treatment for patients who are unable or unwilling to comply with standard observation protocols.

  Strong Recommendation - Moderate quality evidence

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- **RECOMMENDATION 4.8:** Parathyroidectomy is recommended for patients with neurocognitive and/or neuropsychiatric symptoms that may be attributable to pHPT.

  Strong Recommendation - Low quality evidence

  - Parathyroidectomy assessment of symptoms
  - Improvement within 10 days, more over following year (60% reduction)

- **RECOMMENDATION 4-9:** Parathyroidectomy should be offered to surgical candidates who have or are at high risk for cardiovascular disease and who might benefit from mitigation of potential cardiovascular sequelae other than hypertension.

  Weak Recommendation - Low quality evidence

  - Should not be only indication

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- **RECOMMENDATION 5-1:** Patients with pHPT who are candidates for parathyroidectomy should be referred to a surgeon to decide which imaging studies to perform based on their knowledge of regional imaging capabilities.

  Strong Recommendation - Low quality evidence

- **RECOMMENDATION 5-2:** Patients with pHPT who are candidates for surgery and have negative or discordant imaging should still be referred to an expert parathyroid surgeon for evaluation.

- Imaging is not used for diagnosis

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MIP vs. BNE

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Minimally Invasive Parathyroidectomy

- Definition
  - Surgical approach vs technology?
  - Focused neck exploration
  - Video-assisted parathyroidectomy
  - Robot-assisted parathyroidectomy

Focused Neck Exploration

- 2.5cm incision
- Local/general anesthesia
- outpatient

Focused Neck Exploration

- Intraoperative PTH
  - Half life
- Imaging
  - Sestamibi
  - Ultrasound
  - 4D CT

Cure Criteria	Timing of PTH samples in the operating room	Usual # of PTH samples	Cure rates	Recurrence Rates (mean follow-up in months)
Miami: >50% PTH decrease at 10 minutes from the highest level, either pre-incision or pre-excision	1-Pre-incision: before incision 2-Pre-excision: before the blood supply to the gland is ligated 3-Five minute level: 5 minutes after gland removal 4-Ten minute level: 10 minutes after gland removal 5-Other levels++	3 to 4	97-99%	3% (50) Irvin 2004 2% (48) Carneiro 3% (83) Lew 1.2% (13) Lee 2.4% (9*) Schneider 2.9% (21) Rajaei 0.4% (15) Udelsman
Dual: >50% PTH decrease from the pre-incision level *plus* final PTH into normal range	1-Pre-incision: before incision 2-Ten minute level: 10 minutes after gland removal 3-Other levels++	2	97-99%	0.4% (10) Hughes 0.5% (21.6) Wharry n/a (NFS) Heller n/a (NFS) Richards 3.2% (28*) Wachtel

