Intra-operative PTH

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Objectives

- understand utilization of iPTH
- recognized the pitfalls of iPTH
- appreciation of iPTH role in your own practice

Format

- Paradigm shift in parathyroid surgery
- understand the utilization of iPTH
  - how to use it
  - when to use it
- is iPTH a 'must have' instrument?

- 1924 Albert J. under the care Mandl
  - thyroid extract
  - parathyroid extract
  - parathyroid graft
- 1925 parathyroid 'adenoma'

- by 1931 20 more parathyroidectomies
- 1931 Albert J. **reoccurred**
  - 1932 failed re-operative exploration

"success of parathyroid surgery must lie in the ability of the surgeon to know a parathyroid gland when he *(she)* saw it, to know the distribution of the glands, where they hide, and also be delicate enough in technique to be able to use this knowledge."

E. Churchill,
Chief of Surgery MGH, 1931

Parathyroidectomy

- paradigm shift in the last decade
  - move from exposure of all parathyroid glands

  - focused approach
    - unilateral exploration
    - imaged directed

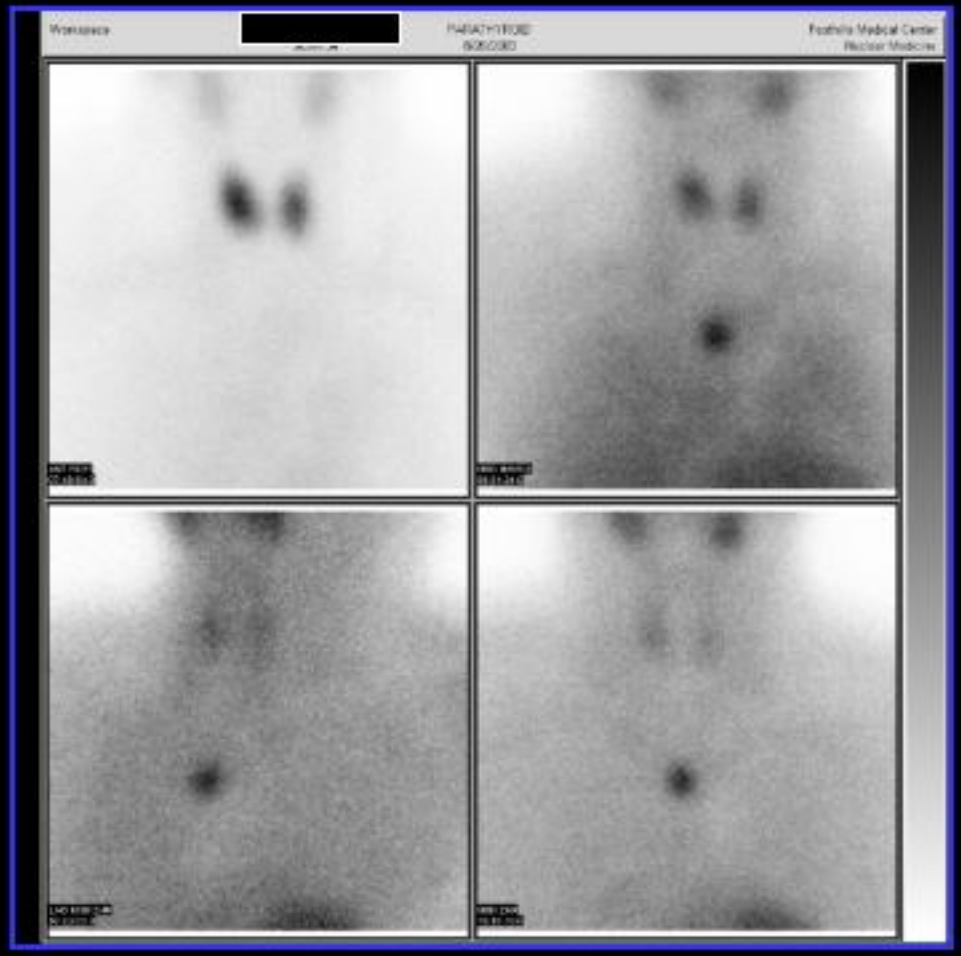
Paradigm Shift in Parathyroidectomy

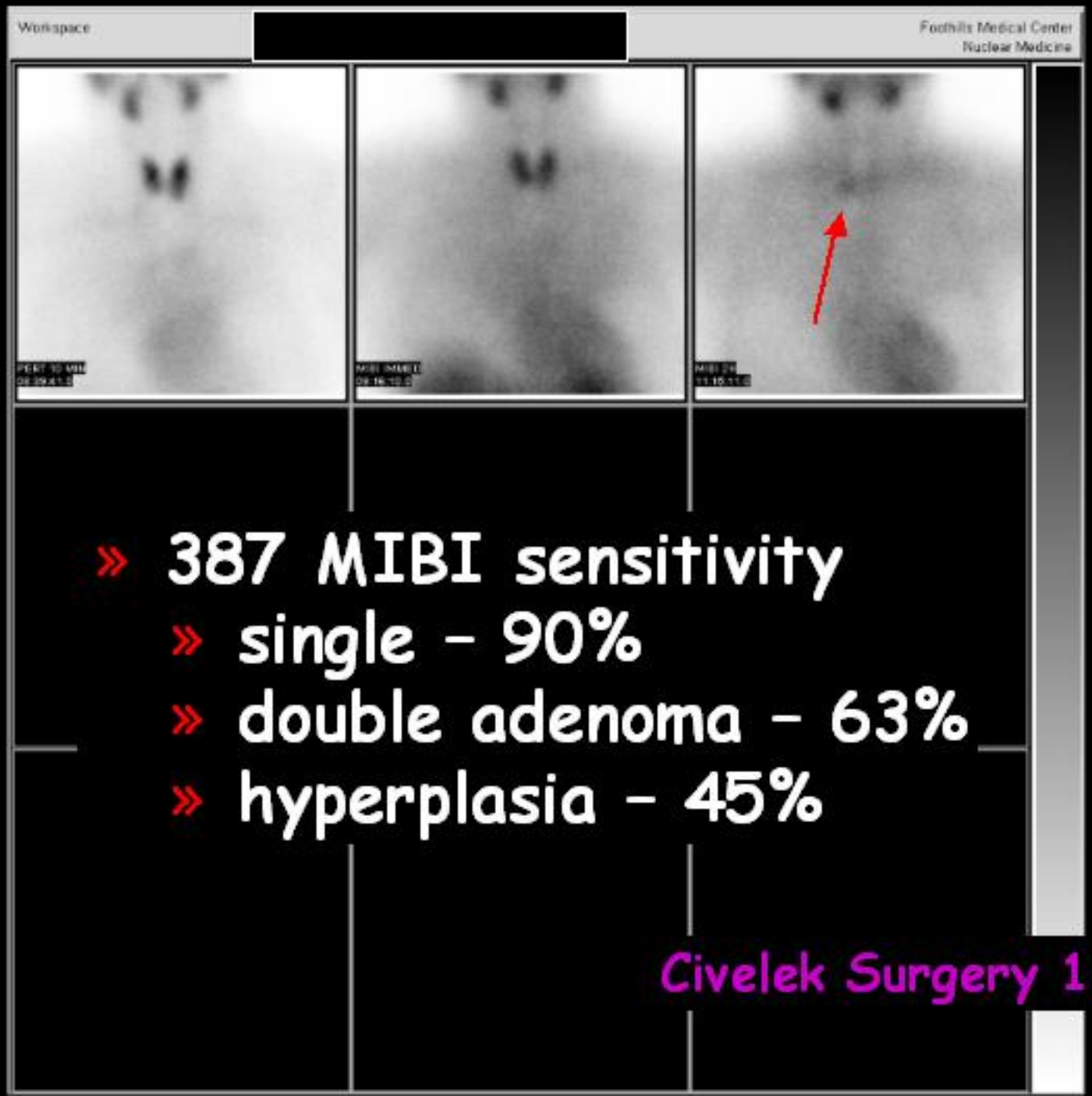
- improvement in pre-operative imaging
- advances in instrumentation, iPTH
- move towards minimally invasive surgeries
- playing the odds

