

# THE IMAGING IN CUSHING'S DISEASE

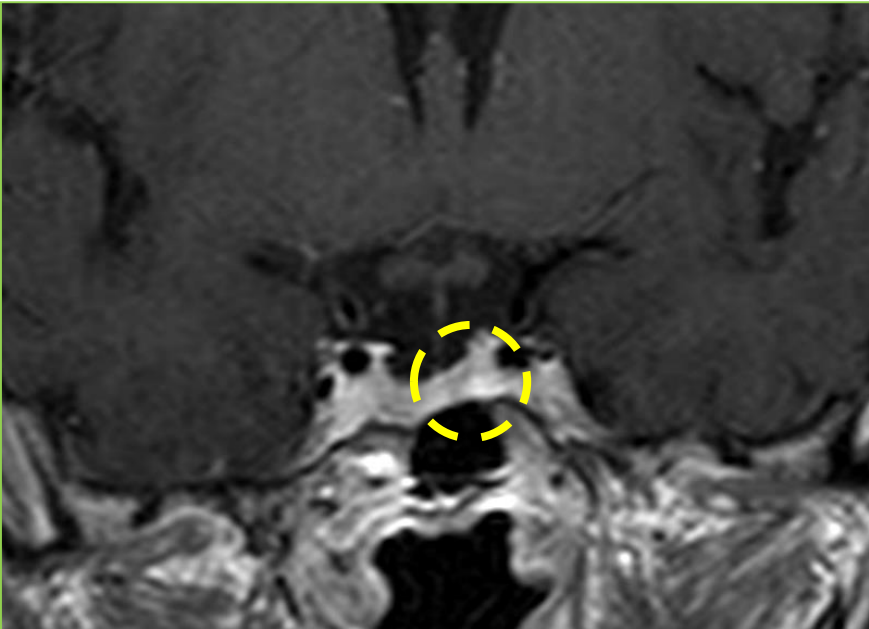
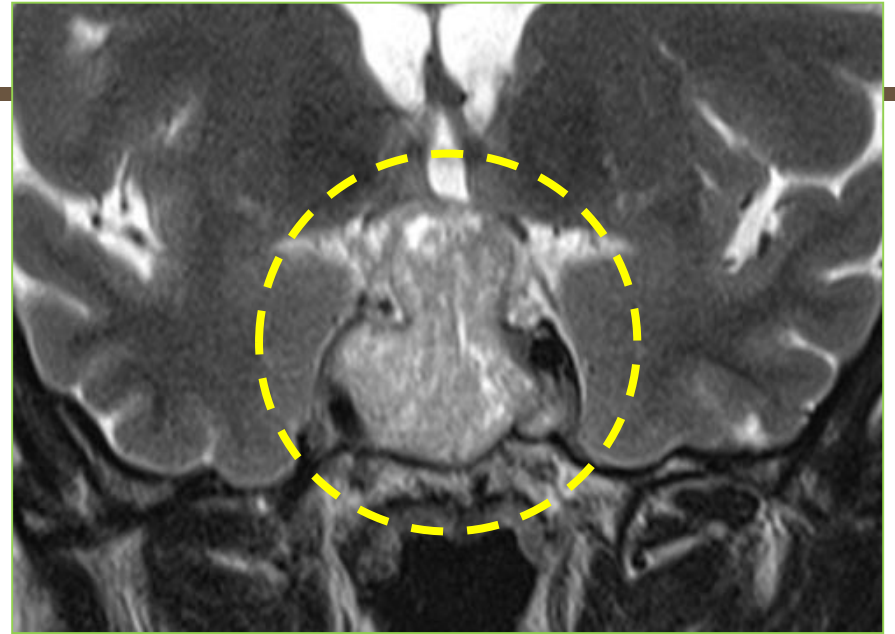
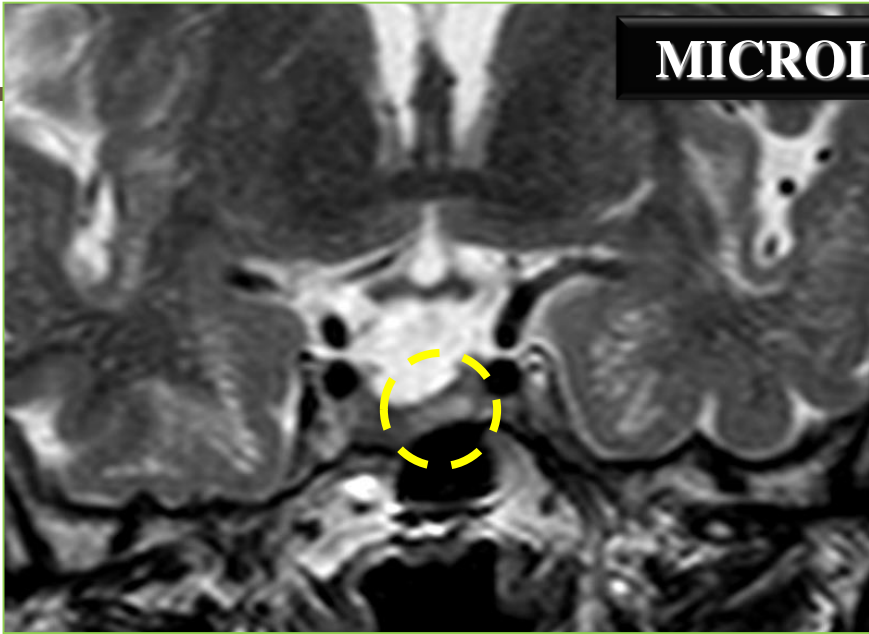
FABIO TORTORA

Dipartimento Medico-Chirurgico  
di Internistica Clinica e Sperimentale  
“ F. Magrassi e A. Lanzara “  
Cattedra di Neuroradiologia  
Seconda Università degli studi di Napoli

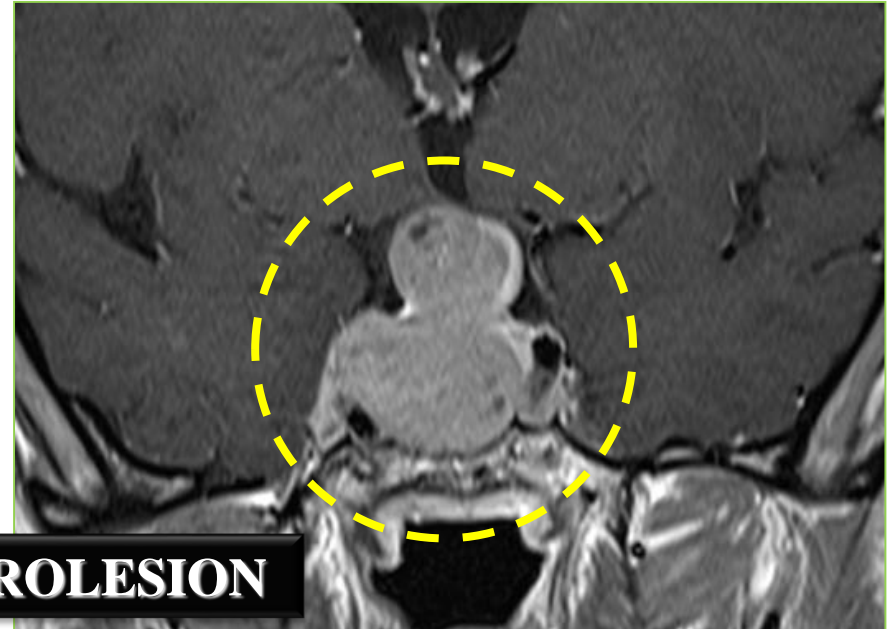


# NEURORADIOLOGICAL STUDY

**MICROLESION**



**MACROLESION**

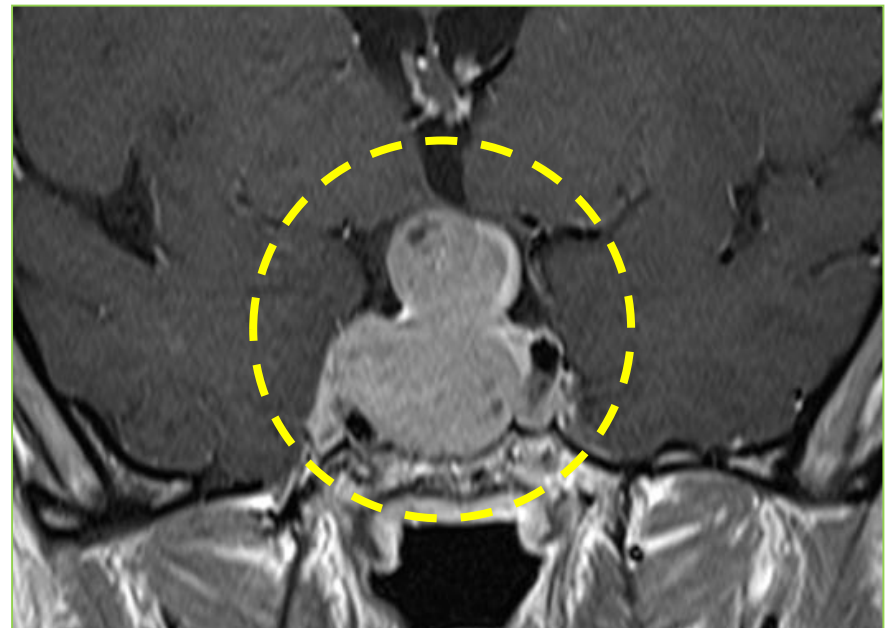
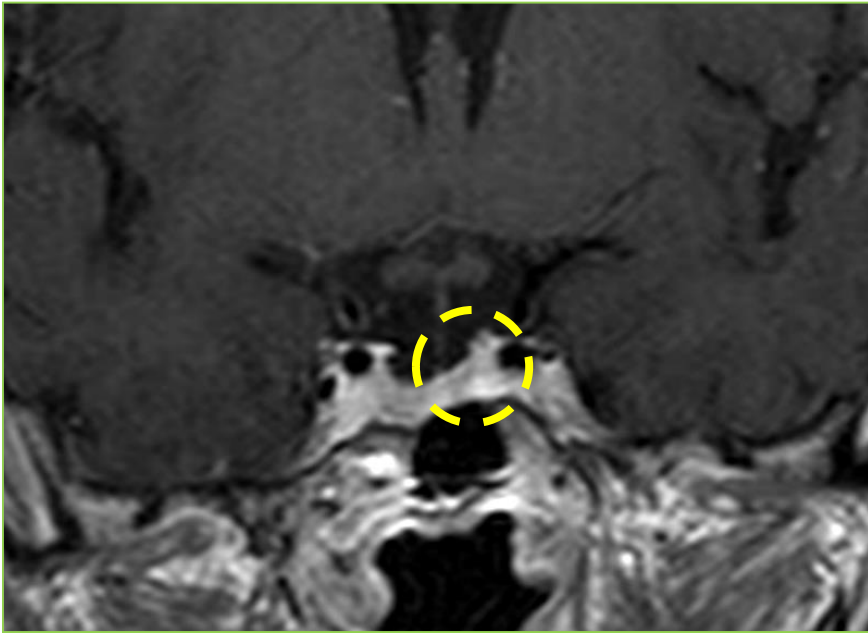


# NEURORADIOLOGICAL STUDY

## PITUITARY MICROADENOMA

- ◆ Thin layer (1-3 mm)
- ◆ Sagittal plane (cavernous region)
- ◆ Frontal plane (pituitary pedicle)
- ◆ Axial plane (sella floor)

- ◆ Thin layer (2-3 mm)
- ◆ Sagittal plane (lateral margins of the lesion)
- ◆ Frontal plane (anterior /posterior margin of the lesion)
- ◆ Axial plane (caudal and cranial margin of the lesion)



# NEURORADIOLOGICAL STUDY

## Cushing

◆ Thin layer (1-3 mm)

◆ Sagittal plane (cavernous region)

◆ Frontal plane (pituitary pedicle)

