

Diagnosis and Treatment of Primary Hyperparathyroidism



Geoffrey B. Thompson, MD
Professor of Surgery
College of Medicine, Mayo Clinic

Disclosure

- Nothing to Disclose

Primary HPT

- Autonomous secretion of excess PTH
- Normal inhibitory feedback lost
- Few patients remain asymptomatic

Primary HPT

- 100,000 new cases annually (U.S.)
- 1/1000 - 1/500 per year (U.S.)
- 8,500 cases recurrent / persistent HPT per year (U.S.)

Primary HPT

- Women > age 50
- All ages, races
- Both sexes

Primary HPT

- Single adenoma: 85%
- MGD: 12-14%
- Cancer: < 1 %

Primary HPT

- Familial (usually MGD)
 - MEN 1 (95%)
 - MEN 2A (10-35%)
 - FIH
 - HPT -- jaw tumor syndrome (SGD)



Clinical Manifestations

- Osteopenia / osteoporosis
- Fractures
- Hypercalciuria
- Renal dysfunction
- Nephrolithiasis, nephrocalcinosis



Clinical Manifestations (HPT)

- Fatigue
- Muscle weakness (aches & pains)
- Neuropsychiatric disturbances
- GI disturbances
- Impaired CV health

Symptomatic HPT (<20%)

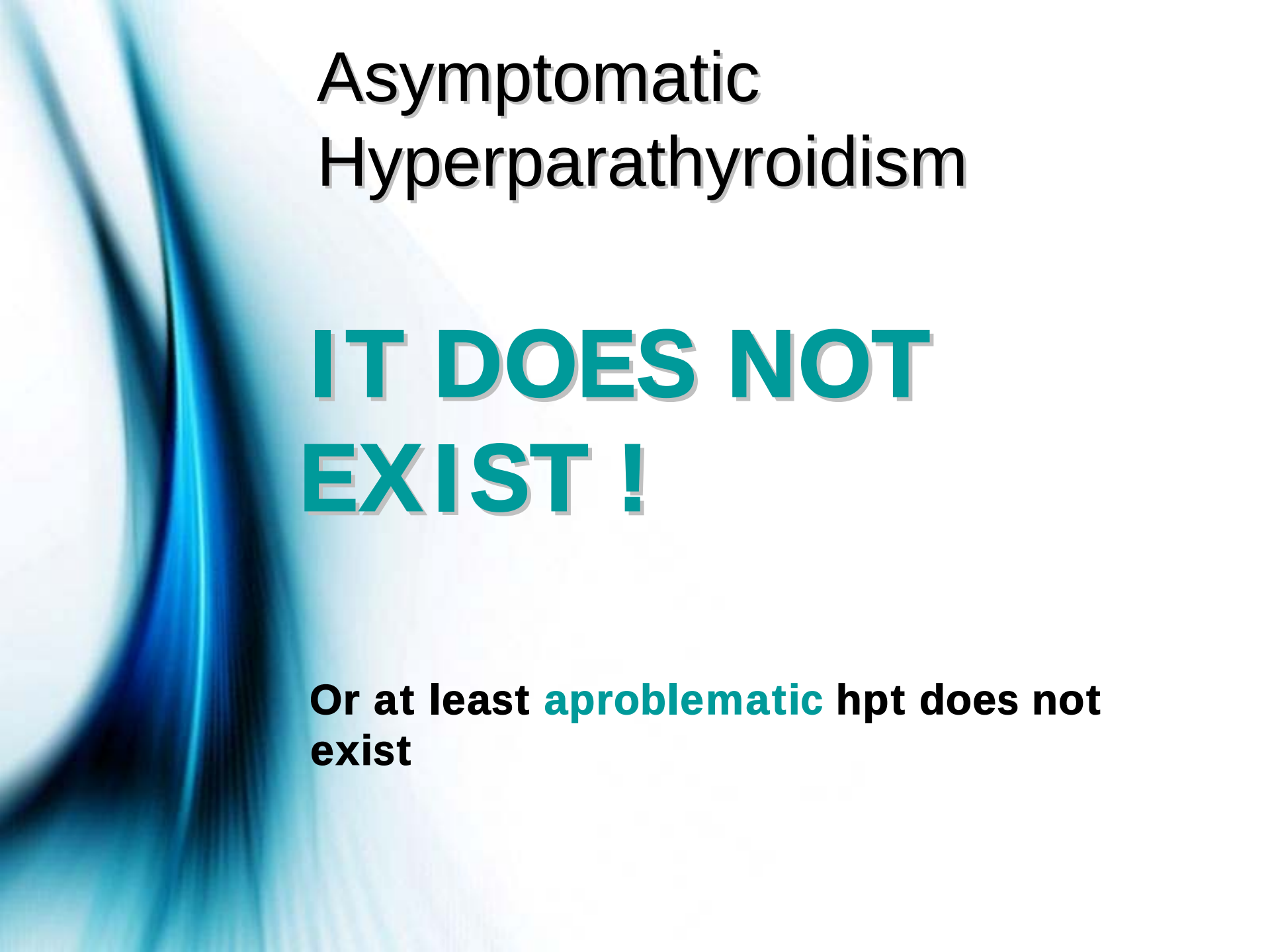
- Nephrolithiasis
- Fractures, osteitis fibrosa cystica
- Hypercalcemic Crisis
- Pancreatitis

NIH Consensus Conference for Parathyroidectomy in Patients with HPT

- Age < 50 years
- Nephrolithiasis
- Markedly elevated serum calcium level :>1.0 mg/dl above normal
- Osteitis fibrosa cystica
- Creatinine clearance 30% less than that of age-matched normal subjects
- History of hypercalcemic crisis
- Urinary calcium > 400mg/day
- Bone density more than 2 std dev below controls
- Documented neuromuscular symptoms
- Medical surveillance not desirable or possible

Primary Hyperparathyroidism

- Over 90% of our operated patients meet the new NIH criteria
- Over 80% of patients have a myriad of non-classical, subclinical signs and symptoms at presentation
- Primary HPT offers something (bad) for everyone if you look for it



Asymptomatic Hyperparathyroidism

**IT DOES NOT
EXIST !**

Or at least **aproblematic** hpt does not
exist

Excess Mortality from HPT

- 896 pts operated between 1953 and 1982
- Increased relative risk for premature death
- Risk ameliorated by successful surgery
- Return to normal risk occurred more quickly in milder cases

Excess Mortality

- Seen in mild and severe hpt
- Diminished by surgery (Palmer, 1987; Ronni-Sivula, 1985)
- Mayo-Wermers 1998: Increased risk of death in more severe untreated cases



Bone Disease

- Often clinically silent until fractures occur
- \$14 billion dollar medical expense in U.S.

Risk of Fracture in HPT

- 407 patients with HPT at Mayo
- Observed increase of 30% over expected in hpt group
- Parathyroid surgery may have protective effect

Effect of Surgery on Bone

- 10-year follow-up study
- ALL symptomatic, non-operated, patients progressed
- After surgery all pts had improved BMD
- No difference in symptomatic vs asymptomatic pts
- No reliable predictors for who will progress

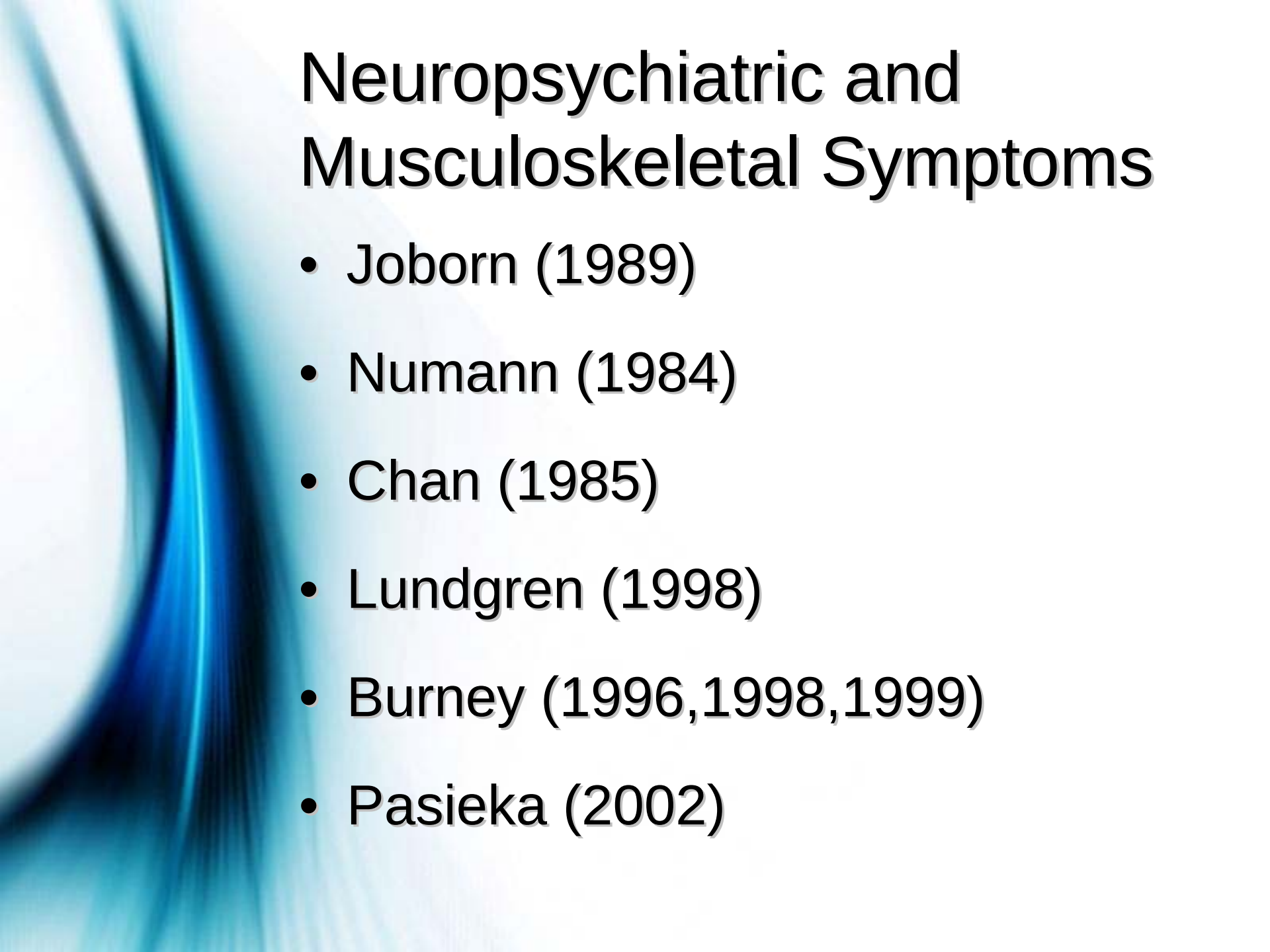
Editorial Comment-R. Utiger

“Asymptomatic does not necessarily mean unharmed”

“Surgical Treatment....should now be recommended for (nearly) all hpt pts.”

PTx vs. Antiresorptive Agents

- Increase in BMD less than 10% over 3 years (Liberian, 1995,1996) with ARA's
- PTx increases BMD 8-12% in 1-3 years (Silverberg, 1999)



Neuropsychiatric and Musculoskeletal Symptoms

- Joborn (1989)
- Numann (1984)
- Chan (1985)
- Lundgren (1998)
- Burney (1996,1998,1999)
- Pasioka (2002)

Burney

- SF-36 Questionnaire
- 140 pts: $Ca < 10.9$, $Ca > 10.9$
- 8 domains: physical function, physical role limit, bodily pain, general health, vitality, social function, emotional role limit, mental health

Burney

- Much lower scores in preops compared to pts without hpt
- Great improvement over 2-6 months post –op in 7 of 8 categories irrespective of calcium level pre-op
- Operate sooner rather than later

Pasieka

- QOL tool based on a visual analog scale
- Given pre- and post-op
- Validated in prospective study
- Pts fulfilling and not fulfilling NIH criteria
- Thyroidectomy pts as controls

Pasieka----Conclusions

- Sx's just as severe in pts not fulfilling NIH criteria for operation
- These pts achieved significant improvement in symptoms with parathyroidectomy
- NIH guidelines need to be broadened

DIAGNOSIS

Elevated Calcium (total or ionized)
Elevated or Inappropriate PTH
Elevated or Normal 24hr Urine Calcium

Normal Creatinine
Low Normal Phosphorus

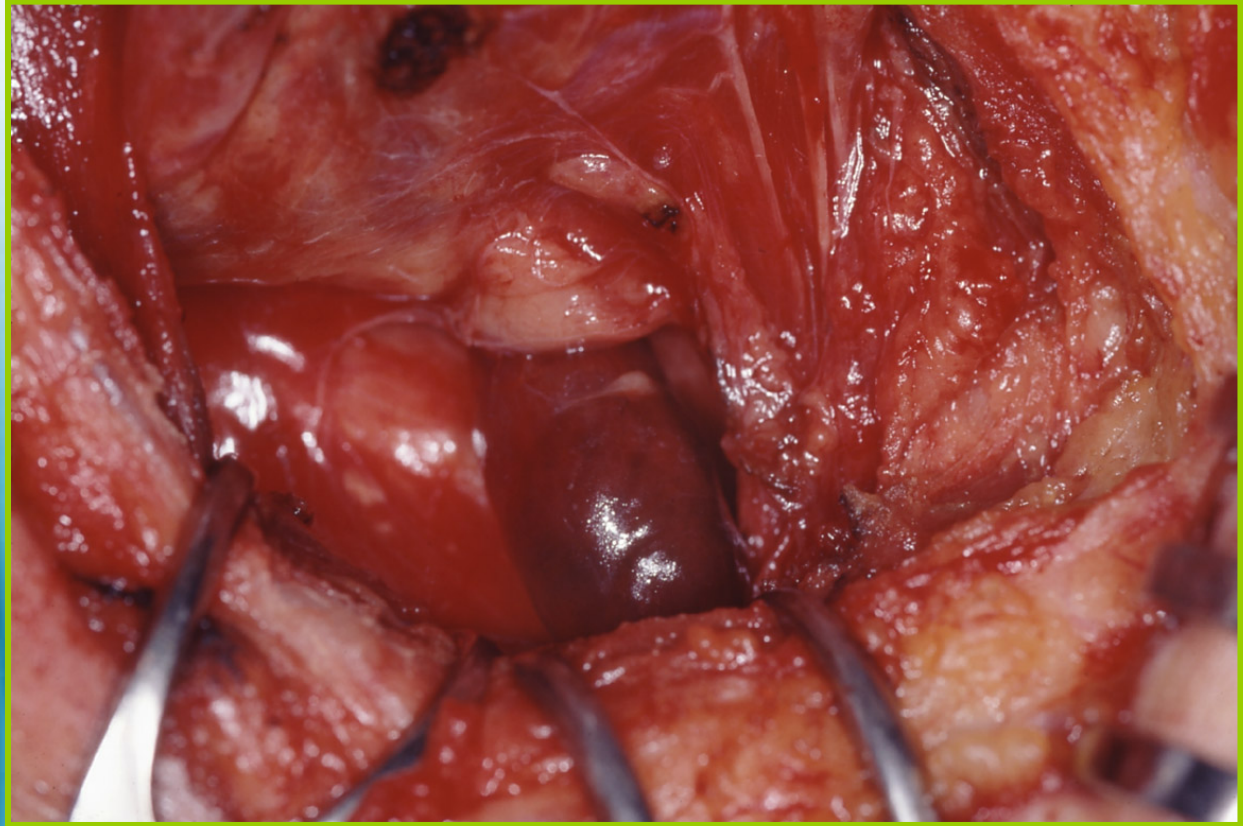
Lithium and Thiazides

Standard Cervical Exploration



- Success: >98%
- Complications: <1%

Reoperative Parathyroid Surgery



- Success: 88%
- RLN injury: 1%
- Hypoparathyroidism: 13%

Minimally Invasive Parathyroidectomy

*Is this a valuable procedure or a
stretch of the imagination?*



Minimally Invasive Surgery

- Cholecystectomy
- Nissen fundoplication
- Colectomy
- Adrenalectomy
- Splenectomy

Minimally Invasive Surgery

Fewer Advantages

Appendectomy

Hernia repair

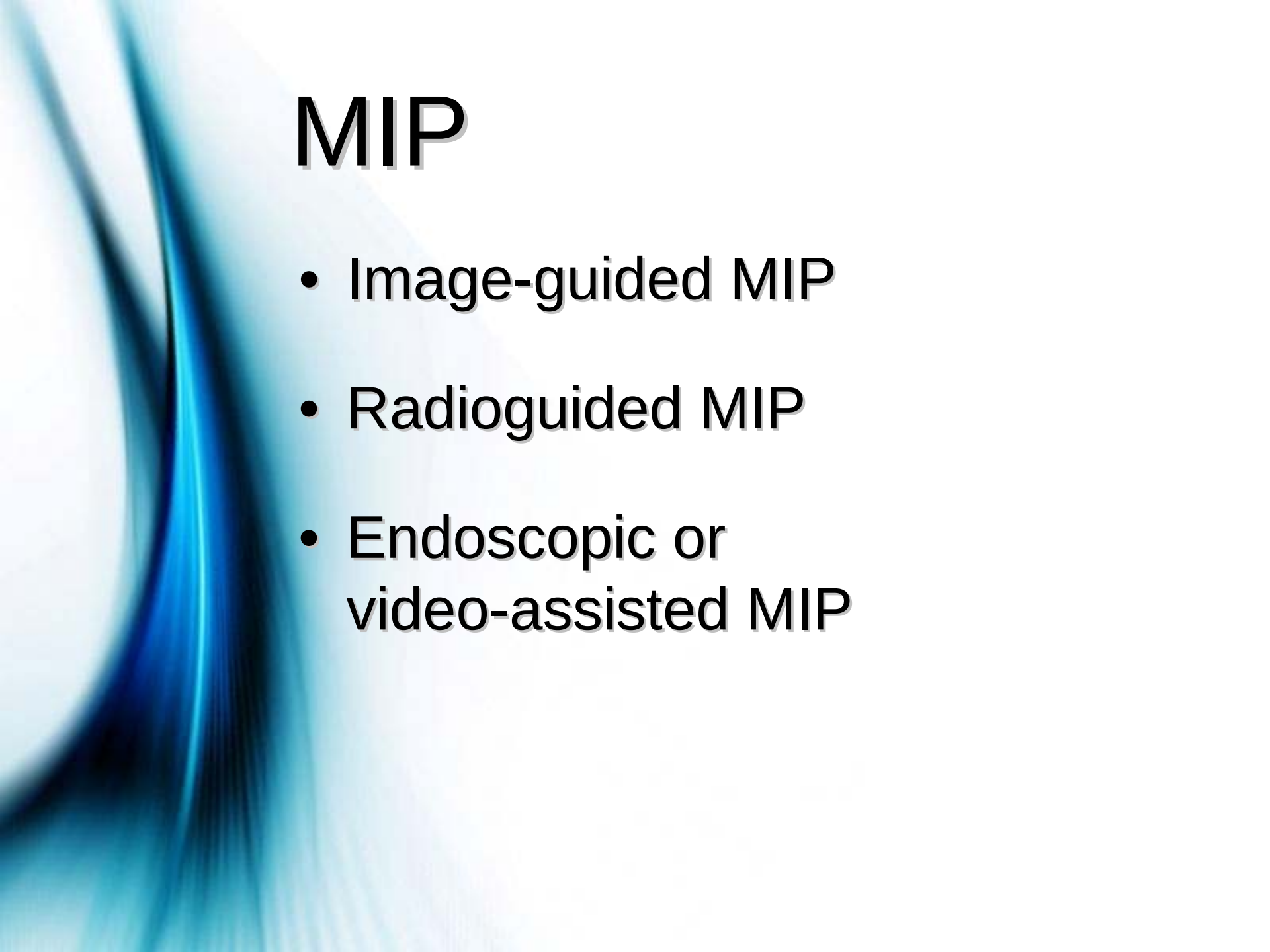


Operative site easily accessible
via small incisions



“New” Outcome Measures

- Patient-Focused
 - General anesthesia after-effects
 - Nausea & vomiting
 - Clouded sensorium
 - Incisional pain
 - Outpatient dismissal
 - Postoperative convalescence