Imaged-Directed Parathyroidectomy

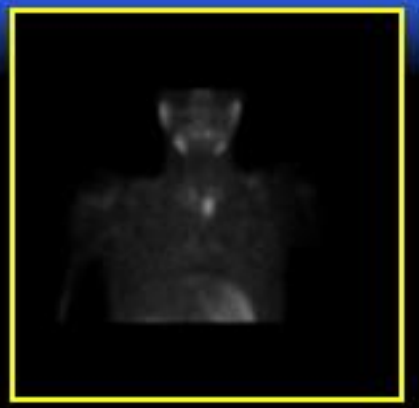
Ultrasound

Sestamibi




Workspace
[redacted]
Foothills Medical Center
Nuclear Medicine
» 387 MIBI sensitivity
» single – 90%
» double adenoma – 63%
» hyperplasia – 45%
Civelek Surgery 131;2002

Imaging only Parathyroidectomy

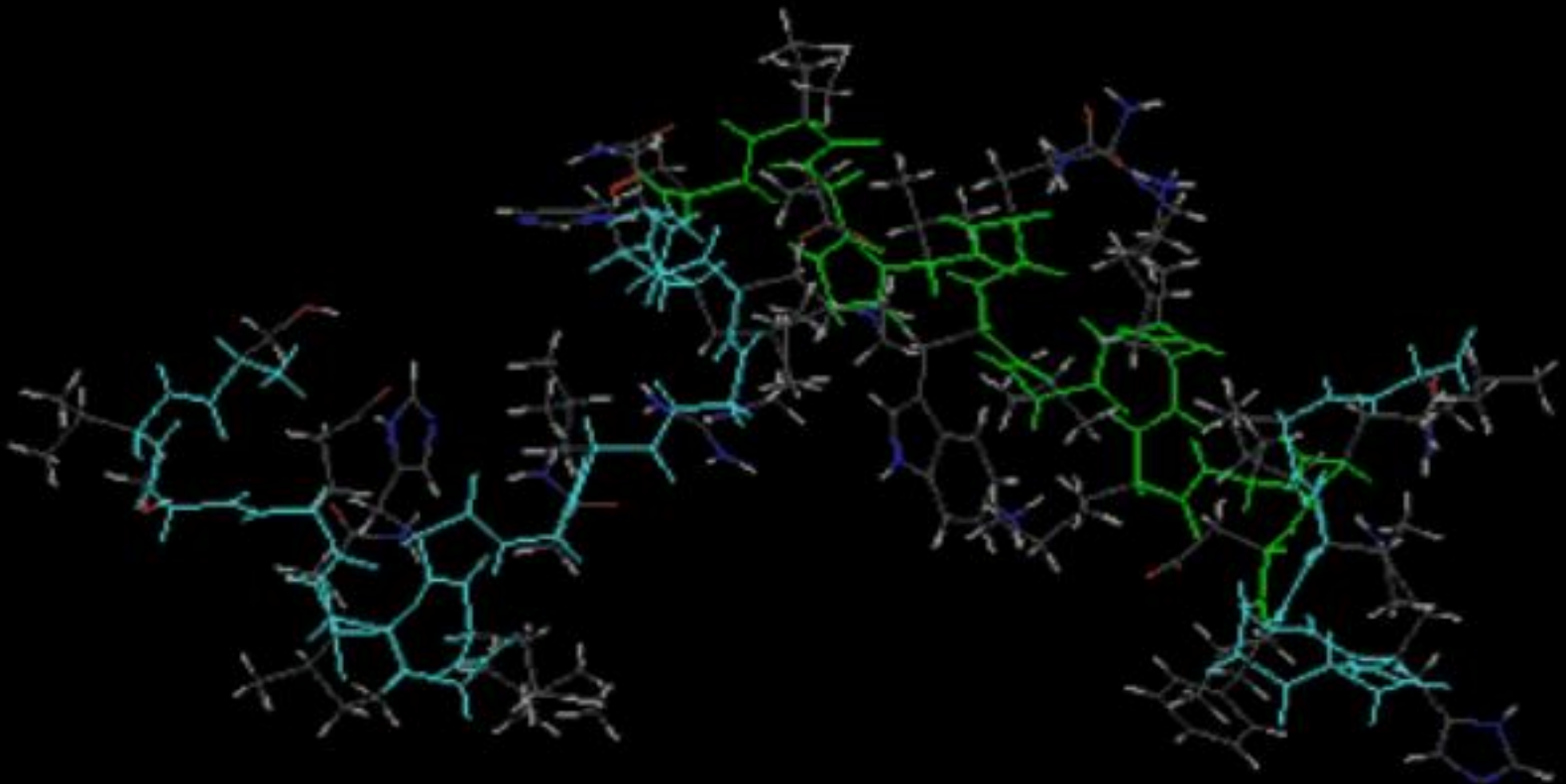


- pitfall is multi-gland disease (MGD)
  - MIBI inaccurate in MGD – 87%
  - U/S inaccurate in MGD – 82%