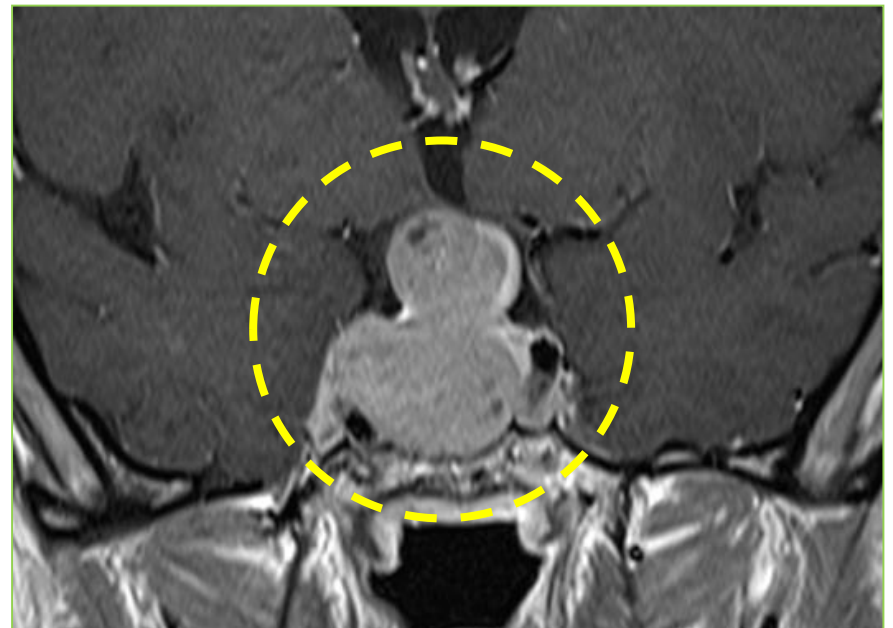
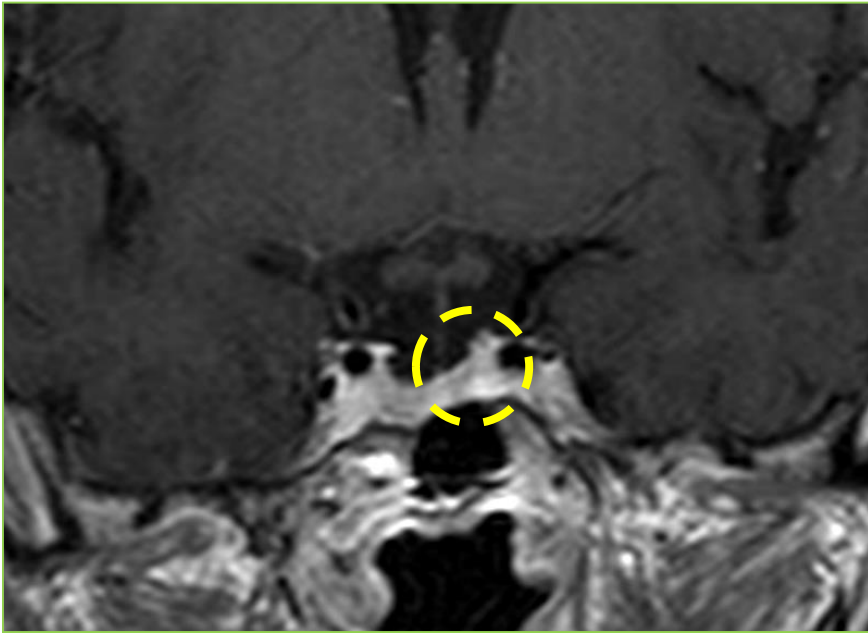
◆ Axial plane (sella floor)

◆ Thin layer (2-3 mm)

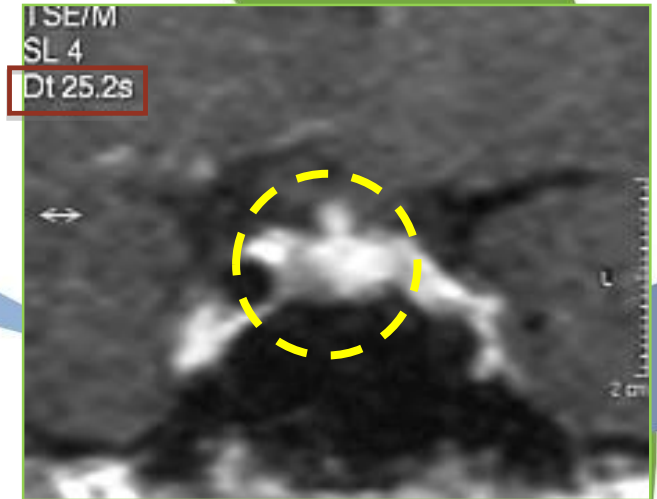
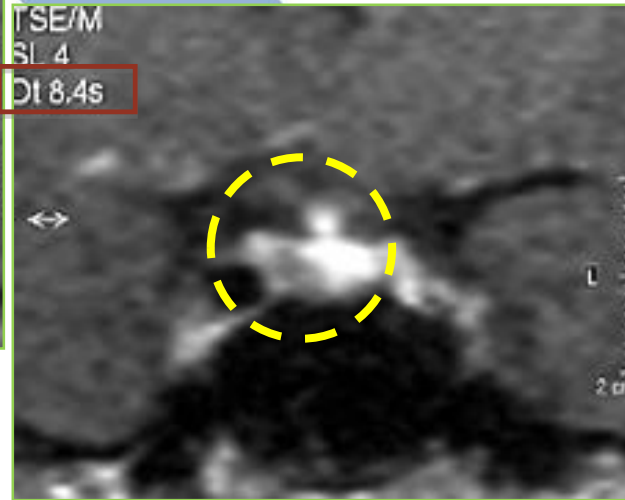
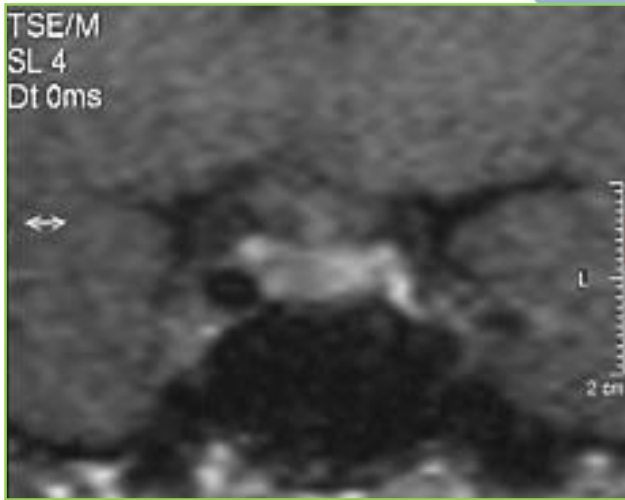
◆ Sagittal plane (lateral margins of the lesion)

◆ Frontal plane (anterior /posterior margin of the lesion)

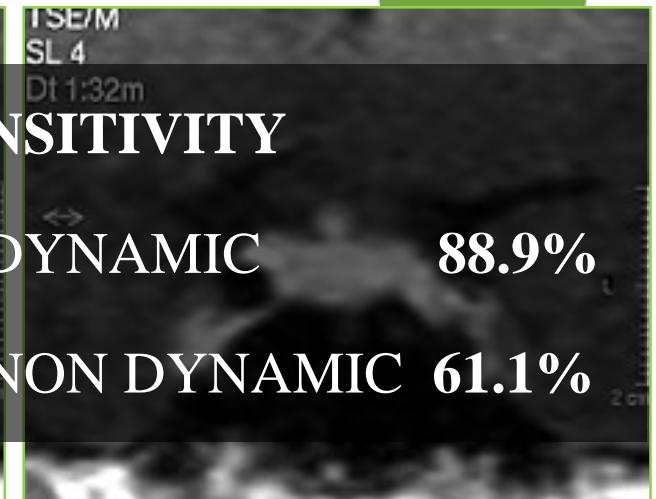
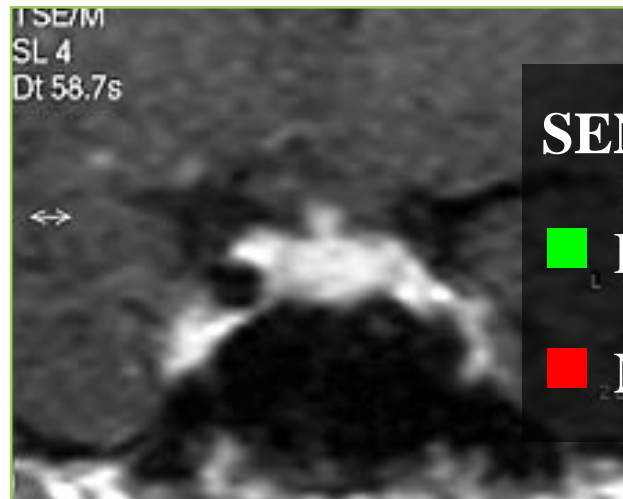
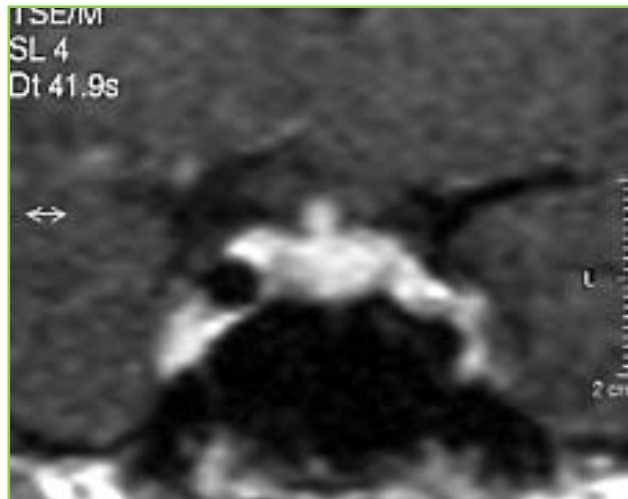
◆ Axial plane (caudal and cranial margin of the lesion)



# PITUITARY MICROADENOMA



**DYNAMIC MRI**



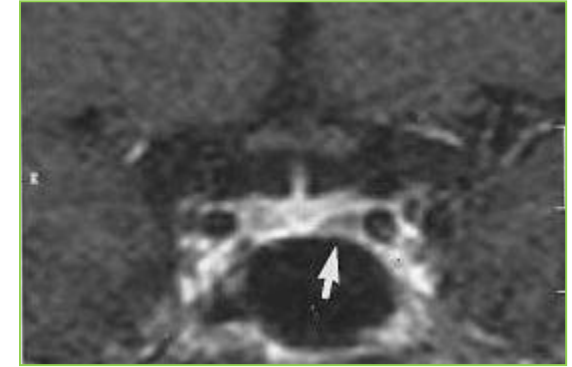
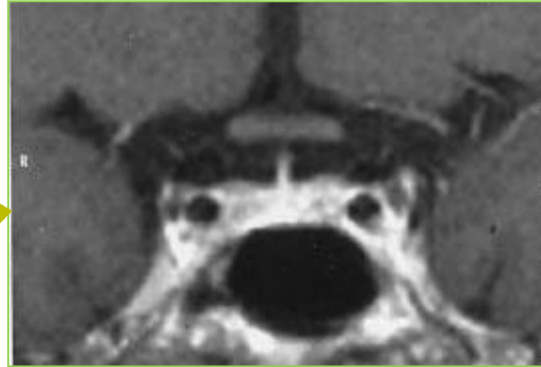
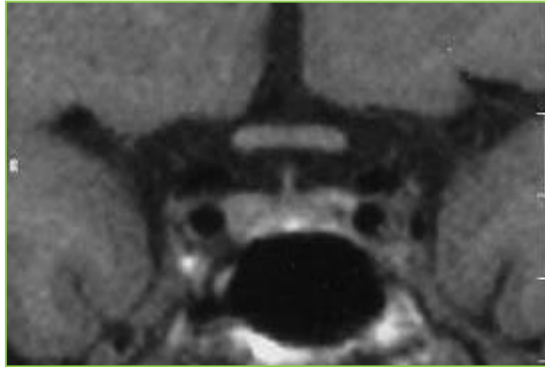
**SENSITIVITY**

 DYNAMIC	88.9%
 NON DYNAMIC	61.1%

Bartynski WS, et Al: *The effect of MR contrast medium dose on pituitary gland enhancement, microlesion enhancement and pituitary gland-to-lesion contrast conspicuity.* **Neuroradiology** 48 449-459, 2006.