MIP

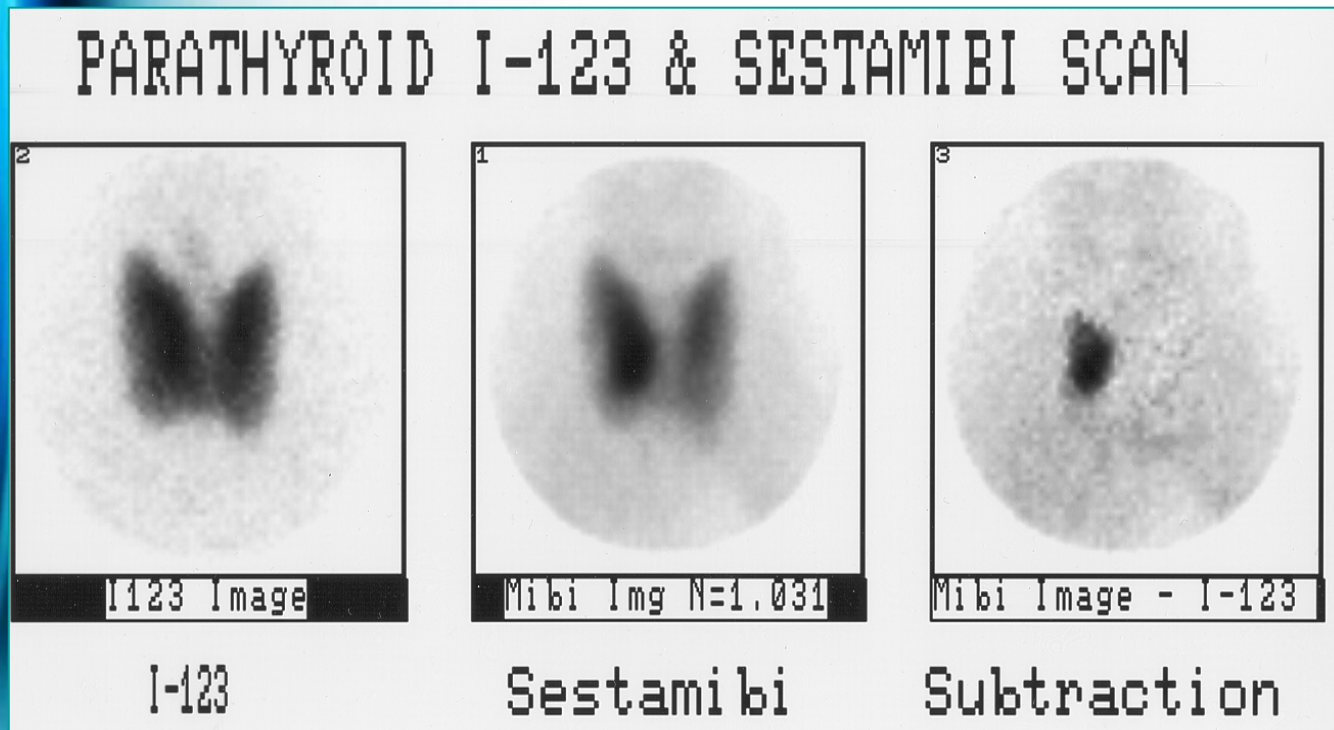
- Image-guided MIP
- Radioguided MIP
- Endoscopic or video-assisted MIP

Minimally Invasive Parathyroid Surgery

- Sestamibi parathyroid scanning
- Ultrasound
- Intraoperative PTH monitoring

Sestamibi Parathyroid Scan

- Dual photon, Subtraction scans
- With Planar, Oblique and SPECT imaging

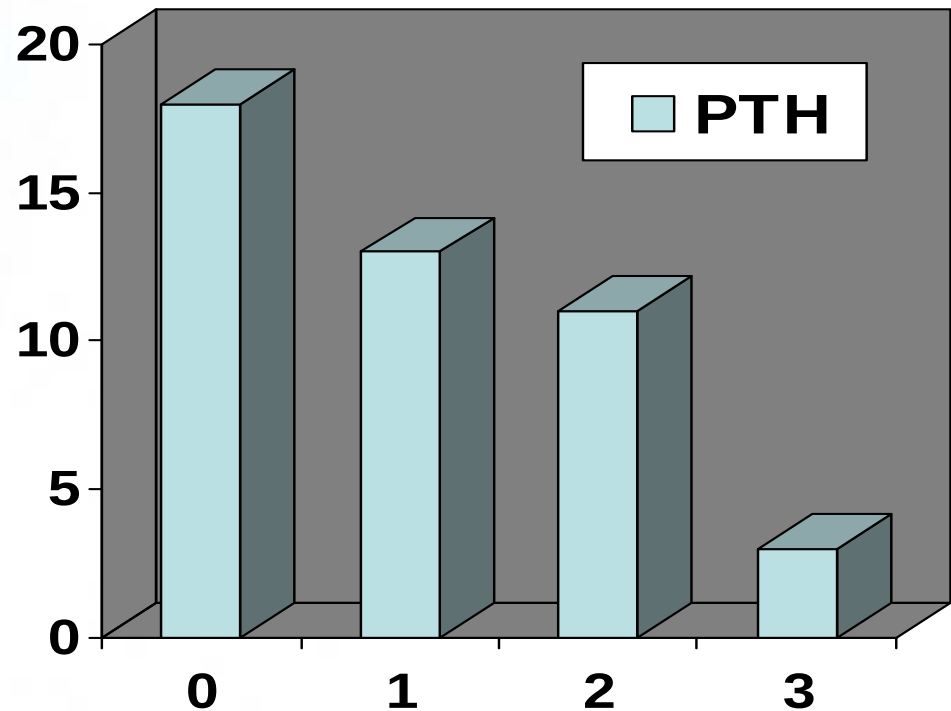


Parathyroid Ultrasound

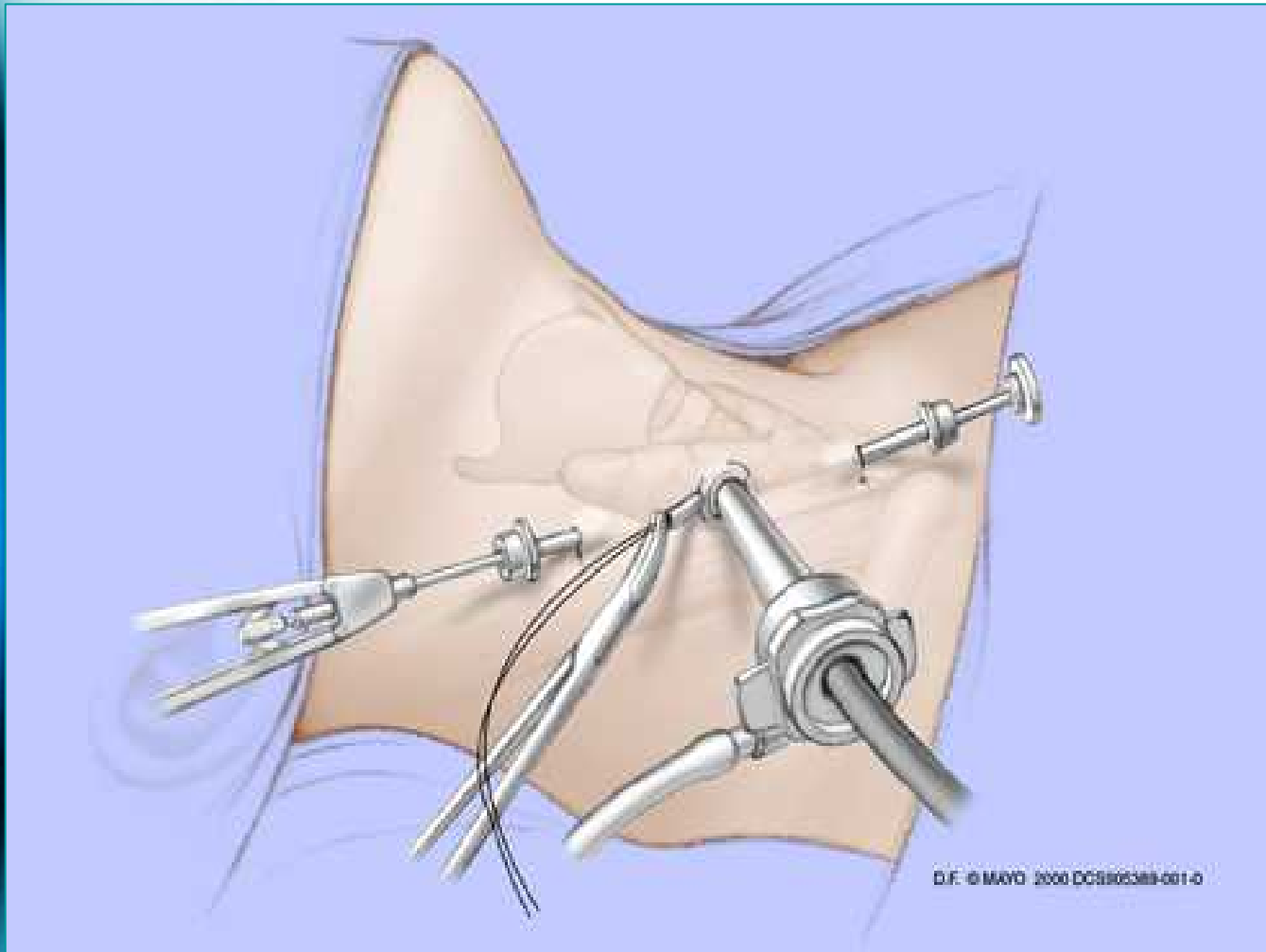


IOPTH

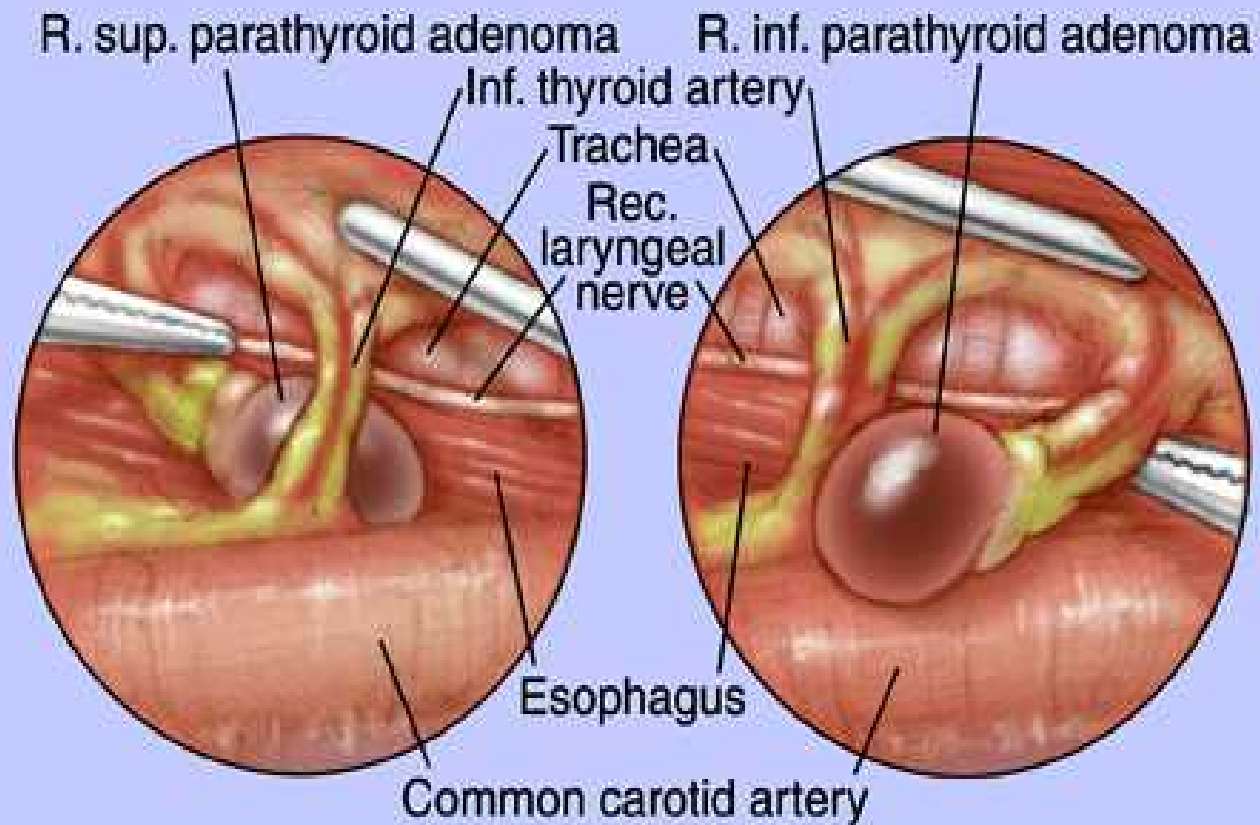
- Rapid results
- Highly reliable: SGD & MGD
- Cost: \$1,000/patient?
- Immulite: \$500



