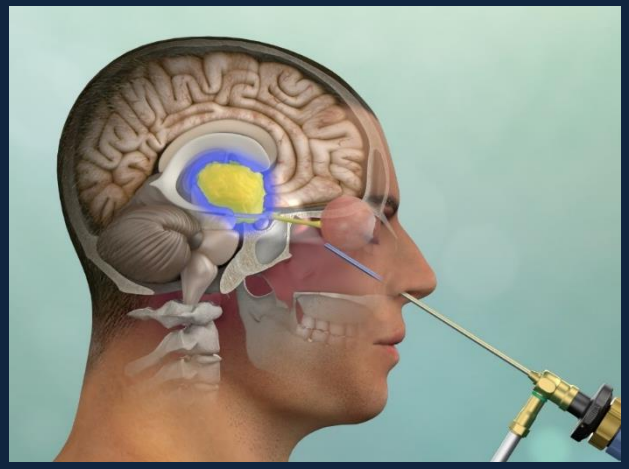
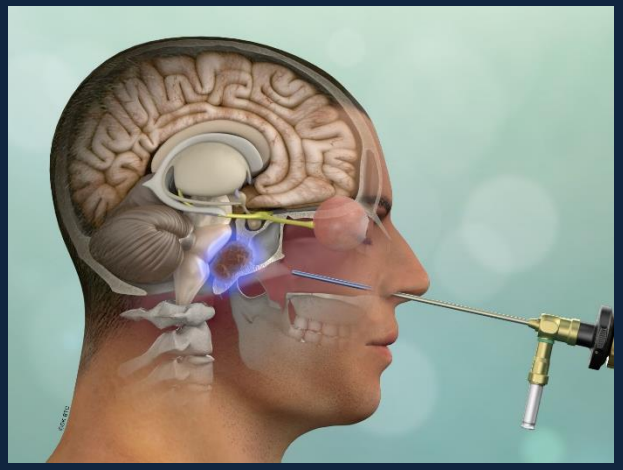
Uncommon Tumors of the Pituitary and Parasellar Region





Garni Barkhoudarian, MD

Colleagues: Daniel F. Kelly, MD, Chester Griffiths, MD
Walavan Sivakumar, MD; Sarah Rettinger, MD; Pejman Cohan, MD

Pacific Brain Tumor Center & Pituitary Disorders Center

Providence Saint John's Health Center & John Wayne Cancer Institute

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Disclosures

- Consultant: VTI
- Anatomy lab receives financial or material support from:
  - Karl-Storz Endoskope America, Inc
  - Stryker Corporation
  - Mizuho America, Inc
  - Surgical West, Inc

Pituitary and Parasellar Tumors

Total No. of patients (55% female)	**509**
Pathology	
Pituitary adenoma	65.7%
Rathke's cleft cyst	7.1%
Meningioma	6.4%
Craniopharyngioma	4.5%
Arachnoid Cyst	2.4%
Chordoma	2.0%
Other *	12%
Total No. of Operations	**551**
No. of extended approaches	**225 (41%)**

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Non-adenomatous Pituitary and Parasellar Tumors

Cysts	n	%		Bone Lesions	n	%
Rathke Cleft Cyst	40	39%		Fibrous Dysplasia	1	1%
Arachnoid Cyst	8	8%		Basilar Invagination	1	1%
Pituitary Cyst	2	2%		Lipomatous bone cyst	1	1%
Cholesterin Granuloma	1	1%		**Total Bone Lesions**	**3**	**3%**
Total Cysts	**51**	**50%**				
				Inflammatory Disease		
Tumors				Lymphocytic Hypophysitis	4	4%
Craniopharyngioma	18	17%		Wegener's Granulomatosis	1	1%
Metastases	4	4%		Giant repairative granuloma	1	1%
Chordoma	3	3%		Granulomatous lesion	1	1%
Chondrosarcoma	1	1%		Pituitary Inflammation	1	1%
Granular cell tumor	1	1%		**Total Inflammatory Disease**	**8**	**8%**
Lymphoma	1	1%				
Meningioma	1	1%		Miscellaneous		
Pituitary Carcinoma	1	1%		Nondiagnostic	3	3%
Oncocytoma	2	2%		Normal gland	2	2%
Total tumors/cysts	**32**	**31%**		Spontaneous CSF Leak	2	2%
				Pituitary Hyperplasia	1	1%
				Aneurysm	1	1%
				Total Miscellaneous	**9**	**9%**

Barkhoudarian and Laws, 2012

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Non-adenomatous Pituitary and Parasellar Tumors