# PITUITARY MICROADENOMA

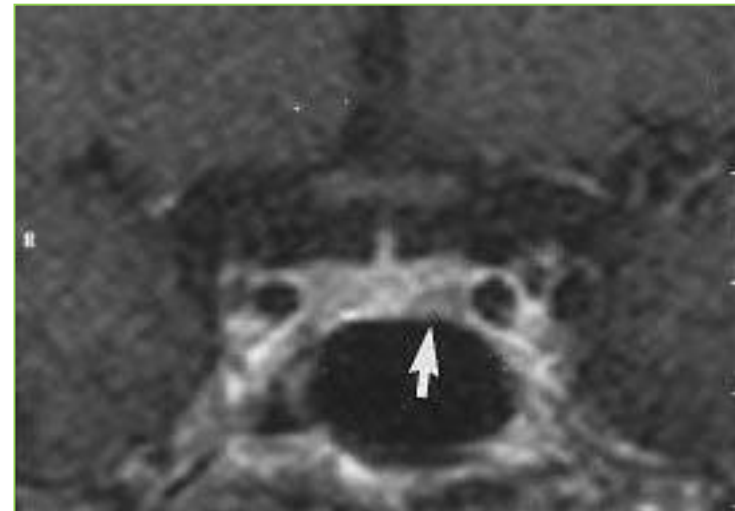
## CUSHING DISEASE



## SENSITIVITY

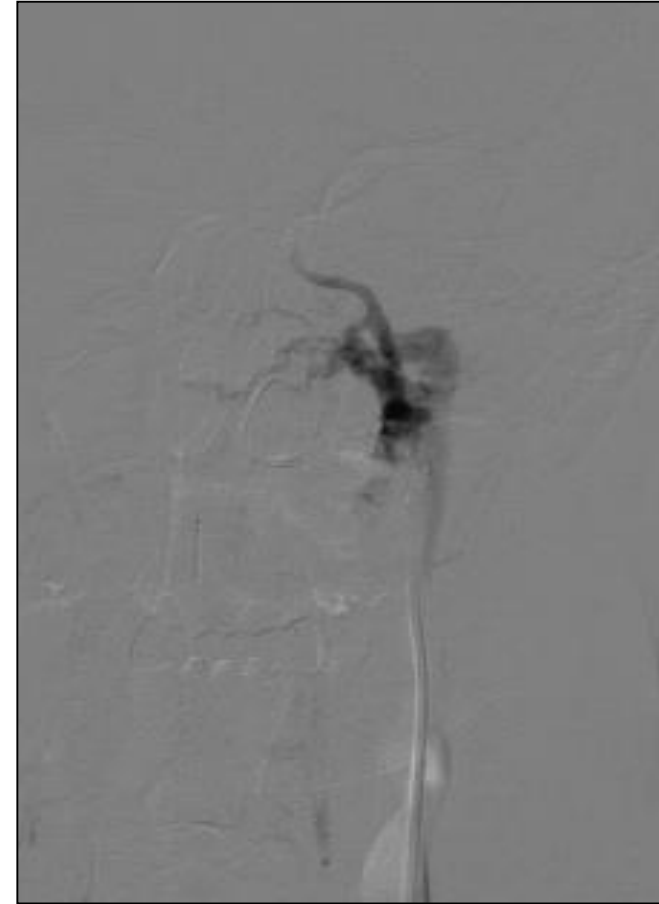
◆ DYNAMIC 67%

◆ NON DYNAMIC 52%



Tabarin A, et Al: Comparative evaluation of conventional and dynamic magnetic resonance imaging of the pituitary gland for the diagnosis of Cushing's disease. Clin Endocrinol (Oxf). 1998 Sep;49(3):293-300.

# PITUITARY MICROADENOMA



# CUSHING DISEASE

Journal of Neurosurgery 2015 Apr;122(4):791-7.

## High-resolution<sup>18</sup>F-fluorodeoxyglucose positron emission tomography and magnetic resonance imaging for pituitary adenoma detection in Cushing disease

**OBJECT** High-resolution PET (hrPET) performed using a high-resolution research tomograph is reported as having a resolution of 2 mm and could be used to detect corticotroph adenomas through uptake of (18)F-fluorodeoxyglucose ((18)F-FDG). To determine the sensitivity of this imaging modality, the authors compared (18)F-FDG hrPET and MRI detection of pituitary adenomas in Cushing disease (CD). **METHODS** Consecutive patients with CD who underwent preoperative (18)F-FDG hrPET and MRI (spin echo [SE] and spoiled gradient recalled [SPGR] sequences) were prospectively analyzed. Standardized uptake values (SUVs) were calculated from hrPET and were compared with MRI findings. Imaging findings were correlated to operative and histological findings. **RESULTS** Ten patients (7 females and 3 males) were included (mean age  $30.8 \pm 19.3$  years; range 11-59 years). MRI revealed a pituitary adenoma in 4 patients (40% of patients) on SE and 7 patients (70%) on SPGR sequences. (18)F-FDG hrPET demonstrated increased (18)F-FDG uptake consistent with an adenoma in 4 patients (40%; adenoma size range 3-14 mm). Maximum SUV was significantly higher for (18)F-FDG hrPET-positive tumors (difference = 5.1, 95% CI 2.1-8.1;  $p = 0.004$ ) than for (18)F-FDG hrPET-negative tumors. (18)F-FDG hrPET positivity was not associated with tumor volume ( $p = 0.2$ ) or dural invasion ( $p = 0.5$ ). Midnight and morning ACTH levels were associated with (18)F-FDG hrPET positivity ( $p = 0.01$  and  $0.04$ , respectively) and correlated with the maximum SUV ( $R = 0.9$ ;  $p = 0.001$ ) and average SUV ( $R = 0.8$ ;  $p = 0.01$ ). All (18)F-FDG hrPET-positive adenomas had a less than a 180% ACTH increase and (18)F-FDG hrPET-negative adenomas had a greater than 180% ACTH increase after CRH stimulation ( $p = 0.03$ ). Three adenomas were detected on SPGR MRI sequences that were not detected by (18)F-FDG hrPET imaging. Two adenomas not detected on SE (but no adenomas not detected on SPGR) were detected on (18)F-FDG hrPET.

**CONCLUSIONS** While (18)F-FDG hrPET imaging can detect small functioning corticotroph adenomas and is more sensitive than SE MRI, SPGR MRI is more sensitive than (18)F-FDG hrPET and SE MRI in the detection of CD-associated pituitary adenomas. Response to CRH stimulation can predict (18)F-FDG hrPET-positive adenomas in CD.



# CUSHING DISEASE

## MRI VARIANTS



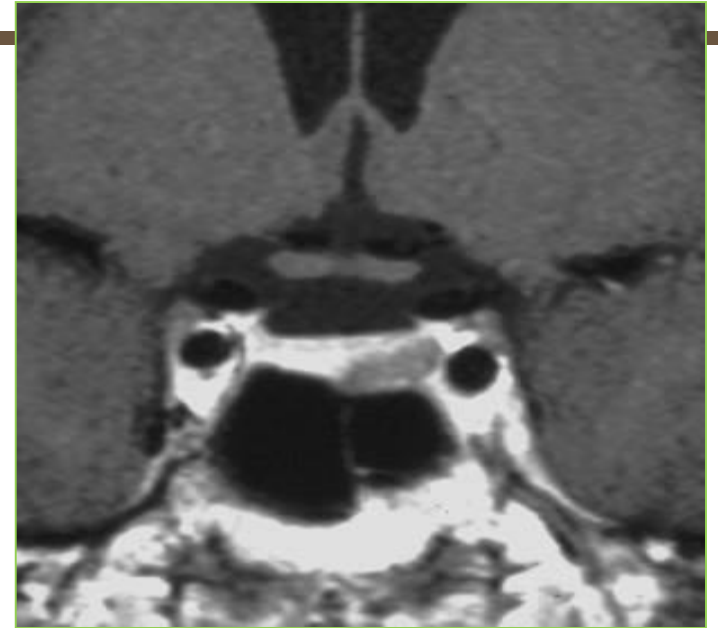
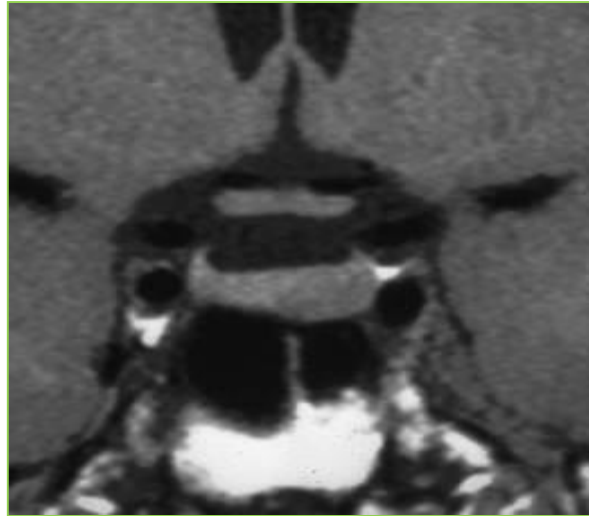
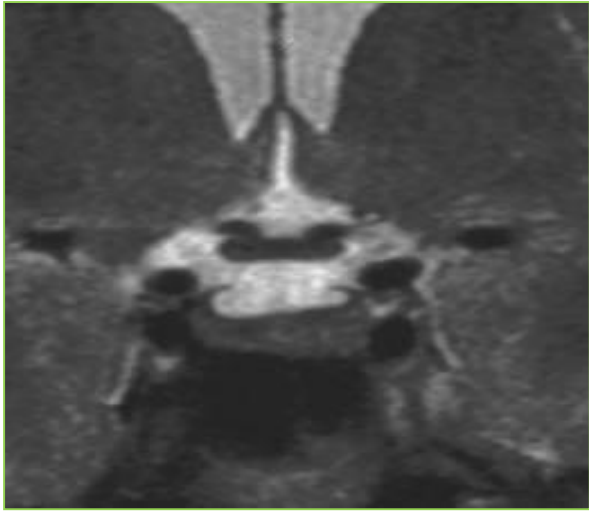
**3T > 1.5 T**

**DOSE:  
Gadolinium**

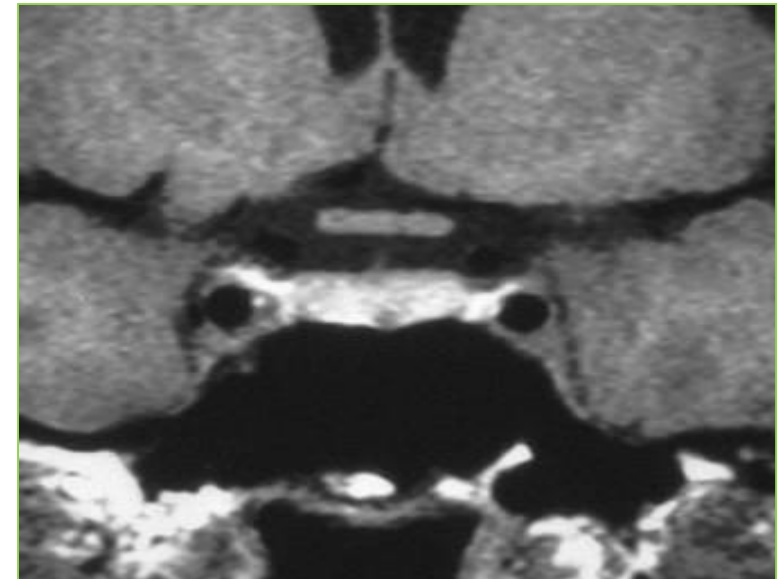
**THE CHOOSE OF  
THE SEQUENCE:  
DYNAMIC SPIN-ECHO,  
SPGR o VI-SGE**

# PITUITARY MICROADENOMA

Gadolinium

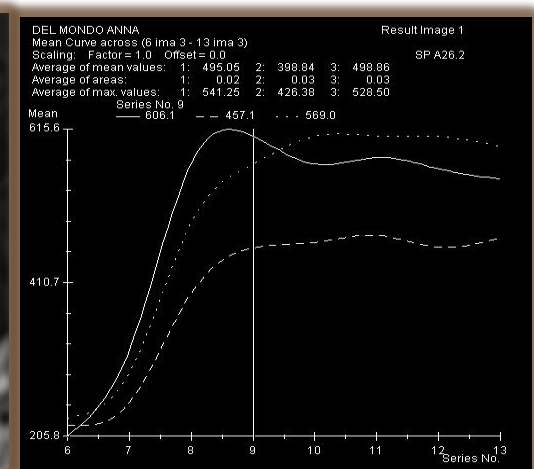
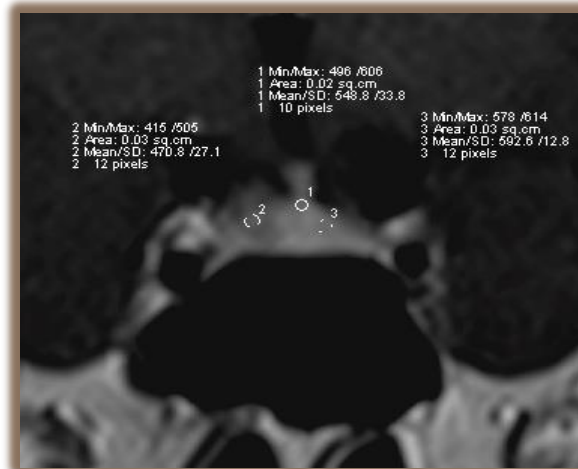
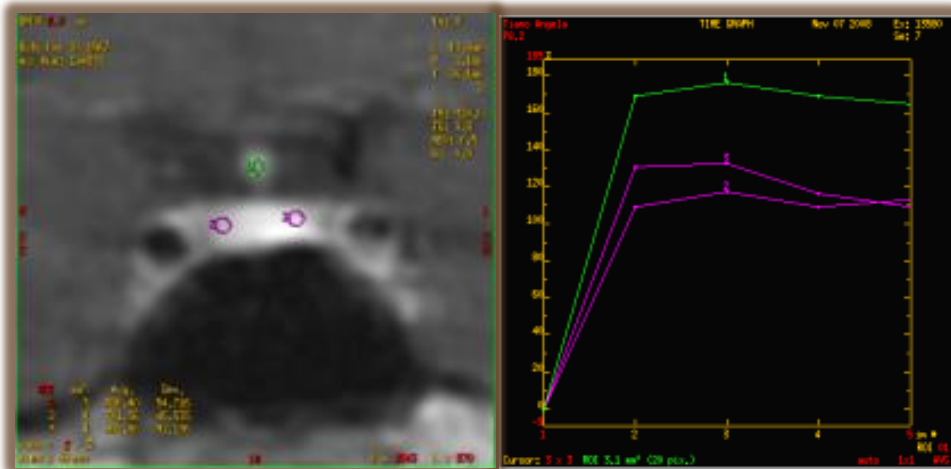
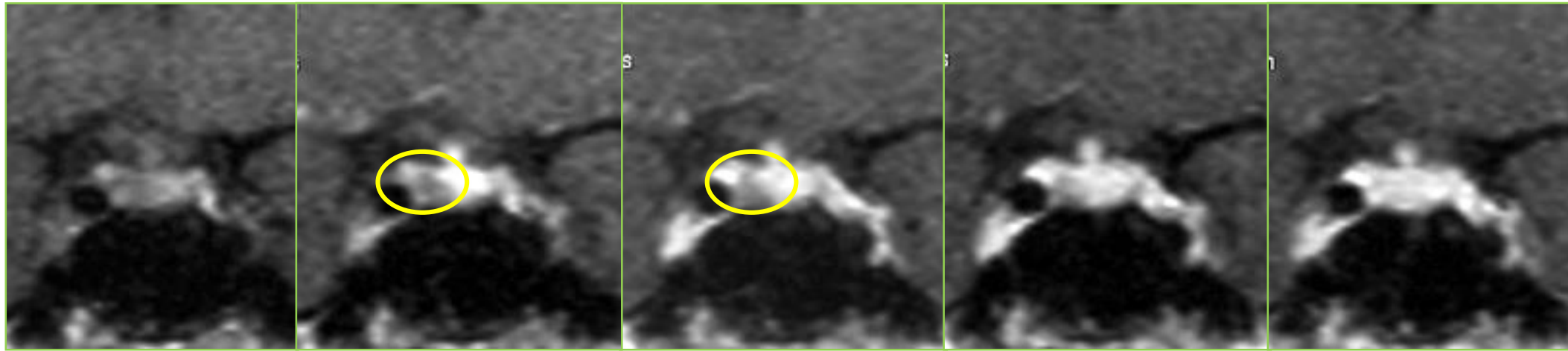