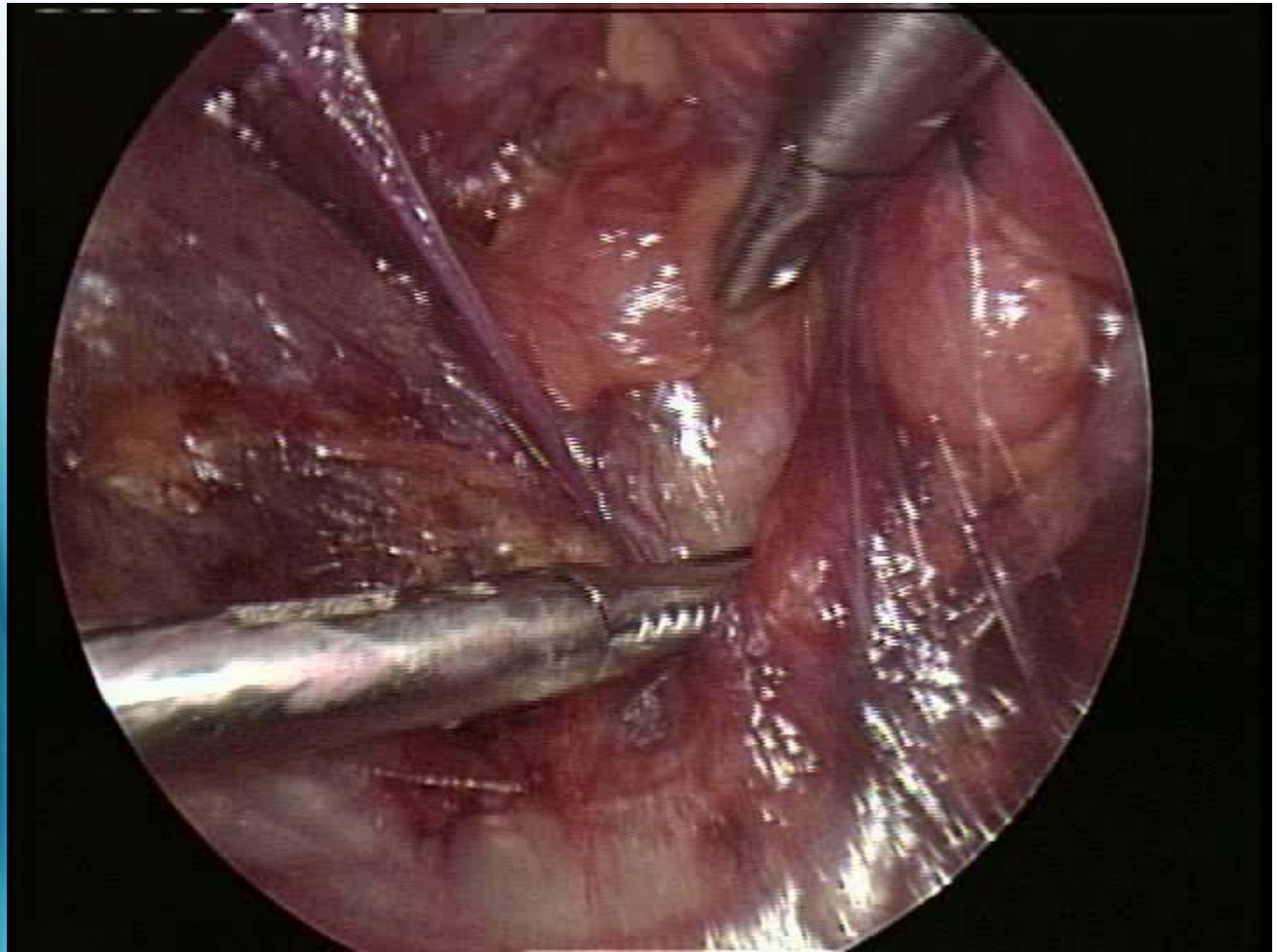
Endoscopic Technique



Endoscopic Technique

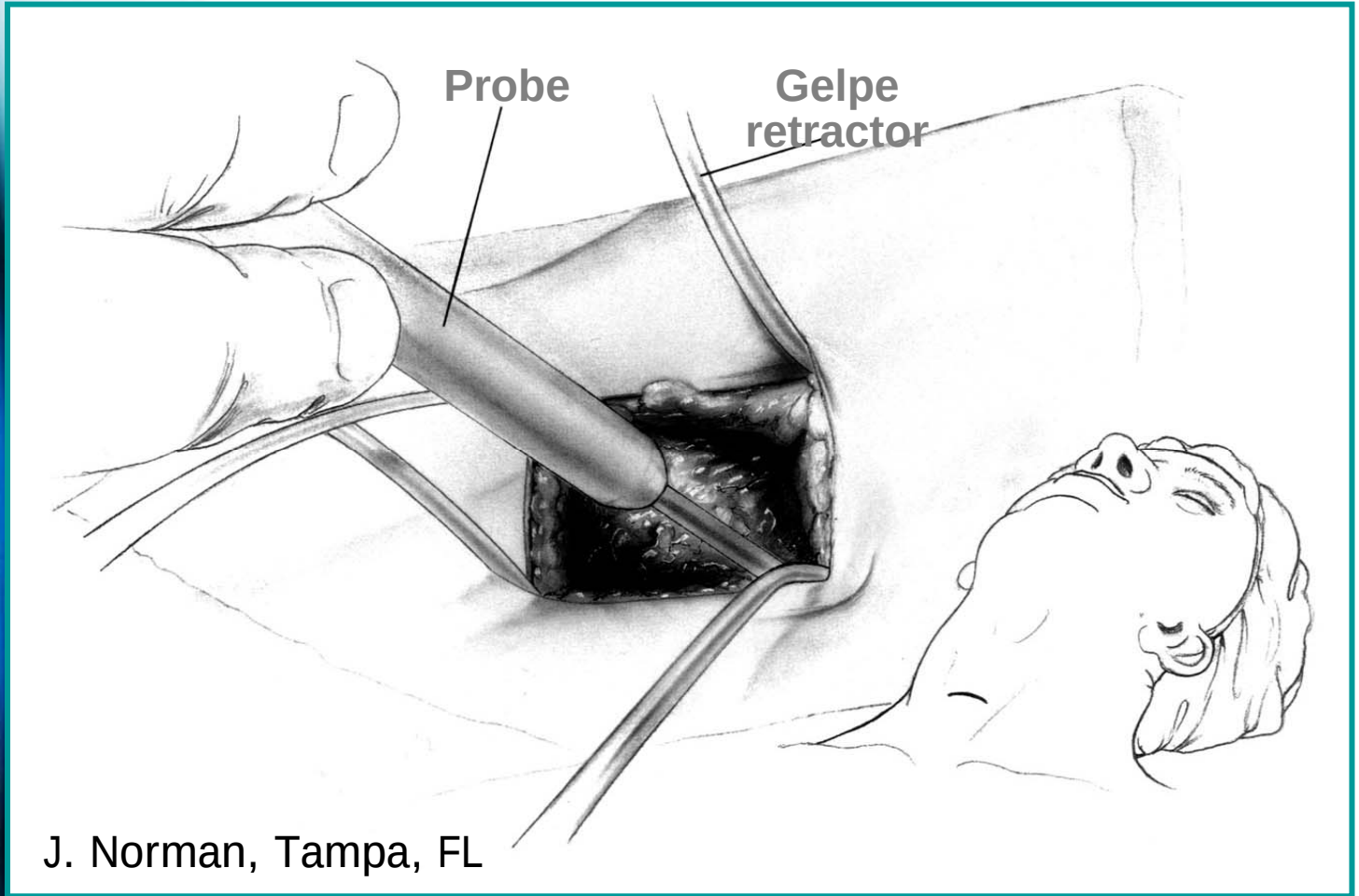


MIP—Endoscopic



Courtesy Dr. Barry Inabnet

Radioguided MIP

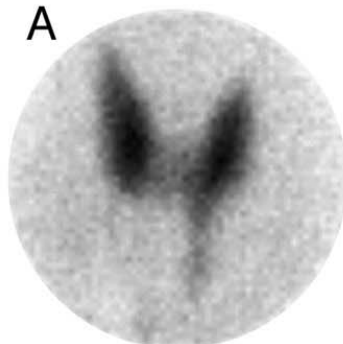


33% failure rate at Mayo Clinic

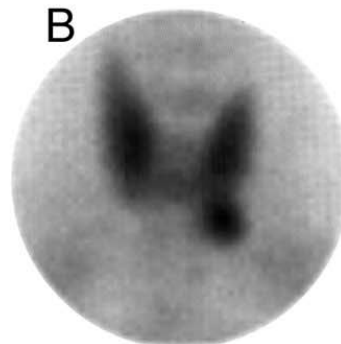
Image-Guided MIP

- Based on highly accurate preop SPS or US images
- IOPTH

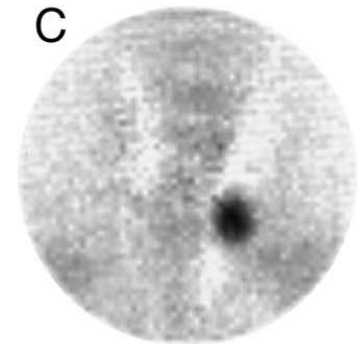
SPS



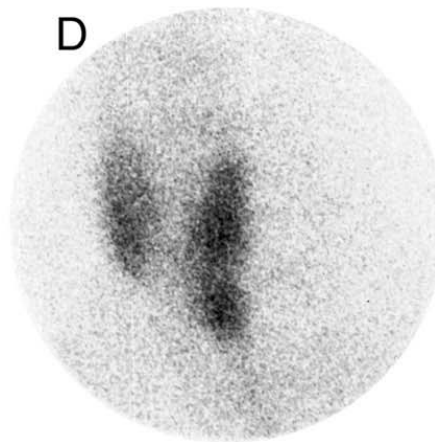
Pertechnetate



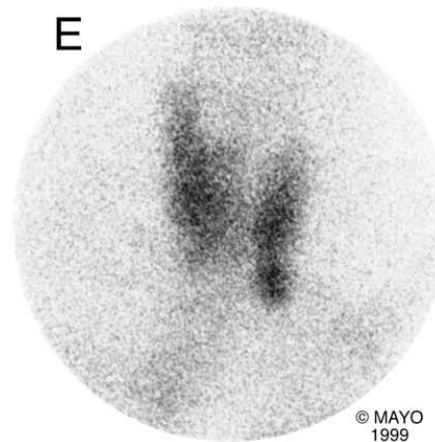
Sestamibi



Subtraction



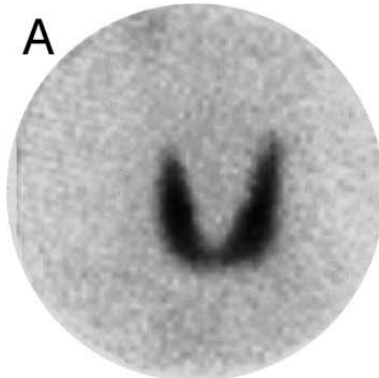
LAO



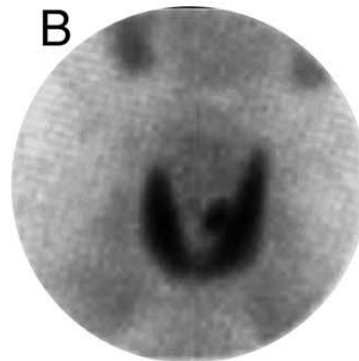
RAO

© MAYO
1999

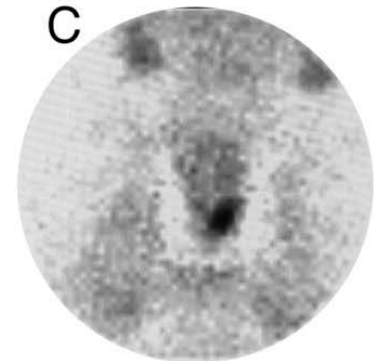
SPS



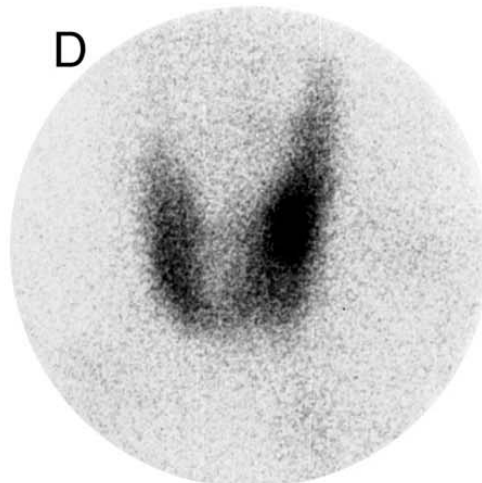
Pertechetate



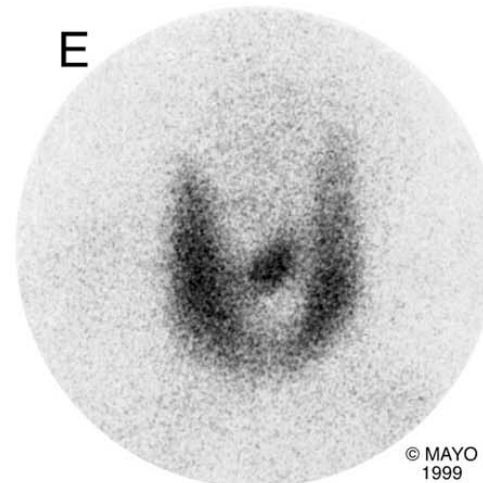
Sestamibi



Subtraction



LAO



RAO

© MAYO
1999

Parathyroid Ultrasound

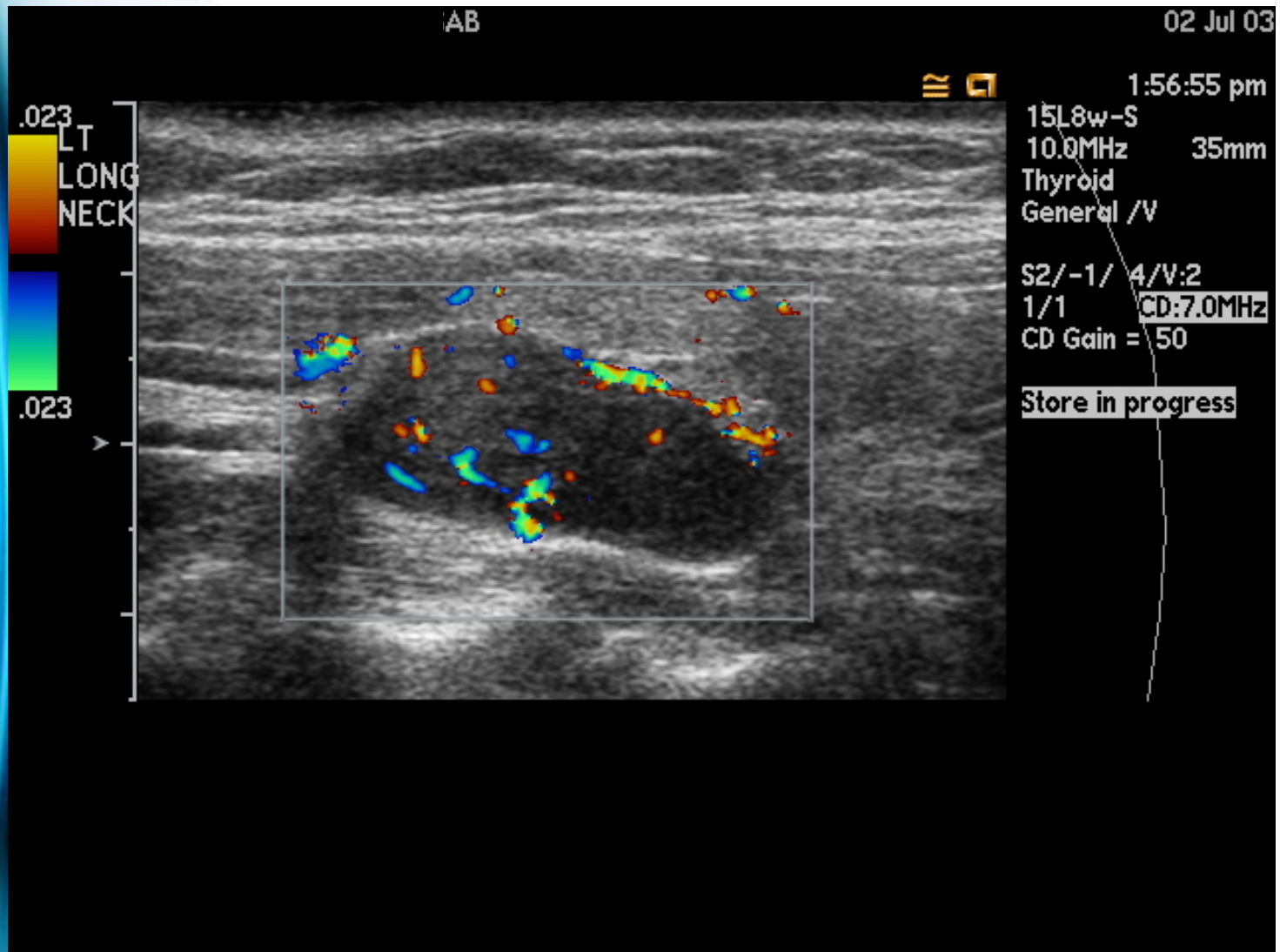
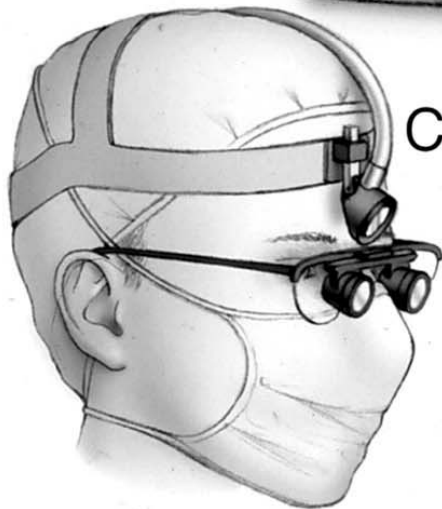
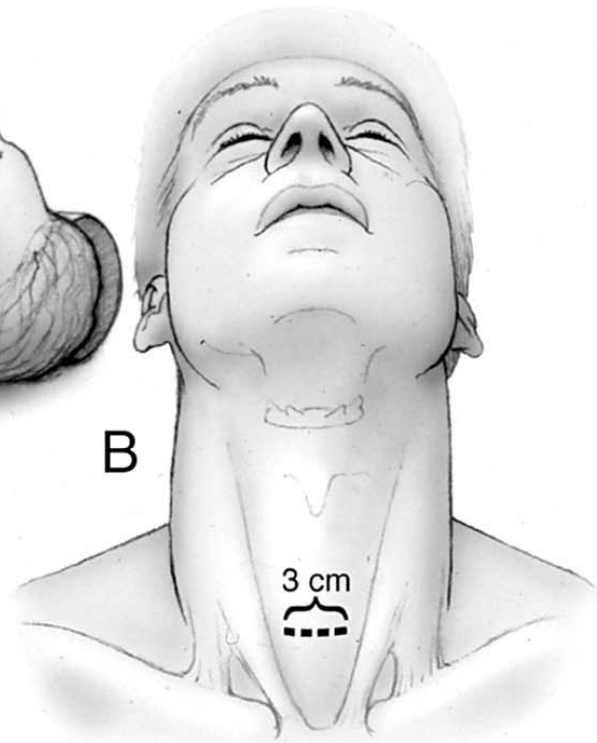
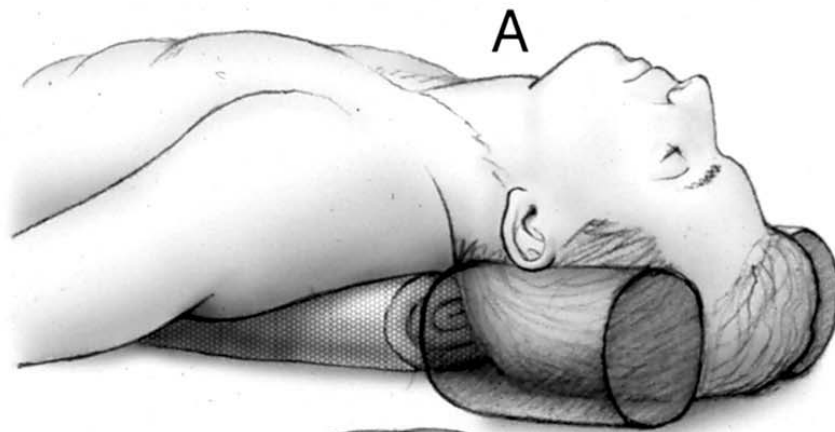