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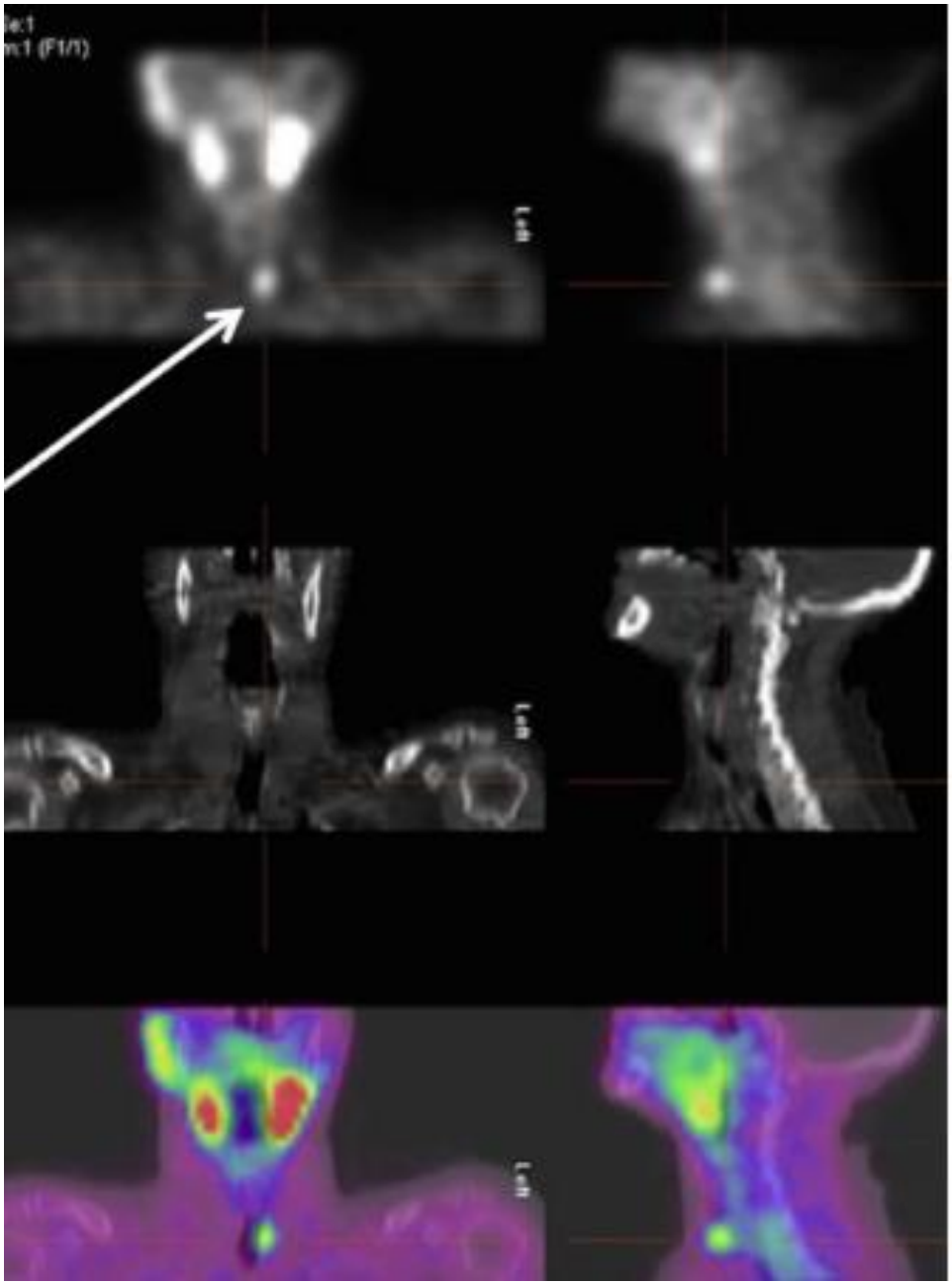
AAES Guidelines