HALF DOSE !!



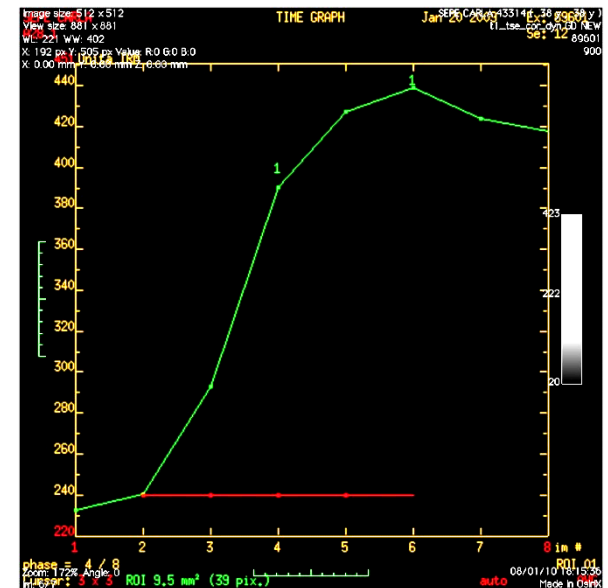
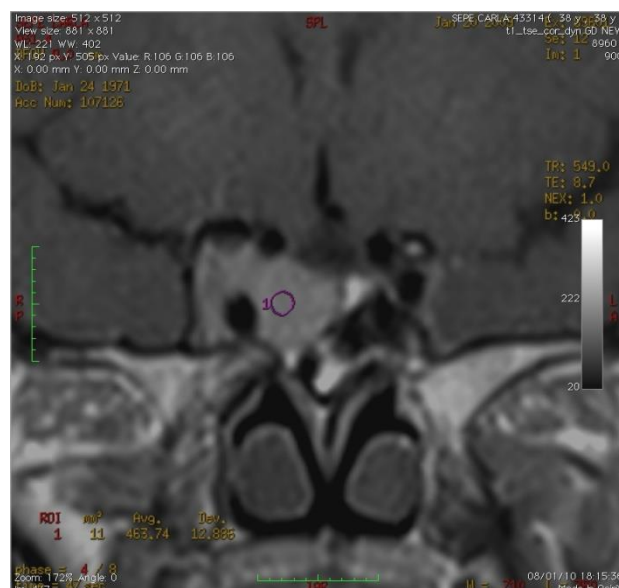
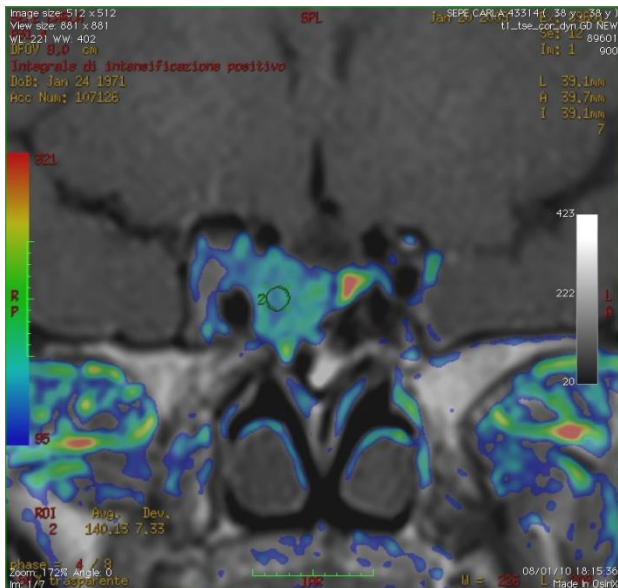
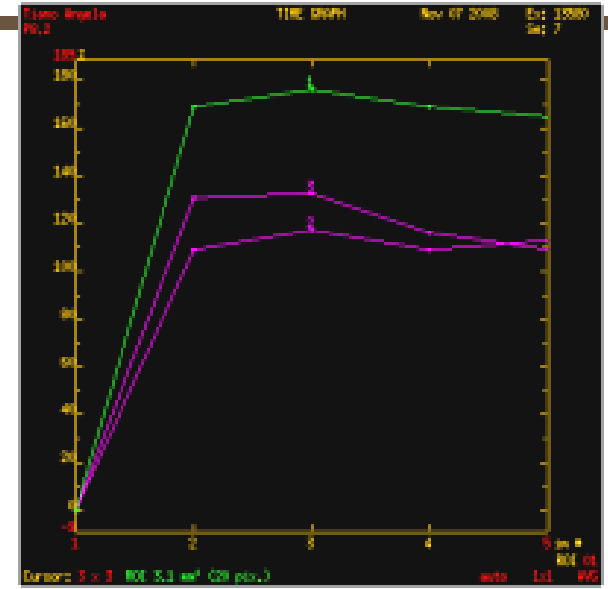
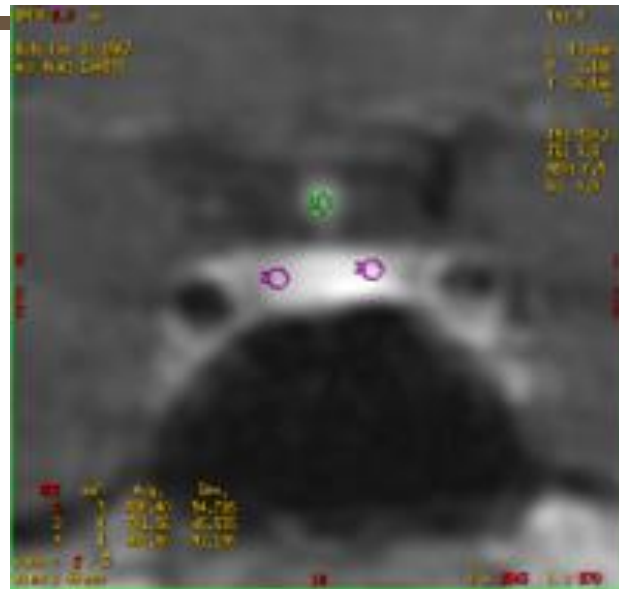
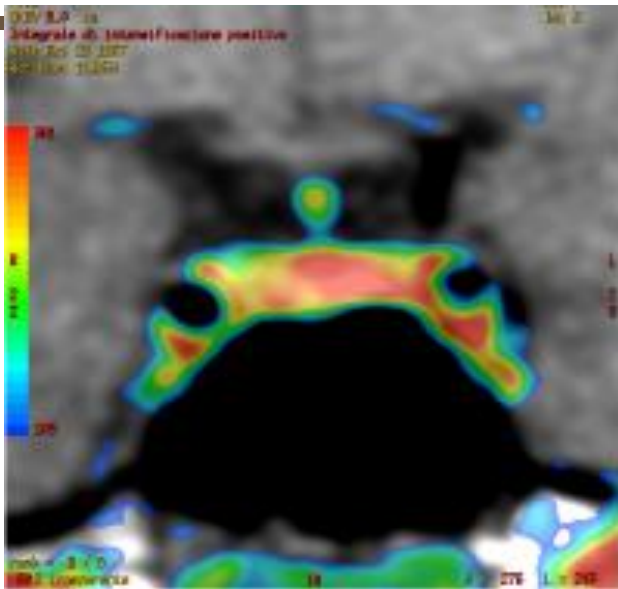
# PITUITARY PATHOLOGY

✓ DynamicMR imaging





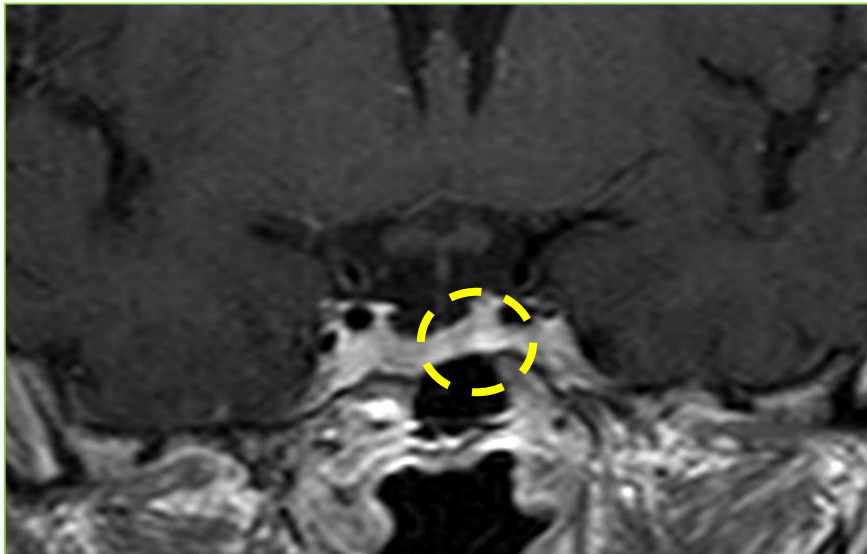
# ✓ EXPEDIENTS: DYNAMIC MDC



# CUSHING DISEASE

## CHOISE OF THE SEQUENCE: SPIN-ECHO or VI-SGE?

- ◆ THIN LAYER (1 mm)
- ◆ SAGITTAL PLANE (cavernous region)
- ◆ FRONTAL PLANE (pituitary pedicle)
- ◆ AXIAL PLANE (sella floor)



### SEQUENZA Spin-Echo 1.5T

TR/TE: 400/9 msec.

FOV: 12\*12cm.

Slice Thickness: 3mm.

### SEQUENZA VI-SGE 1.5T

TR/TE: 10/3,3 msec.

FOV: 16\*16cm.

Slice Thickness: 1-2mm.