- Pituitary / Parasellar Cysts
- Craniopharyngiomas
- Meningiomas
- Chordomas

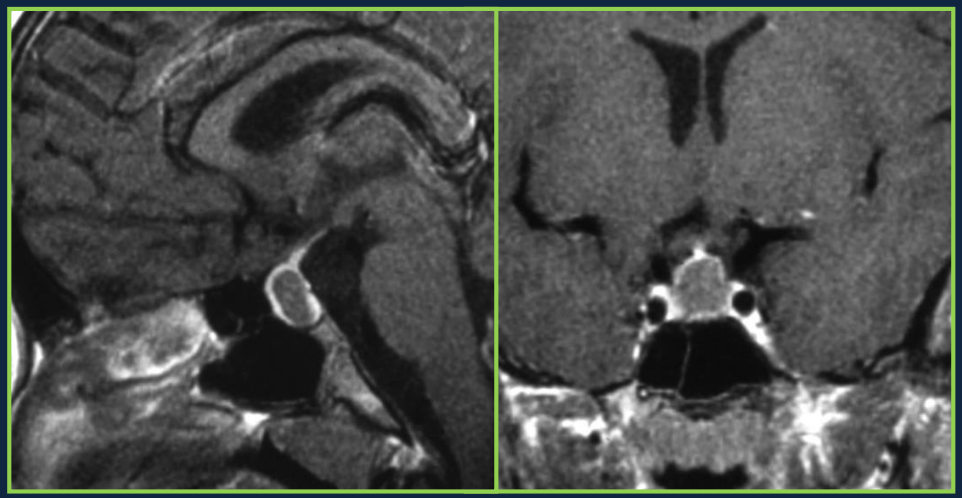
Pituitary / Parasellar Cysts

- Rathke's Cleft Cyst
- Arachnoid Cyst
- Cholesterin Granuloma

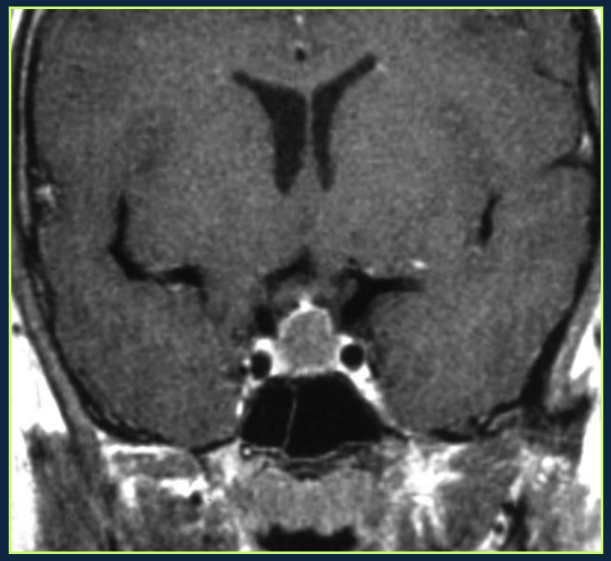
- (Cystic Adenoma)
- (Craniopharyngioma)

