



Surgical treatment of cushing disease

Luigi Maria Cavallo

DIVISION OF NEUROSURGERY

DEPARTMENT OF NEUROSCIENCES & *reproductive*
& *odontostomatological sciences*

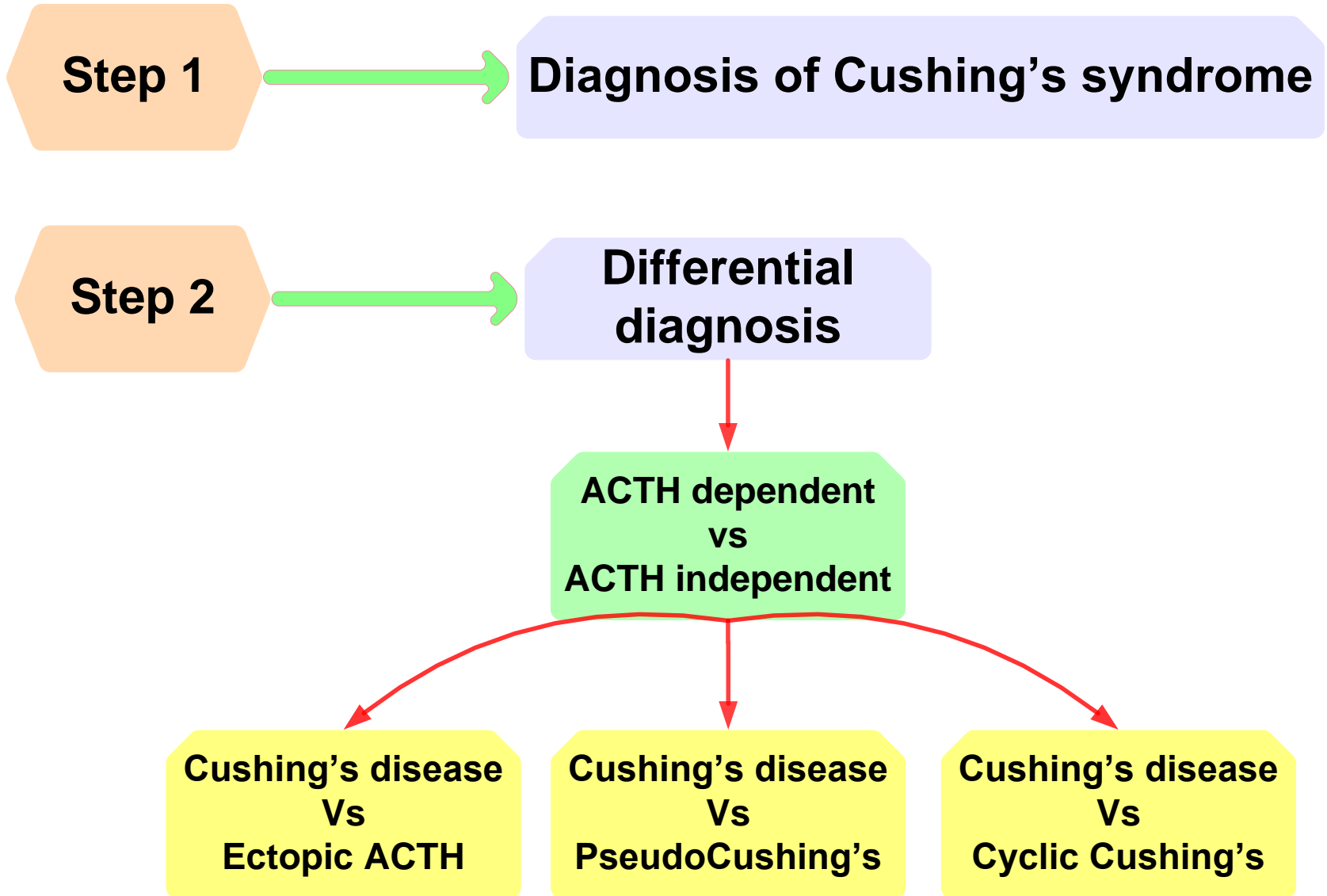
(Chief: Prof. Paolo Cappabianca)

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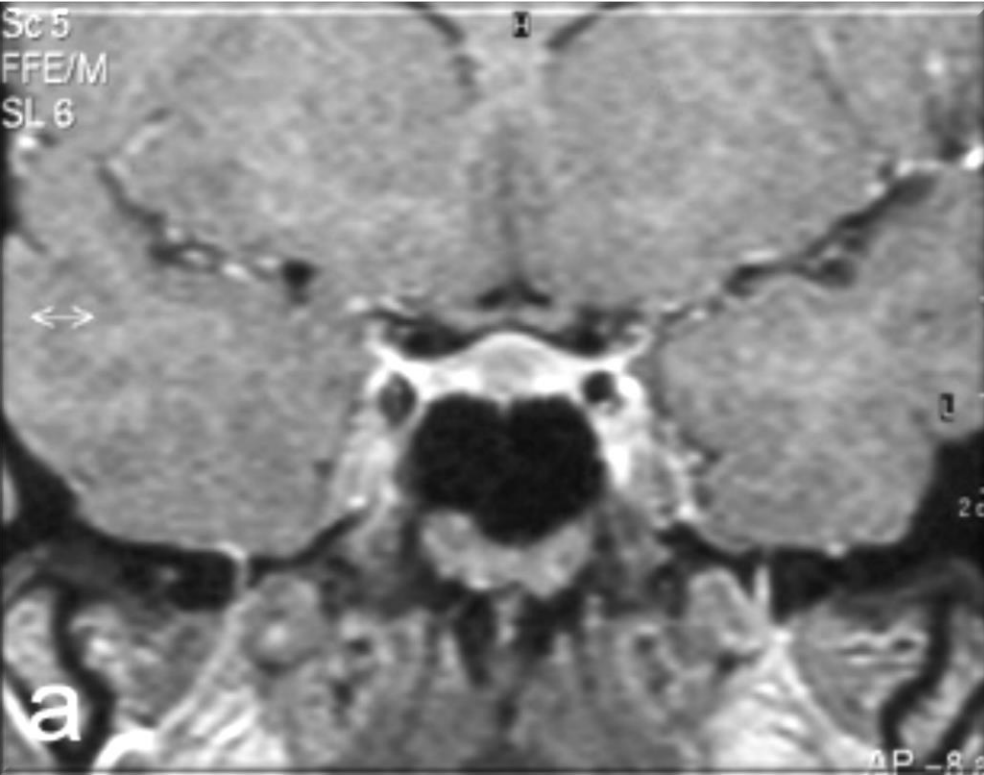
NAPLES, ITALY

Cushing's disease

Diagnosis



Sellar MRI



Microadenoma: 80%

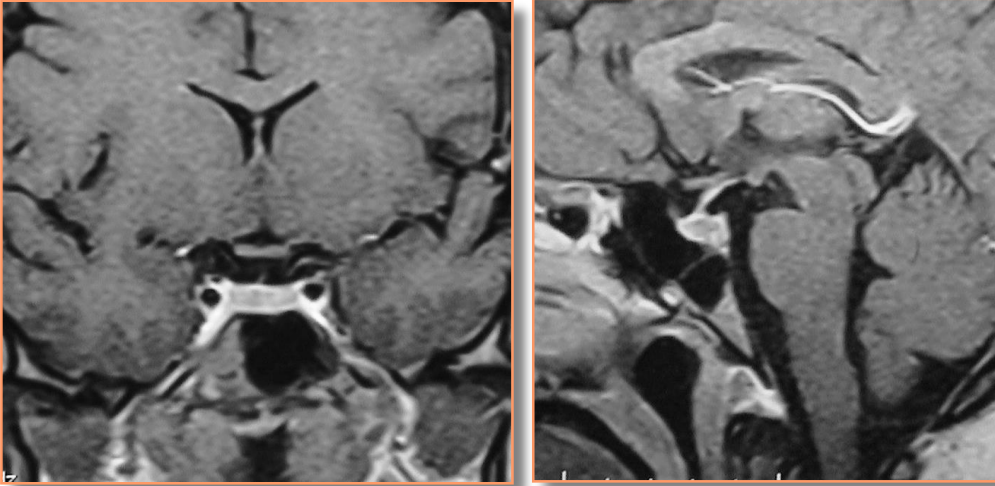
Macroadenoma: 10%

Hyperplasia: 10%

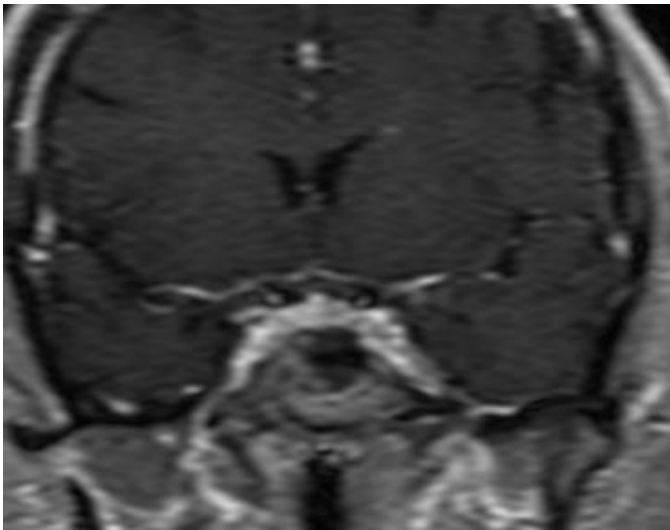
Sensitivity: 70%

Specificity: 87%

Sellar MRI



Conventional 1.5 T
MRI



Dynamic contrast-enhanced
T₁ SPGR [multi-phase spoiled gradient
recalled echo] MRI

Inferior Petrosal Sinus Sampling

Petrosal sinus sampling can yield 2 different types of evidence:

1) it can differentiate between pituitary and ectopic tumoral ACTH secretion (Endocrinologist)