Miura *et al* WJS:26;2002

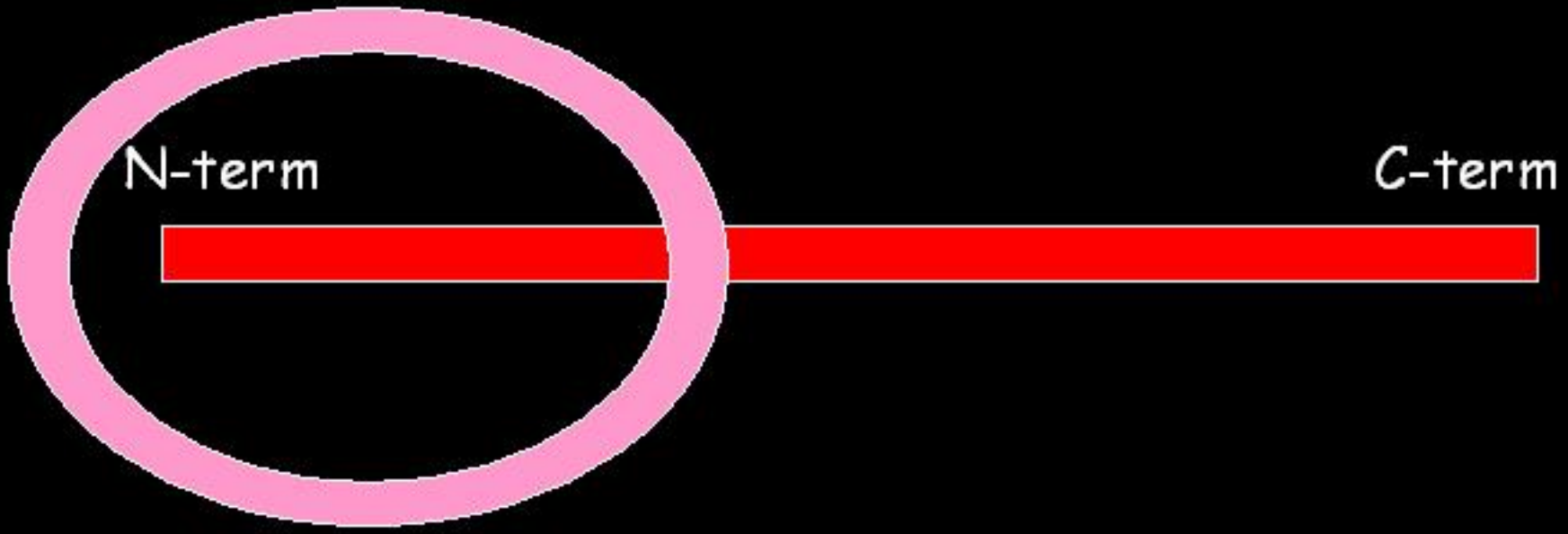
Imaged-Directed Parathyroidectomy

- pre-operative imaging
  - can be misleading in MGD
  - no morphological data
- iPTH (when to stop)
- 95% post-operative cure