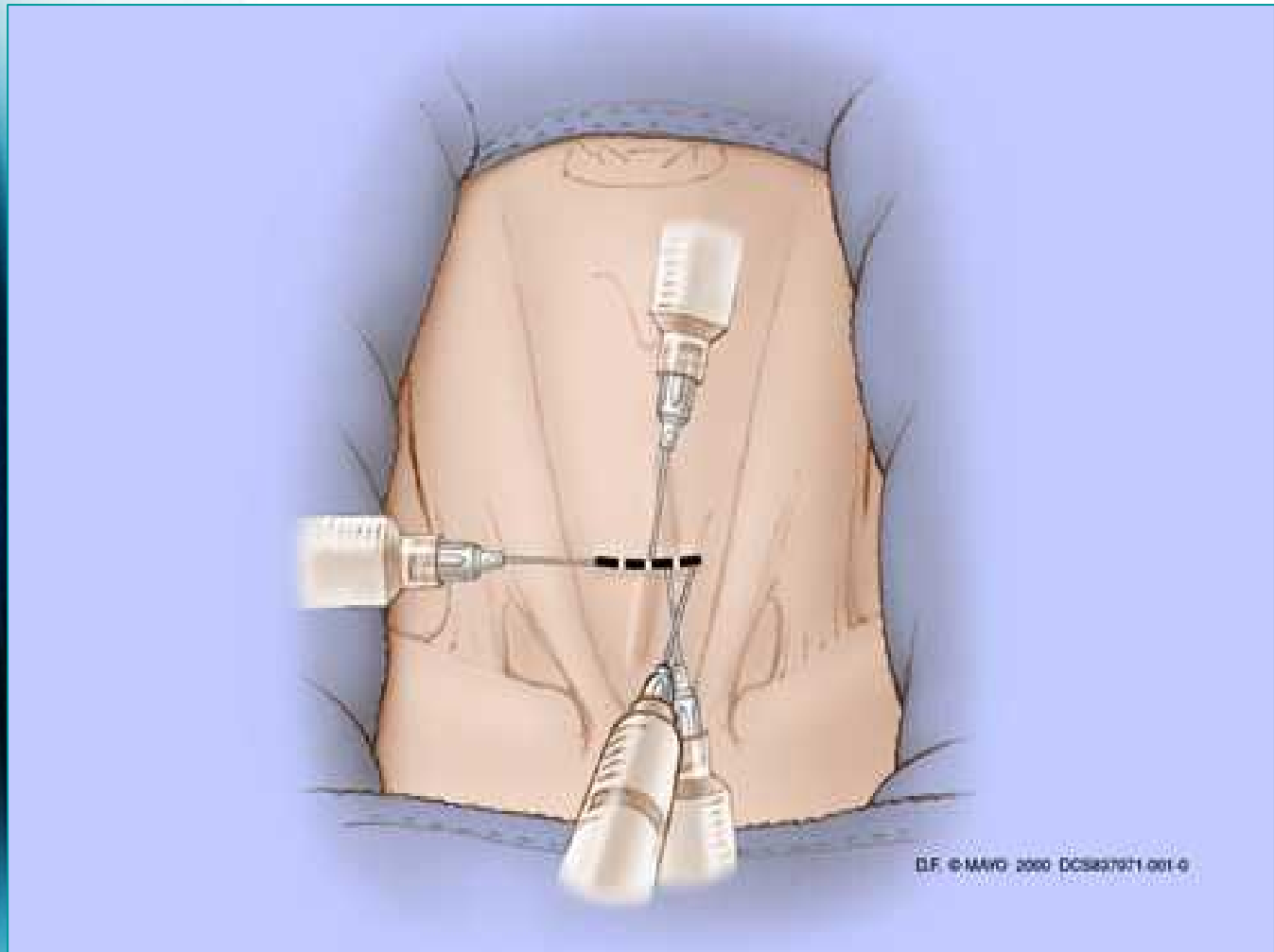
Image-Guided MIP

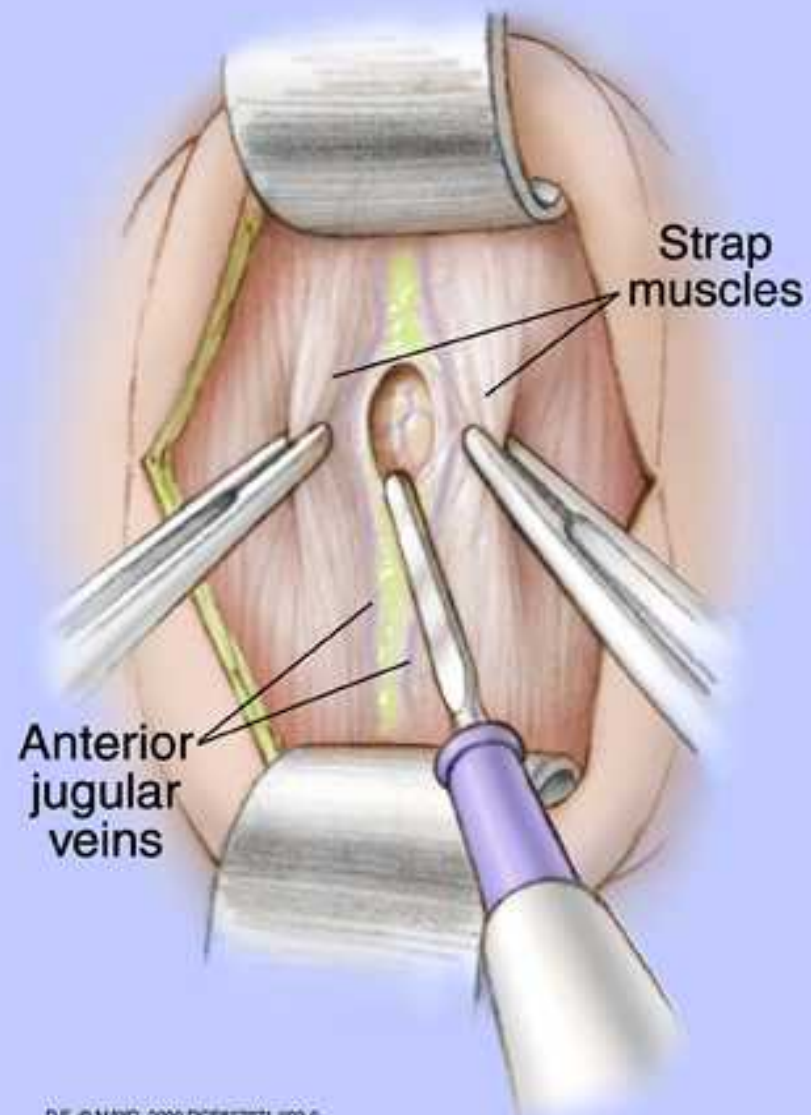
- 3-cm collar incision/unilateral exploration
- Local anesthesia/general anesthesia
- Outpatient setting
- Less nausea, pain
- Confirm results with IOPTH