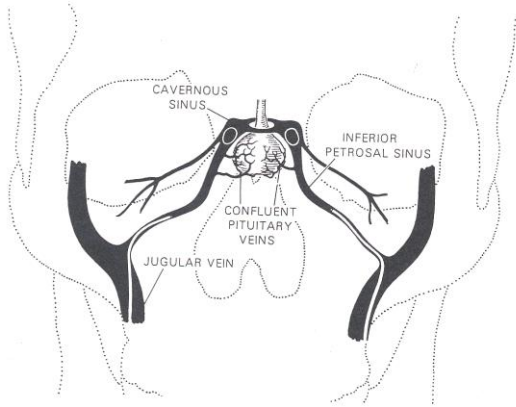
2) it can provide clues as to the site of a patient's pituitary adenoma (i.e., midline or right or left of midline). (Neurosurgeon)

The role of inferior petrosal sinus sampling in ACTH-dependent Cushing's syndrome: review and joint opinion statement by members of the Italian Society for Endocrinology, Italian Society for Neurosurgery, and Italian Society for Neuroradiology

Francesca Pecori Giraldi, MD,^{1,2} Luigi Maria Cavallo, MD, PhD,³ Fabio Tortora, MD, PhD,⁴ Rosario Pivonello, MD, PhD,⁶ Annamaria Colao, MD, PhD,⁶ Paolo Cappabianca, MD,³ and Franco Mantero, MD, PhD,⁵ on behalf of the Altogether to Beat Cushing's Syndrome Group

Inferior Petrosal Sinus Sampling

Criterion for diagnosis of Cushing's disease



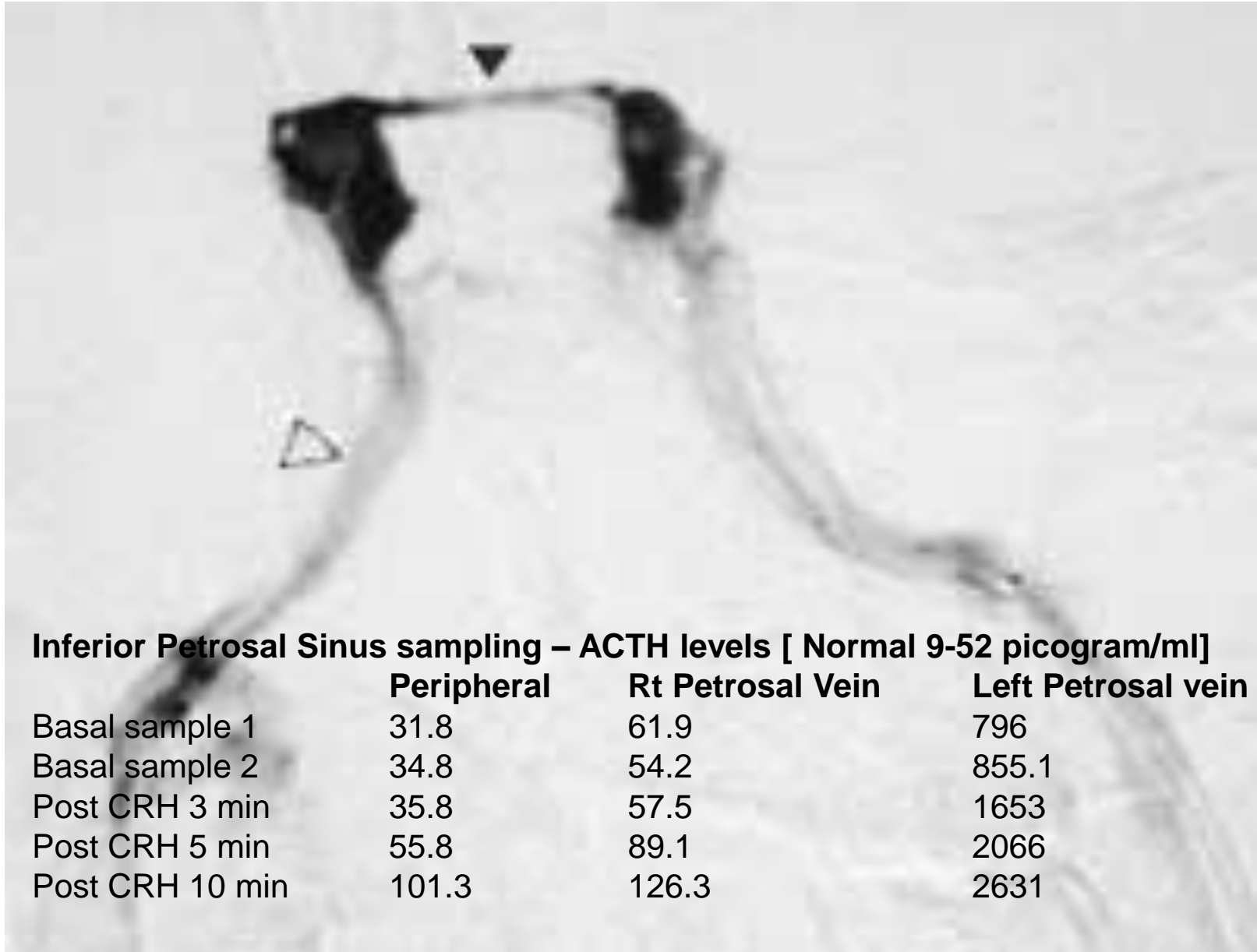
ACTH central/peripheral >2.0 in baseline
or central/peripheral >3.0 after CRH

Sensitivity: ~ 97%

Specificity: ~ 100%

Indications: when differential diagnosis is uncertain on the basis of biochemical tests and neuroimaging techniques.

Inferior Petrosal Sinus Sampling



Inferior Petrosal Sinus Sampling

Criterion for localization of pituitary tumor

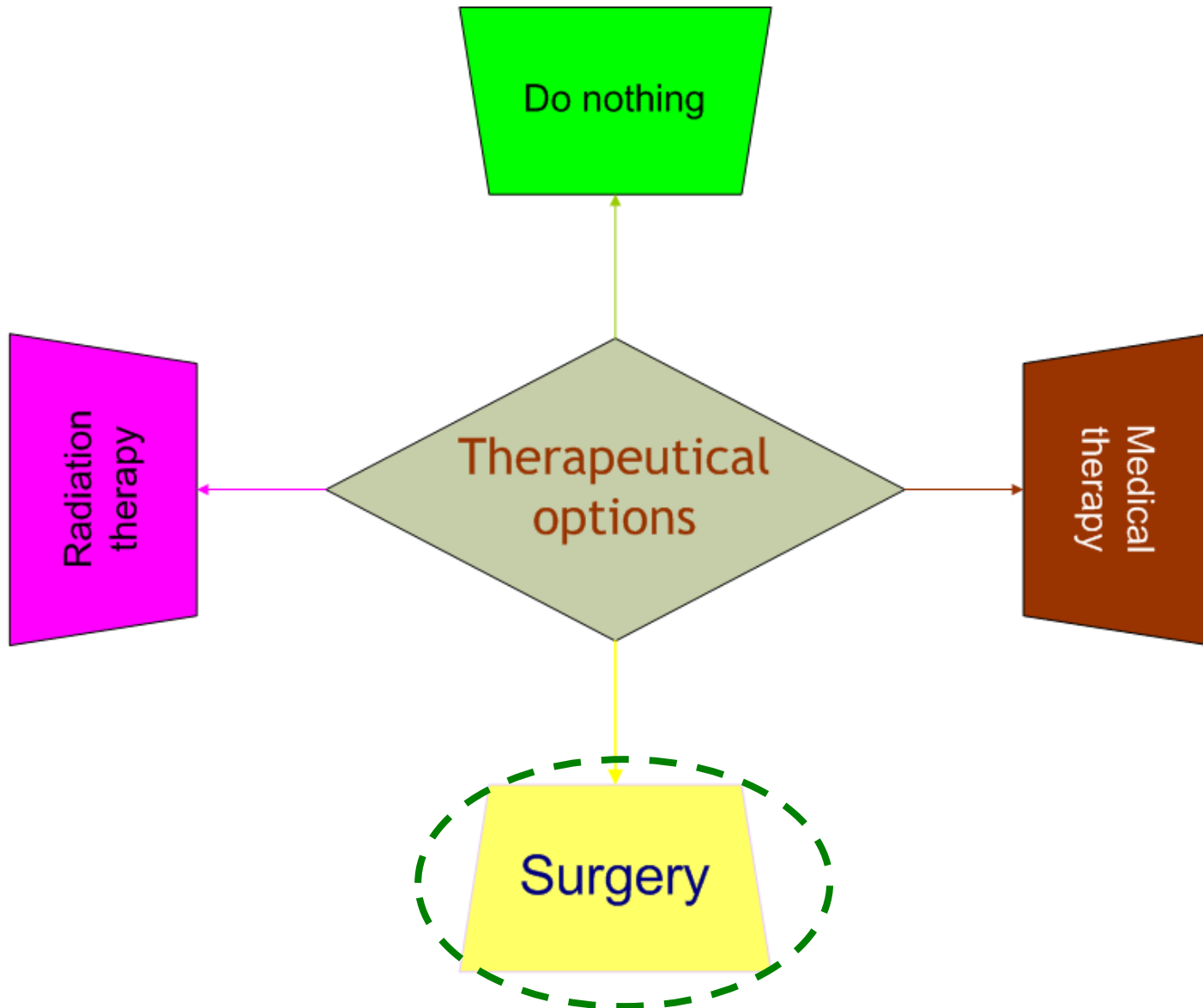
ACTH right/left ratio >1.4

Problems:

- ✘ Median tumors
- ✘ Multifocal tumors
- ✘ Pituitary hyperplasia

Sensitivity: ~ 50%

Management of cushing disease



NO single therapy is successful
in **controlling** the disease

Medical therapy

Adrenal-blocking Drugs

Ketoconazole

Etomidate

Trilostane

Aminogluthetimide

Mitotane

Metyrapone

Rosiglitazone

Neuromodulatory Drugs

Valproic acid

Cyproheptadine

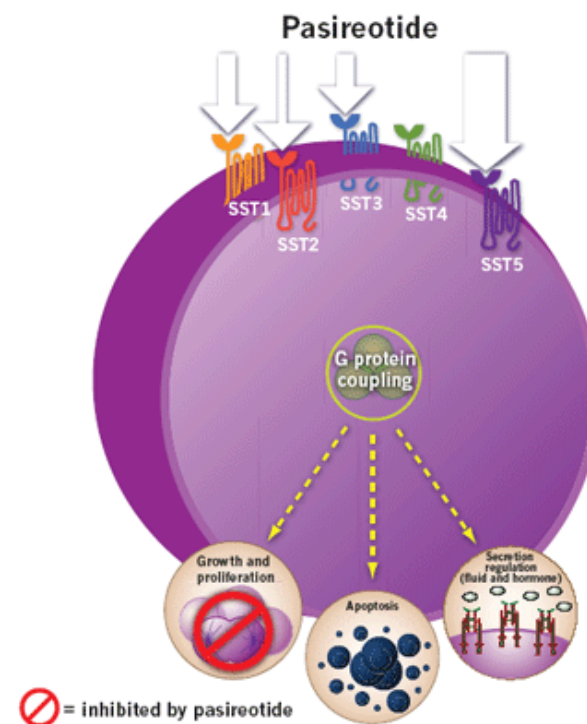
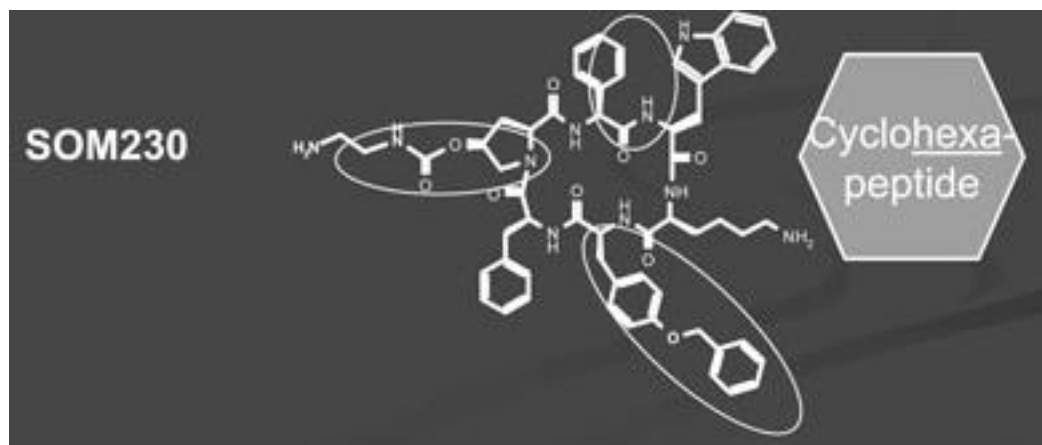
Octreotide

Bromocriptine

ORIGINAL ARTICLE

Pasireotide treatment significantly improves clinical signs and symptoms in patients with Cushing's disease: results from a Phase III study

Rosario Pivonello*, Stephan Petersen†, John Newell-Price‡, James W. Findling§, Feng Gu¶, Mario Maldonado**, Andrew Trovato**, Gareth Hughes††, Luiz R. Salgado‡‡, André Lacroix§§, Jochen Schopohl¶¶ and Beverly M.K. Biller*** on behalf of the Pasireotide B2305 Study Group¹



Radiotherapy / Radiosurgery

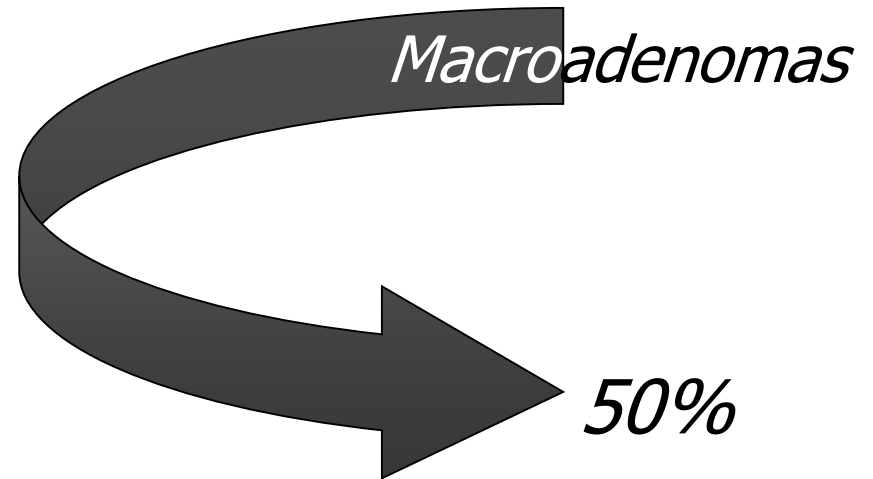
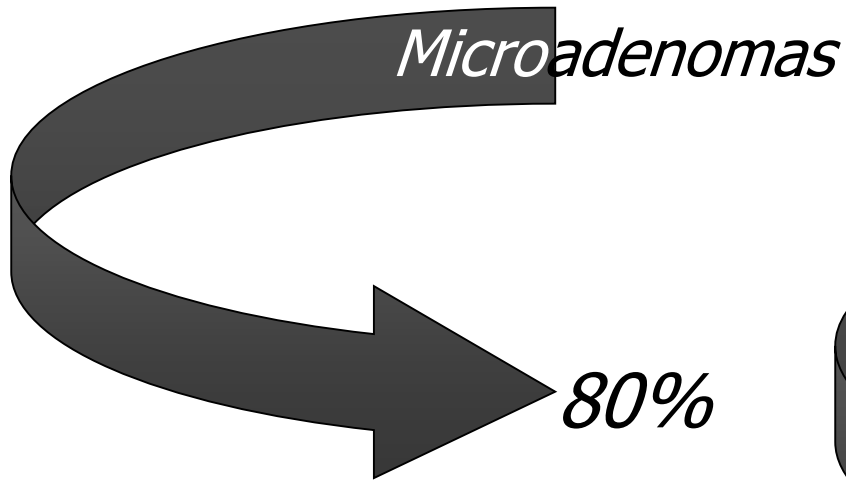
Indications