- Sensitivity: 70-90%

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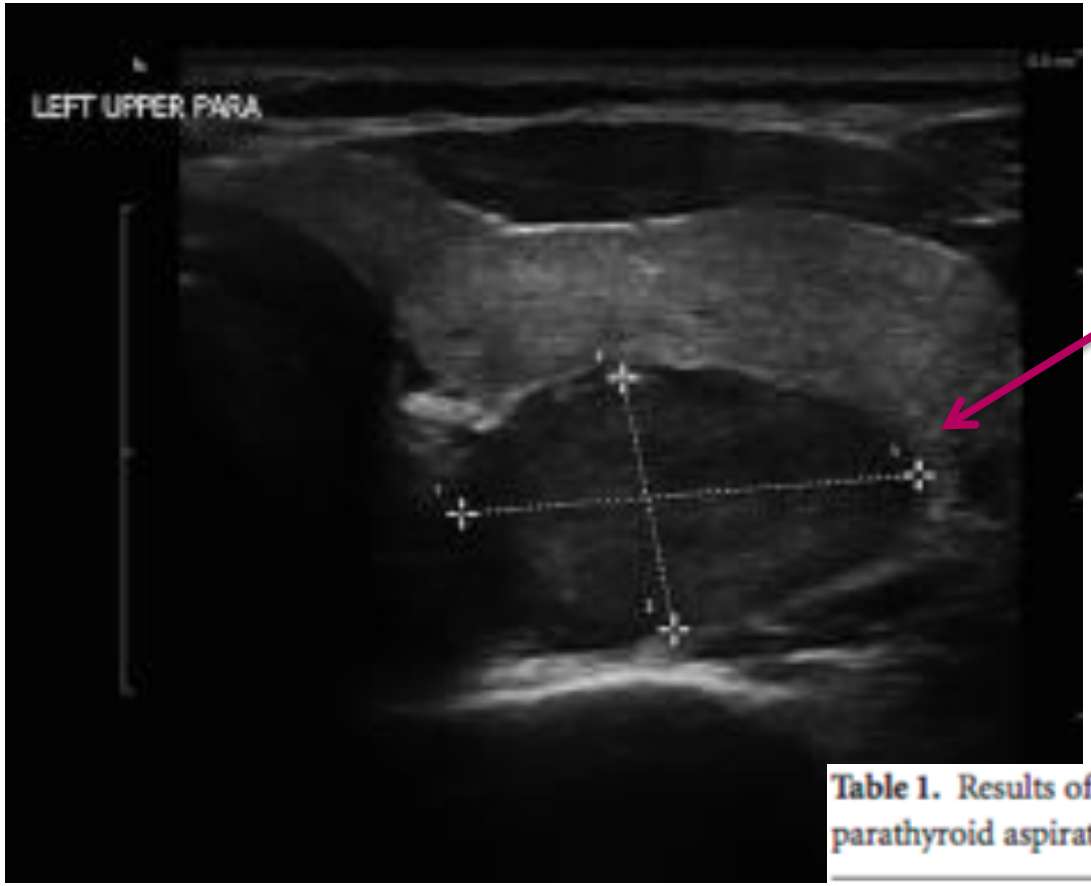

- Variability between groups
- Know institutional rates

Table 1. Results of imaging studies: SS, US and US + iPTH assay of parathyroid aspirates according to absence or presence of goitre

Technique	*n*	TP (%)	FN (%)	FP (%)	Sensitivity (%)	PPV (%)
SS, total	121	93 (76·9)	17 (14·0)	11 (9·1)	84·5	89·4
SS, no goitre	78	67 (85·9)	8 (10·2)	3 (3·8)	89·3	95·7
SS, with goitre	43	26 (60·5)	9 (20·9)	8 (18·6)	74·3	76·5
US, total	121	96 (79·3)	14 (11·6)	11 (9·1)	87·3	89·7
US, no goitre	78	73 (93·6)	3 (3·8)	2 (2·6)	96·0	97·3
US, with goitre	43	23 (53·5)	11 (25·6)	9 (20·9)	67·7	71·9
US + iPTH*	43	39 (90·7)	4 (9·3)	0 (0)	90·7	100

Barczynski M. Clin Endo 2006

Image-guided Parathyroidectomy

- Variety of localization techniques
  - Ultrasound, sestamibi most common

Table VII. Operative success rates compared with the results of preoperative US and sestamibi imaging

US	*Sestamibi*	*Success rate (%)*
+	+	30/32 (94)
–	+	16/17 (94)
+	–	12/12 (100)
–	–	0/1 (0)

+, Suspicious lesion identified; –, no lesion identified.

- May be a substitute for IOPTH if not available

Feingold DL, et al. Surgery. Dec 2000

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Bilateral Neck Exploration

- Previously standard
- All 4 glands must be identified
- +/- IOPTH
- Necessary if multigland disease
  - MEN 1
  - MEN 2a
  - ?lithium-induced HPT

Bilateral Neck Exploration

TABLE 4. Surgical Findings in Bilateral Neck Exploration When Localizing Studies Suggested a Solitary Adenoma–Simulated Unilateral Approach

Surgical Findings in Bilateral Neck Exploration	MIBI n = 682		US n = 731		MIBI and US n = 588	
	n:	(%)	n:	(%)	n:	(%)
Single adenoma, correct side identified (PPV)	483	71	548	75	454	77
Additional cases of success by:						
Converting to bilateral Exploration*	95	14	81	11	57	10
Adding IOPTH†	24	4	23	3	17	3
Failure‡	67	10	79	11	60	10

*When 2 normal or 2 abnormal glands were found during LE a bilateral neck exploration was performed.

†Failure of IOPTH to drop more than 50%, 10 min after resection forced a bilateral neck exploration.