MIP

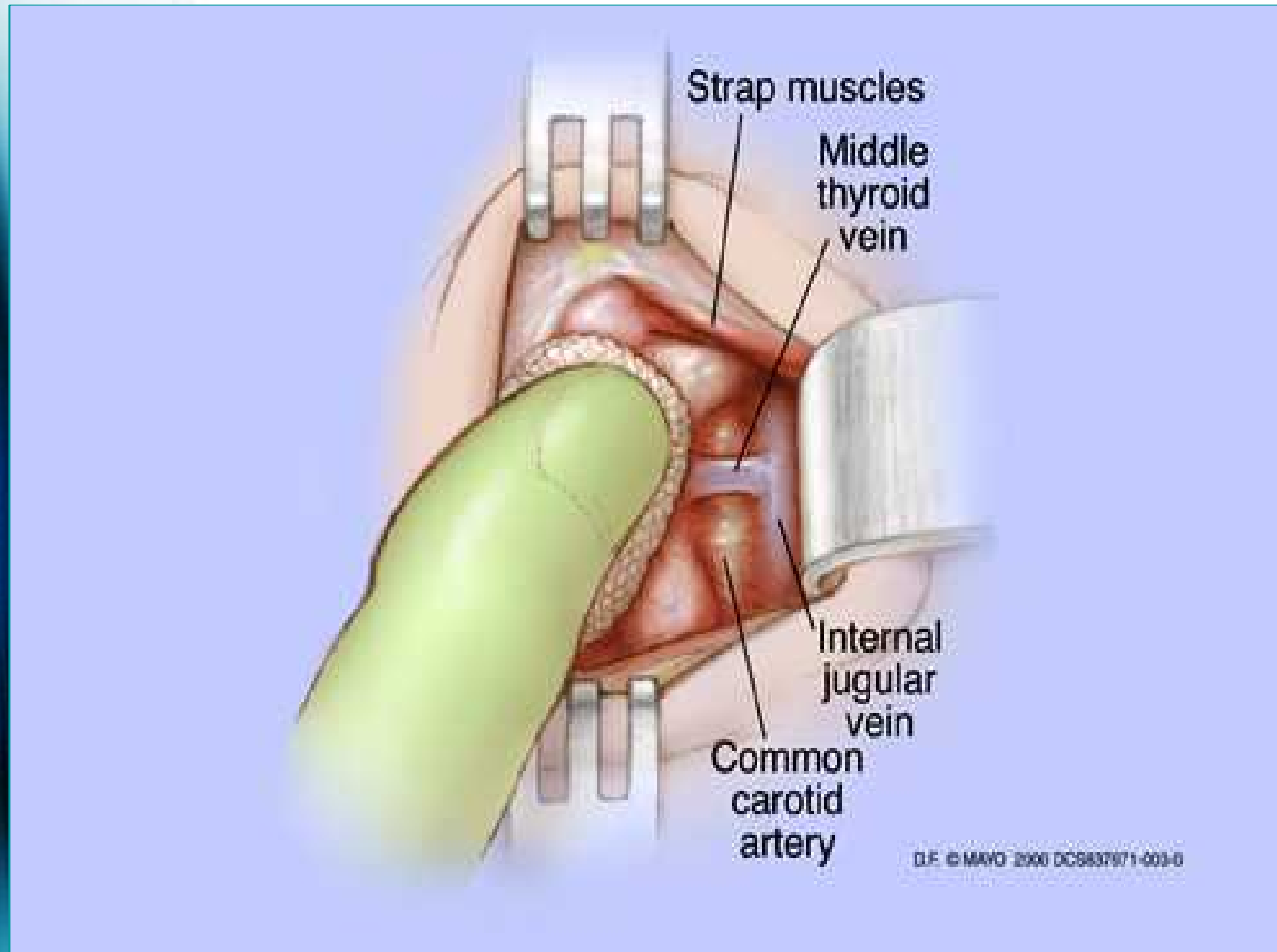


MIP Technique

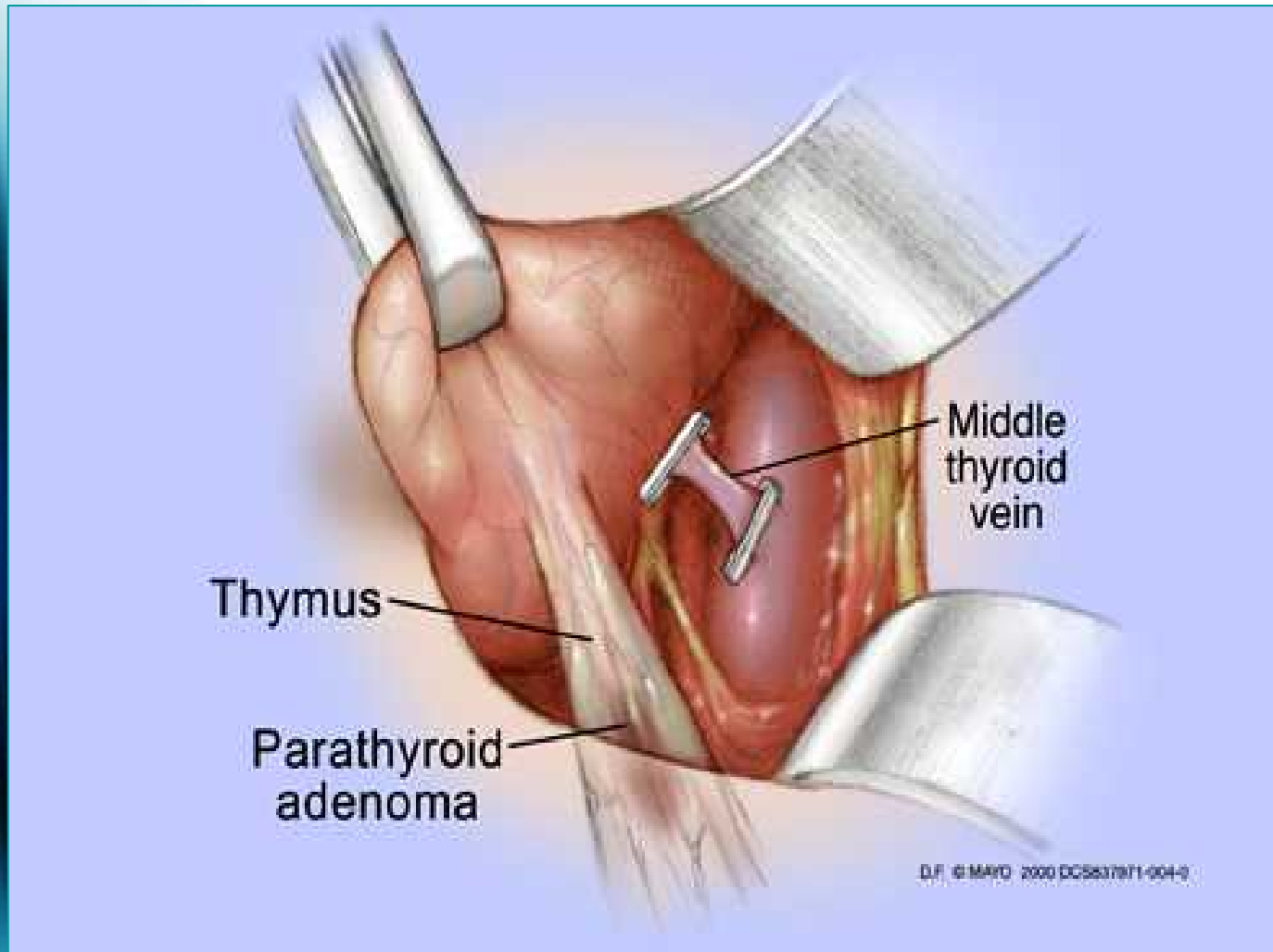




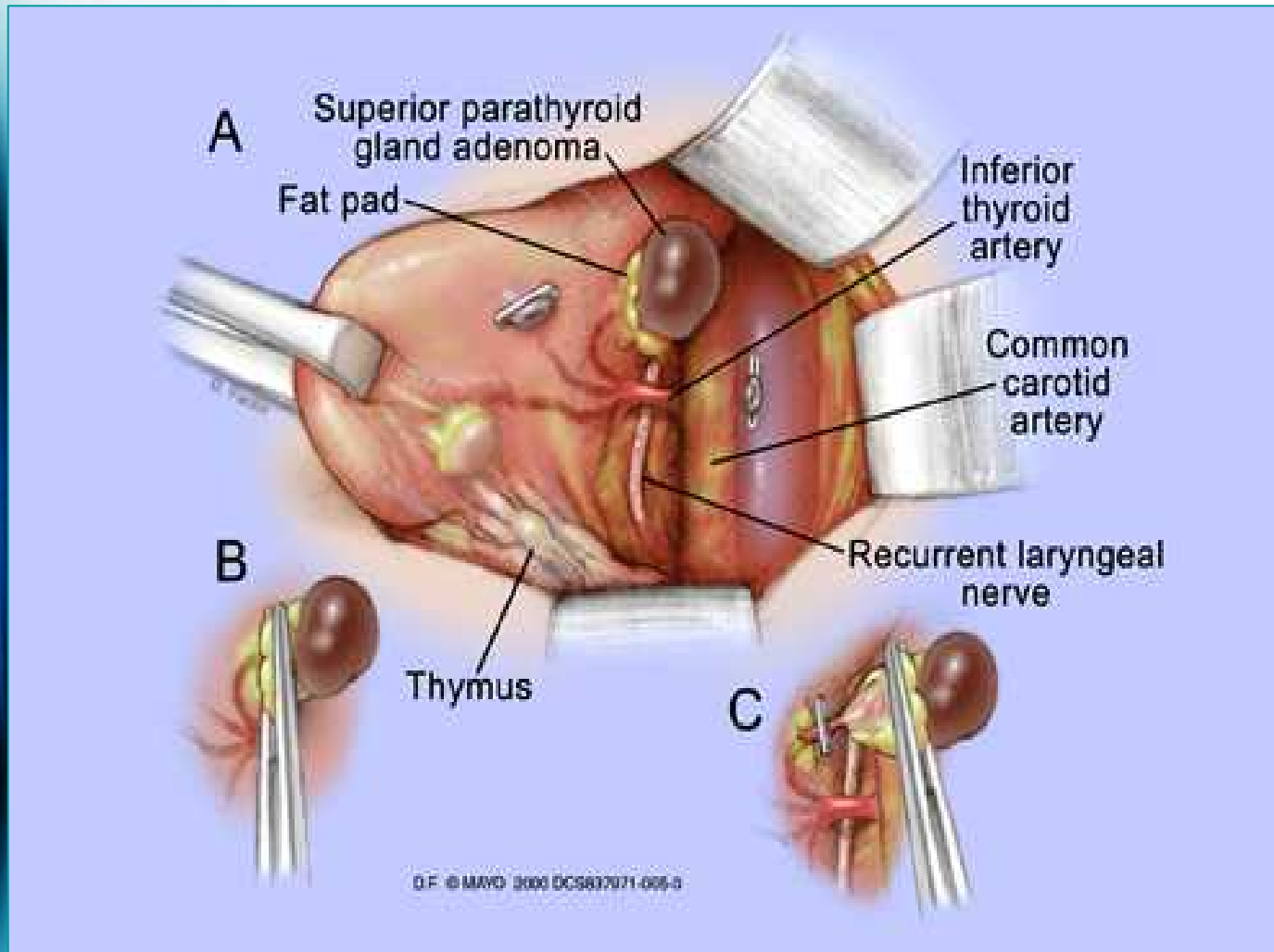
MIP Technique



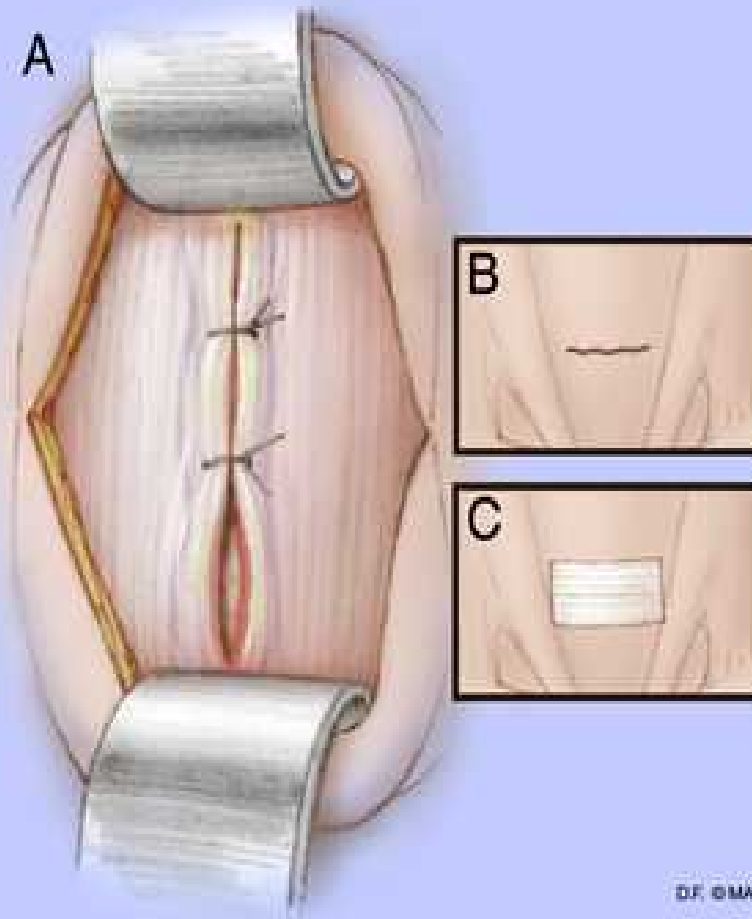
MIP Technique



MIP Technique

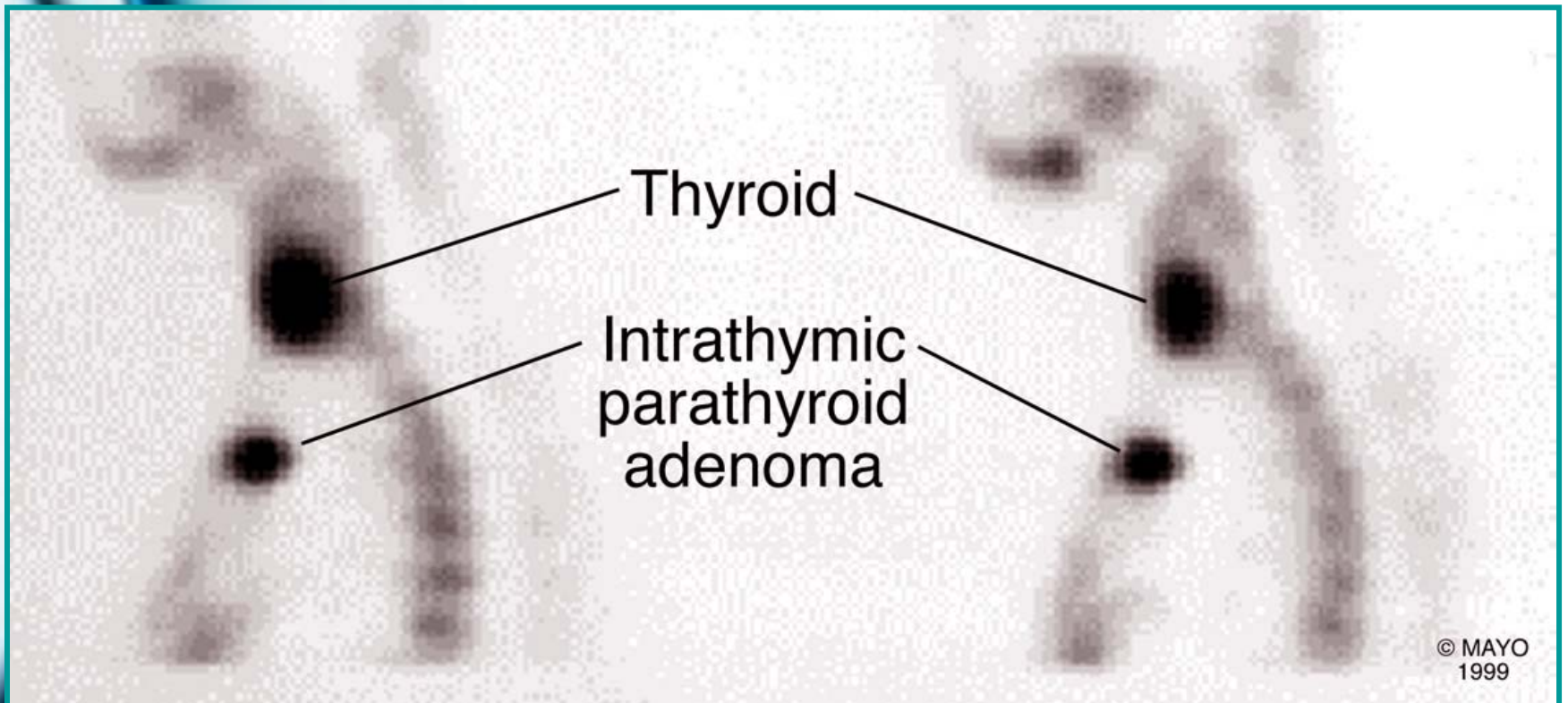


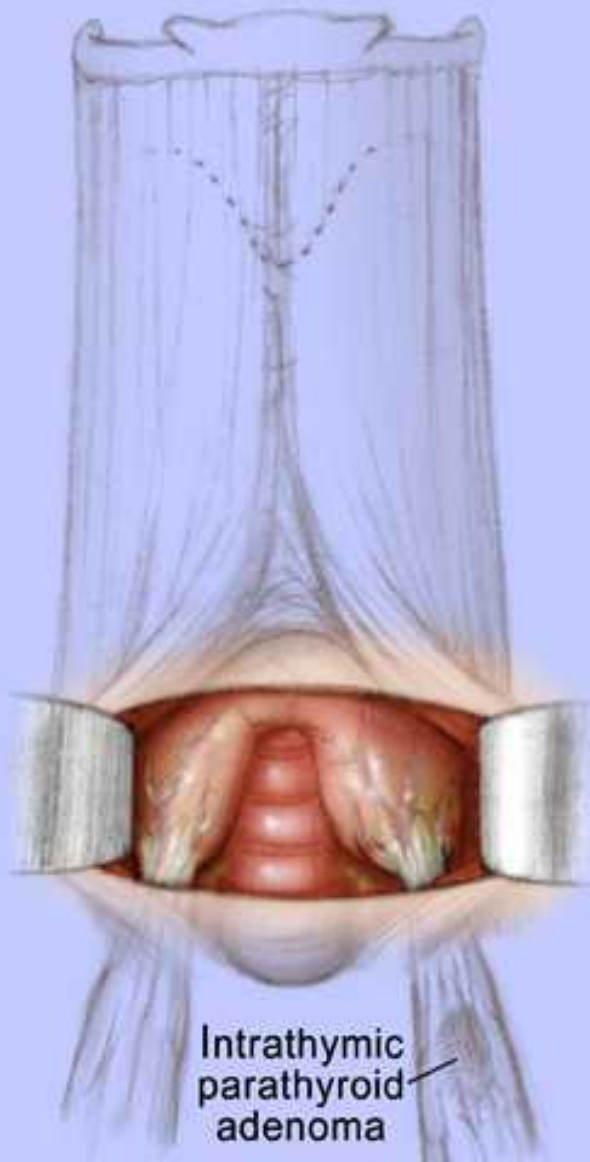
MIP Technique



Scar @ 3 Months

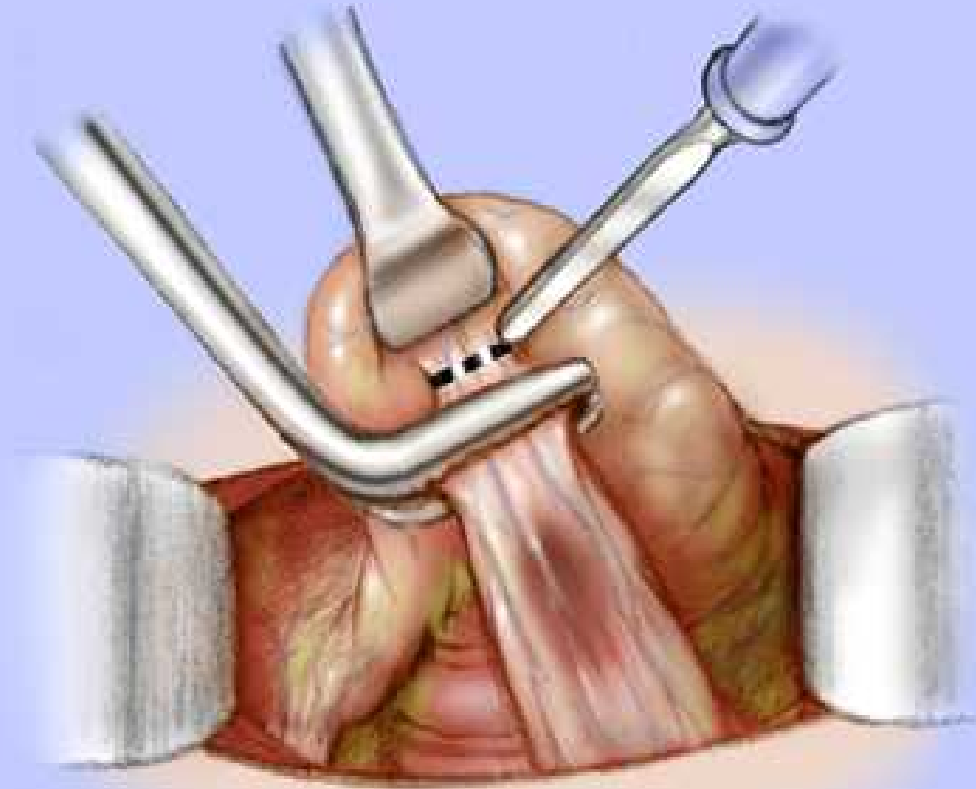






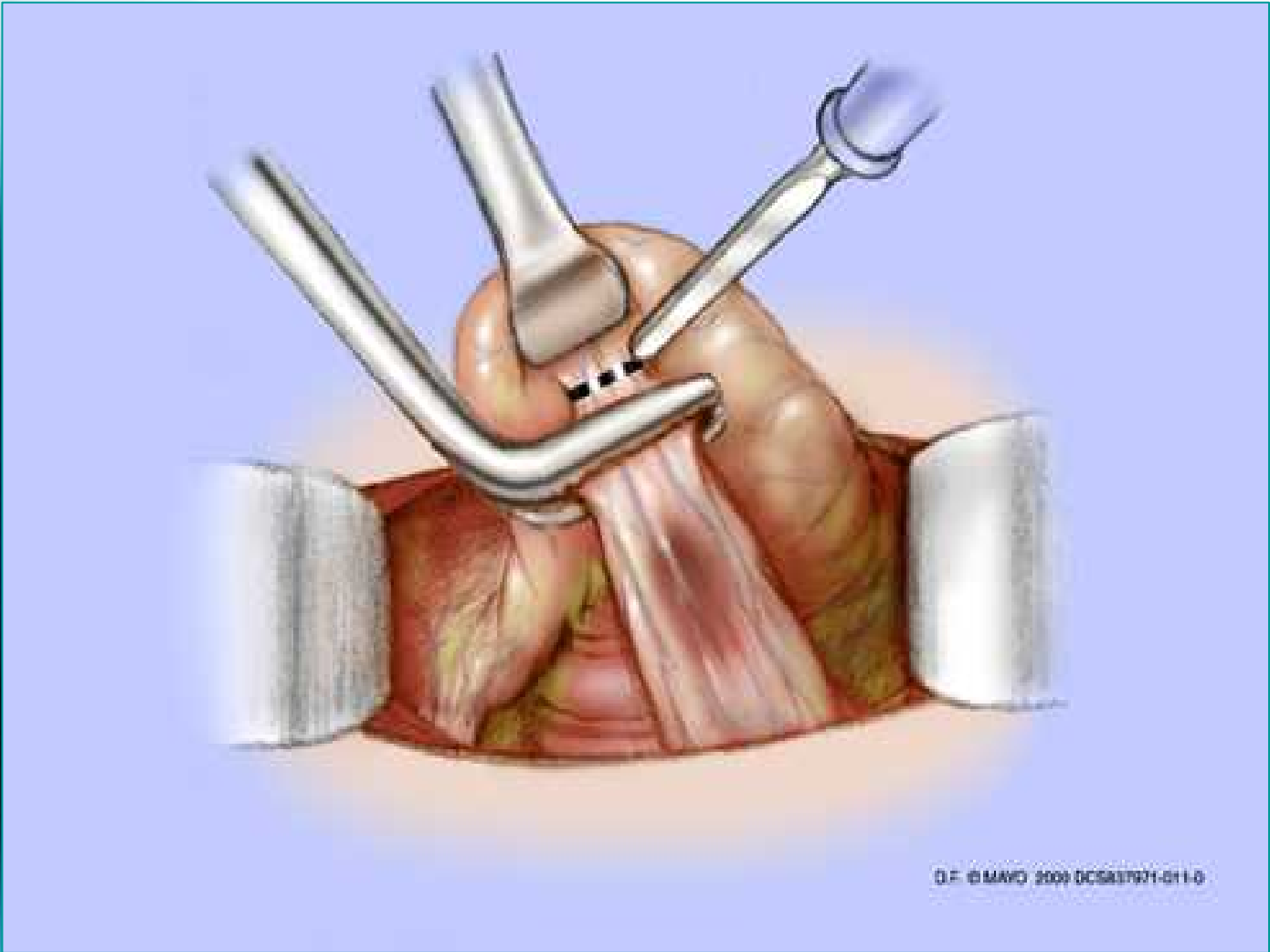
D.F. © MAYO, 2000 DC5837971-007-0

MIP Technique



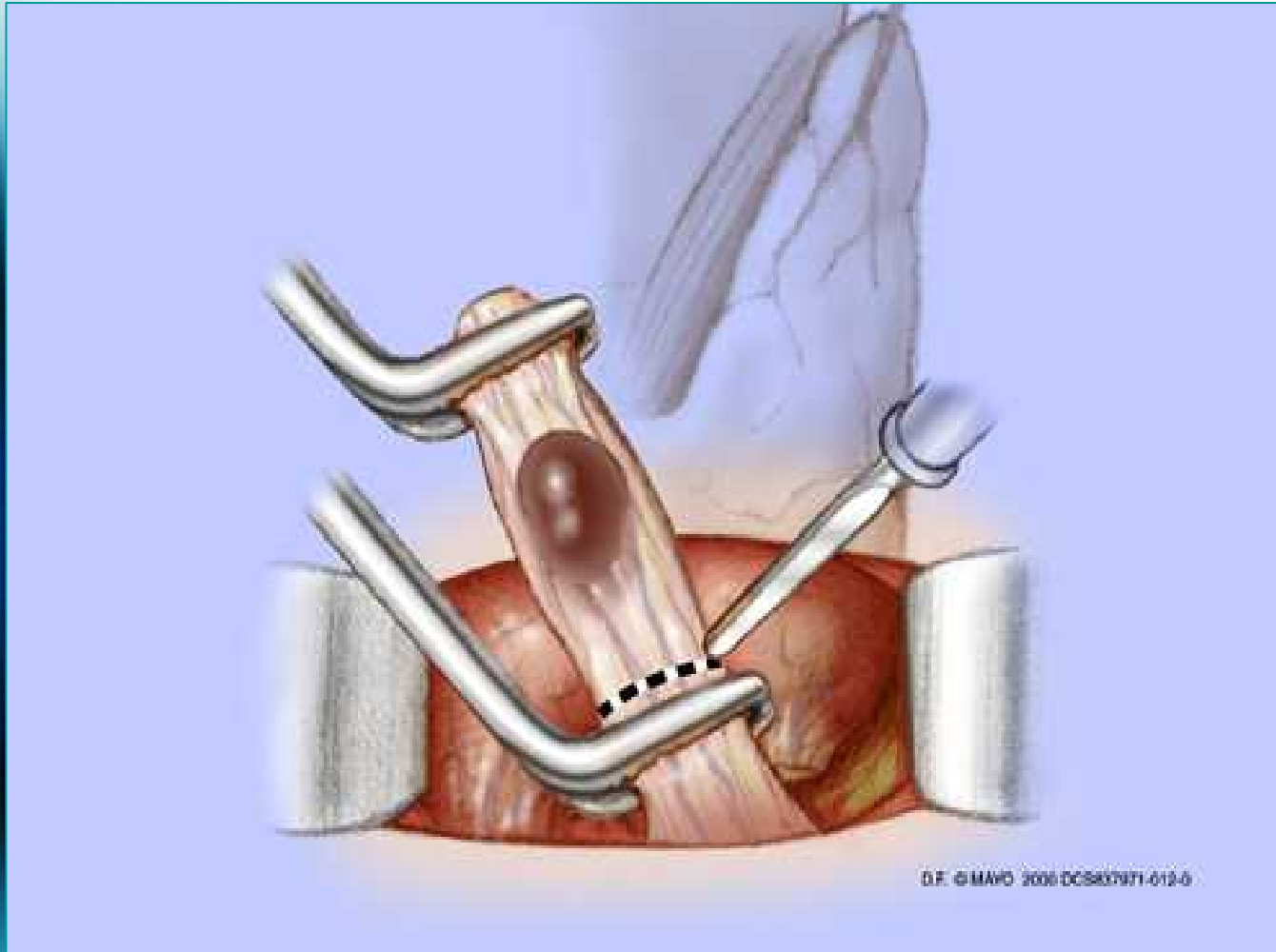
This anatomical illustration depicts the MIP (Minimally Invasive Piriformis) technique for hip surgery. It shows a lateral view of the hip joint with the femoral head and neck. A minimally invasive surgical approach is shown, involving a small incision and the use of specialized instruments. A retractor system is used to hold back muscle and soft tissue, providing a clear view of the femoral head and neck. A surgical instrument is shown performing a minimally invasive approach to the femoral head and neck, likely for a total hip arthroplasty. The illustration highlights the minimally invasive nature of the technique, showing the small incision and the use of specialized instruments.