- ✘ Failure of Neurosurgery
- ✘ Nelson's syndrome

Complications and Problems

- ✘ Permanent hypopituitarism
- ✘ Long latency before the results

Neurosurgery



Complications

- ✘ Hypocortisolism
- ✘ Multiple hypopituitarism
- ✘ Diabetes insipidus

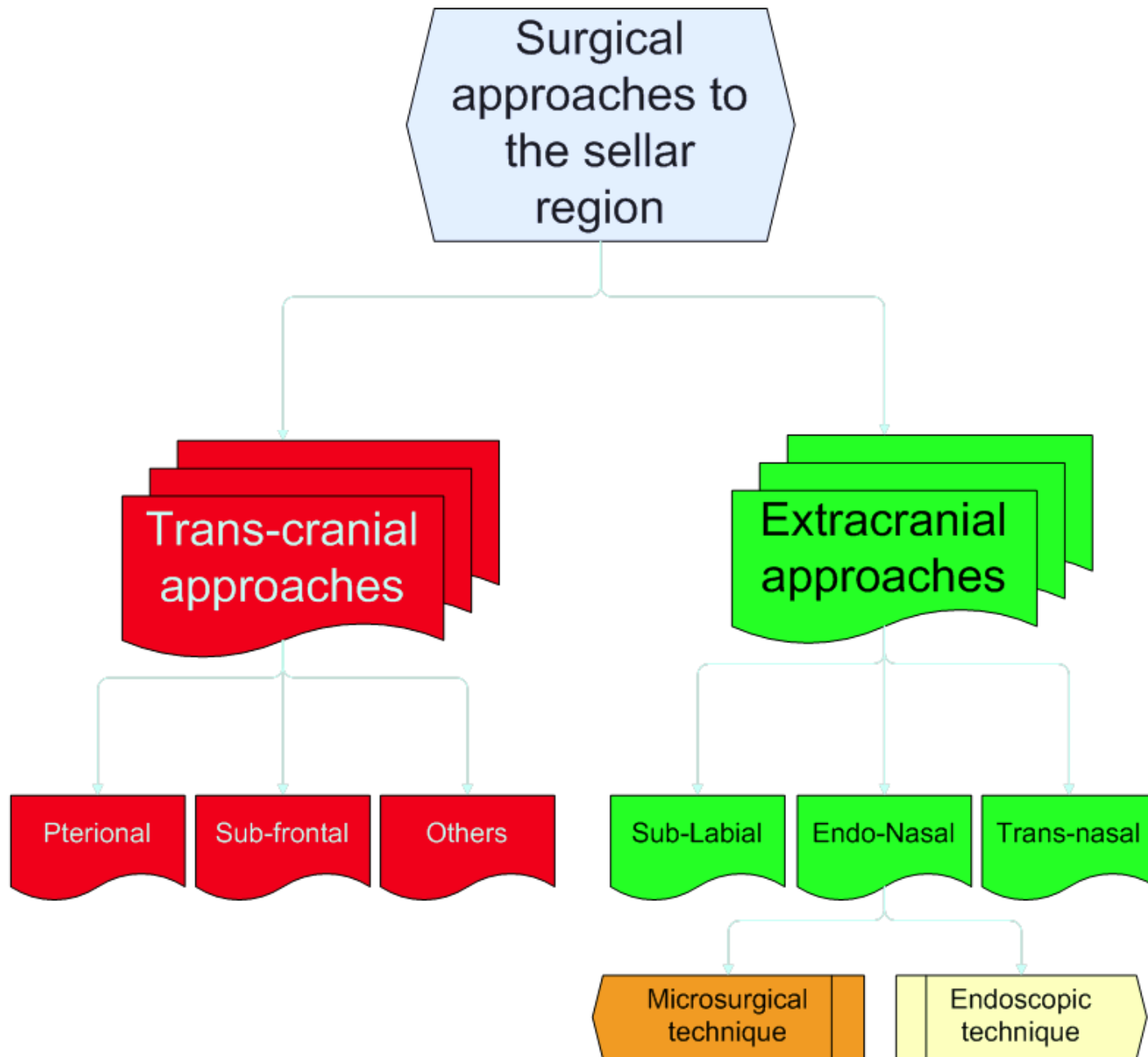
Problems

- ✘ No evidence of pituitary tumor
- ✘ Multifocal tumor
- ✘ Hyperplasia

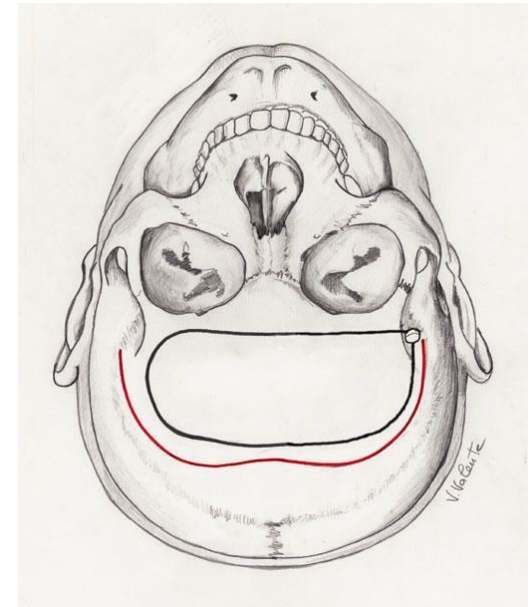
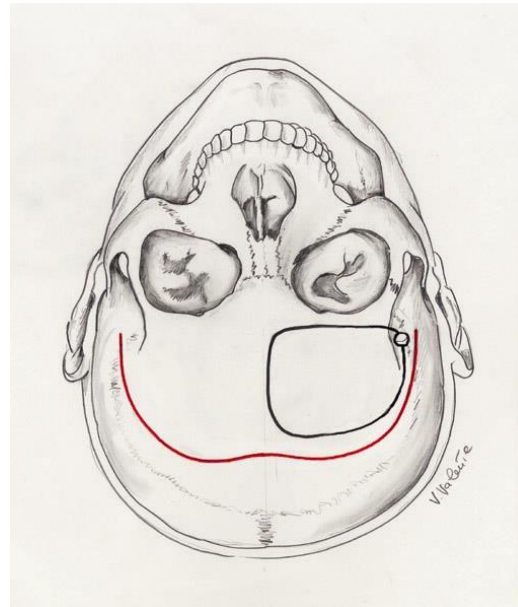
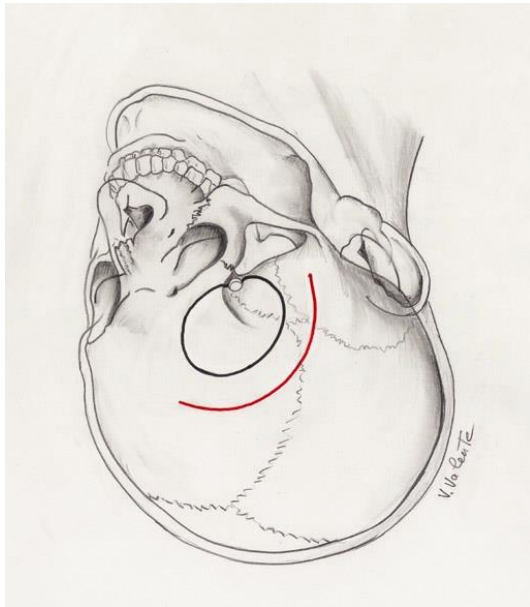
Neurosurgery

Principles

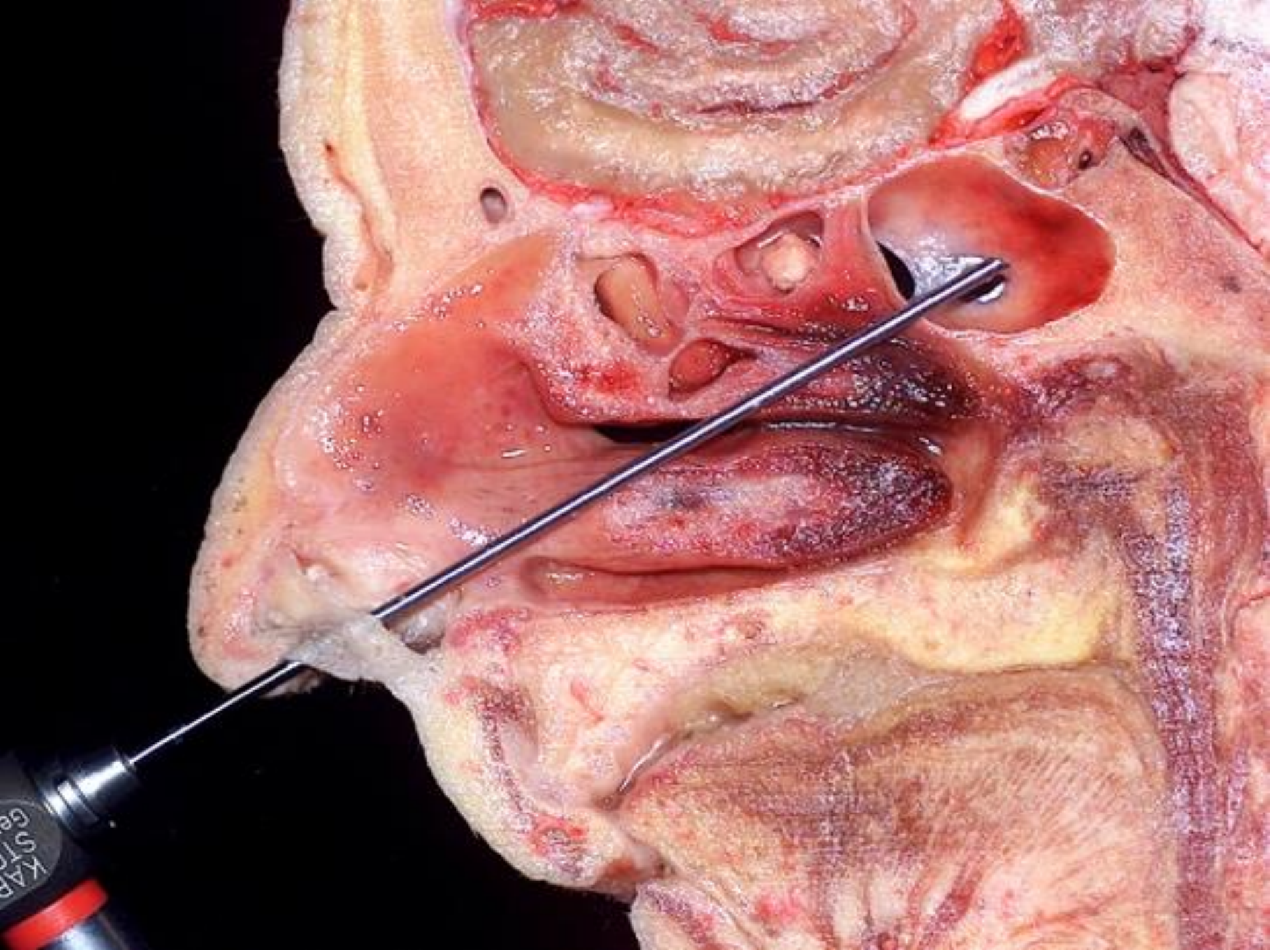
- ✓ *Relief of mass effect*
- ✓ *Normalization of hormonal hypersecretion*
- ✓ *Preservation/restoration of normal pituitary function*
- ✓ *Prevention of recurrence*
- ✓ *Sampling for tissue diagnosis and scientific study*