## FOV ADEGUATO

## ACTH ADENOMAS



(TR)/ (TE) 422/26 ms;  
(FOV) 15,8 - 18, 0 cm

*“Not all ‘T1-weighted SE scans are equally accurate. MRI technique, particularly FOV and TR/TE value, influences Results “.*

## PITUITARY MICROADENOMA



TR/TE 400/10 ms;  
FOV 12 - 12 cm

Iffat N. Chowdhury A change in pituitary magnetic resonance imaging protocol detects ACTH-secreting tumours in patients with previously negative results  
Clinical Endocrinology (2010) 72, 502–506

## ACTH ADENOMAS

Spin-Echo MR



Spin-Echo MR



## PITUITARY MICROADENOMA

3D Spoiled-Gradient-Echo MR



3D-Spoiled Gradient Echo MR

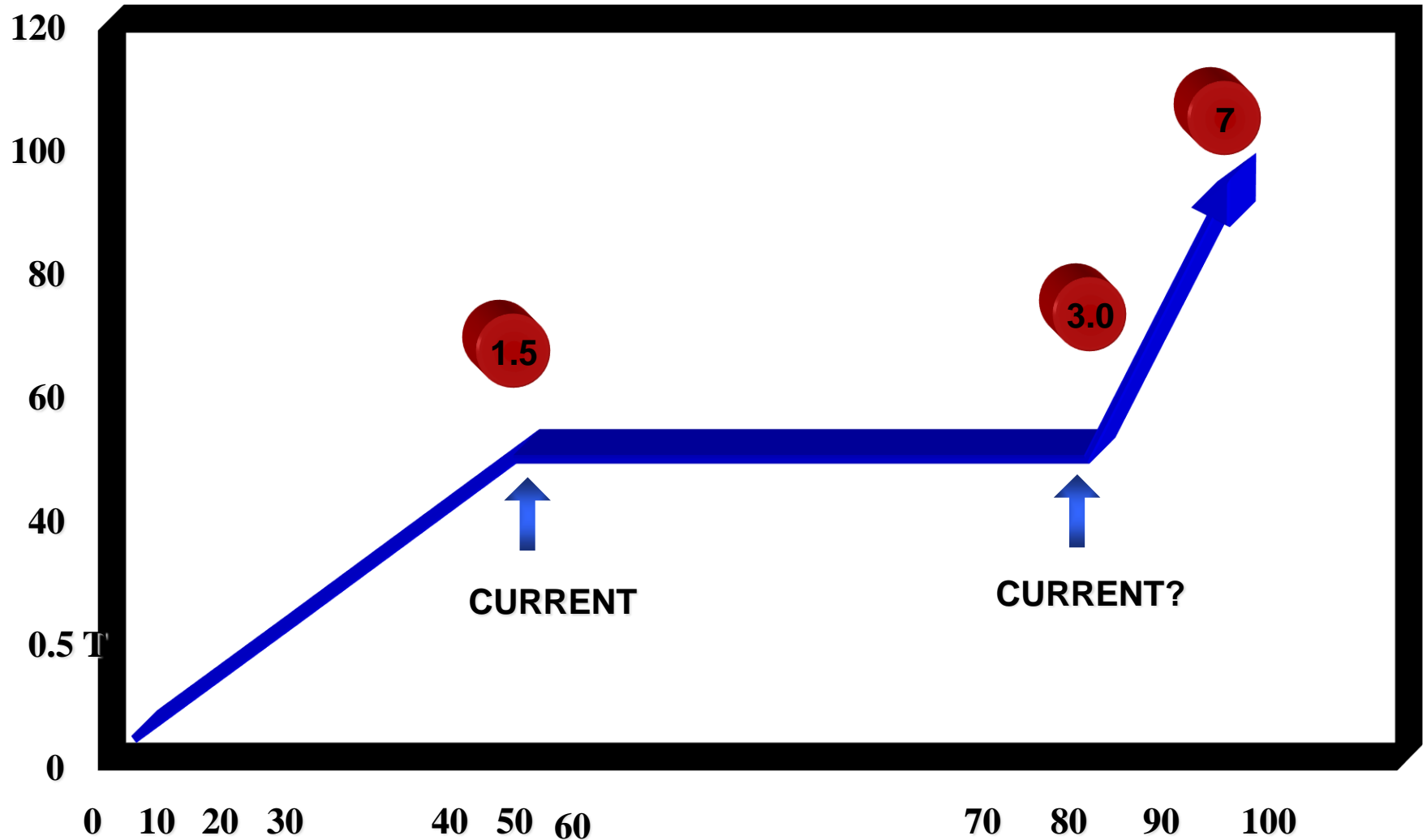


*Kasaliwal R, et Al: Volume interpolated 3D-spoiled gradient echo sequence is better than dynamic contrast spin echo sequence for MRI detection of corticotropin secreting pituitary microadenomas. Clin Endocrinol (Oxf*

**VOLUMETRIC  
SEQUENCE**

# PITUITARY MICROADENOMA

MAGNETIC FIELD



SENSITIVITY



# PITUITARY MICROADENOMA



## ACTH ADENOMAS



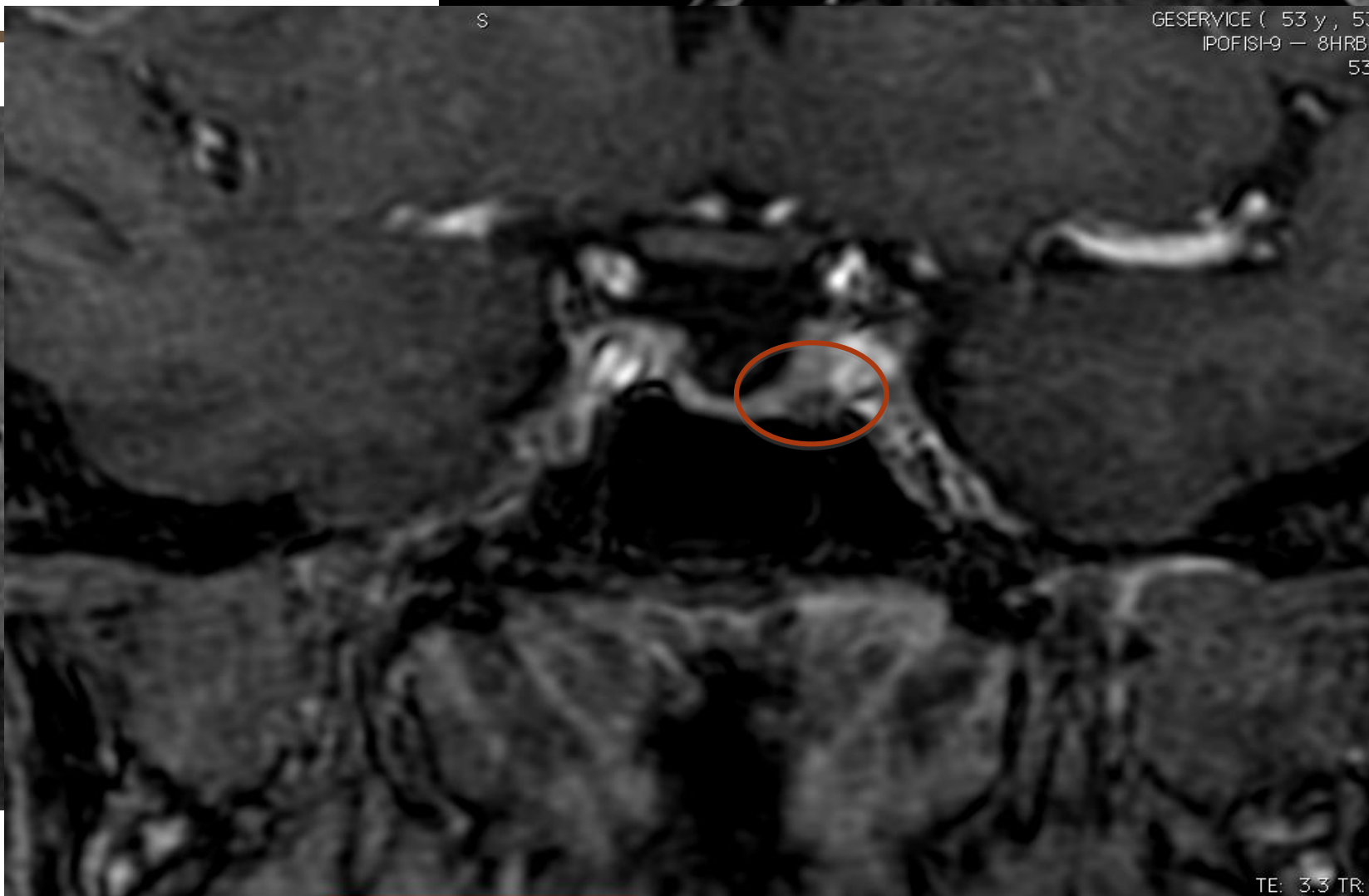
Sensitivity that increases even beyond 3 mm if performed with high magnetic fields

Ono, E., Ozawa, A., et al: *Diagnostic usefulness of 3 tesla MRI of the brain for cushing disease in a child.* Clinical Pediatric Endocrinology (2011). 20 (4) , pp. 89-93.

# CASE N1

Image size: 256 x 256  
View size: 762 x 762  
WL: 753 WW: 861

GESERVICE ( 53 y , 53 y )  
HIPOFISIS 8C-6 — DINAMICO FSPGR  
53118  
10



Zoom: 298% Angle: 0  
Im: 1/45 A (A -> P)  
Uncompressed  
Thickness: 2.00 mm Location: -47.06 mm

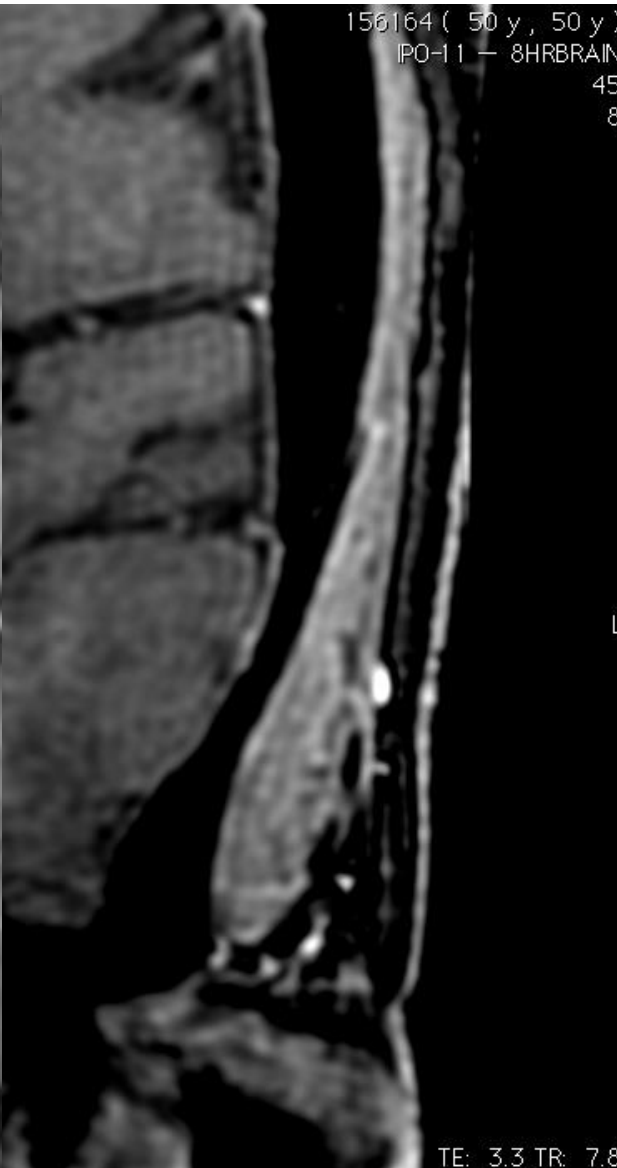
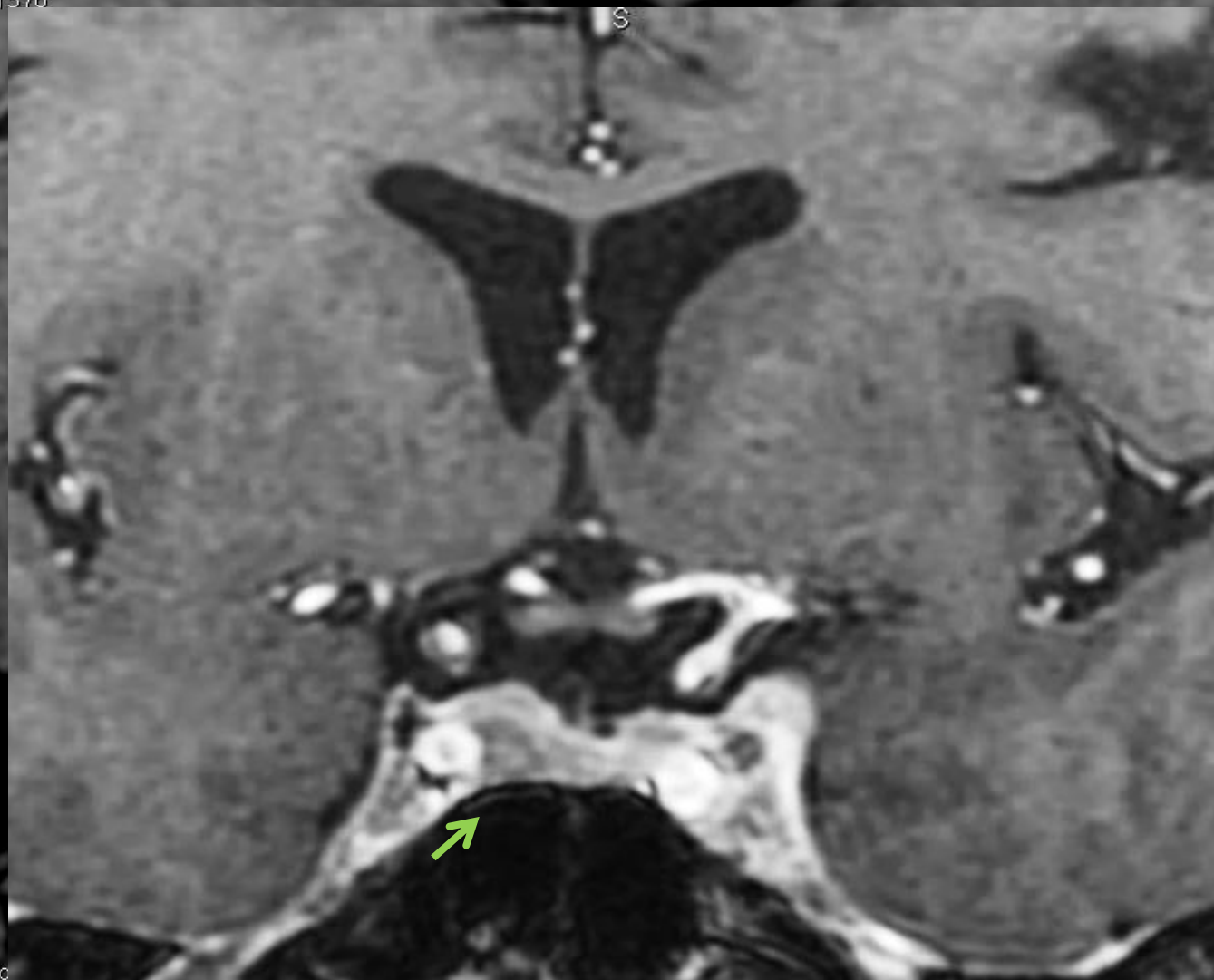
**NOT FOR MEDICAL USAGE**