‡Failure is the finding of unsuspected multiple gland disease in the subsequent bilateral neck exploration, after finding and resecting the index gland, and an adequate drop in the IOPTH.

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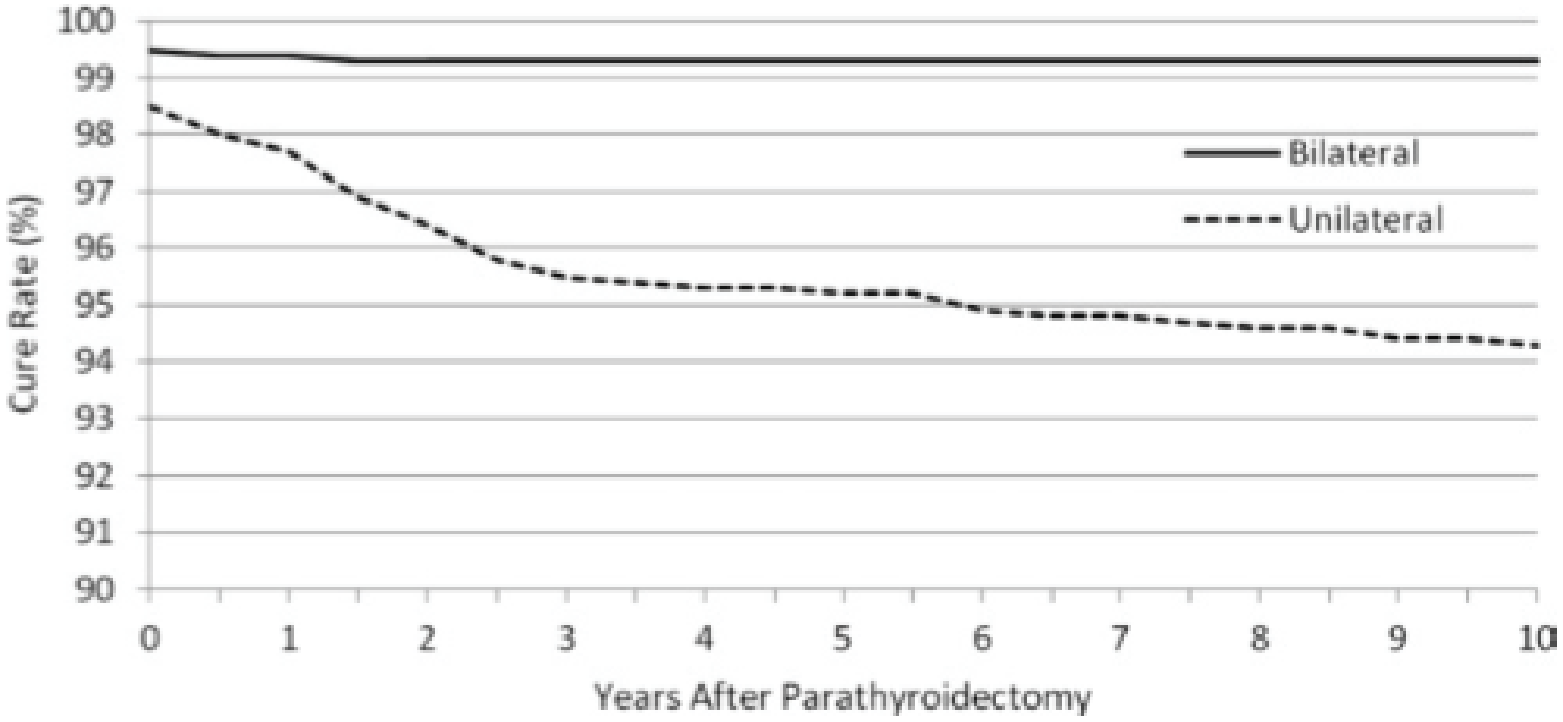
Siperstein A. Ann Surg 2008

Bilateral Neck Exploration



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Norman J. JACS 2012

Table 2
Randomized and retrospective series comparing focused neck exploration and bilateral neck exploration