TRANSCRANIAL APPROACH

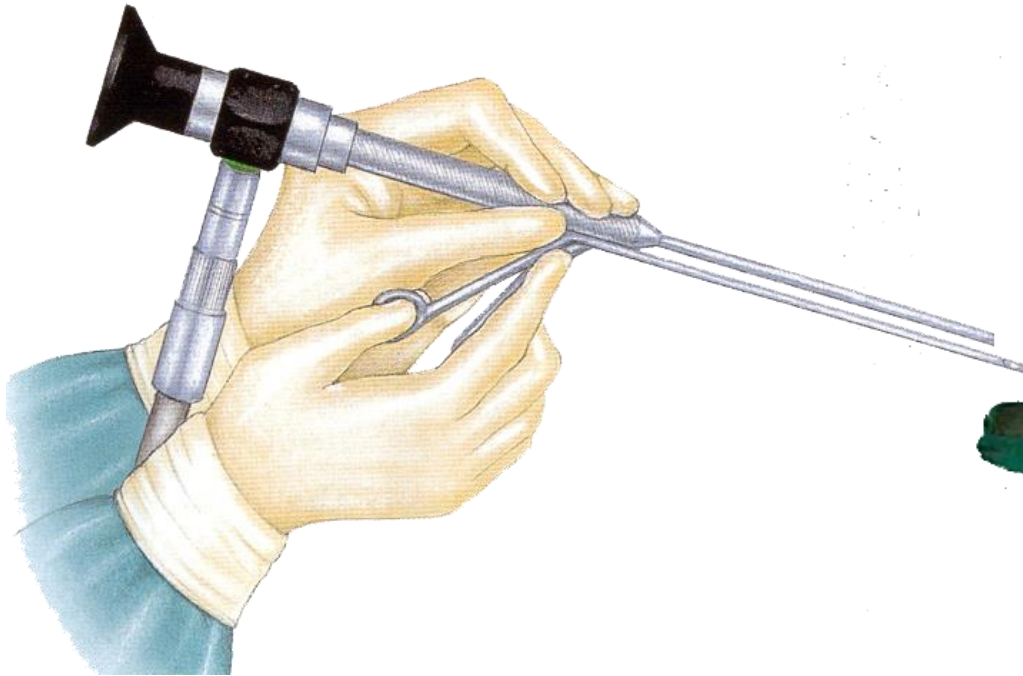


< 1% of cases



KAR
ST
Ge

Endoscopic endonasal surgery

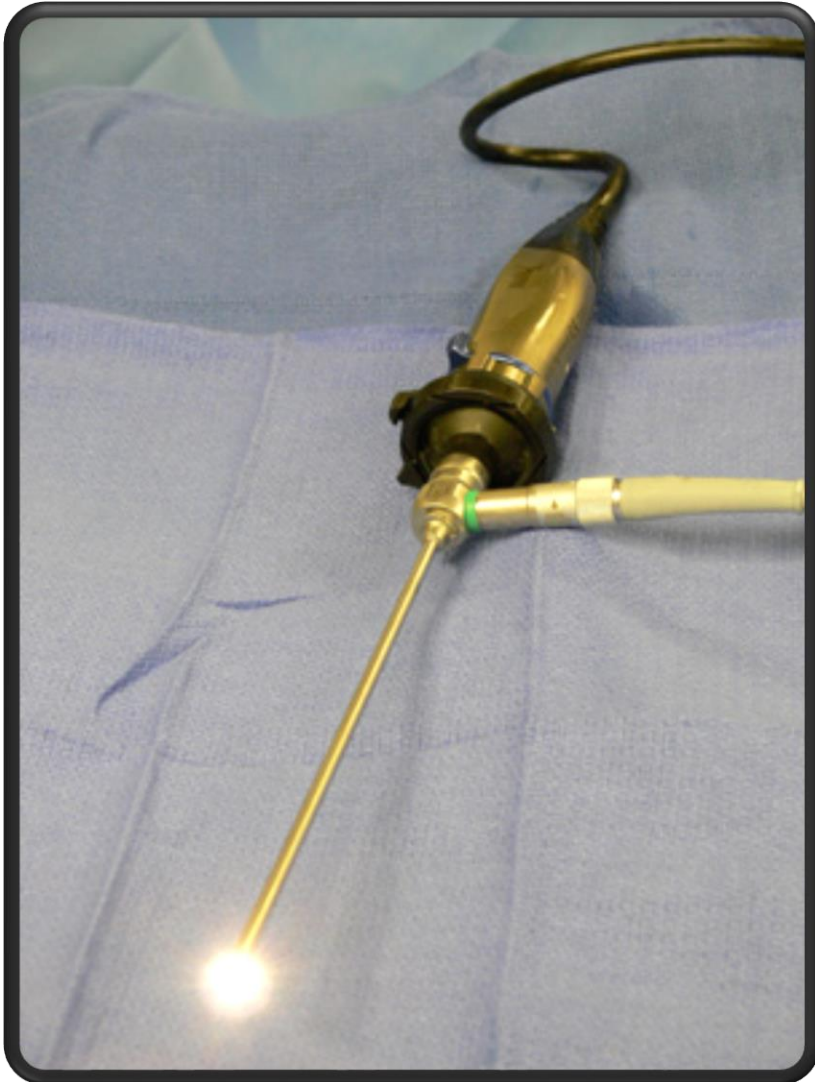


The endoscope is the sole visualizing tool



NO nasal speculum

Endoscopic endonasal surgery



- ✓ rigid endoscopes
- ✓ no working channel
- ✓ 18 cm in length

Microsurgical attitude



Standard endoscopic endonasal approach

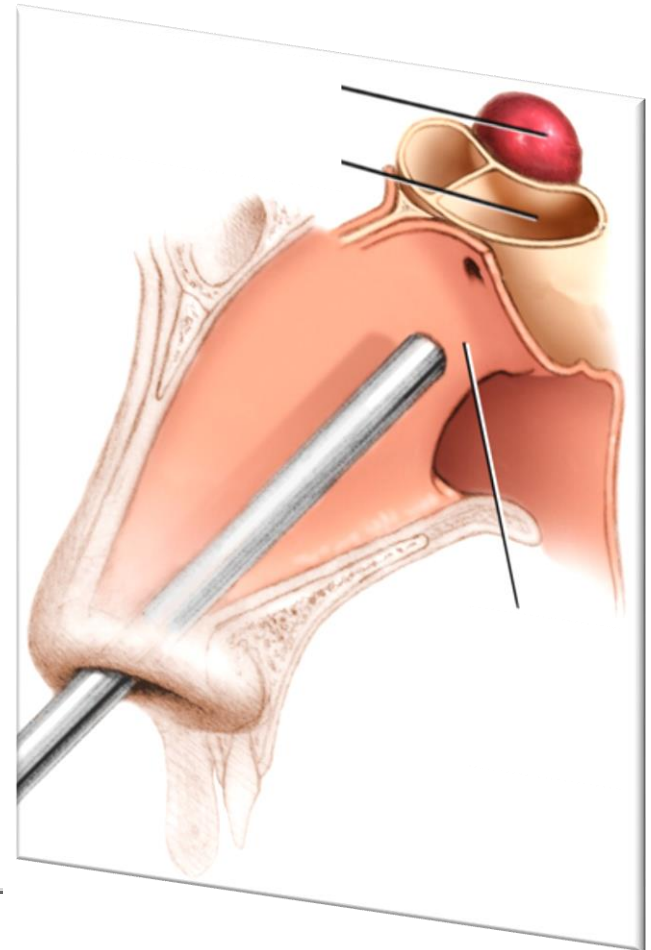
Basic concepts

*....three main aspects: exposure of the lesion,
removal of the relevant pathology and reconstruction
go through...
nasal, sphenoid and sellar step.*

Pituitary (2008) 11:385–390
DOI 10.1007/s11102-008-0087-5

Endoscopic pituitary surgery

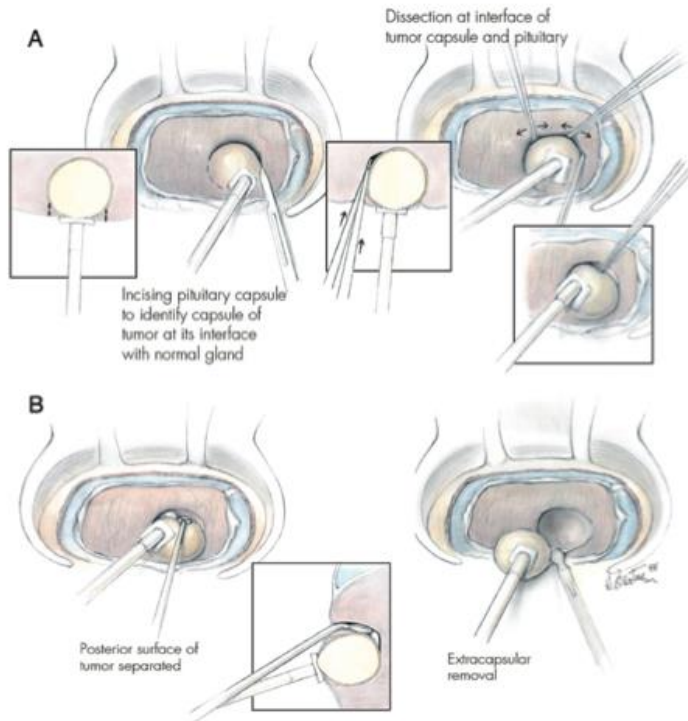
**Paolo Cappabianca · Luigi Maria Cavallo · Oreste de Divitiis ·
Domenico Solari · Felice Esposito · Annamaria Colao**



sellar steps

1. WIDE exposure of sellar floor
2. WIDE exposure of dura (four blues)
3. WIDE opening of dura and exposure of gland

Pseudocapsule concept

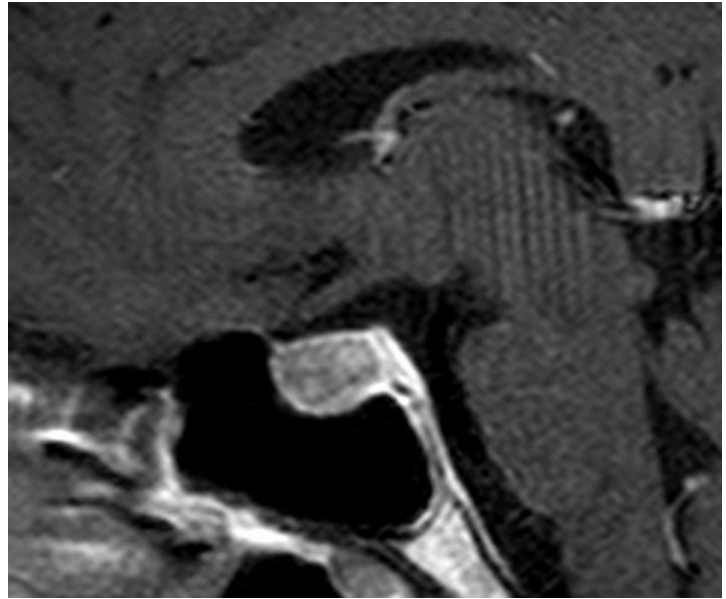
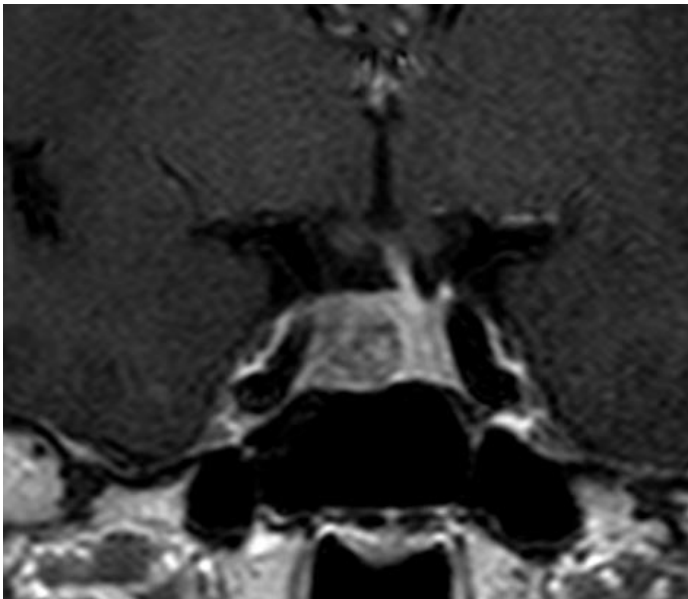


