Bilateral Inferior Petrosal Sinus Sampling (BIPSS) in the Diagnosis of Cushing's Disease

The Neurosurgical point of view

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Cushing Disease

- Most patients with CS have a Pituitary corticotrophic microadenomas (< 10 mm)
- Localization of corticotropic adenomas remains a major challenge in many cases of Cushing's disease
- Small size and imaging features similar to normal gland

Standard diagnostic workup of Cushing's syndrome

- Clinical examination
- Biochemical studies:

1. Serum cortisol
2. 24 h urine cortisol
3. low- and high-dose dexamethasone suppression tests
4. CRH stimulating test

- Neuroimaging: Magnetic resonance (1,5-3 Tesla)

Neuroradiological Diagnosis

- Recent developments: MRI sequences that provide increased sensitivity for pituitary tumor detection

1. spoiled gradient recalled echo (SPGR)
2. dynamic contrast enhanced MRI, (dMRI)
3. 3 Tesla MRI

Neuroradiological diagnosis

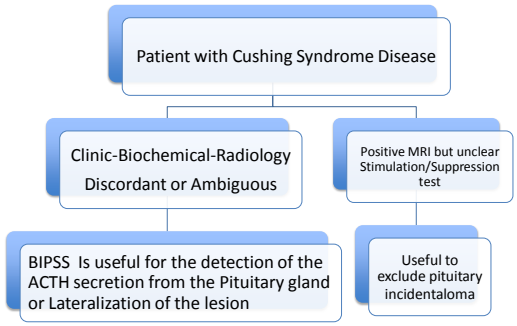
- limited value in the differential diagnosis of CS:

3 reasons:

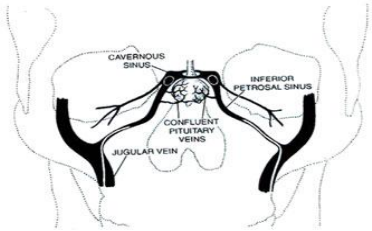
1. low sensitivity of MRI
2. significant incidence of pituitary asymptomatic microadenomas in the general population
3. Possible ectopic sites

20-50% of patients with Cushing's disease have negative MRI (Patronas et al 2003)

Standard diagnostic workup of Cushing's syndrome



BIPSS



BIPSS

- The best diagnostic test for differentiation of ACTH Cushing's syndrome
- Serial samples for central and peripheral plasma ACTH concentrations then are drawn at -1 and 0 minutes before and at 3, 5, and 10 minutes after the administration of desmopressin or most commonly CRH

BIPSS

Central to periphery baseline ratio >2

Gradient >3 following CRH or Desmopressin stimulation

Findings suggestive of Cushing's disease

Sensitivity

- Diagnostic sensitivity and specificity for BIPSS 94%


Endocrinol Metab Clin N Am 34 (2005) 403–421

Differential Diagnosis and Imaging in Cushing's Syndrome

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BIPSS

- Useful for localization of microadenomas
- An intersinus ratio of 1.4 or greater would be consistent with the ipsilateral localization of a microadenoma
- the mean diagnostic accuracy of BIPSS for correct lateralization is 78% Vilar et Al (2007)

Surgery

- The main challenge in patients with Cushing disease and a negative MRI is the exploration of the pituitary to find the microadenoma
- BIPSS should at the most suggest the initial side of the gland to be explored

Surgery

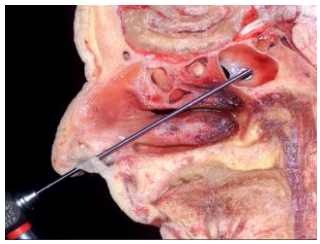
- Wide sellar floor opening
- Wide dura opening
- Gland first explored on the side suggested by BIPSS test

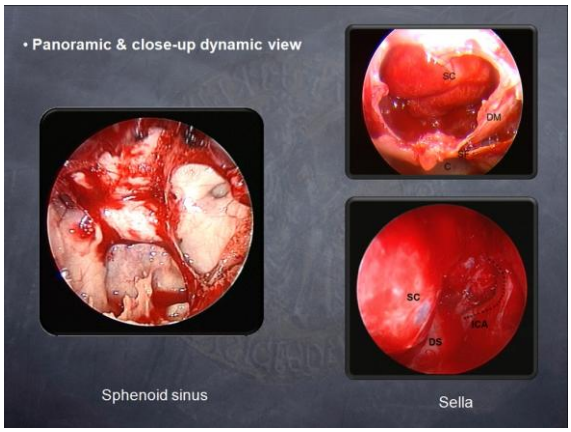
In case of failure

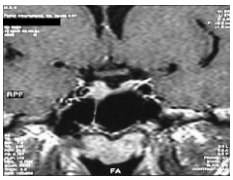
Whole gland exploration

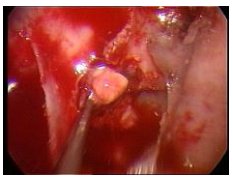
New Technique

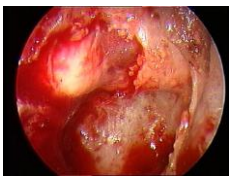
- Endoscopic endonasal approach

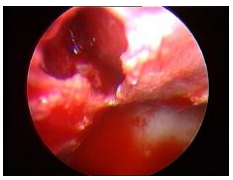


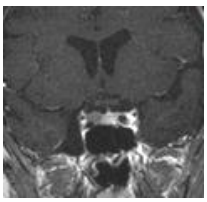






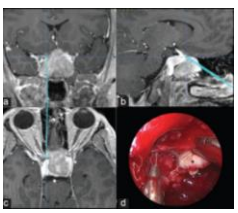






New Tool

- Neuronavigator

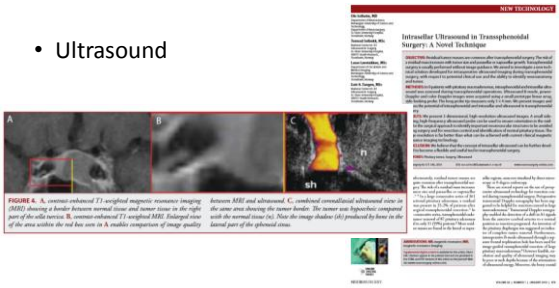


New Tool

- Microdoppler probe

New Tool

- Ultrasound



Knappe UJ, Engelbach M, Konz K, Lakomek HJ, Saeger W, Schonmayr R, Mann WA: **Ultrasound assisted microsurgery for Cushing's disease**. Exp Clin Endocrinol Diabetes 2011; 119(4): 191-200

New Tool

- Intraoperative MRI

Nimsky C, von Keller B, Ganslandt O, Fahlbusch R.
Intraoperative high-field magnetic resonance imaging in transsphenoidal surgery of hormonally inactive pituitary macroadenomas.
Neurosurgery. 2006 Jul;59(1):105-14; discussion 105-14.

Berkmann S[1], Fandino J, Müller B, Remonda L, Landolt H.
Intraoperative MRI and endocrinological outcome of transsphenoidal surgery for non-functioning pituitary adenoma.
Acta Neurochir (Wien). 2012 Apr;154(4):639-47. doi: 10.1007/s00701-012-1285-5.

Failure of intraoperative tumor identification

- Lack of surgical experience
- Misdiagnosis
- Very small pituitary tumor
- Corticotroph hyperplasia
- Extrapituitary parasellar adenoma

Kim LJ and Al: J Neurosurg 98:1312-1317,2003.

Intraoperative Neuropathologist consultation