Series	Study Type	Outcome
Westerdahl & Bergenfelz,[90] 2007	Randomized	= Cure rate at 5 y
Bergenfelz et al,[5] 2002	Randomized	= Cure rate; increased cost and operative time in FNE; increased postoperative hypocalcemia with BNE
Slepavicius et al,[91] 2008	Randomized	= OR time and cure rate; increased cost with FNE; increased postoperative hypocalcemia with BNE
Aarum et al,[93] 2007	Randomized	= Cure rate; = complication rate; increased cost with FNE
Grant et al,[92] 2005	Retrospective	= Cure rate; = complication rate
Udelsman et al,[8] 2011	Retrospective	Increased cure rate and lower complication rate with FNE

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Laird AM. Surg Clinics. Sept 2015

Table 1 Operative variables in 77 patients who underwent reoperative parathyroidectomy, divided by the type of initial operation—minimally invasive parathyroidectomy or standard cervical exploration

Operative variable (median) (minimum, maximum)	Initial MIP	Initial SCE	*P* value
Operating room time (min)	121 (62, 344)	143 (64, 307)	.22
Dissection time (min)	74 (21, 286)	84 (18, 255)	.55
Days hospitalized	1 (0, 3)	1 (0, 8)	.08
Focused reoperation (MIP)	13 (65%)	44 (77%)	.37

MIP = minimally invasive parathyroidectomy; SCE = standard cervical exploration.

Table 2 Postoperative variables in 77 patients who underwent reoperative parathyroidectomy, divided by the type of initial operation—minimally invasive parathyroidectomy or standard cervical exploration

Postoperative variable	Total	Initial MIP	Initial SCE	*P* value
Any postoperative event	27 (35%)	3 (15%)	24 (42%)	.03
Symptomatic hypocalcemia	17 (22%)	3 (15%)	14 (25%)	.53
Emergency department visit	5 (6.4%)	0	5 (9%)	.32
Readmission	2 (2.6%)	1 (5%)	1 (2%)	.45
Cured at 6 months*	44 (88%)	11 (73%)	33 (94%)	.06
Permanent hypoparathyroidism*	4 (8%)	0	4 (11%)	.30

MIP = minimally invasive parathyroidectomy; SCE = standard cervical exploration.

*Fifty patients were followed for ≥6 months postoperatively. There was no significant difference by prior procedure group (MIP versus SCE) in percentage of patients followed for at least 6 months.

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Morris LM. Am J Surg 2014

Advantages of FNE	Advantages of BNE
Smaller incision	May be done through small incision
Shorter operative time	Shorter operative time
Reduced cost compared to BNE	Reduced cost compared to FNE
Outpatient surgery	May be done in outpatient setting
Lower complication rate compared with BNE	Detects multigland disease better than BNE
Cure rate equals BNE	Does not require localization or IOPTH
Less postoperative pain	

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Laird AM. Surg Clinics. Sept 2015

TABLE 1. Demographics, Symptoms, and Signs*

	Standard	MIP	*P*
Age, y (mean ± SD)	57.0 ± 14.2	58.7 ± 13.8	
Female%	72.9	75.9	
Preoperative PTH pg/mL (median [IQR])	114 (79)	107 (60)	
Preoperative calcium mg/dL	11.5 ± 1.0	11.2 ± 0.7	
Symptoms (%)			
Fatigue	38.0	57.7	<0.001
Mental impairment	32.3	46.4	<0.001
Depression	17.8	24.4	<0.002
Gastrointestinal	31.3	42.5	<0.001
Signs (%)			
Bone disease	52.8	72.7	<0.001
Nephrolithiasis	30.0	22.8	<0.001
Cardiovascular disease	13.9	23.6	<0.001
Asymptomatic (%)	10.8	3.8	<0.001

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Udelsman R. Ann Surg 2011

Where are we now?