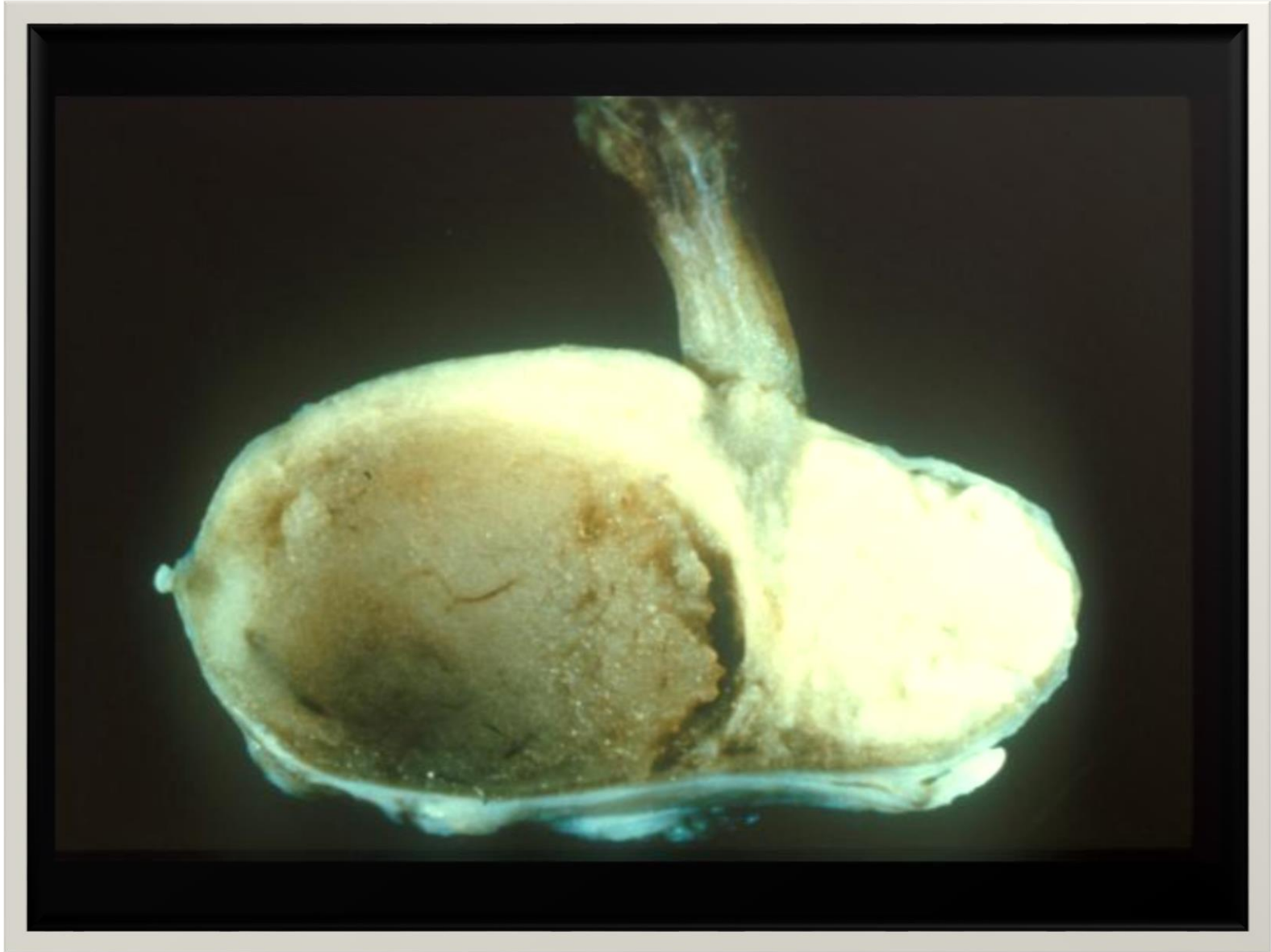
...all types of pituitary adenomas enlarge slowly and compress the surrounding tissue, producing a histological pseudocapsule that can be used as a surgical capsule.

...tumor tissue is frequently present within the pseudocapsule, suggesting that any tumor remnant in the pseudocapsule could be a source of recurrence and an obstacle to achieving complete remission.

Lee EJ et al.: Tumor tissue identification in the pseudocapsule of pituitary adenoma: should the pseudocapsule be removed for total resection of pituitary adenoma?. *Neurosurg*, 2008, Mar;64(3 Suppl):ons62-9; discussion ons69-70

Jagannathan J et al.: Outcome of using the histological pseudocapsule as a surgical capsule in Cushing disease. *J Neurosurg*, 2009, Sep;111(3):531-9



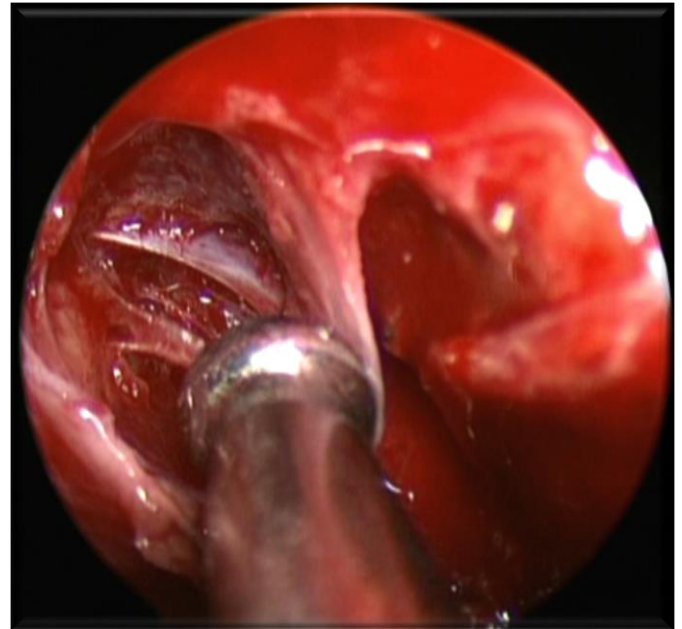
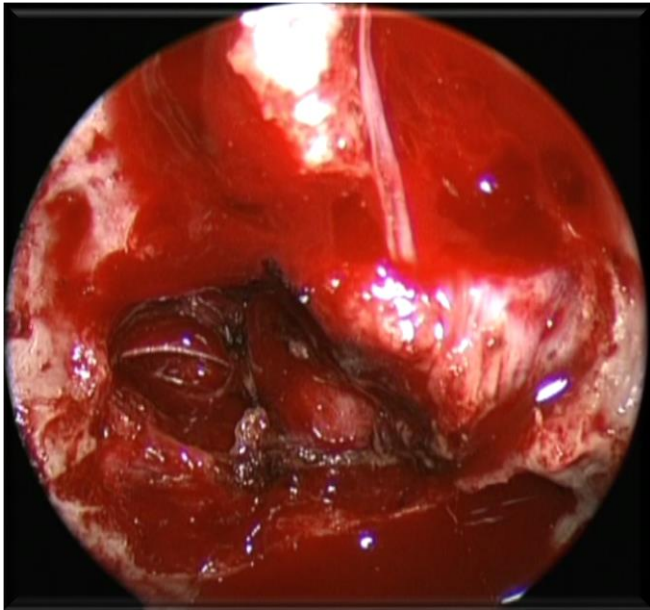
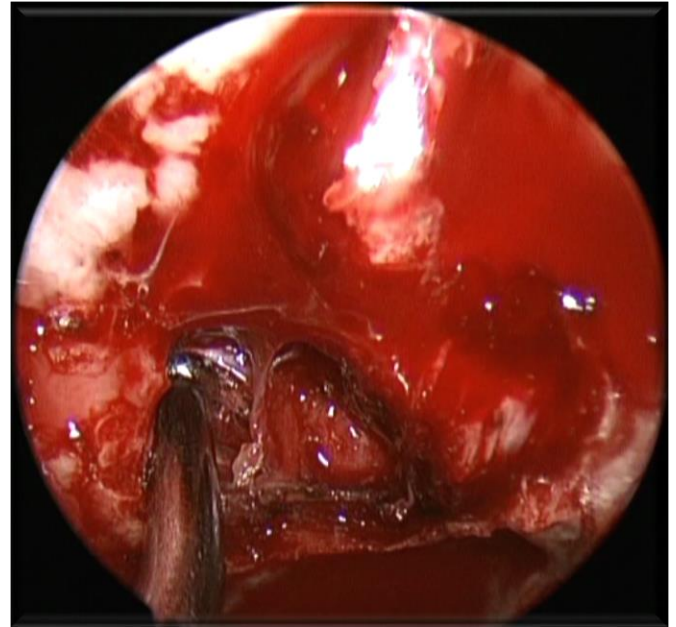
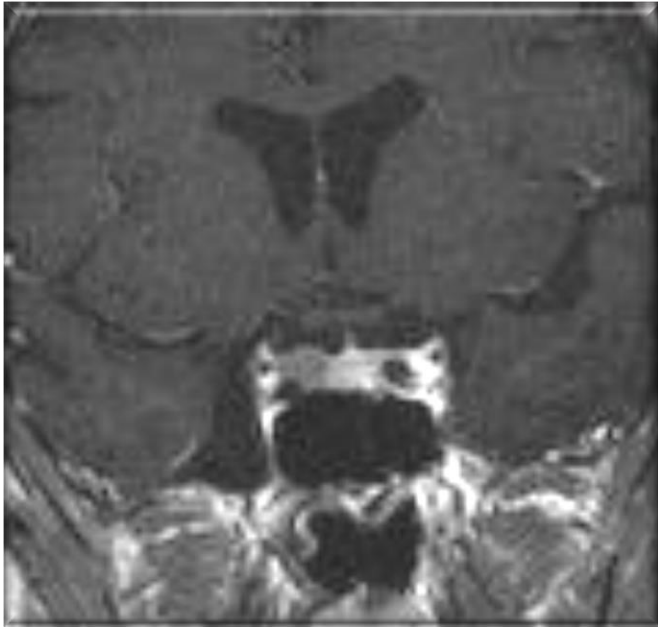




Endoscopic endonasal surgery

Advantages

- ✓ *wider and orientable view of the surgical field*
- ✓ *closer look “inside” the anatomy*
- ✓ *view in hidden corners with angled lenses*



ADVANTAGES FOR THE PATIENT

- ✓ *Less nasal traumatism*
- ✓ *No nasal packing*
- ✓ *Less post-op pain*
- ✓ *Decreased rate of complications*
- ✓ *Quick recovery*