TE: 3.1 TR: 51  
FS: 3  
20/01/14 14:32:19  
Made In OsiriX

# CASE N2

Image size: 512 x 512  
View size: 1298 x 762  
WL: 1331 WW: 1576

156164 ( 50 y, 50 y )  
IPO-11 - 8HRBRAIN  
45  
8



Zoom: 299% Ang  
Im: 1/36 P (P -> A)  
Uncompressed  
Thickness: 1.00 mm Location: +28.16 mm

NOT FOR MEDICAL USAGE

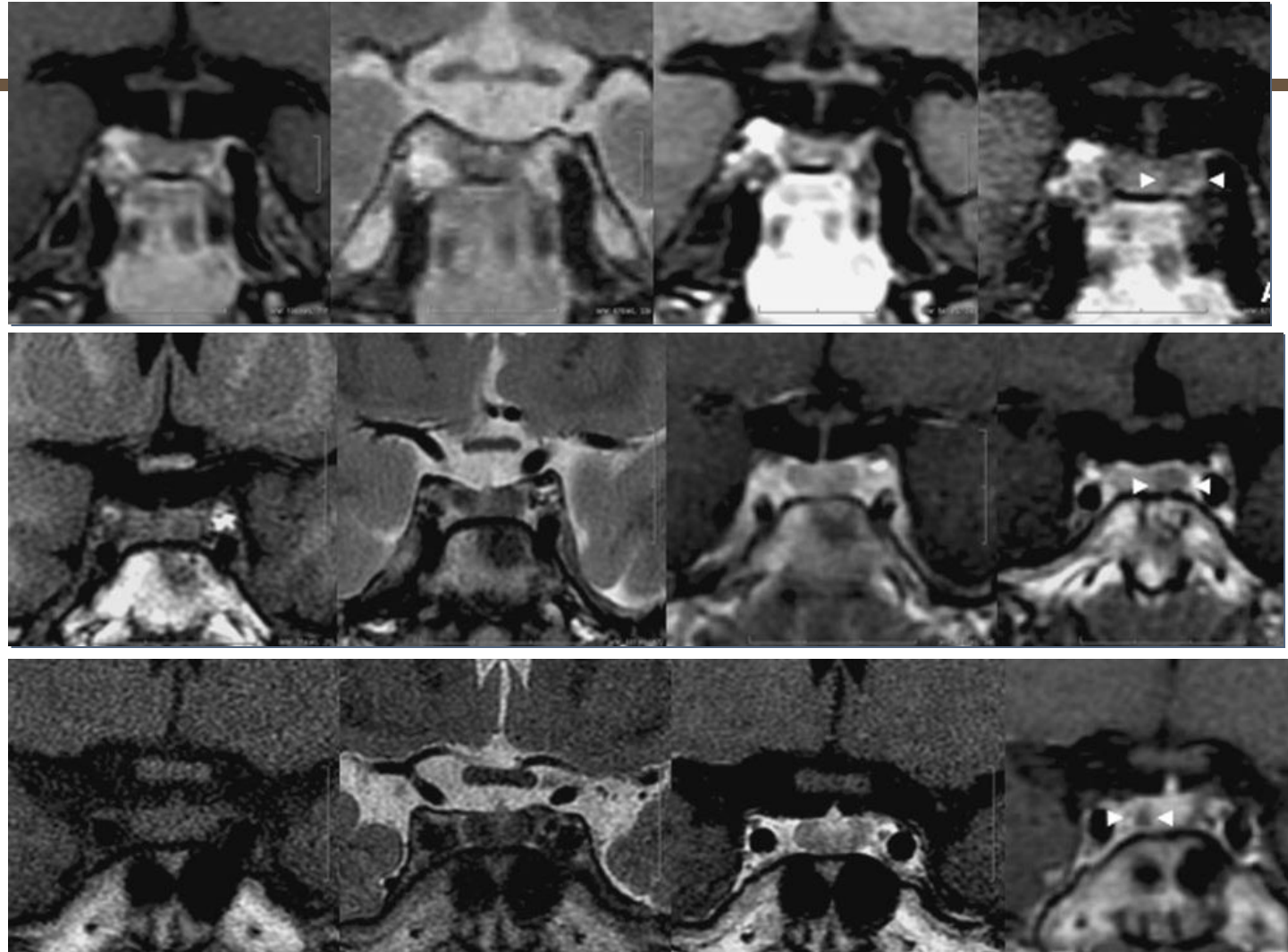
TE: 3.3 TR: 7.8  
FS: 3  
10/02/14 10:21:03  
Made In Oquirrh

# PITUITARY MICROADENOMA

◆ High magnetic field

◆ TR , TE e FOV

◆ Gadolinium dose



**SENSITIVITY 100 %**

*Lesly Portocarrero-Ortiz A modified protocol using half-dose gadolinium in dynamic 3-Tesla magnetic resonance imaging for detection of ACTH-secreting pituitary tumors Pituitary (2010) 13:230–235*

# BILATERAL PETROUS SINUS SAMPLING

---

## 1

Two microcatheters are introduced in 2 guiding catheters, by a bilateral femoral venous approach or, in some cases with a unilateral approach.

## 2

The positions of the catheter tips are controlled before and after the venous sinus sampling. Venous blood is sampled simultaneously from both petrosal sinuses and the peripheral vein.

## 3

Three venous blood samples are taken 1) **Inferior Vena Cava (IVC)** 2) **Right atrium** and 3) **Superior Vena Cava (SVC)** respectively, with a single **6-F catheter**; a non-scrubbed assistant obtained simultaneous peripheral samples from a vein of the arm.

# IBPSS: *TECNICA DI ESECUZIONE*

## *Accesso bilaterale*

a) Cateterismo bilaterale vene femorali comuni (4 o 5 French)



b) Singolo catetere (4F) utilizzato per prelievi simultanei:

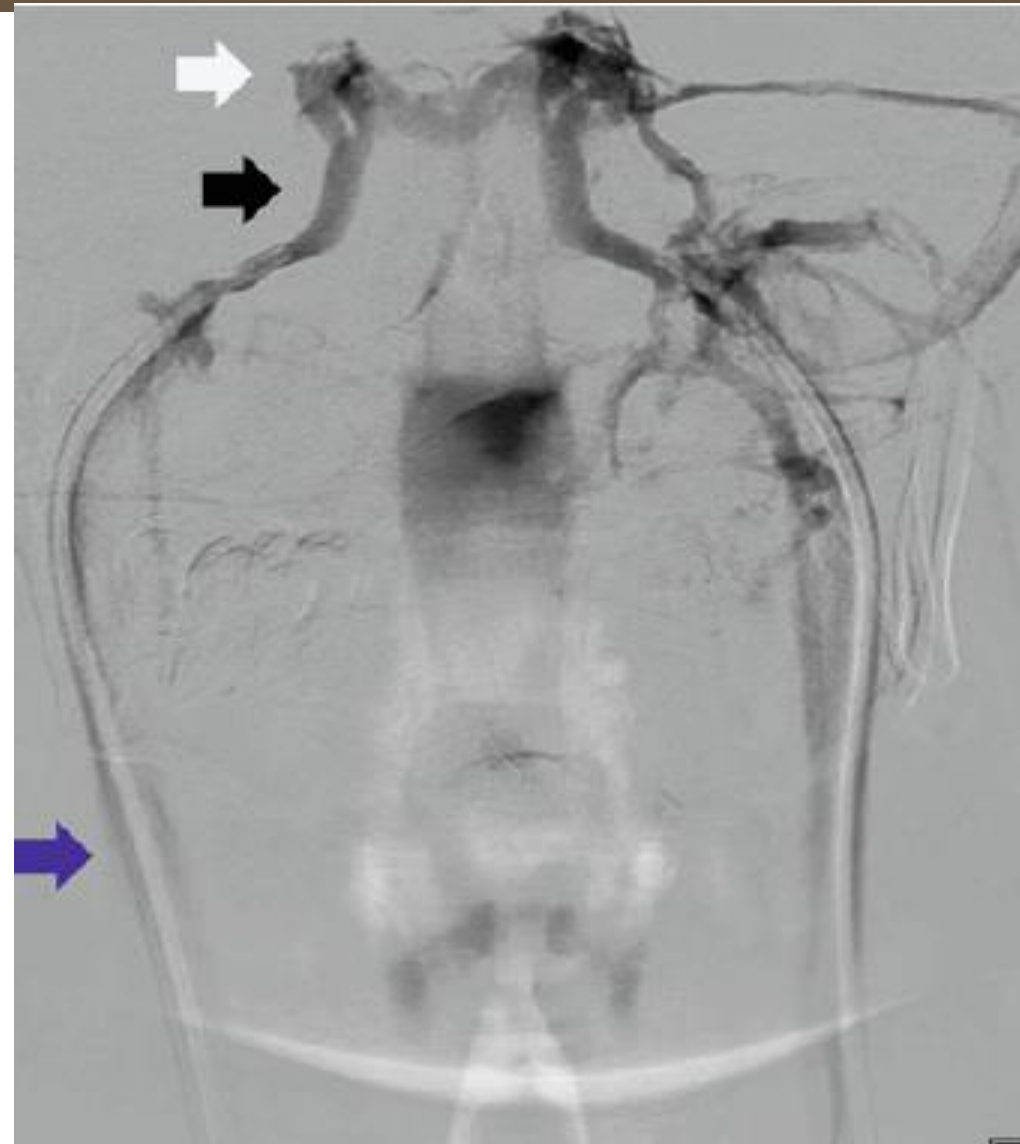
- VCI → periferico
- Atrio Dx → periferico
- VCS → periferico