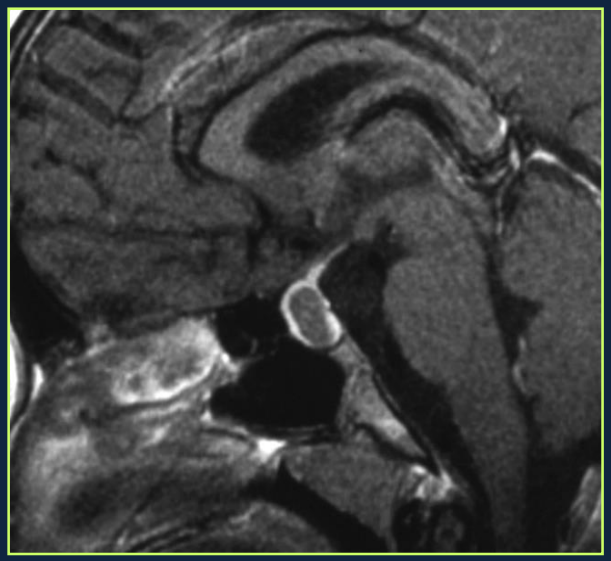
Rathke's Cleft Cyst

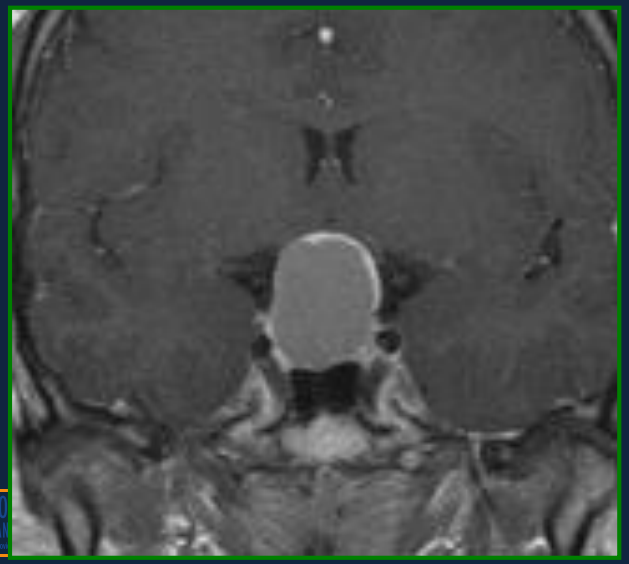
- Non-neoplastic cyst arising from remnants of embryonic Rathke's pouch.
- Nonenhancing, noncalcified and may be intrasellar or suprasellar. Most located between anterior and posterior lobes
- Many are asymptomatic. Symptoms increase with size.
- Contain proteinaceous fluid which has different appearances on MR depending on protein concentration.
- Can rupture or hemorrhage and present as pituitary apoplexy.