PTH – The hormone

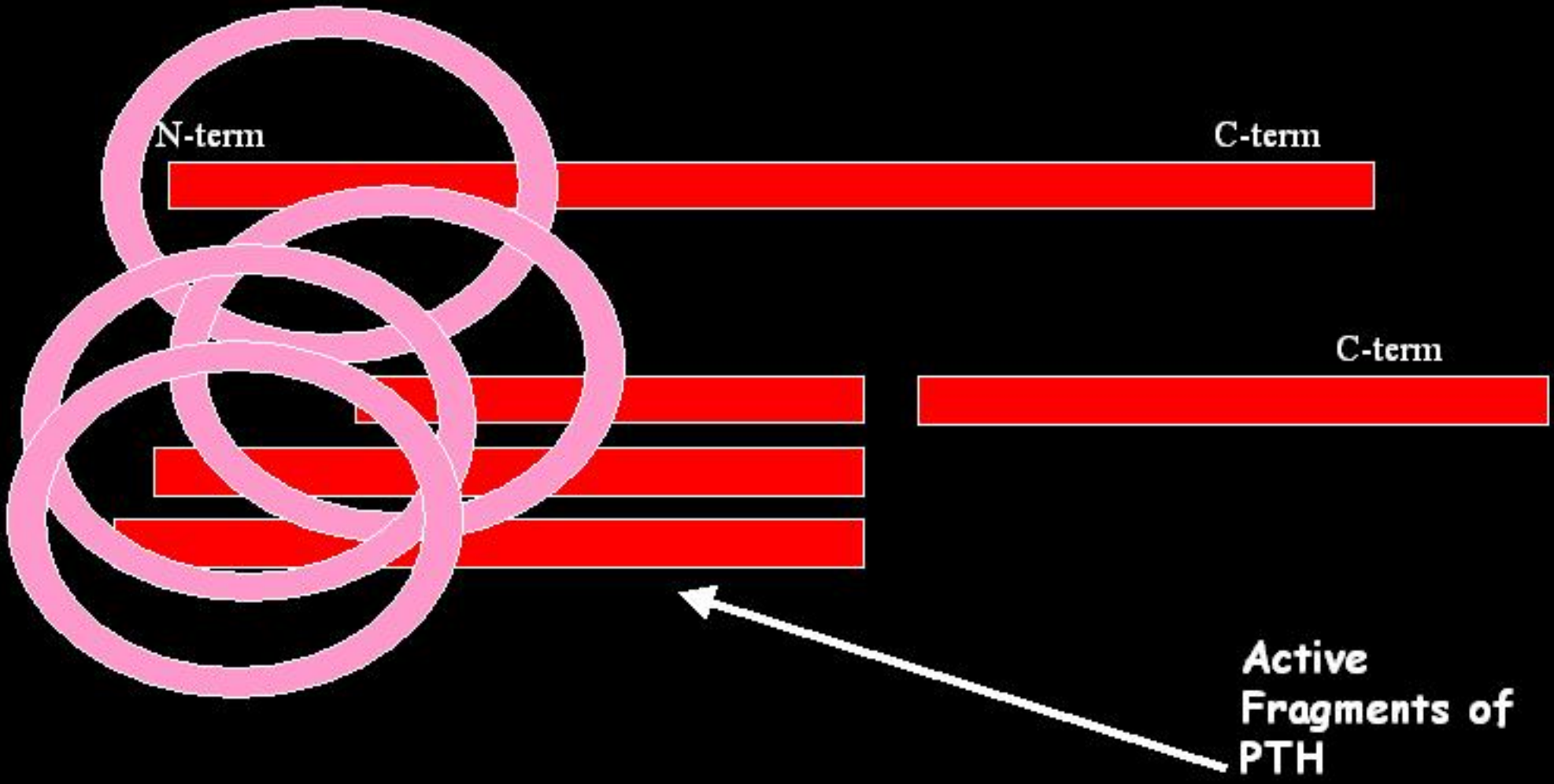
- 84 amino acids



Half-Life 2 – 3 minutes

1% intact PTH gets to target organ

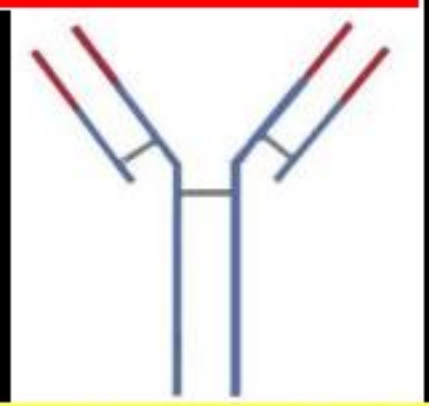
PTH – The hormone



Assays of "Intact PTH"

All "Intact" assays are
NOT created equally!!!

Extent of cross-reaction
with the 7-84 fragment
is vendor specific.

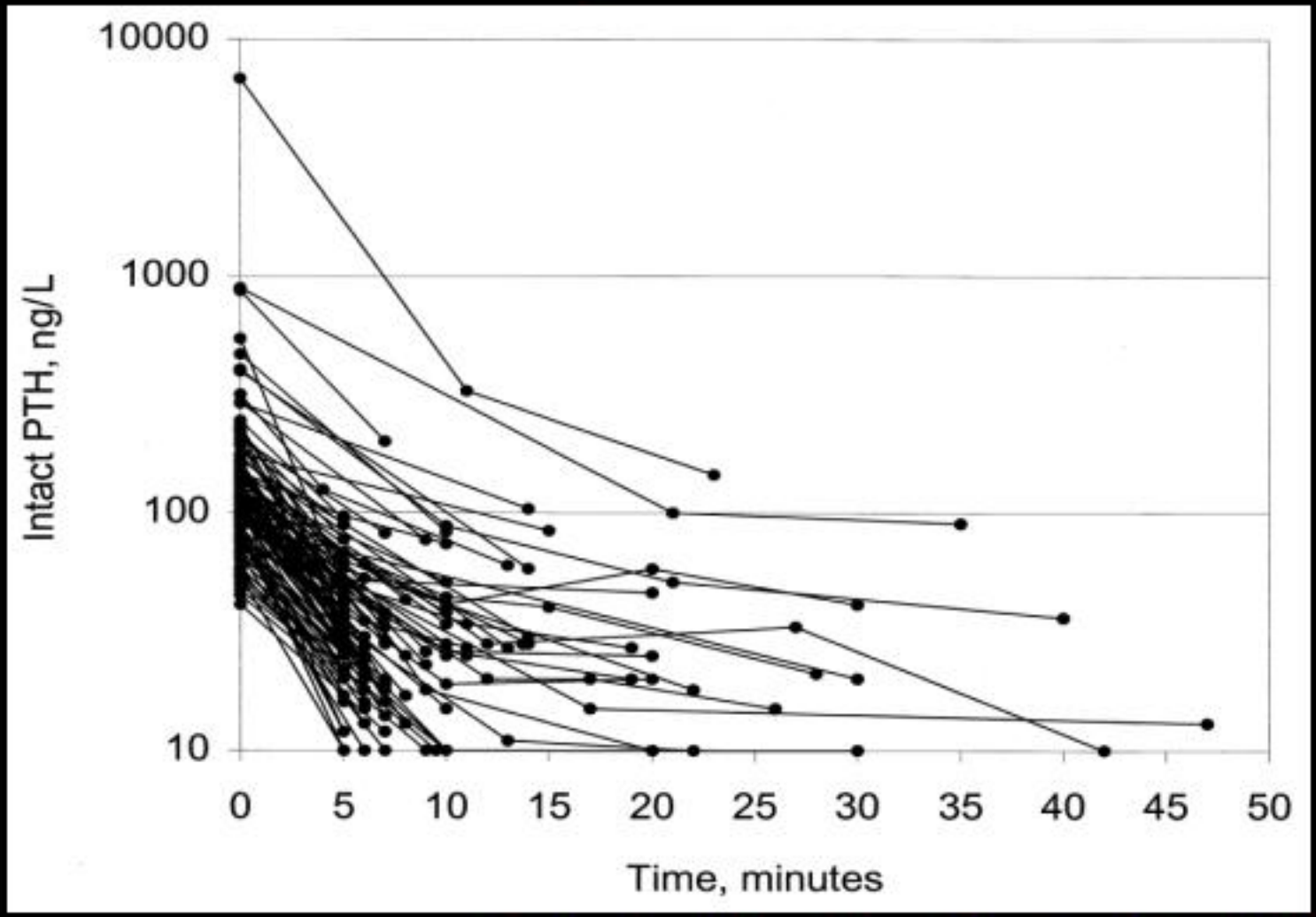


Antibody-coated tube

Parathyroid Hormone (PTH)