c) Posizionamento secondo catetere (4F) controlateralmente



d) Cateterismo bilaterale seni petrosi Inferiori



## ***Accesso monolaterale***

**Cateterismo monolaterale vena femorale (8 o 9 French)**

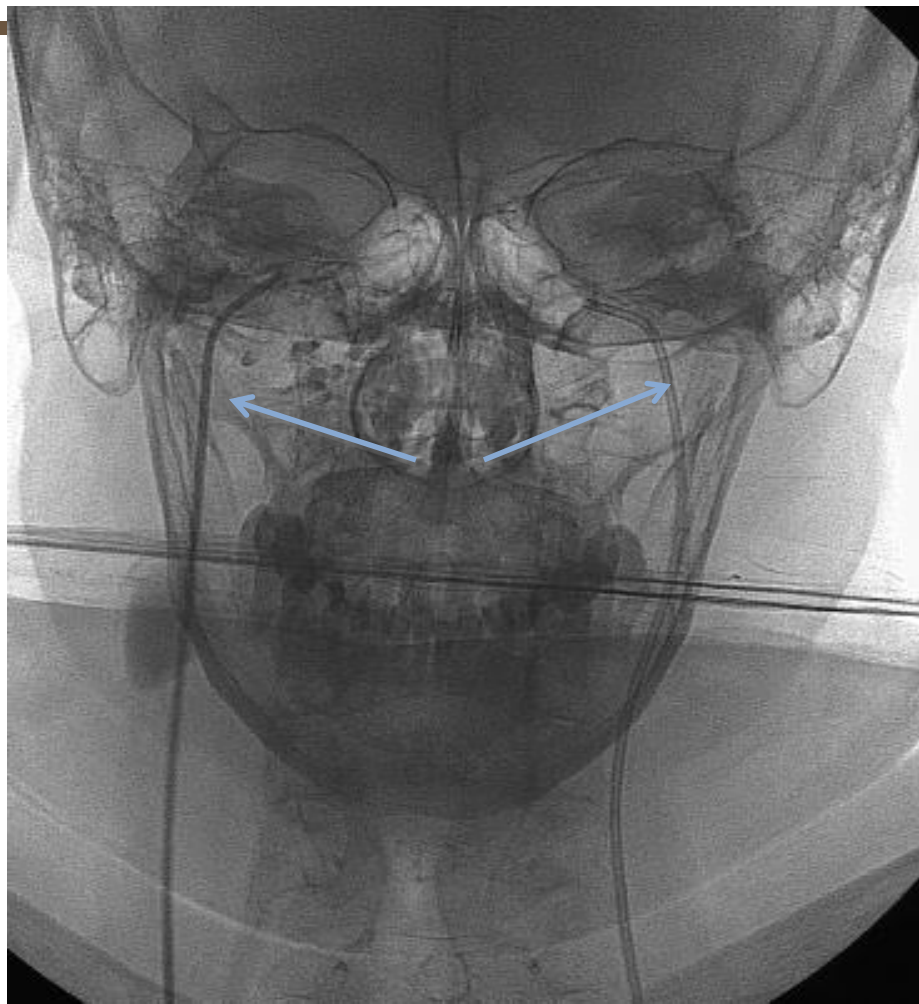


**b) Posizionamento dal singolo accesso di 2 cateteri da 4 French)**

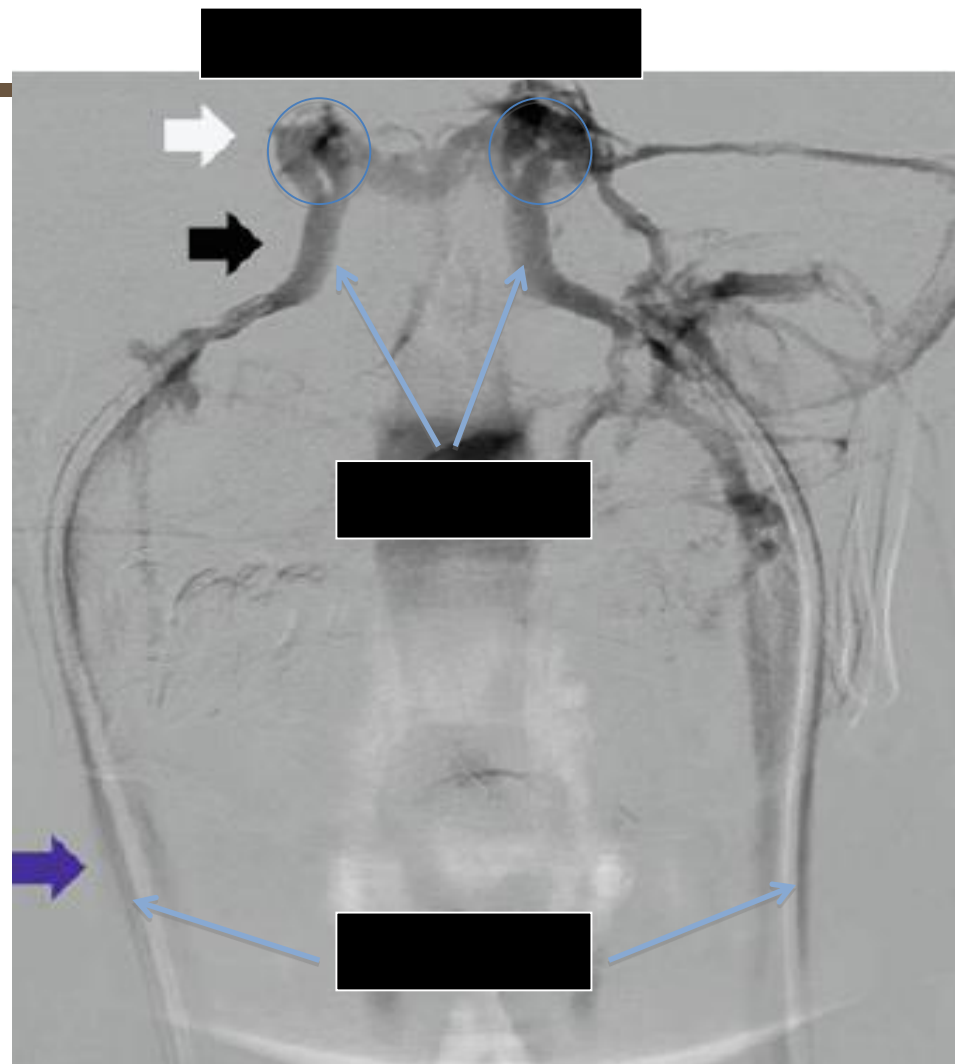


**c) Cateterismo bilaterale seni petrosi**

# IBPSS: *TECNICA DI ESECUZIONE*



**Posizionamento cateteri**



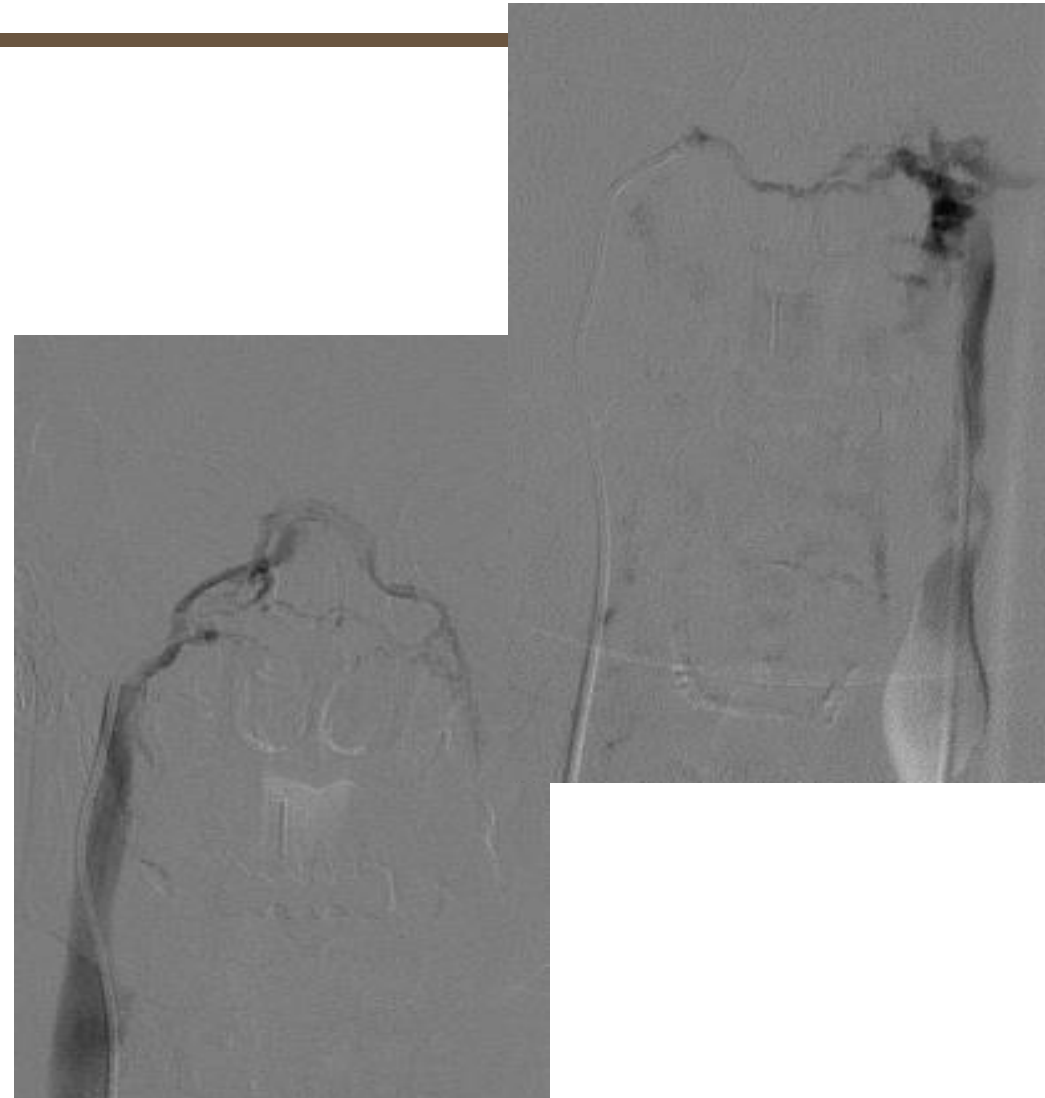


# IBPSS: *TECNICA DI ESECUZIONE*

**Prelievo bilaterale e simultaneo dei due seni petrosi e del sangue periferico**

**Stimolo farmacologico  
- CRH ( $1 \mu\text{g}/\text{kg}$  peso)**

**e) Prelievo a 3, 5, e 10 min dallo stimolo farmacologico**



*La sensibilità del test scende al 70% se il cateterismo non è bilaterale e simultaneo*

# IBPSS: *TECNICA DI ESECUZIONE*

## *FALSI POSITIVI (BIPSS + in assenza di adenoma)*

Cyclic Cushing syndrome

Farmaci (inibizione del Cortisolo: Ketoconazolo, Metirapone, Mitotane)

Adrenalectomia Bilaterale

Ipercortisolemia factitia

Pseudo-Cushing's syndrome

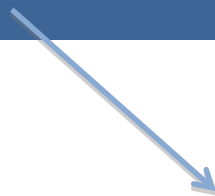
Adrenal Cushing's syndrome (con lieve ipercortisolemia)

Tumori secernenti CRH

## *FALSI NEGATIVI (BIPSS – in presenza di adenoma)*

Drenaggio venoso ipofisario aberrante

Tecnica IBPSS non corretta



*La sensibilità del test scende al 70% se il cateterismo non è bilaterale e simultaneo*

# PROCEDURA SUPERSELETTIVA

**1**

**In our institute all BIPSS were performed by an interventional neuroradiologist with a local anesthesia and a unilateral femoral venous approach, using a 9 F femoral venous sheath.**

**2**

**Two 4-F guiding catheters were used for venous sampling and for internal jugular vein catheterization. Heparin is infused, in flushing fluid during the catheterism, to avoid complications.**

**3**

**Thereafter the tips of two 2.7 F microcatheters were placed in IPS bilaterally; both catheters were placed symmetrically, and contrast injection was used to confirm their correct position. Two baseline samples were obtained from both petrosal sinuses and one peripheral vein of the arm, at the same time.**

**4**

**After systemic administration of a bolus of a CRH, venous blood samples were obtained from the IPS and peripheral vein simultaneously at 3, 5, 15 minutes to measure ACTH levels**