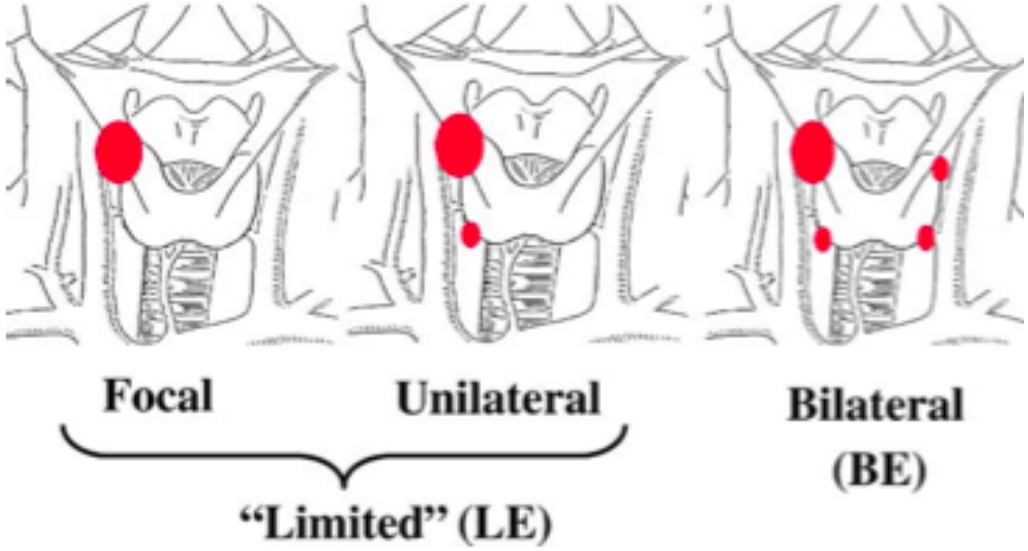

Figure 1. Three philosophical approaches to parathyroidectomy.

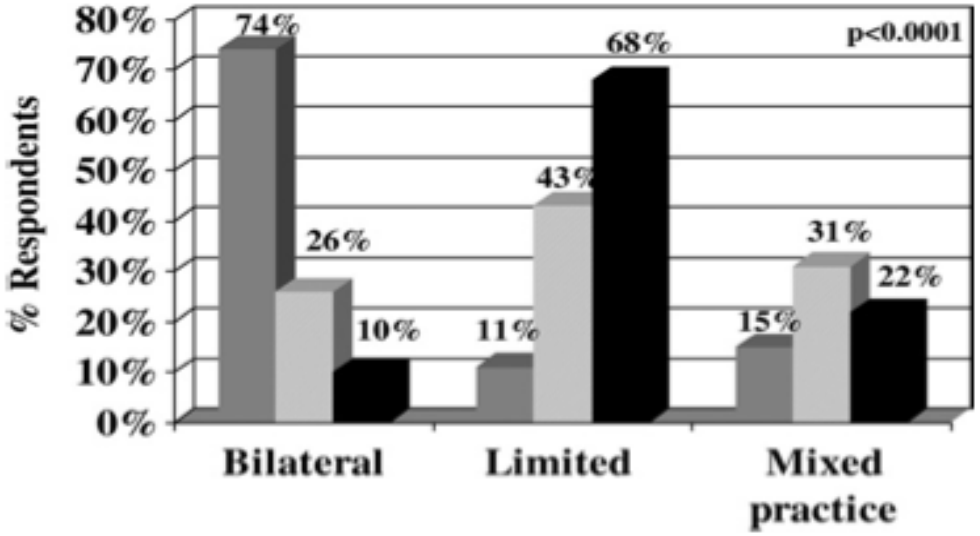

Figure 2. The shift in overall philosophy of practice with regard to parathyroid surgery from 1998 to 2008. Gray bar, 10 years ago; striped bar, 5 years ago; black bar, currently.

Greene, et al. JACS. September 2009

Focused Neck Exploration

- Parathyroidectomy done through a small incision on the anterior neck
- Obtain preoperative localization—sestamibi, surgeon-performed ultrasound
- Use intraoperative PTH monitoring, same way every time
- Outpatient procedure
- +/- general anesthesia

Summary

- Standard treatment of 1ºHPT is cervical exploration and identification of all 4 glands
- Current guidelines define indications for surgery and strongly recommend surgical over medical tx
- Debate surrounds optimal surgical management given equivalent cure rates of focused vs. bilateral neck exploration
- Advantages of focused exploration: reduced operating time, reduced recovery time, lower complication rates

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