© F. © MAYO 2000 DCS837971-011-0

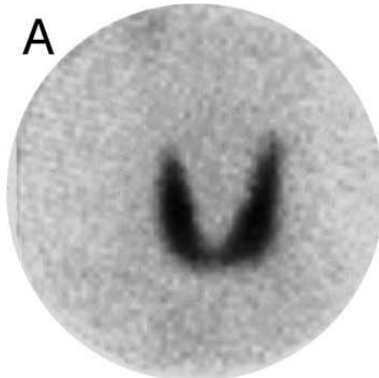


U.F. 49 MAY 2000 DEC 31 1997-01 1-0

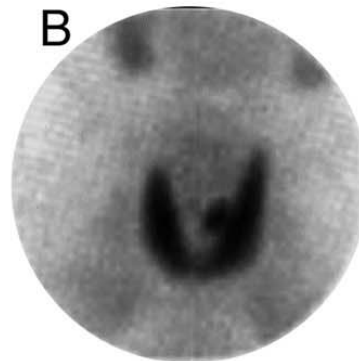
MIP Technique



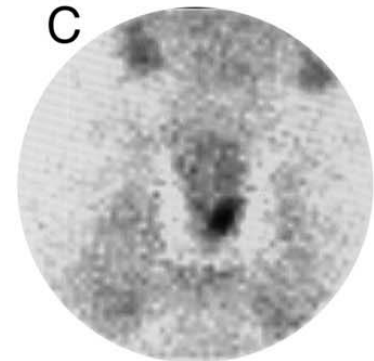
SPS



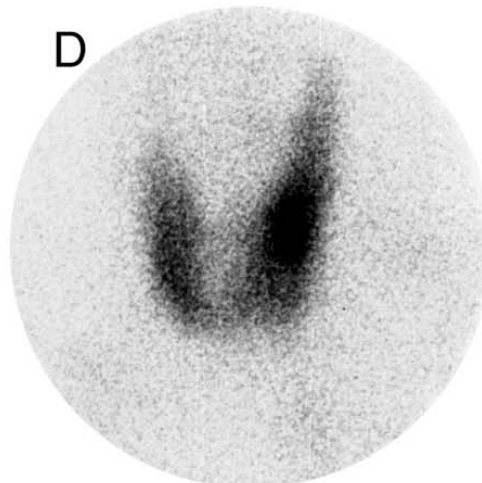
Pertechnetate



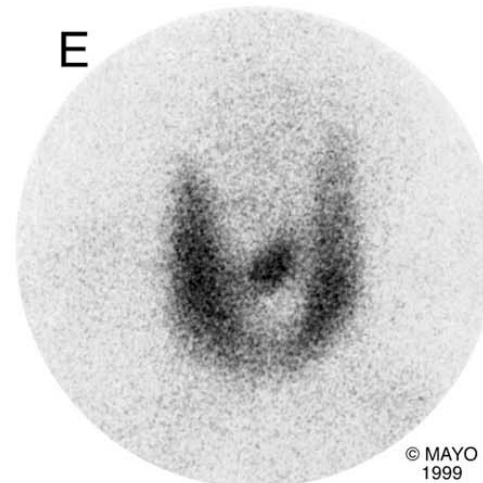
Sestamibi



Subtraction

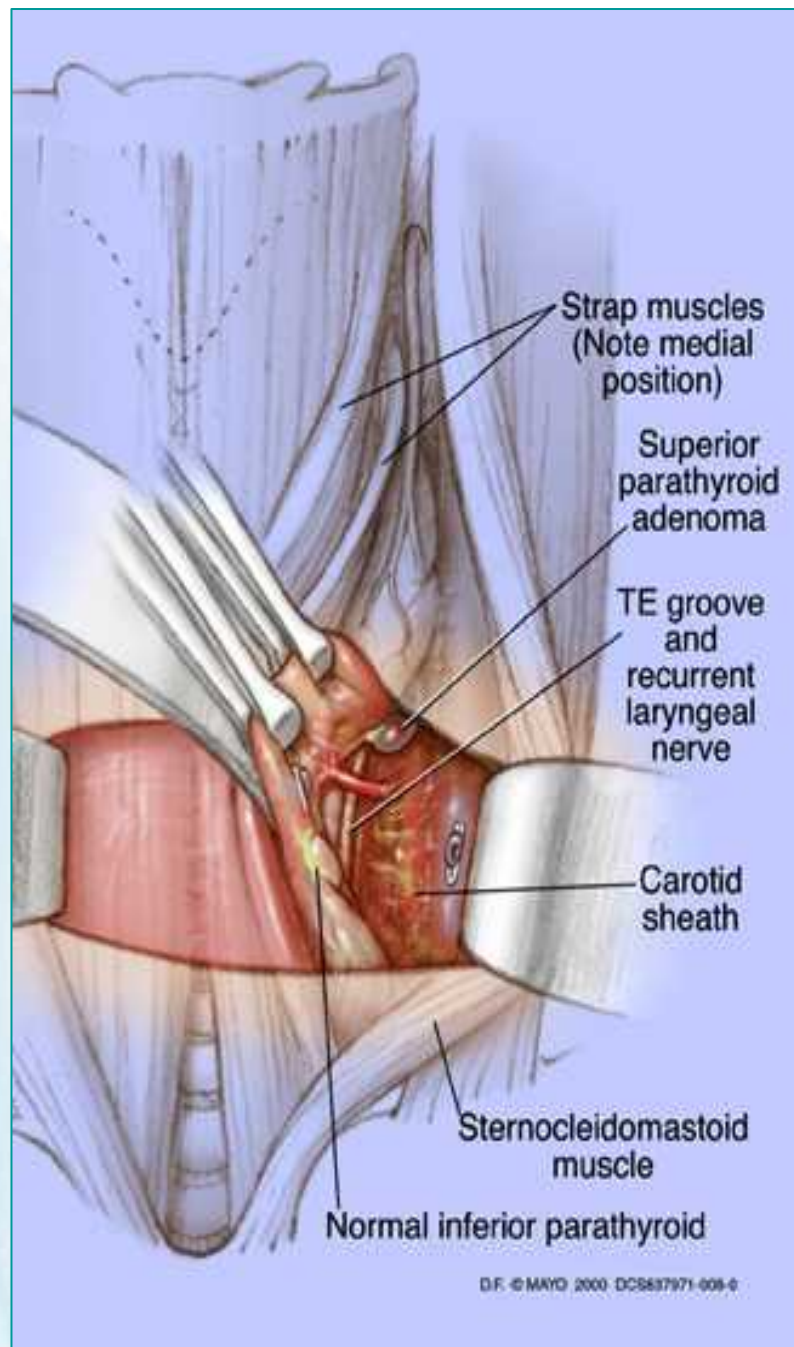


LAO



RAO

© MAYO
1999



A

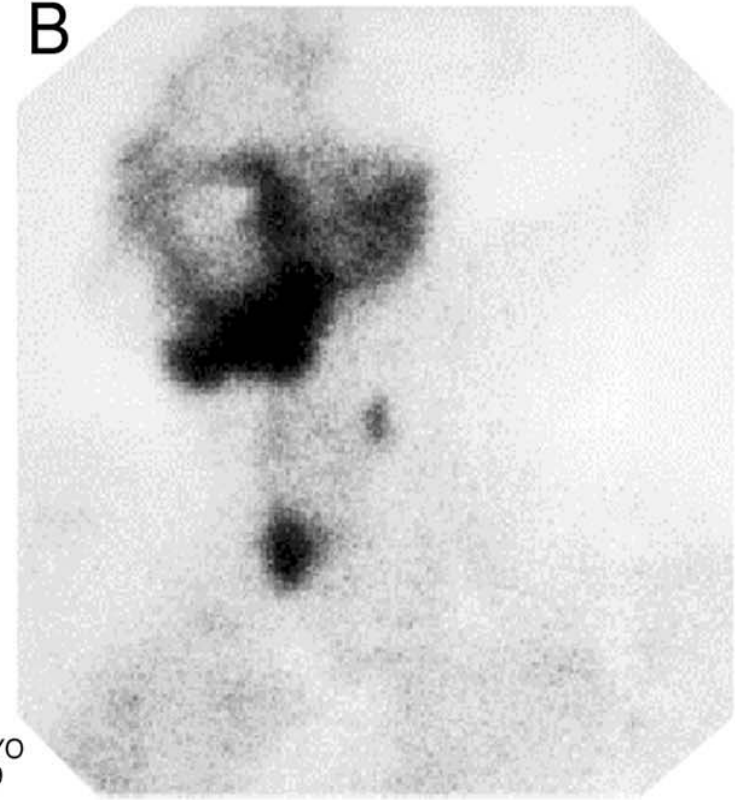


Right

Anterior

Left

B



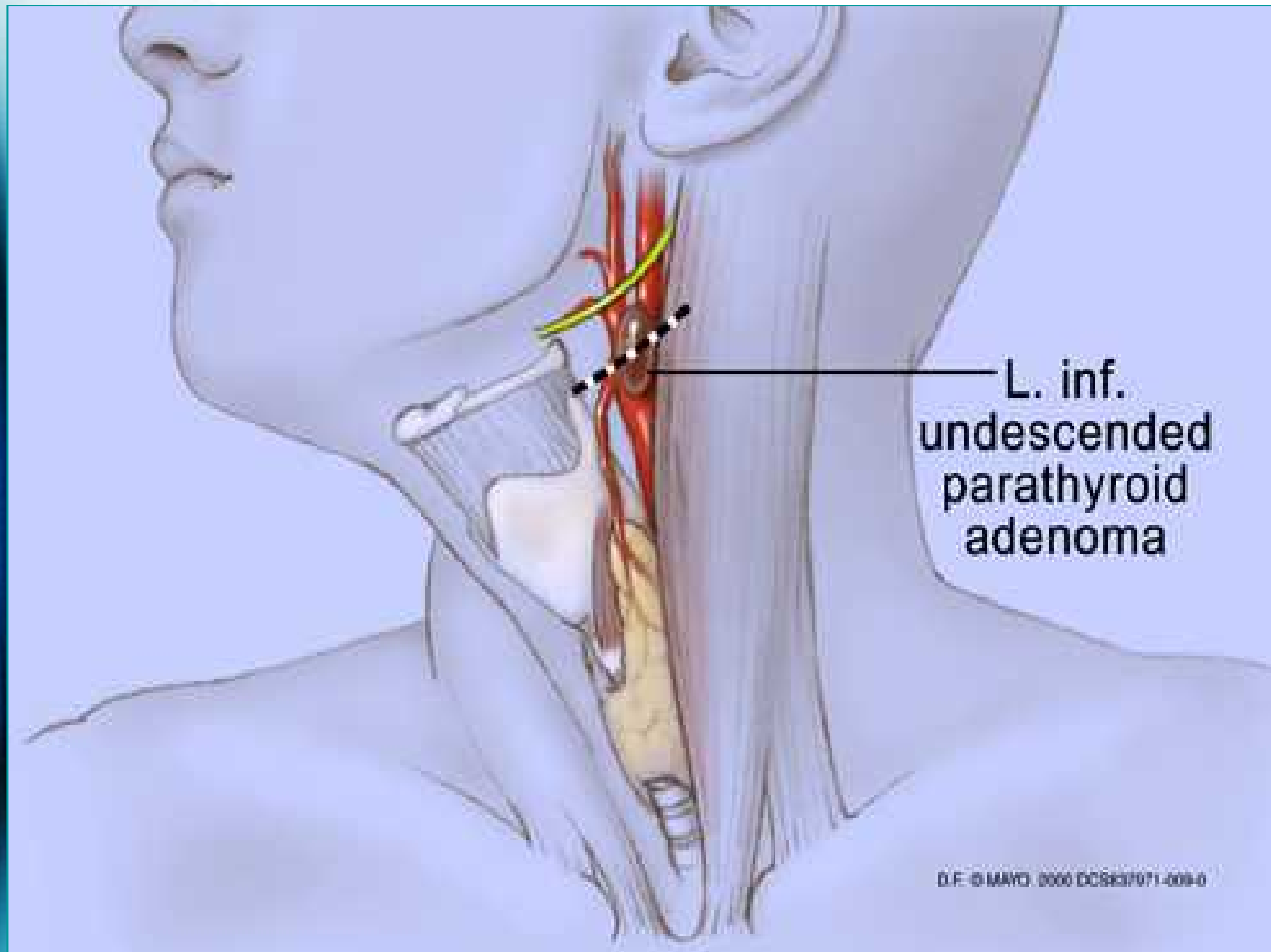
Ant

Left Lateral

Post

© MAYO
1999

MIP Technique



First Fifty Patients

- Outcomes similar
- Morbidity <1%

- Return to normal
- Overall satisfaction
- Scar satisfaction

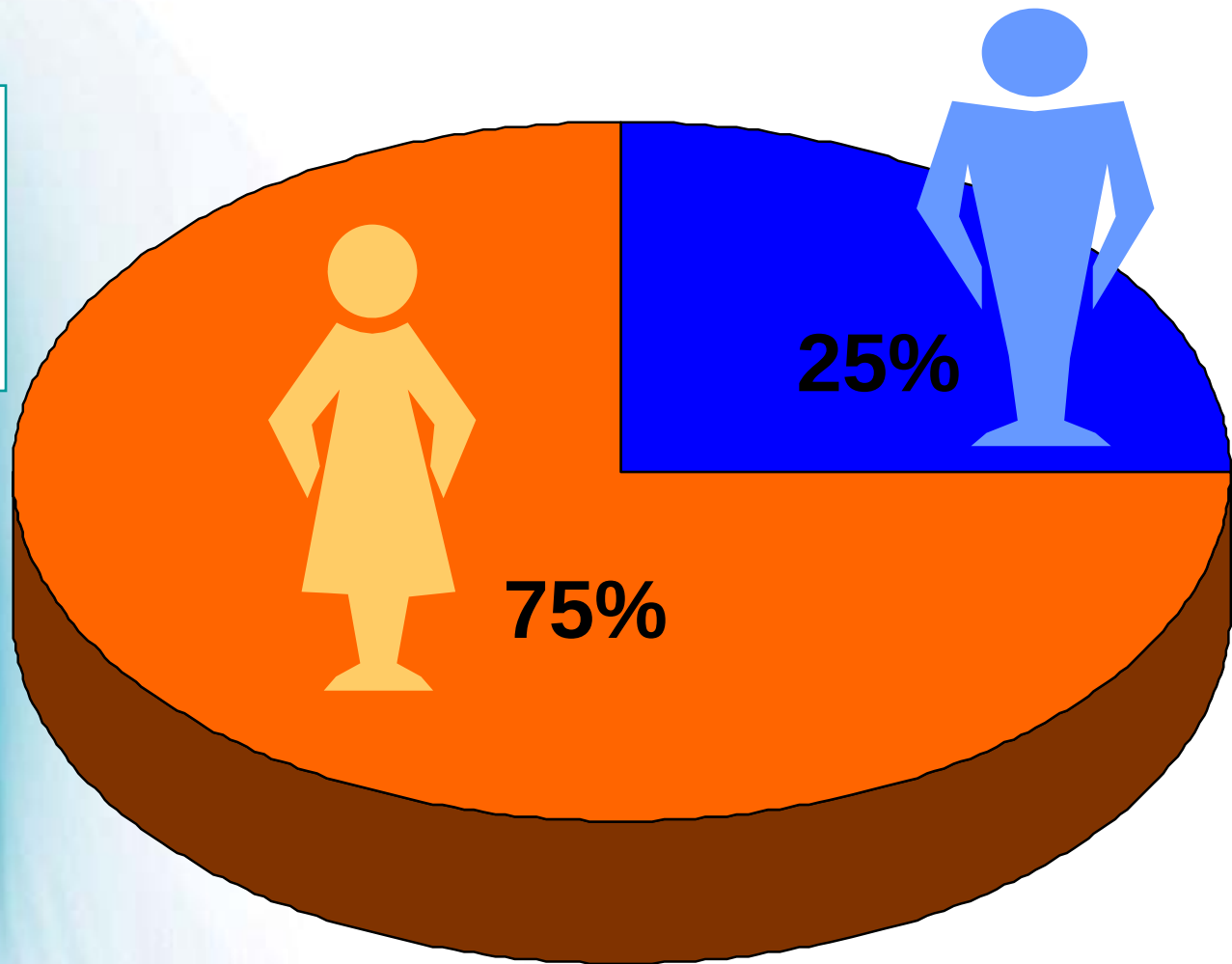
Similar

- Pain and nausea* less in MIP group
- Cosmesis better?

*When performed under local anesthesia

HPT: Mayo 6/98-9/09

3,187 pts
Age 61
(10-97)