ADVANTAGES FOR THE SURGEON

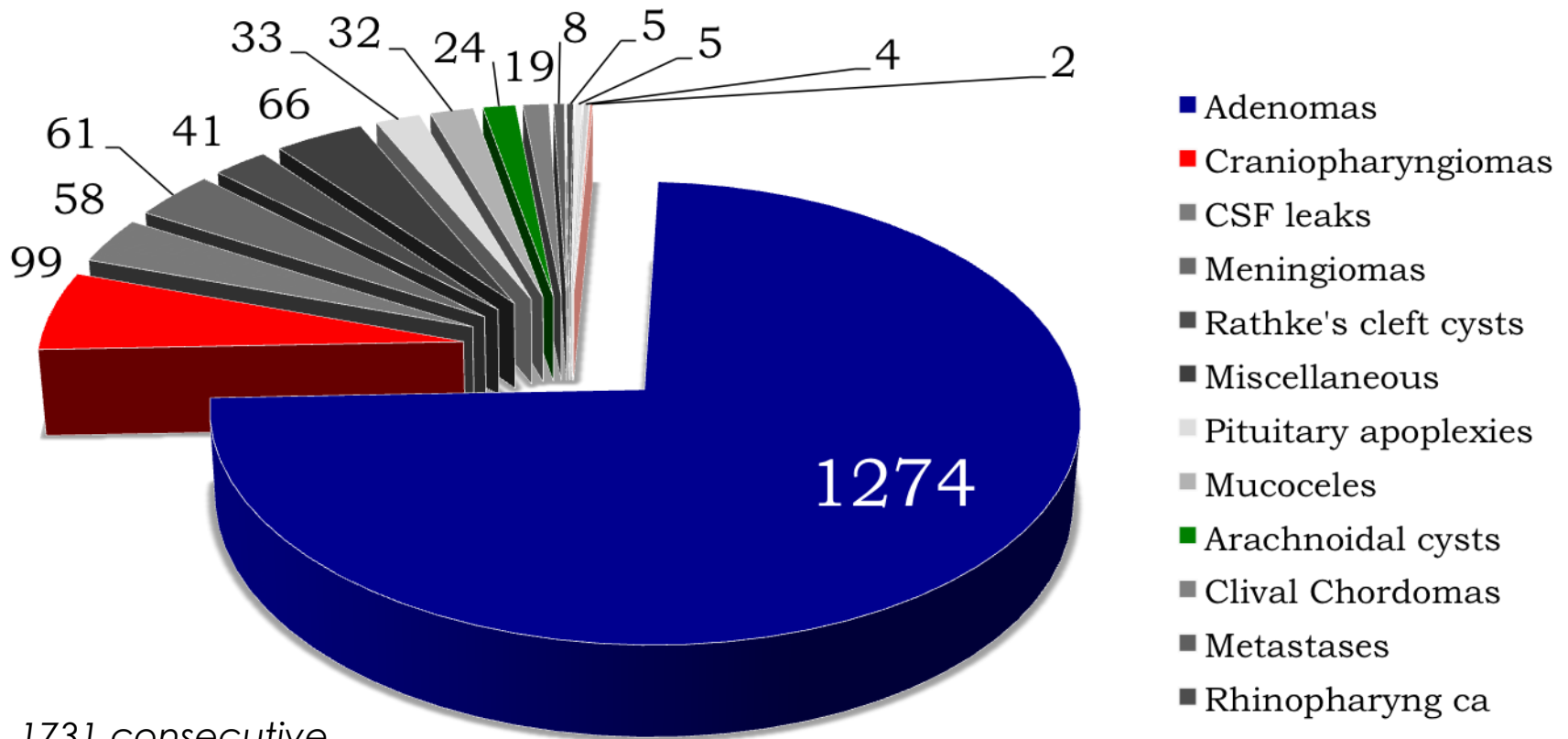
- ✓ *Wider and orientable view of the surgical field*
- ✓ *Closer look “inside” the anatomy*
- ✓ *Easier treatment of recurrences*
- ✓ *Increase of the scientific and research activity*
- ✓ *Promoted interdisciplinary co-operation*

ADVANTAGES FOR THE INSTITUTION

- ✓ *Shorter post-op hospital stay*
- ✓ *Earlier “back to work”*
- ✓ *Easier insurance reimbursement*
- ✓ *Increase of the case load*

Endoscopic Endonasal Skull Base Surgery

(1997-2017)



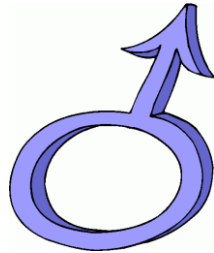
1731 consecutive
procedures
931 females
800 males
Mean age 47.6 yrs

UniNa experience

ACTH adenomas



106

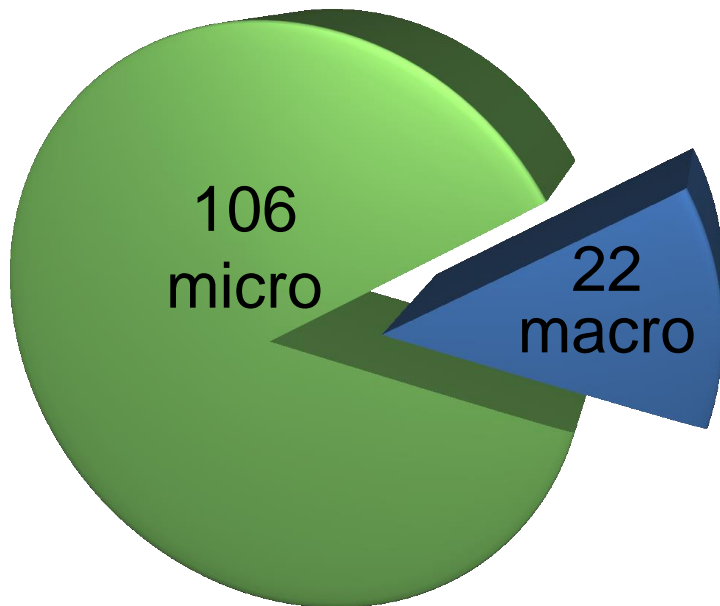


22

F:M = 5:1

Age: mean 41y

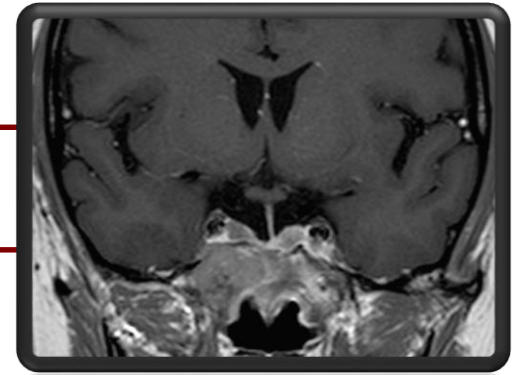
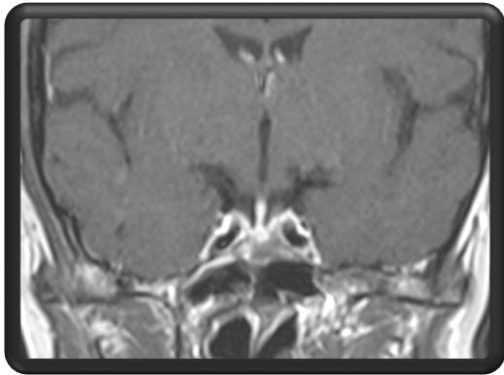
(19 ÷ 74)



128 patients

UniNa experience

ACTH adenomas

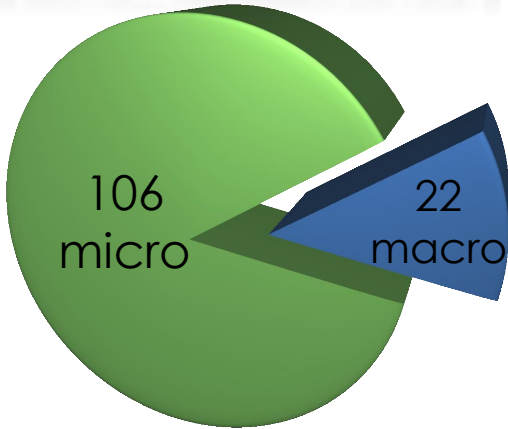


18 recurrences (14%)



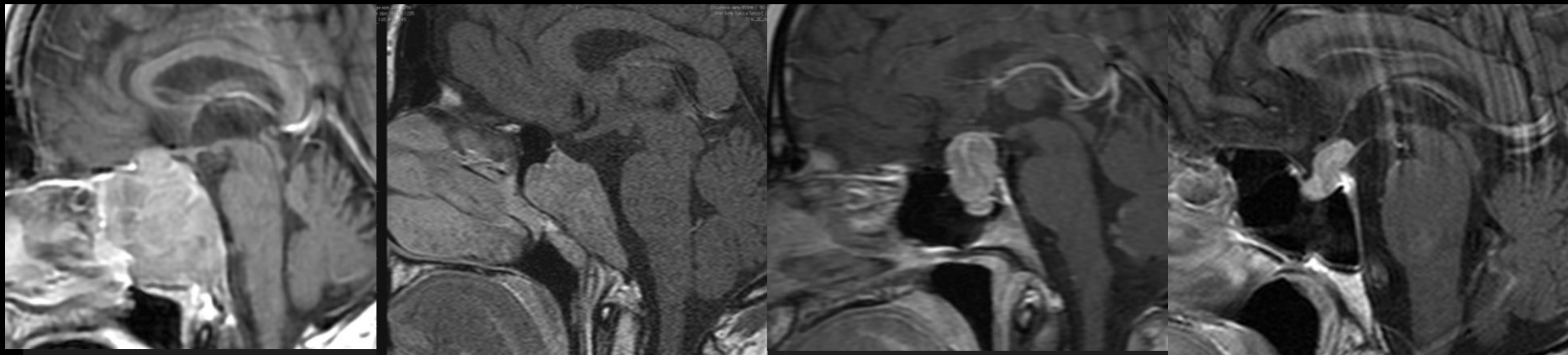
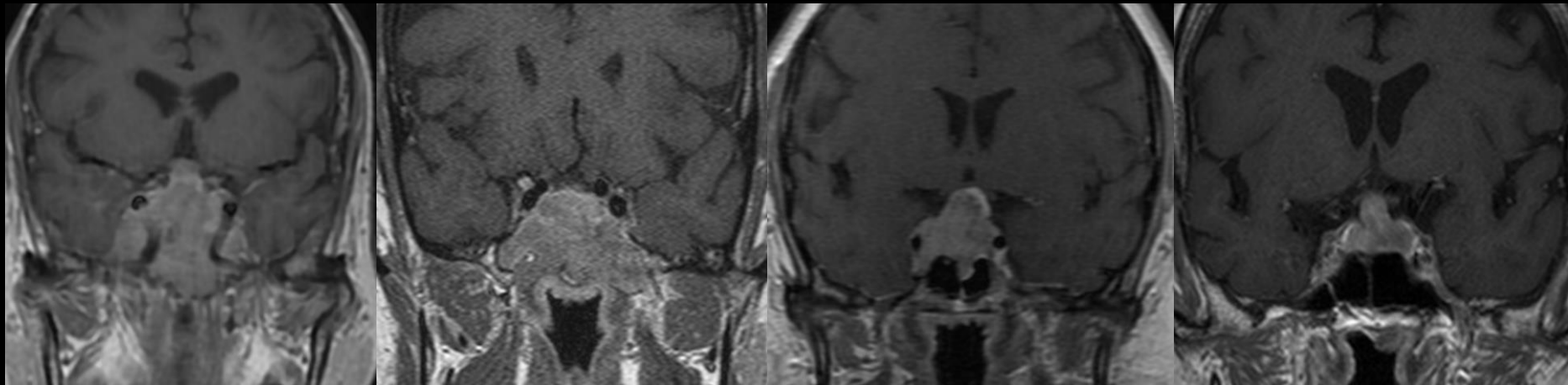
| | Micro | Macro |
|------------|------------|-----------|
| Recurrence | 15 (14,2%) | 3 (13,6%) |