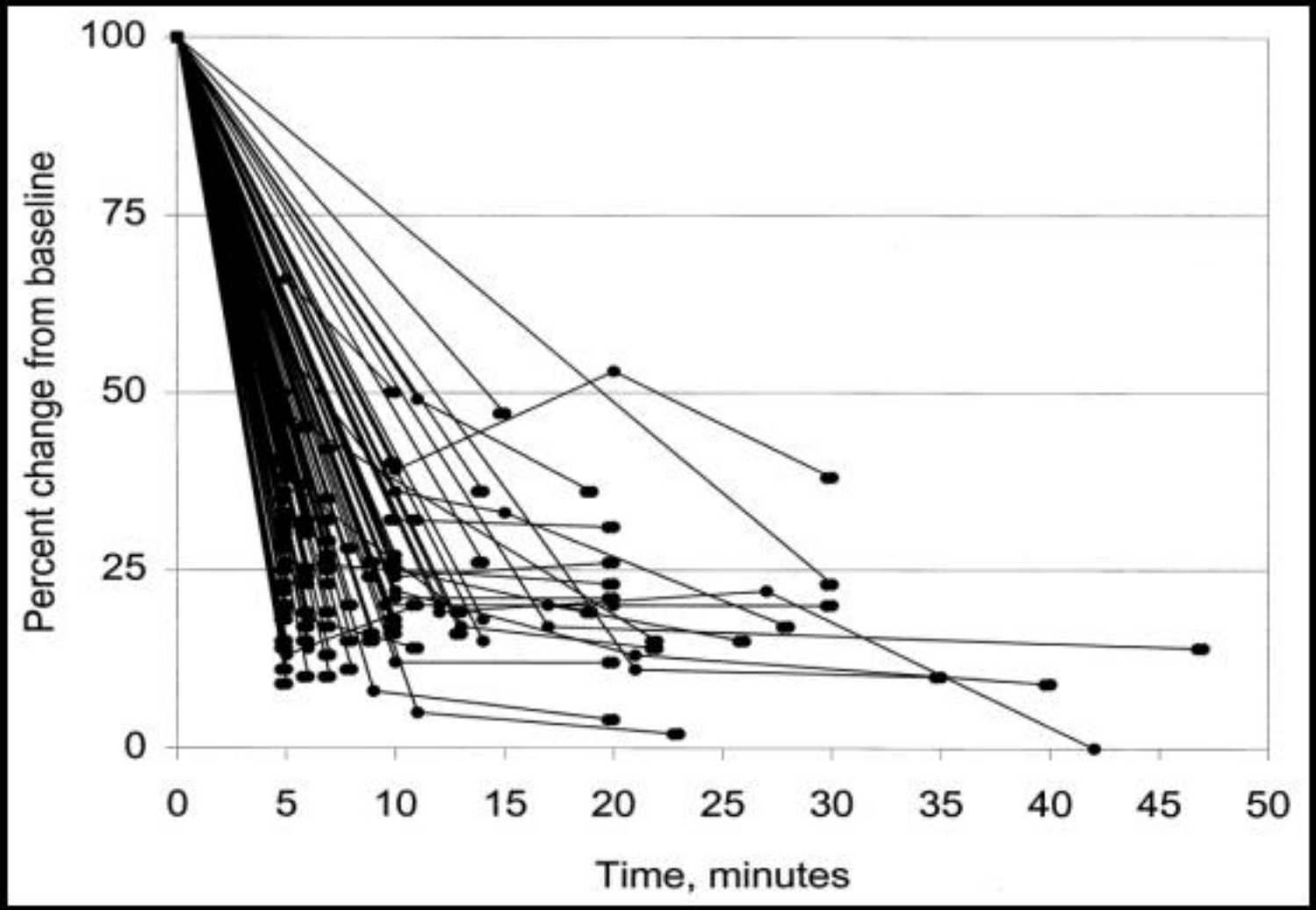
	Assay Time
• 1960s: Bioassay: Measure incorporation of $^{32}PO_4$ into cAMP in cultured cells, triggered by PTH.	1 day
• 1970s: Radio-immunoassay	3 days
• 1980s: Enzyme-linked Immuno-Sorbant assay (Elisa)	½ day
• 1990-present: Automated Immunoassays	12 - 30 min.

Concentration of Intact PTH in 149 1⁰ HPT patients with single adenomas



Sokoll, LJ. Clin Chem 46;2000

Percentage change in intact PTH from baseline



Sokoll, L JClin Chem 2000;46

iPTH Guided Surgery

- Irwin - 96% success rate
  - follow-up 6 months
- 3% MGD - hyper-secretion
- not over-functioning at the time ?
- definition of MGD ?

Carneiro et al Surgery:128;2000

Criteria	Sensitivity	Specificity	Accuracy
≥ 50% 10 min Highest	97%	96%	97%
≥ 50% 10 min Pre -incision	83%	99%	86%
≥ 50% 10 min Highest & Normal range	75%	98%	79%
≥ 50% 10 min Highest & below pre inc	94%	97%	95%
≥ 50% highest 5 min	88%	97%	90%
≥ 50% 10 min Pre excision	85%	97%	87%

Carneiro *et al* Surgery:134;2003

Utilization of iPTH

- when to stop
- add comfort to 'cure'
- lateralize in complex cases
- re-operative - get it all
- identification of parathyroid
- post thyroidectomy

Pitfalls to iPTH

- cost effective - how many will benefit
- Achilles heal - detect MGD
- too sensitive - slow to drop
- add a new complexity (11% WJS 29;2005)

Surgeon's Achilles Heal

- MGD on Sestamibi scan
  - 1/3 - non-visualization
  - 1/3 - multi-glands seen
  - 1/3 - solitary (misleading)
- 23% MGD - 8% misleading
- success decreased 98.5% - 90%

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Intra-Operative PTH

- ? cost-effectiveness of iPTH
- benefits 3-8% of sporadic 1^0 HPT

Agarwal *et al* Surg:130;2001
Miura *et al* WJS:26;2002
Burkey *et al* WJS:26;2002

Parathyroidectomy

	4 Gland / Unilateral	Imaged Directed	Plus iPTH
Cure	95 - 98%	90 - 92%	95 - 97%
Long term	same	unknown	unknown
Pre-op image	no	yes	yes
GA/Regional	GA/LA	Regional	Regional
Surgeon	experienced	experienced	? more
Cost	$	$$	$$$