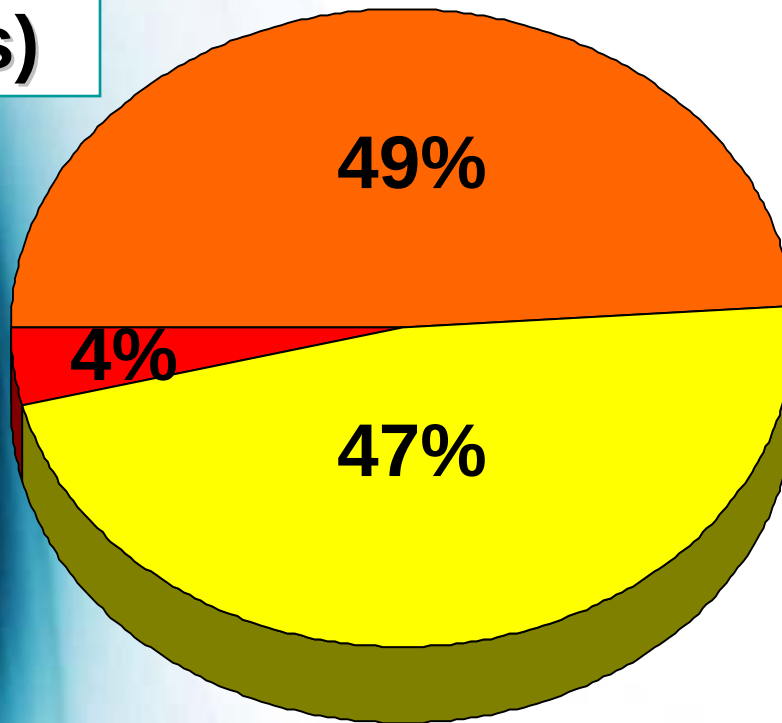


HPT: Mayo Clinic Experience

**3,187 pts
(3,203 ops)**

Conventional

**MIP
converted**



**Median gland wt:
430 mg
(range, 20-56,000 mg)**

88% SGD

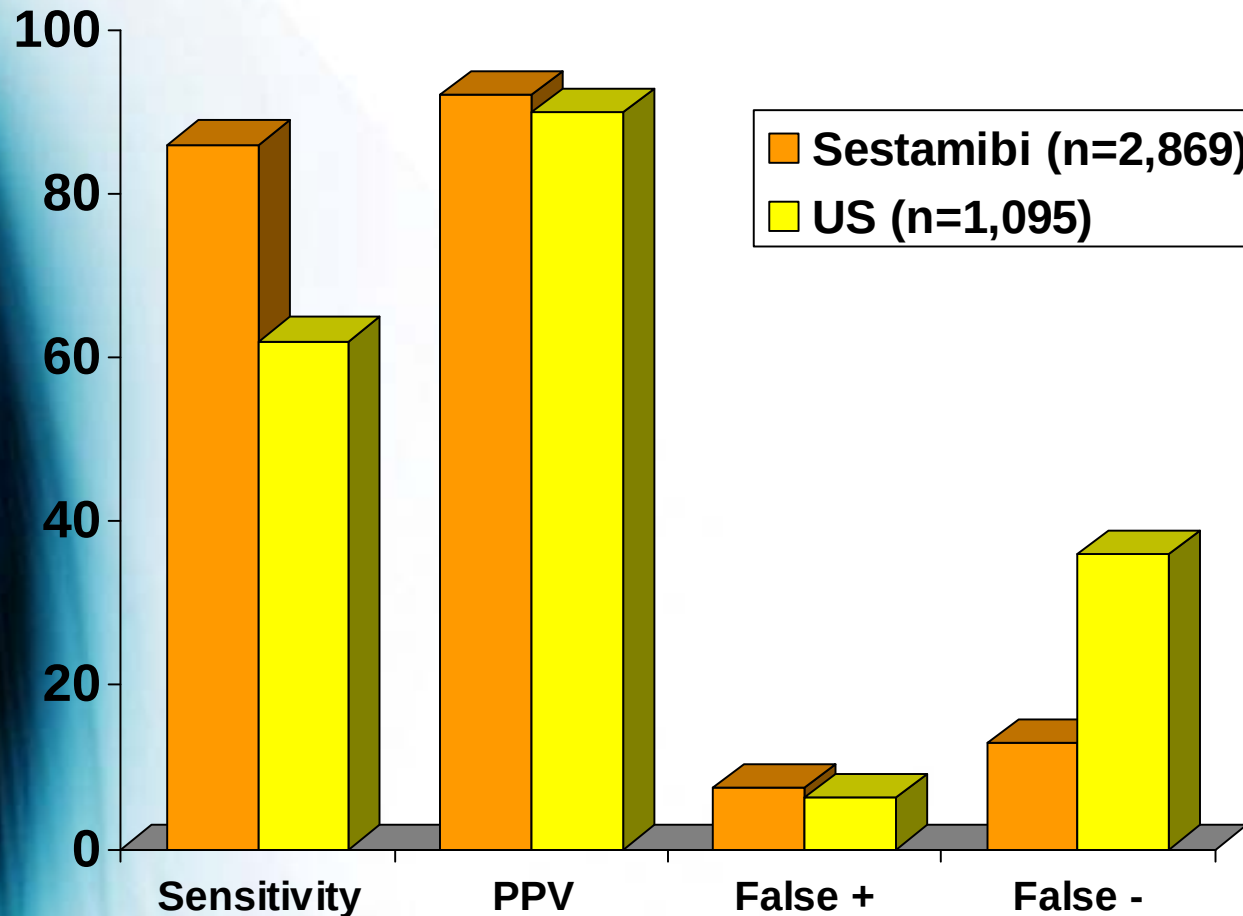
12% MGD

Mean Ca⁺⁺ 11.0 mg/dL

MIP

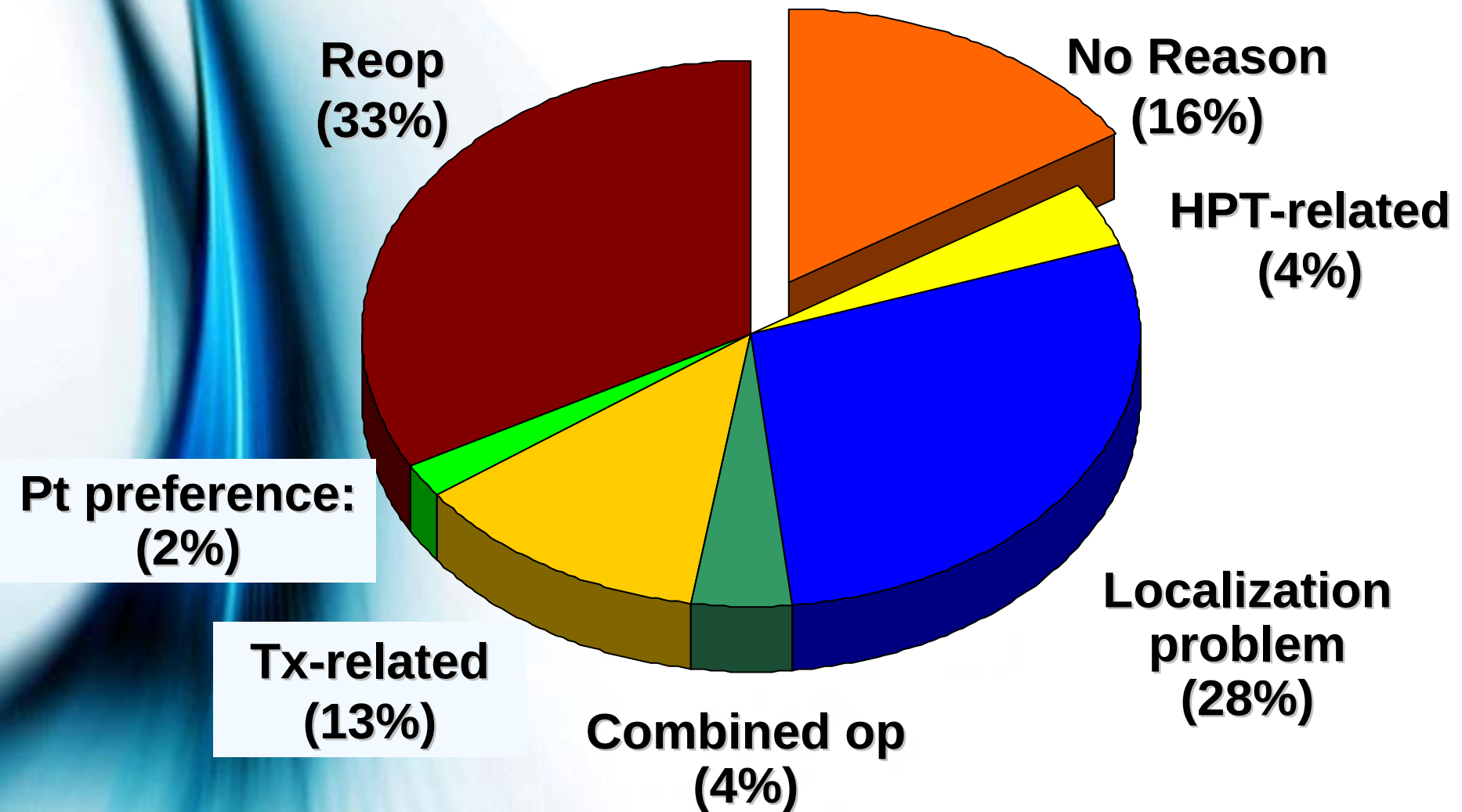
HPT: Localization

Overall



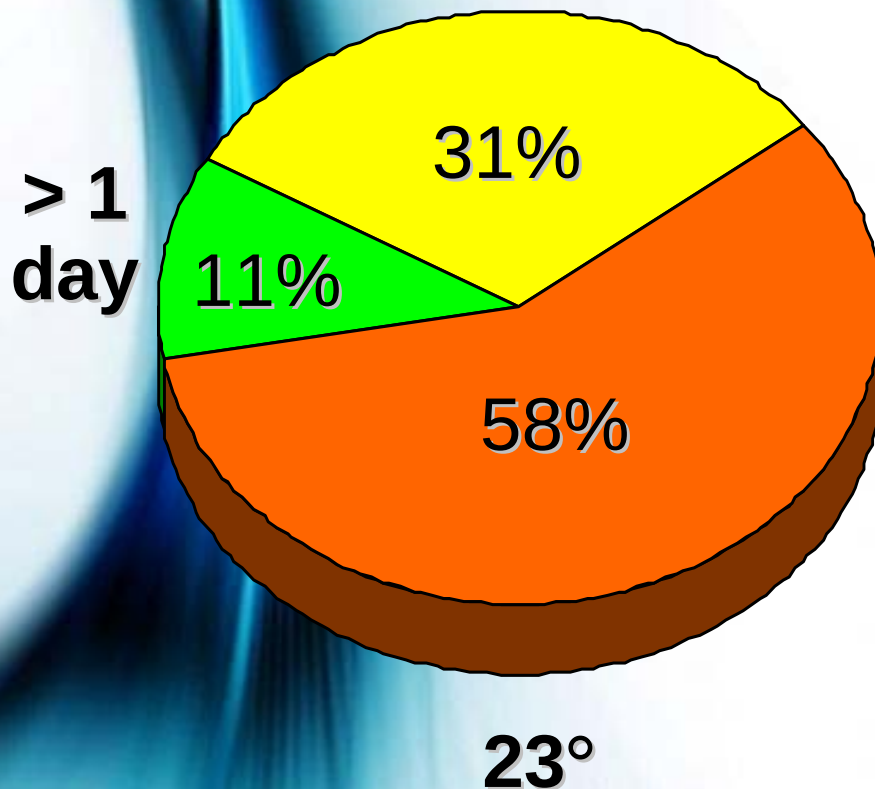
Reasons: Conventional Op

1,257 pts (includes reops)

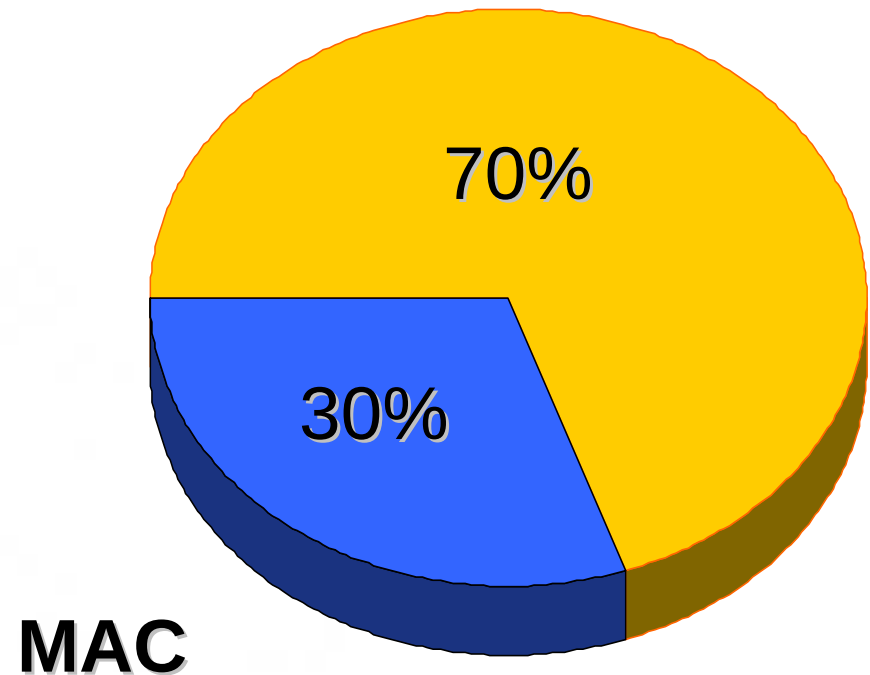


MIP: Length of Stay/Anesthesia

Outpatient



General



MIP: Methodology

- Influences

- SPS: 2,869 cases (90%); Sensitivity 86%, PPV 92%, FP 7.4%, FN 13.0%
- IOPTH: 2,422 cases (76%); accuracy: 97%
 - 194 (8%) true negatives – most beneficial
- Gamma-probe inaccurate in 32% of 93 cases
- Thyroid resected in 439 cases (14%)

HPT: Success

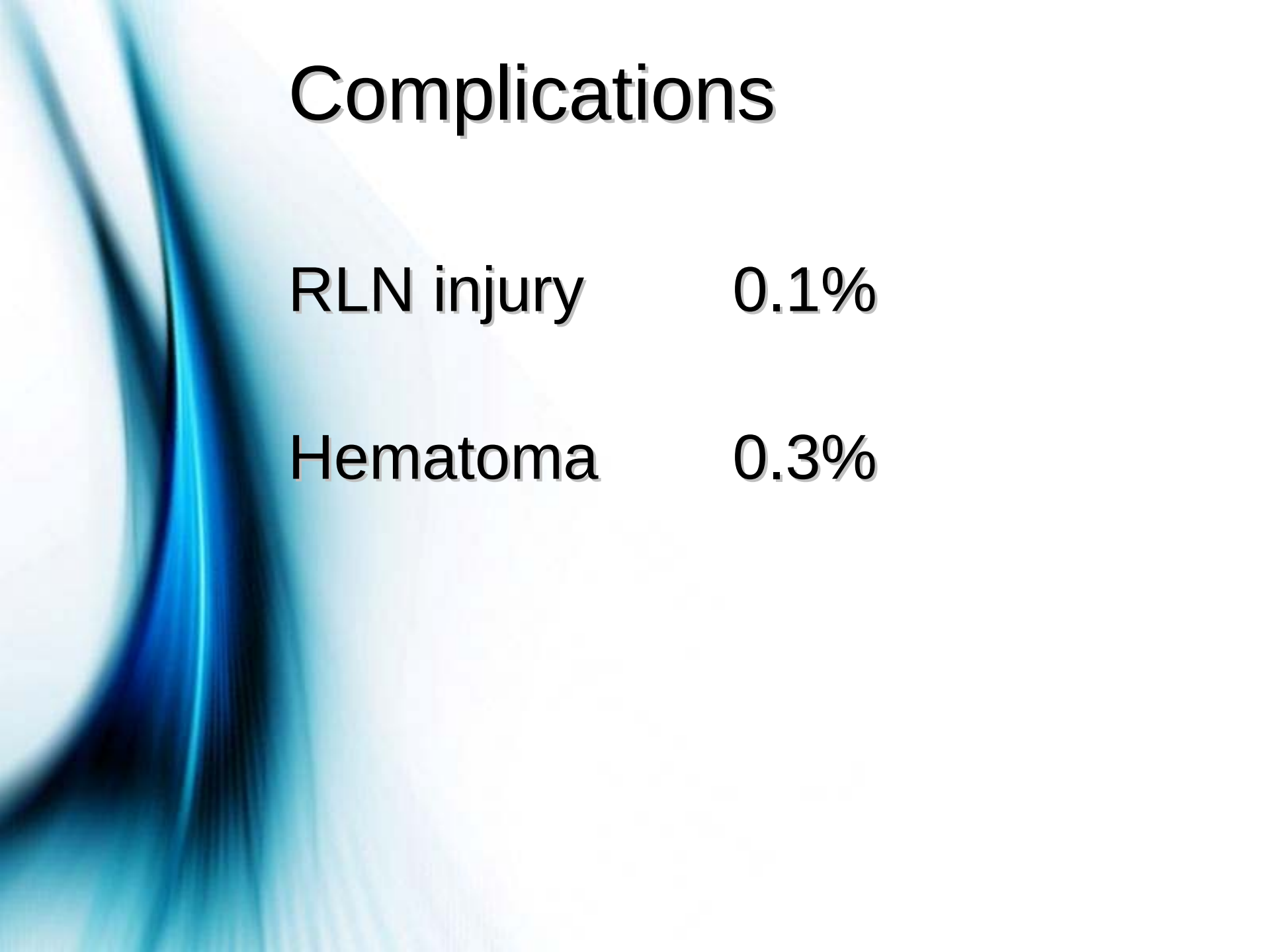
Cure Rates (3,187 patients)

Conventional (exc reops)	96%
--------------------------	-----

MIP (exc reops)	98%
-----------------	-----

Overall (inc reops)	97%
---------------------	-----

MGD	95%
-----	-----



Complications

RLN injury	0.1%
------------	------

Hematoma	0.3%
----------	------

MIP: Assessment

- Advance
 - Estimate 60-70% eligible for image-guided MIP
 - Dependent on high-quality imaging and interpretation
 - IOPTH truly valuable in <10%, but quite reassuring in others
 - With the use of IOPTH, cure should be very little different from standard open procedure
 - γ - probe not valuable in our hands

MIP: Assessment-2

- Added Value
 - Small incision
 - Local anesthesia
 - for majority of patients (no longer critical)
 - minimize pain, nausea, mental “fogginess”
 - outpatient
 - General anesthesia **if** pt still outpatient
 - Expense equivalent or increased

Modest step forward---not a quantum leap

Indications for Standard Exploration

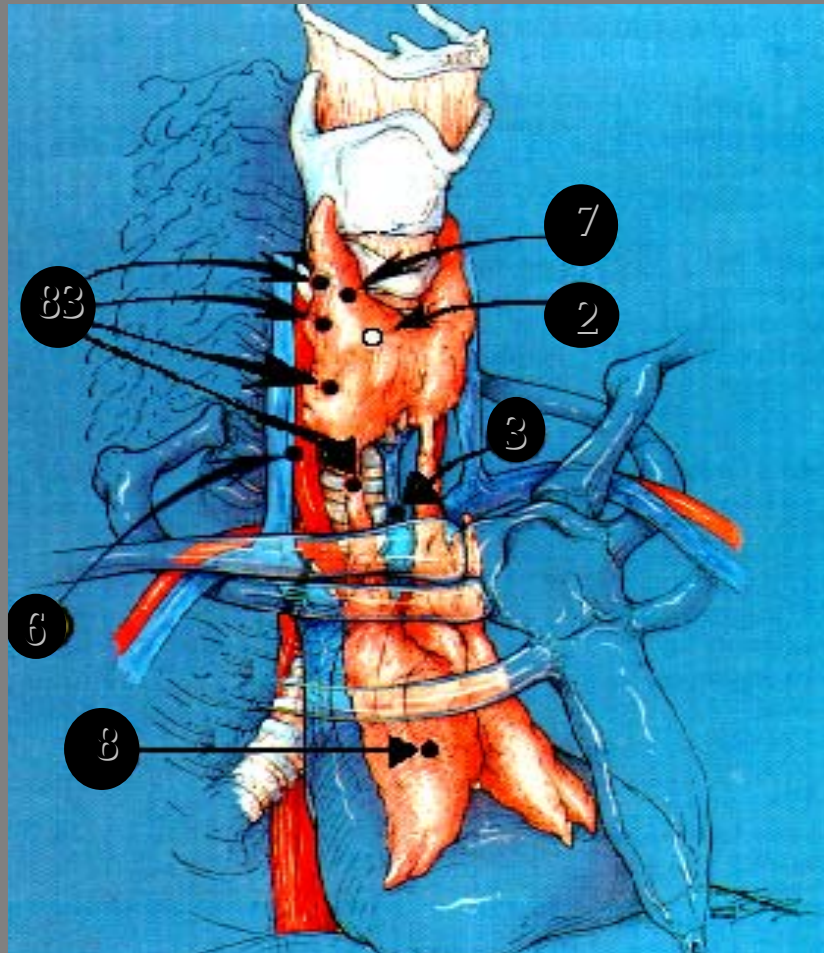
- Negative preoperative imaging
- Concomitant thyroid pathology *
- Family history of endocrinopathy
- Family history of HPT *
- Imaging suggesting MGD *
- History of neck irradiation *
- Certain reoperations

*Relative contraindications for MIP

Persistent/Recurrent HPT

- Confirm Diagnosis: R/O FHH, Thiazides, Lithium
- Assess the risks of not reoperating
- Vocal cord examination
- Operative Reports-talk to surgeon
- Pathology blocks and slides (not just reports)