| | | |
|--|--|--|
| | | |
|--|--|--|



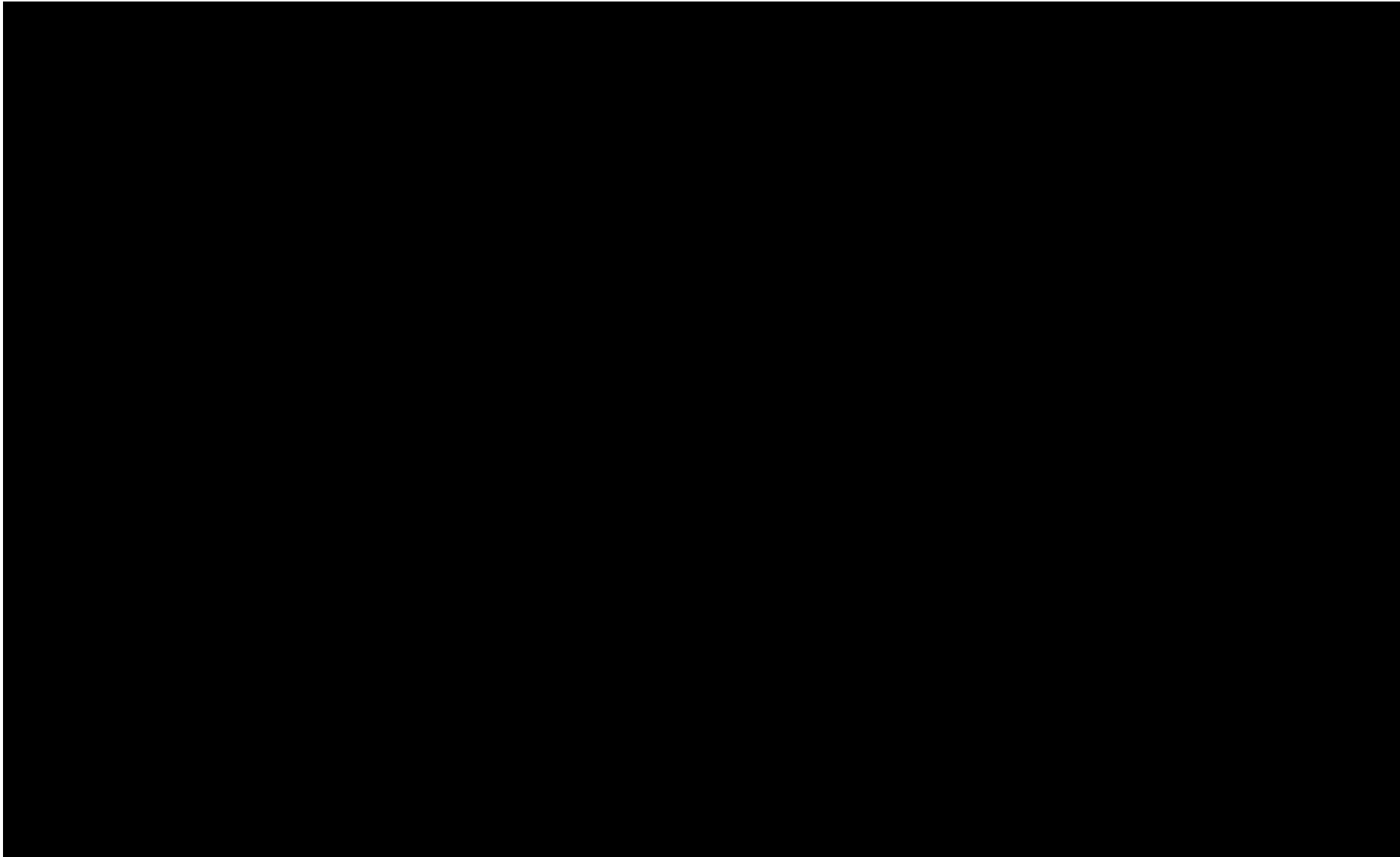
Further treatments

- ✓ *Re-operation: 14 pts*
- ✓ *Adrenalectomy: 6 pts*
- ✓ *Radiotherapy: 8 pts*
- ✓ *Radio-Chemotherapy: 1 pt*



Ki67: 5%

Ki67: 15%



Complications in Cushing Disease

- ✓ *Thromboembolism (3,1%)*
- ✓ *Epistaxis (1,5%)*
- ✓ *Diabetic ketoacidosis (0,8%)*
- ✓ *Respiratory Failure (0,8%)*
- ✓ *Meningitis (0,8%)*
- ✓ *Death (0,8%)*

Future perspectives

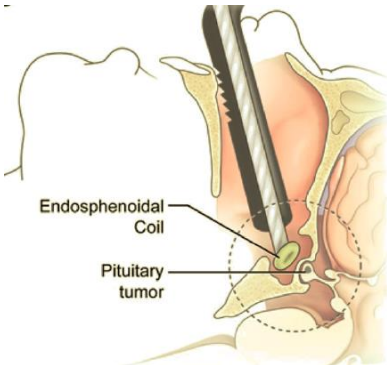
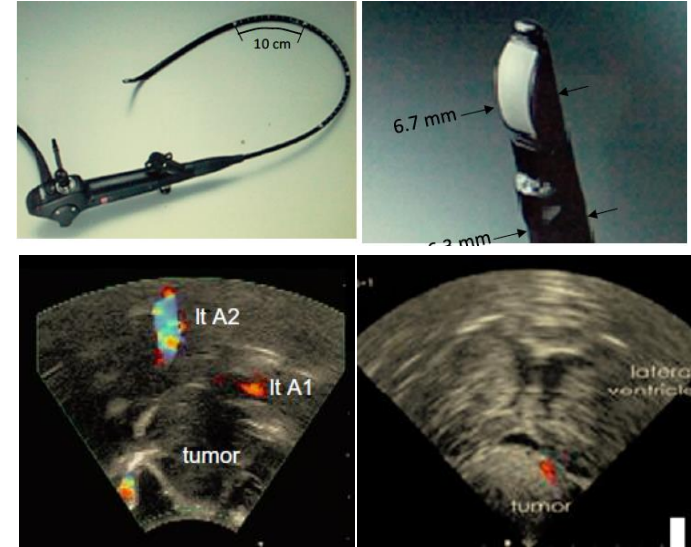
Acta Neurochir
DOI 10.1007/s00701-015-2382-z

23 February, 2015

CASE REPORT - BRAIN TUMORS

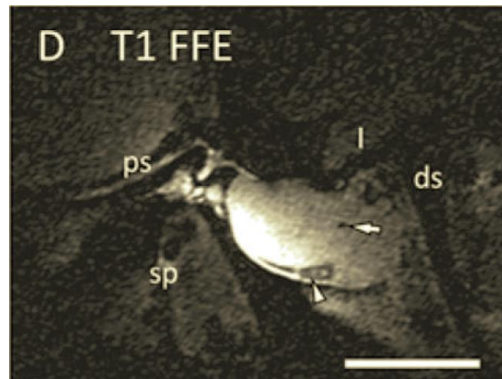
Endonasal ultrasonography-assisted neuroendoscopic transsphenoidal surgery

Mami Ishikawa • Yasushi Ota • Naohiro Yoshida •
Yukiko Iino • Yuichi Tanaka • Eiju Watanabe



JNS

LABORATORY INVESTIGATION
J Neurosurg 125:1451–1459, 2016



Endosphenoidal coil for intraoperative magnetic resonance imaging of the pituitary gland during transsphenoidal surgery

Prashant Chittiboina, MD, MPH,¹ S. Lalith Talagala, PhD,² Hellmut Merkle, PhD,³
Joelle E. Sarlls, PhD,² Blake K. Montgomery, BA,¹ Martin G. Piazza, MS,¹
Gretchen Scott, BSN, RN,¹ Abhik Ray-Chaudhury, MD,¹ Russell R. Lonser, MD,^{1,5}
Edward H. Oldfield, MD,^{1,6} Alan P. Koretsky, PhD,³ and John A. Butman, MD, PhD⁴



Expert team

- ✓ Specialized centres
- ✓ Team approach
 - ✓ surgery
 - ✓ endocrinology
 - ✓ Neuroradiology
 - ✓ Pathologist
 - ✓ Radiation oncology
 - ✓ etc.
- ✓ Surgeon
 - ✓ > 100 previous cases
 - ✓ > 25 cases/year (?)

Team approach



Made of **givers** rather than **takers**

We must move from the "I" to the "We" towards successful outcomes



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May 26, 2017

20 years of Endoscopic Endonasal Surgery History, ideas and friends on the gulf of Naples

HAVE THE DATE!



Organizing secretariat
MCM Eventi e Congressi
Dr. Stefania Acanfora
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PUT ITALY ON THE MAP PUT NAPLES ON THE MAP

AUSPICES

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THE ORGANIZERS GRATEFULLY
ACKNOWLEDGE THE SUPPORT OF



Baxter INTEGRA



Medtronic **STORZ**
KARL STORZ ENDOSKOPY



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<http://www.mcmcongressi.it/eventi/>