- 100/188 select patients for MIP
- overall - MGD 18% in HPT population
- drew PTH - analysis post-op
- 2% not cured MIP
- 13% unnecessary conversion (false neg)

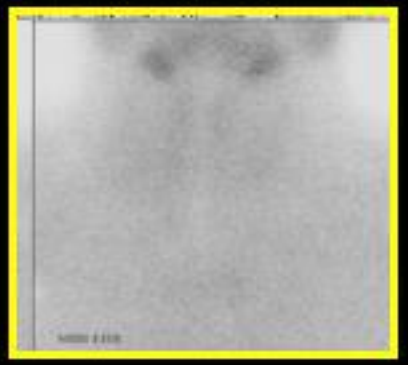
Stalberg J Am Coll Surg;203;2006

- Positive U/S and MIBI - 4% MGD

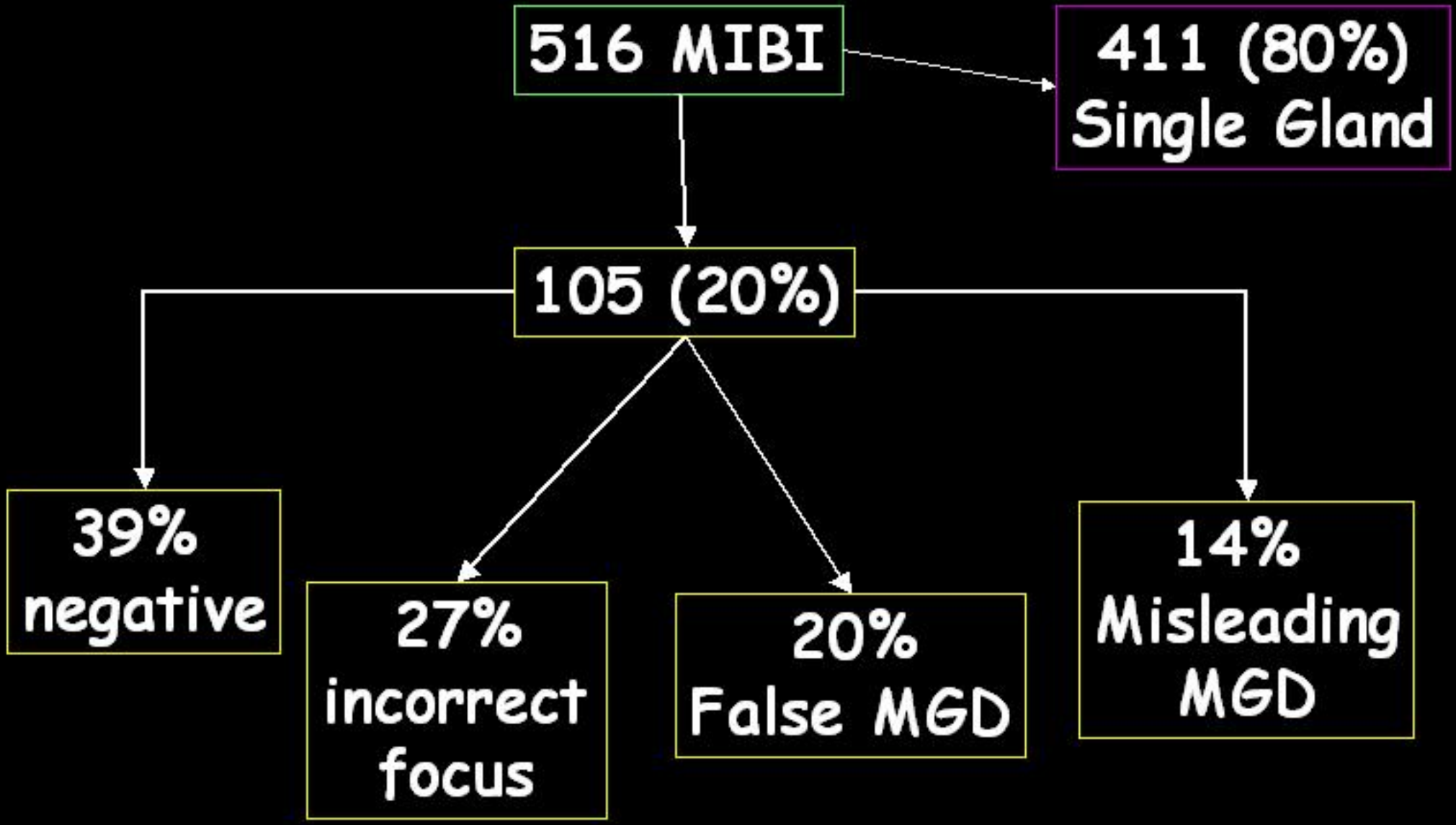
- Negative U/S and MIBI - 32% MGD
  - recommended iPTH

or

  - exposure of ALL glands



Sebag *et al* Surg:134;2003



Carneiro-Pla J Am Coll Surg 202;2006

- iPTH changed management 17%
- MIBI missed 87% of MGD
- only 4% of patients had MGD
- 15 MGD - iPTH correct in 10 (67%)*
- success @ 6 months - 97%