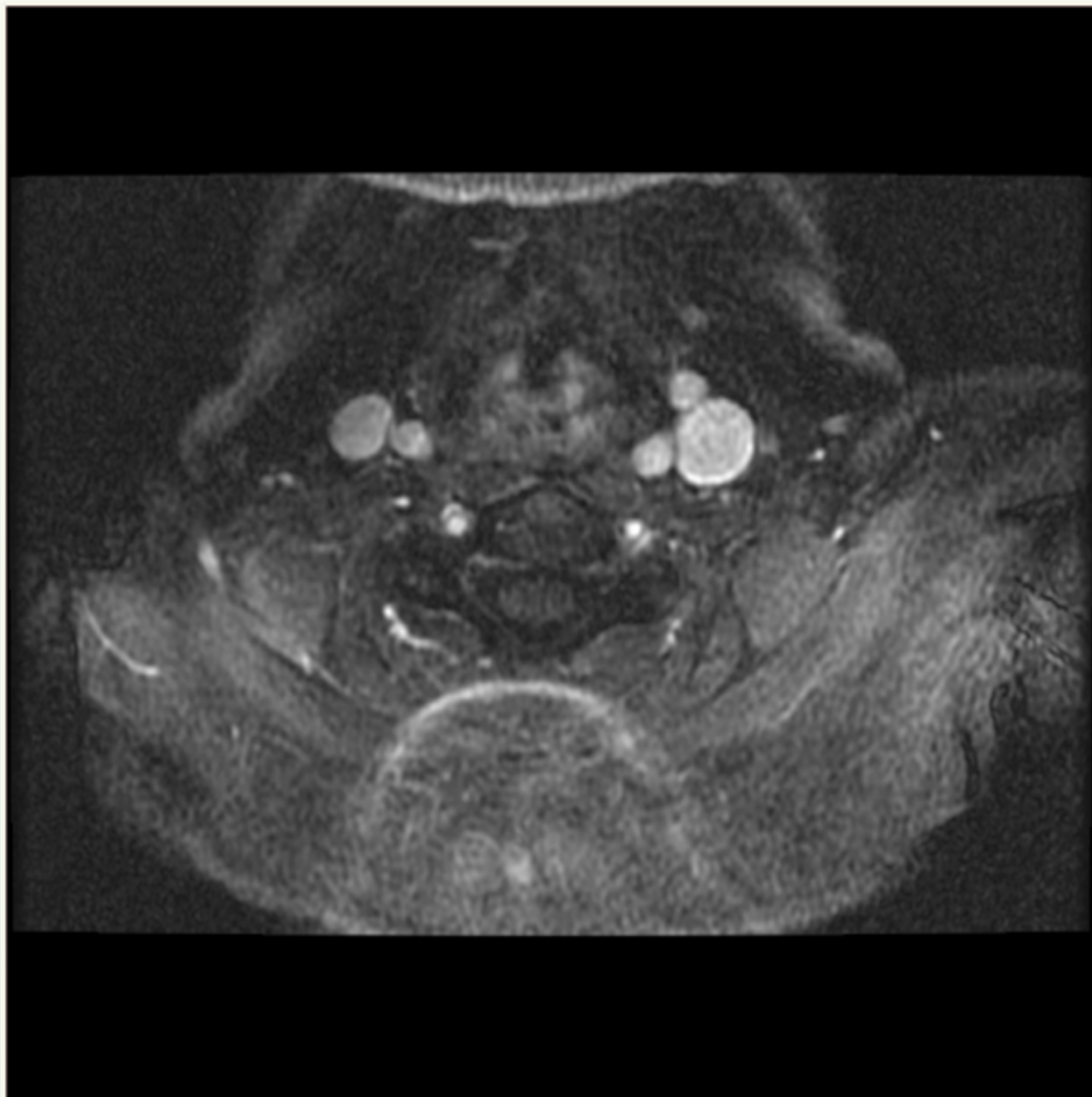
Reoperative Parathyroid Surgery: Location of Missed Glands in Cured Patients

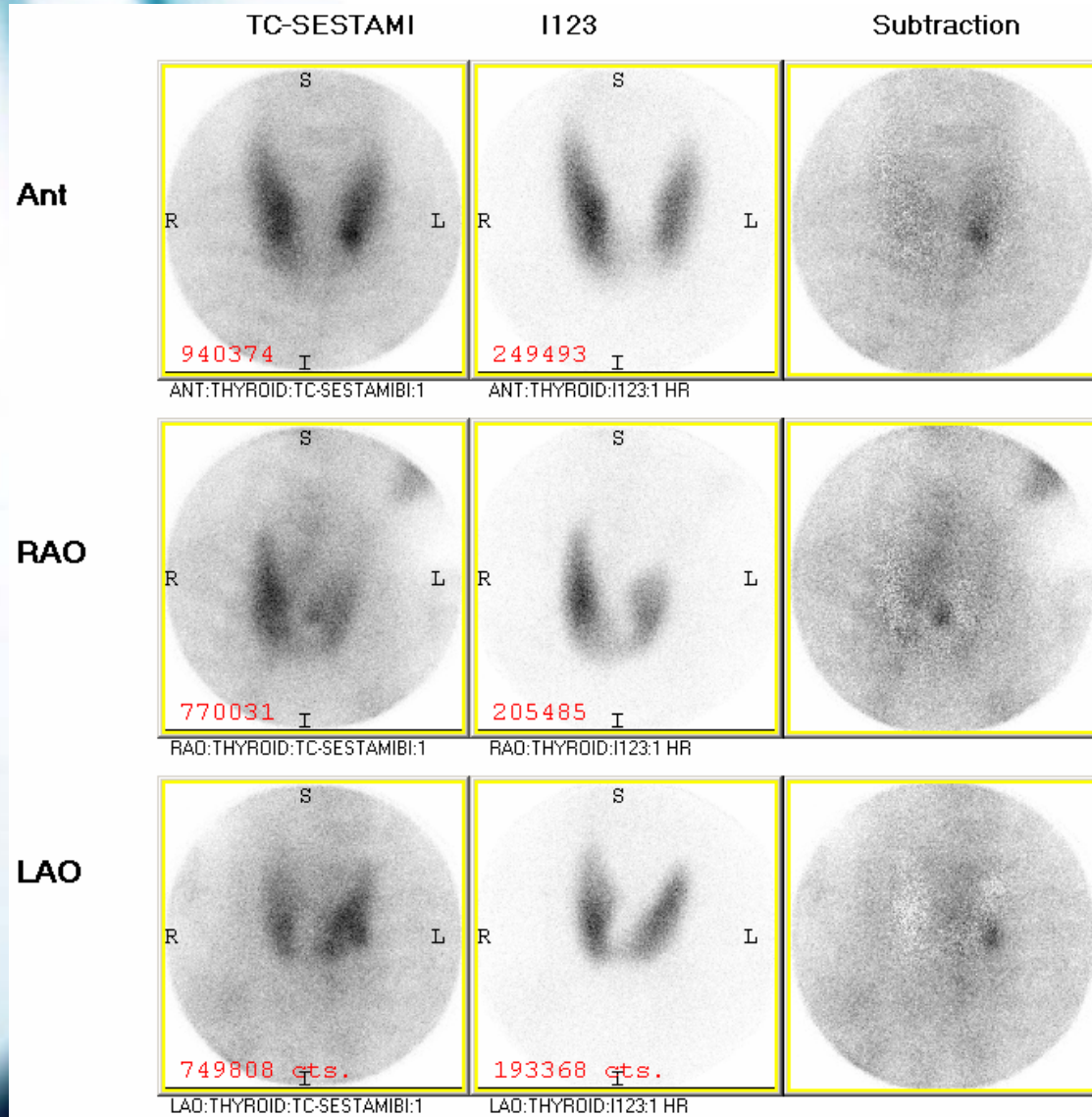


- Normal 83
- Mediastinum 8
- Intrathyroidal 7
- Carotid sheath 6
- Anterior trachea 3
- Retroesophageal 2

Persistent/Recurrent HPT(cont.)

- **Imaging**-the more the better ?
- **SPS, US plus FNA for PTH**, SPS/CT fusion with Hawkeye camera, **Venous sampling**, MRI, **4D CT**, Arteriography
- Alternative ablative therapies (embolization and PEI) and surgical approaches
- Autotransplantation vs cryopreservation





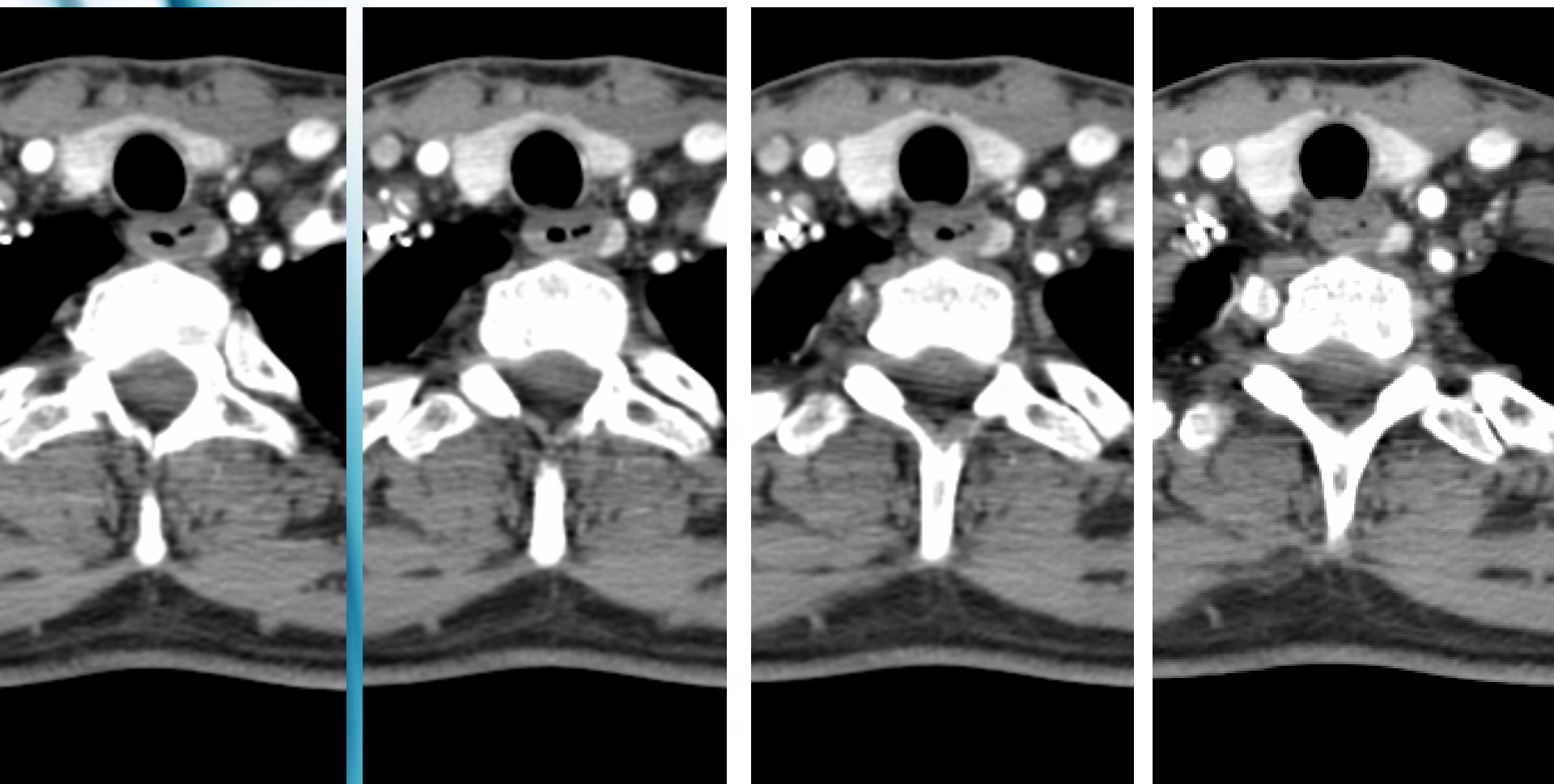
Nucs-

Left thyroid pole to left
tracheoesophageal groove

US-

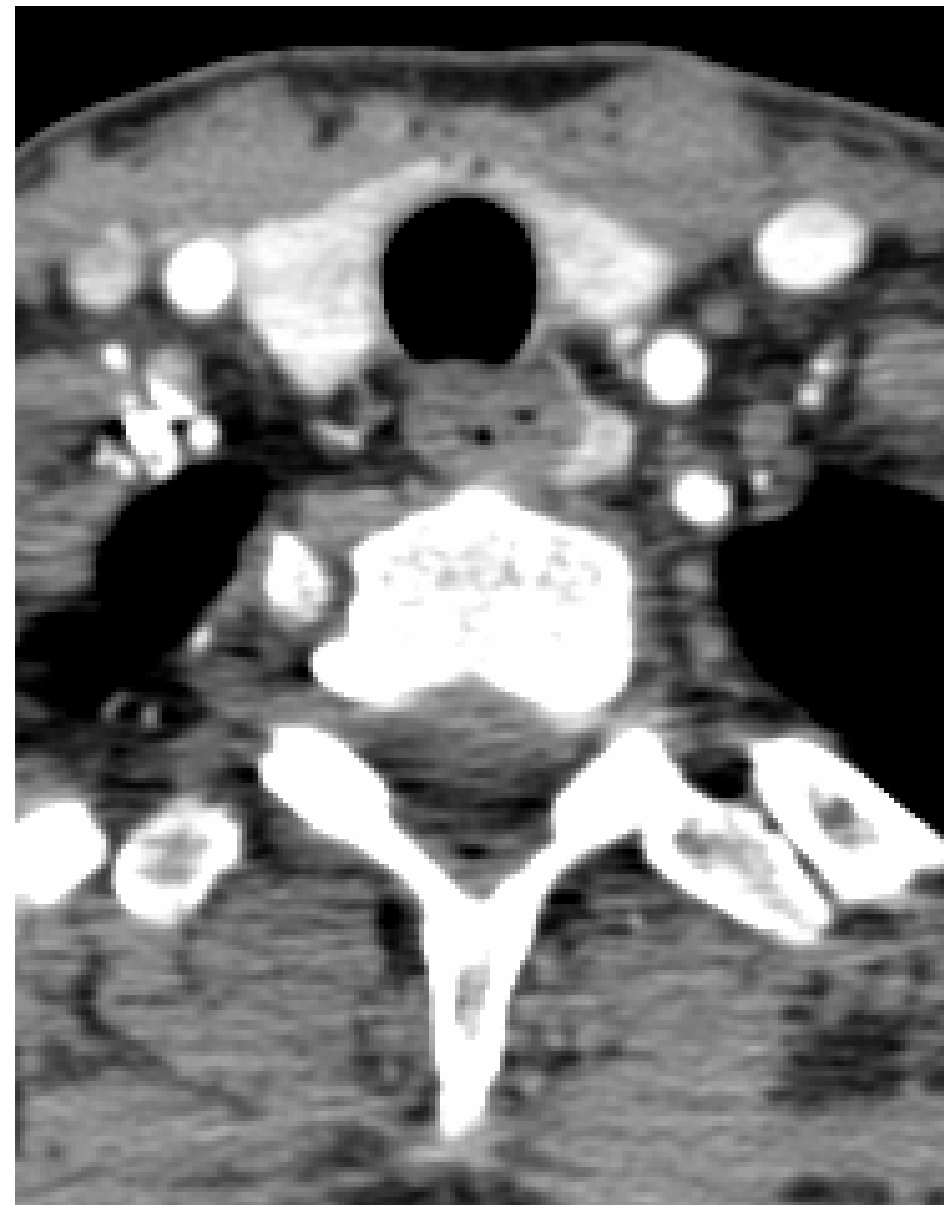
Nothing convincing

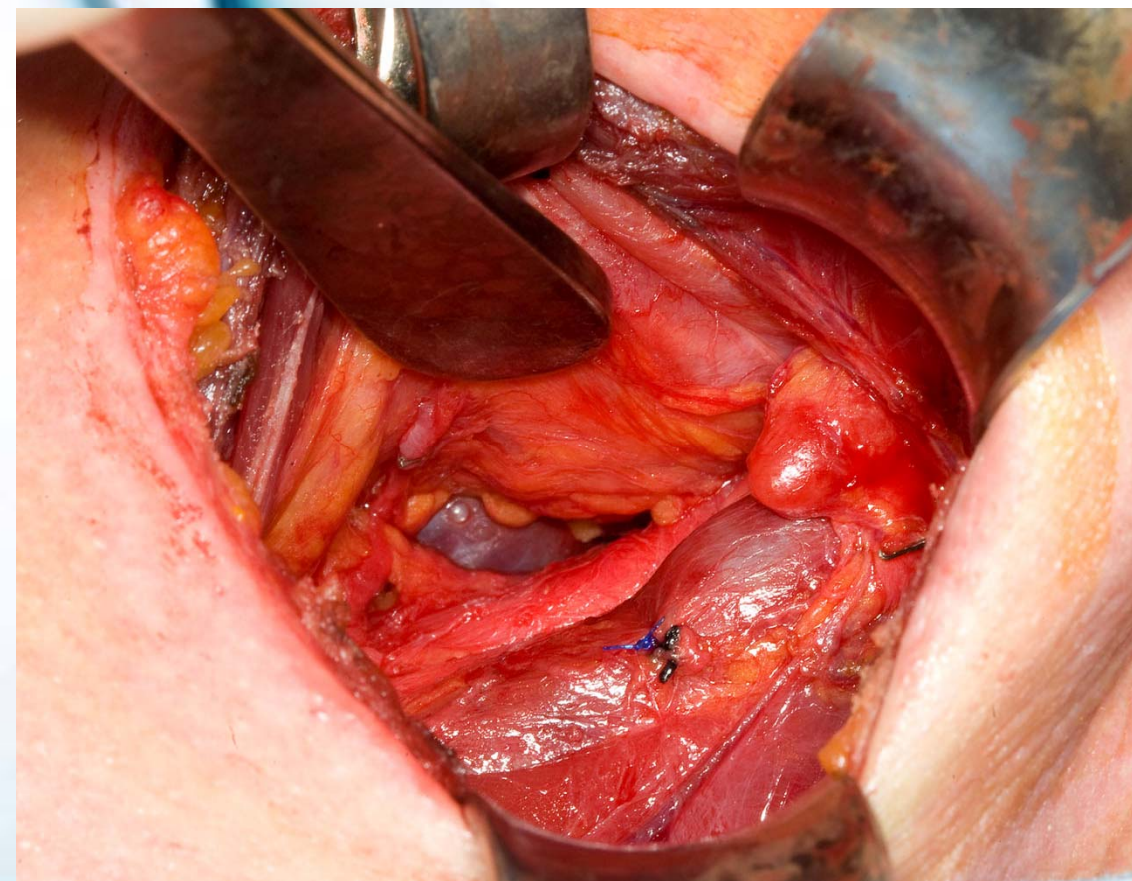
prior exploration



Arterial, 2mm slices, adenoma measured 8x4x14mm on CT







Courtesy Geoffrey Thompson, MD

Thank You