Image size: 512 x 512  
View size: 711 x 711  
WL: 124 WW: 259

Onorato Anna 9238 ( 26 y , 26 y )  
Cerebrale — unnamed  
0  
1

Zoom: 139% Angle: 0

Im: 1/450

JPEGLossless:Non-hierarchicalHistOrderPrediction

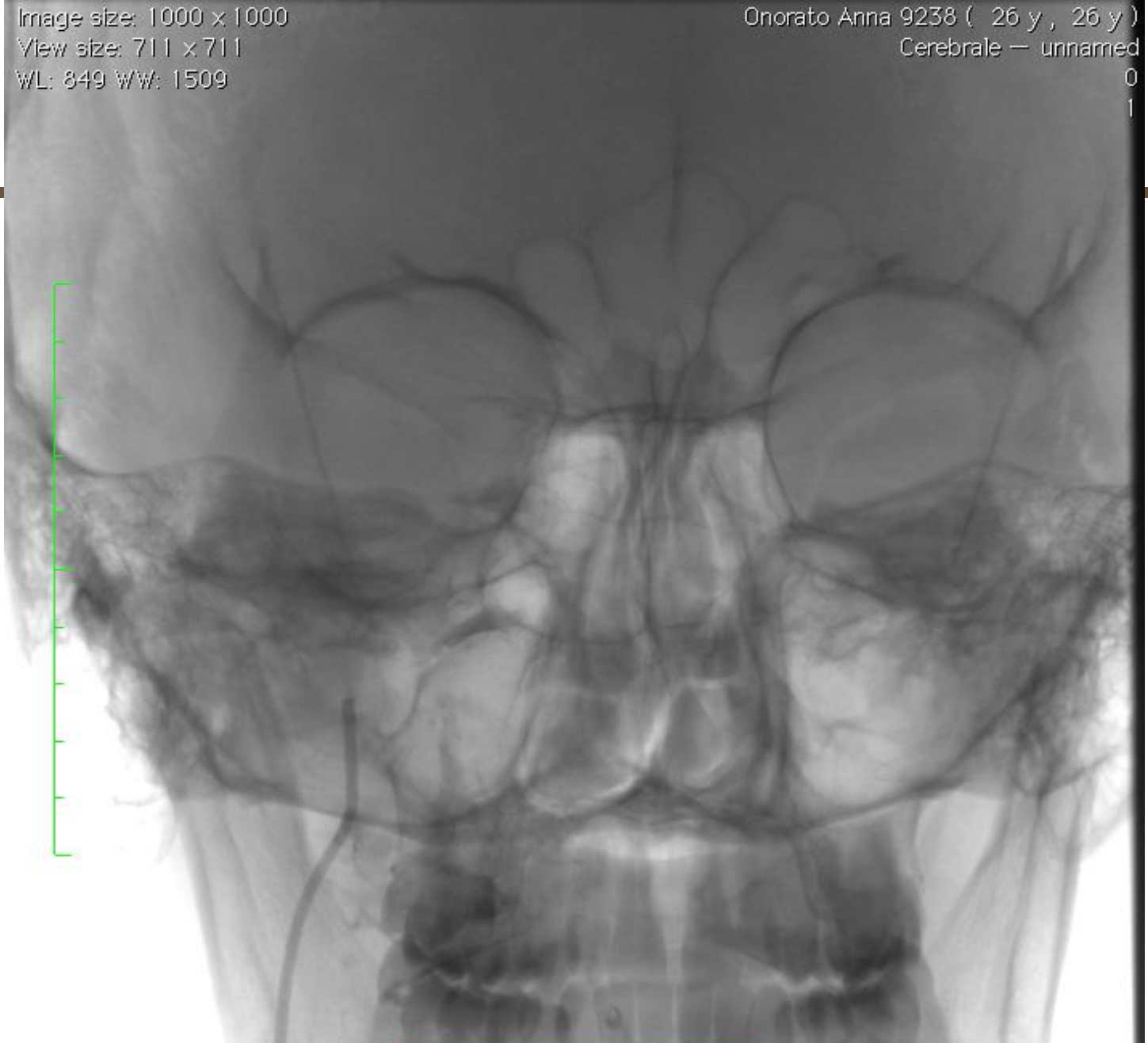
**NOT FOR MEDICAL USAGE**

11/02/15 10:42:33

Made In Osirix

Image size: 1000 x 1000  
View size: 711 x 711  
WL: 849 WW: 1509

Onorato Anna 9238 ( 26 y , 26 y )  
Cerebrale — unnamed  
0  
1



Zoom: 71% Angle: 0  
Im: 2/24

**NOT FOR MEDICAL USAGE**

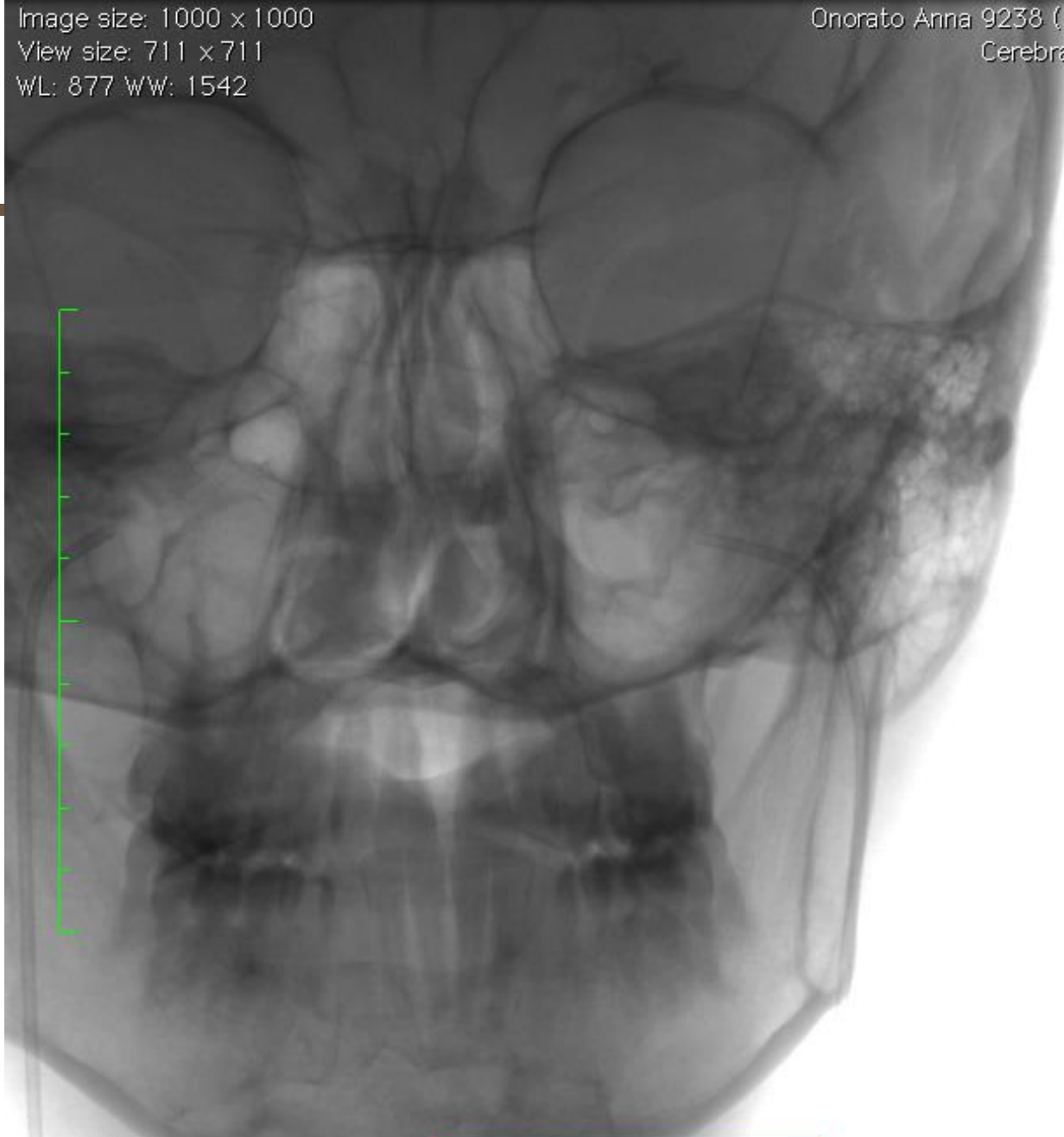
11/02/15 10:45:49

JPEGLossless: f|on-hierarchical-I|stOrderPrediction

Made In OsiriX

Image size: 1000 x 1000  
View size: 711 x 711  
WL: 877 WW: 1542

Onorato Anna 9238 ( 26 y , 26 y )  
Cerebrale - unnamed  
0  
1



Zoom: 71% Angle: 0  
In: 2/32

**NOT FOR MEDICAL USAGE**



11/02/15 11:12:27

Made In OsiriX

JPEGLossless:flon-hierarchical-H stOrderPrediction



## 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,<sup>1,2</sup> Luigi Maria Cavallo, MD, PhD,<sup>3</sup> Fabio Tortora, MD, PhD,<sup>4</sup> Rosario Pivonello, MD, PhD,<sup>6</sup> Annamaria Colao, MD, PhD,<sup>6</sup> Paolo Cappabianca, MD,<sup>3</sup> and Franco Mantero, MD, PhD,<sup>5</sup> on behalf of the Altogether to Beat Cushing's Syndrome Group

<sup>1</sup>Department of Clinical Sciences and Community Health, University of Milan; <sup>2</sup>Neuroendocrine Research Laboratory, Istituto Auxologico Italiano, Milan; <sup>3</sup>Division of Neurosurgery, Department of Neurosciences and Reproductive and Odontostomatological Sciences, and <sup>4</sup>Department of Clinical Medicine and Surgery, University of Naples Federico II; <sup>5</sup>Department of Neuroradiology, "Magrassi Lanzara" Clinical-Surgical Department, Second University of Naples, Naples; and <sup>6</sup>Endocrinology Unit, Department of Medicine, University of Padua, Italy

In the management of adrenocorticotrophic hormone (ACTH)-dependent Cushing's syndrome, inferior petrosal sinus sampling (IPSS) provides information for the endocrinologist, the neurosurgeon, and the neuroradiologist. To the endocrinologist who performs the etiological diagnosis, results of IPSS confirm or exclude the diagnosis of Cushing's disease with 80%–100% sensitivity and over 95% specificity. Baseline central-peripheral gradients have suboptimal accuracy, and stimulation with corticotropin-releasing hormone (CRH), possibly desmopressin, has to be performed. The rationale for the use of IPSS in this context depends on other diagnostic means, taking availability of CRH and reliability of dynamic testing and pituitary imaging into account. As regards the other specialists, the neuroradiologist may collate results of IPSS with findings at imaging, while IPSS may prove useful to the neurosurgeon to chart a surgical course. The present review illustrates the current standpoint of these 3 specialists on the role of IPSS.

<http://thejns.org/doi/abs/10.3171/2014.11.FOCUS14766>

**KEY WORDS** inferior petrosal sinus sampling; Cushing's disease; Cushing's syndrome; diagnosis; pituitary adenoma; pituitary surgery; pituitary imaging



# CUSHING DISEASE

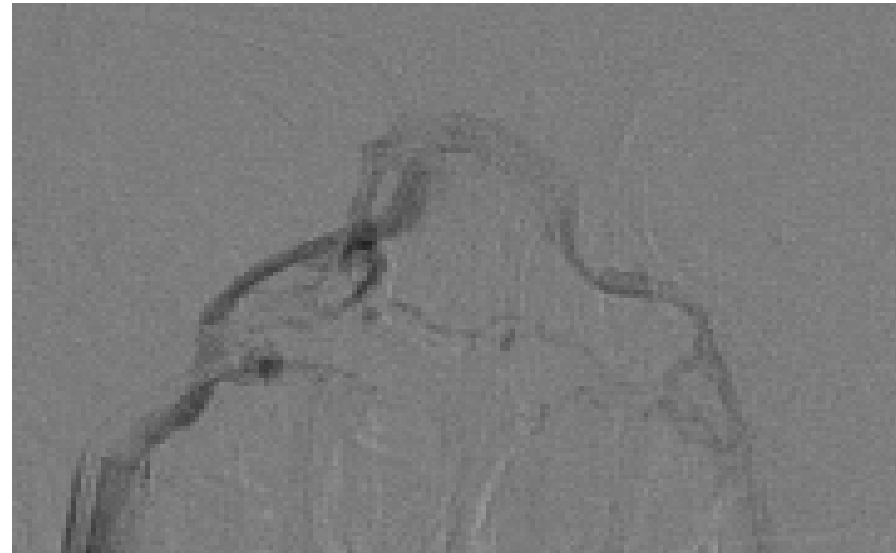
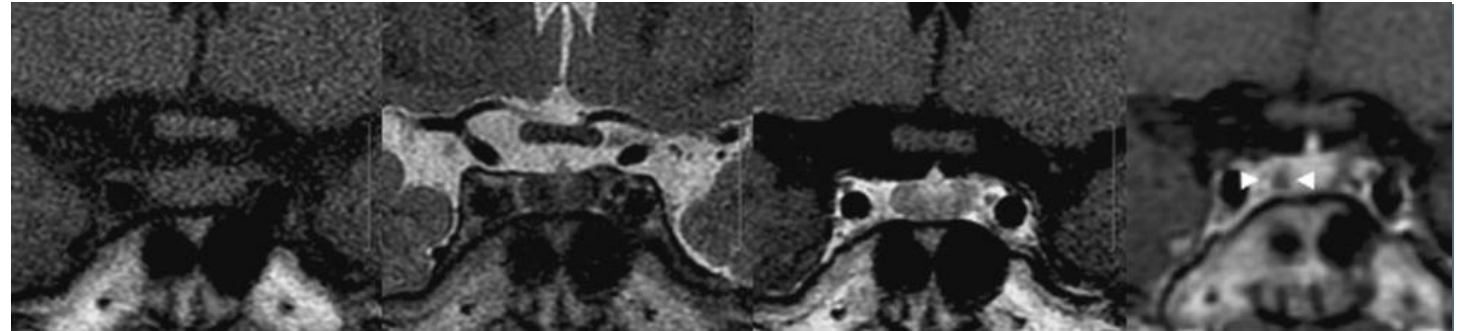
## CONCLUSIONS

◆ High magnetic field

◆ TR , TE e FOV

◆ Gadolinium dose

◆ BILATERAL  
SUPERSELECTIVE  
PETROUS SINUS  
SAMPLING



**SENSITIVITY 100 %**

*Lesly Portocarrero-Ortiz A modified protocol using half-dose gadolinium in dynamic 3-Tesla magnetic resonance imaging for detection of ACTH-secreting pituitary tumors*  
*Pituitary (2010) 13:230–235*



***THANK YOU FOR YOUR ATTENTION!***