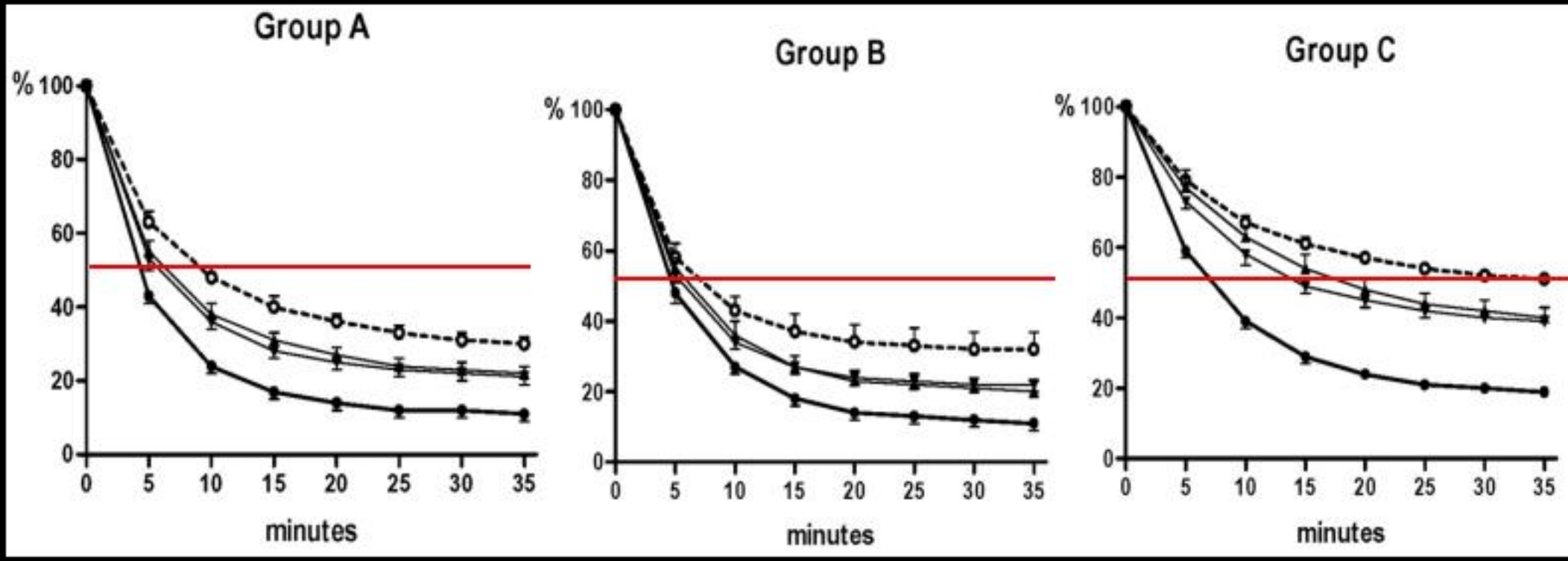
Carneiro-Pla J Am Coll Surg 202;2006

Intra-Operative PTH

- 350 U/S and iPTH - predicted solitary disease
- explore the contra-lateral side
- 15% - iPTH failed to predict MGD

Siperstein *et al* Surg:Oct;2004

- not functioning at surgery - ? Future
- long-term follow-up needed



Dialysis Tx Normal Cr Tx impaired

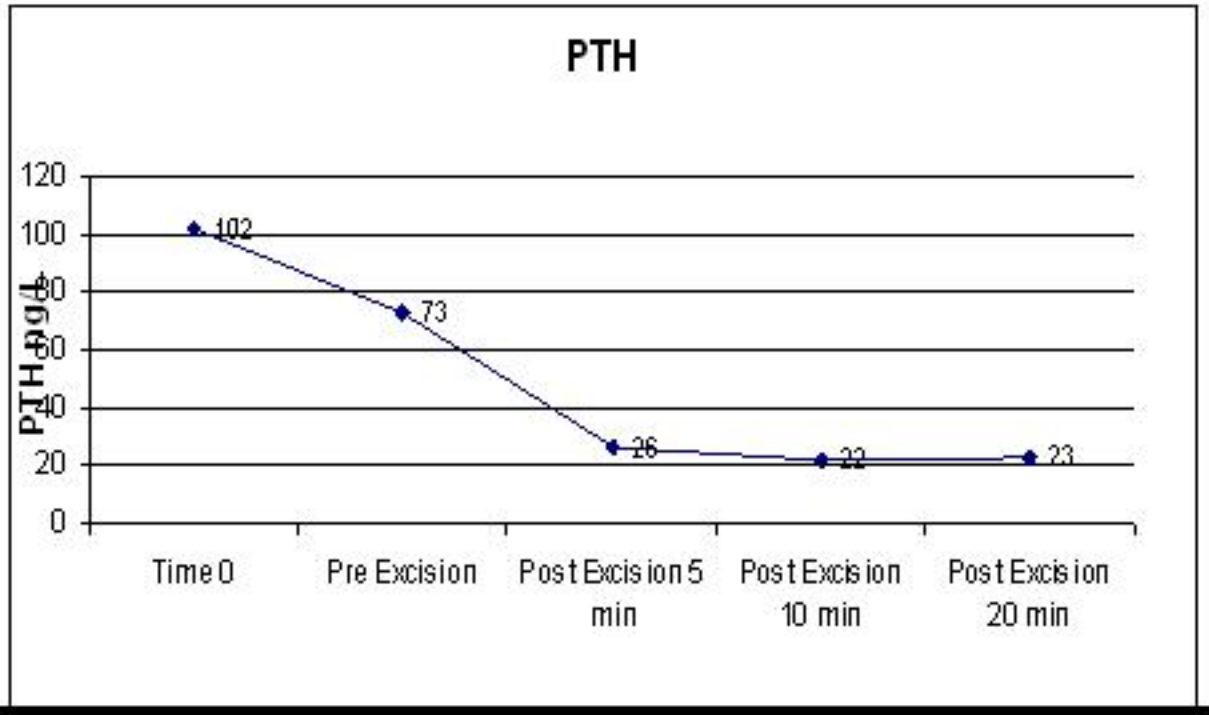
Bieglmayer C. Clin Chem 52;2006

iPTH

- 50% drop from highest value @ 10 min
- AND below normal value (< 54 pg/ml)
- normal renal function
- 80 - 90% drop @ 20 minutes in 3^0 HPT

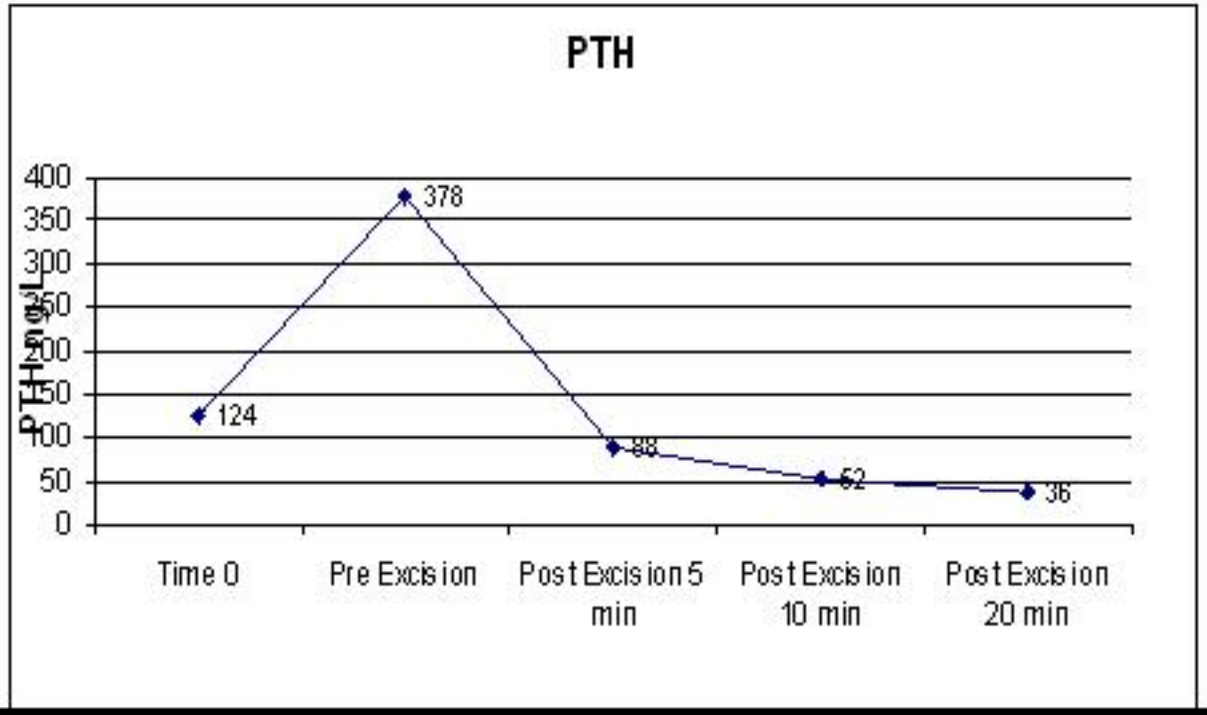
Weber T *et al* WJS 29;2005

Sample #	Description	Collection Time	Results ng/L	% Change
1	Time 0	13:30	102	0.0%
2	Pre Excision	14:05	73	-28.4%
3	Post Excision 5 min	14:15	26	-74.5%
4	Post Excision 10 min	14:20	22	-78.4%
5	Post Excision 20 min	14:30	23	-77.5%

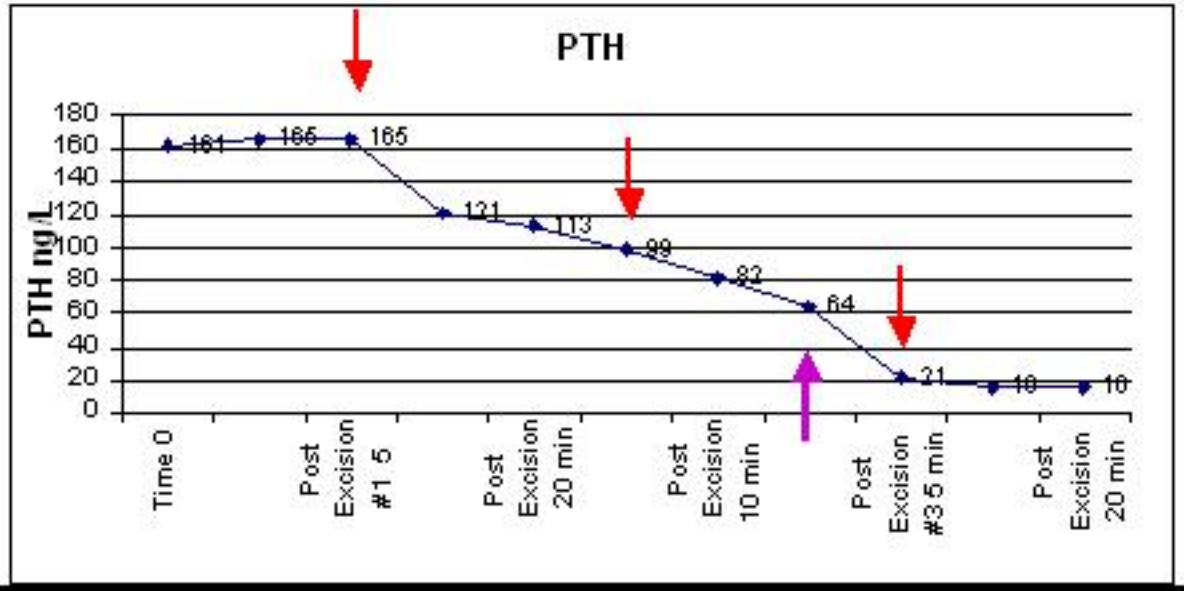


- Ca^{++} - 2.34 PO_4 - 1.12 2003 post-op
- Ca^{++} - 2.24 PO_4 - 1.03 2004
- Ca^{++} - 2.56 PO_4 - 0.95 2005
  - PTH 42 (13 - 54 pg/ml)
- Ca^{++} - 2.67 PO_4 - 0.87 2006
  - PTH 63

Sample #	Description	Collection Time	Results ng/L	% Change
1	Time 0	11:15	124	0.0%
2	Pre Excision	11:48	378	0.0%
3	Post Excision 5 min	11:55	88	-76.7%
4	Post Excision 10 min	12:00	52	-86.2%
5	Post Excision 20 min	12:10	36	-90.5%



Sample #	Description	Collection Time	Results ng/L	% Change
1	Time 0	8:34	161	0.0%
2	Pre Excision	9:35	165	0.0%
3	Post Excision #1 5 min	9:55	165	0.0%
4	Post Excision 10 min	10:00	121	-26.7%
5	Post Excision 20 min	10:11	113	-31.5%
6	Post Excision #2 5 min	10:33	99	-40.0%
7	Post Excision 10 min	10:36	82	-50.3%
8	Post Excision 20 min	10:50	64	-61.2%
9	Post Excision #3 5 min	11:22	21	-87.3%
10	Post Excision 10 min	11:27	16	-90.3%
11	Post Excision 20 min	11:37	16	-90.3%



Objectives

- understand utilization of iPTH
  - imaged directed
  - re-operative
- recognized the pitfalls of iPTH
  - MGD - definition
  - kinetics of the drop
  - cost-effectiveness
- appreciation of iPTH role in your own practice