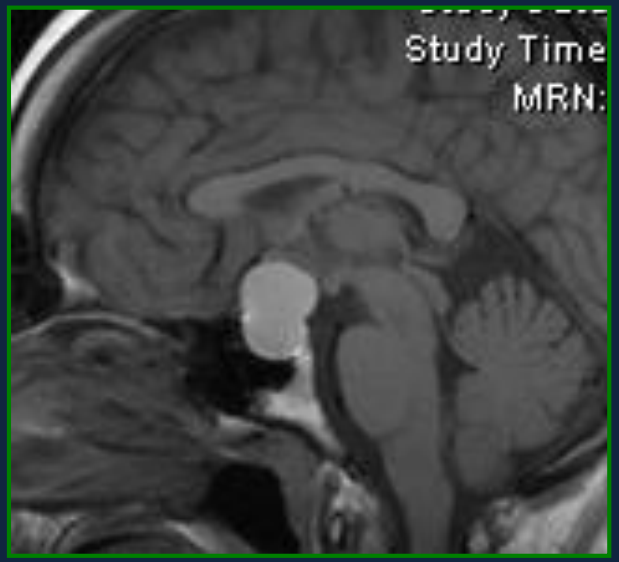


Rathke's Cleft Cyst









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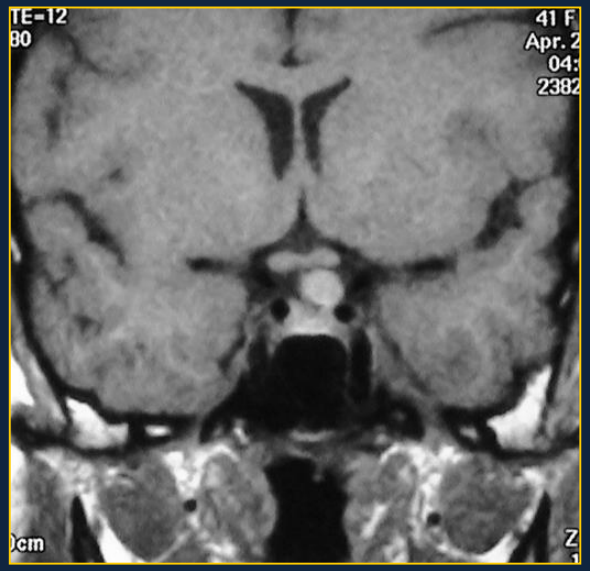
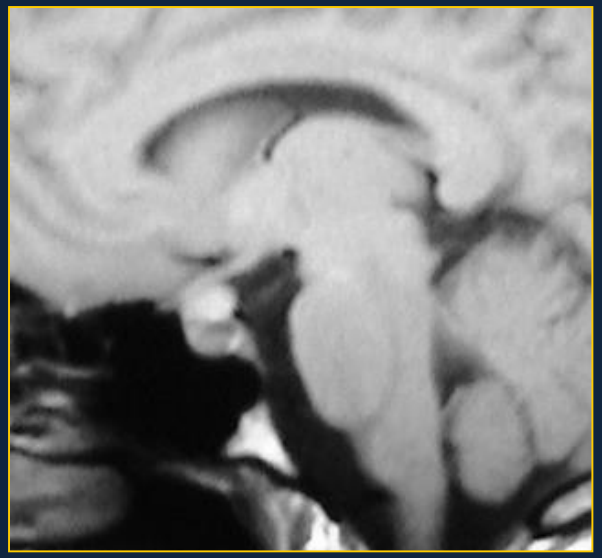
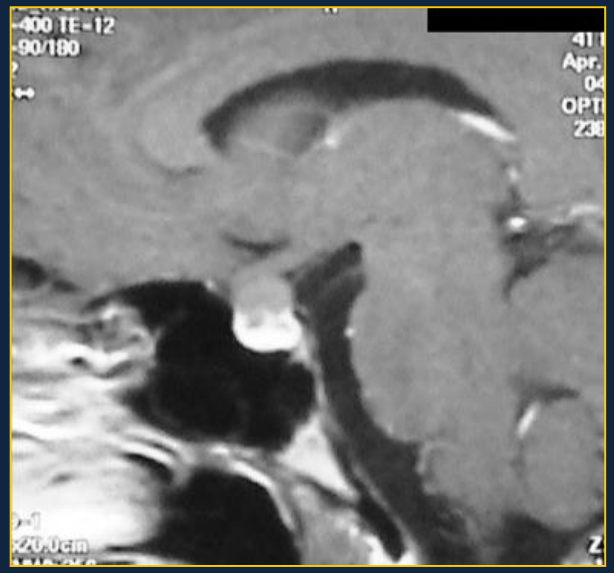
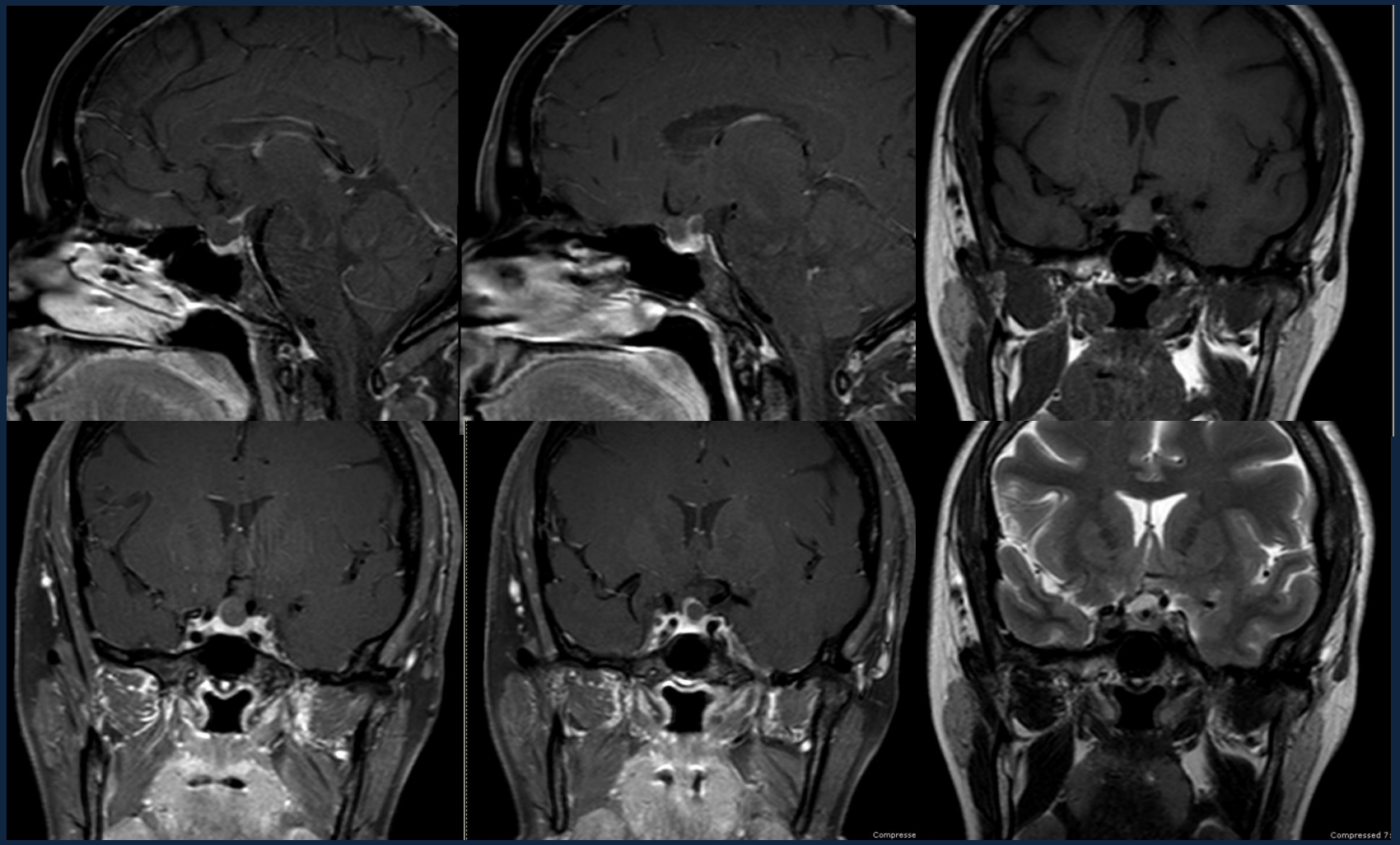
Supraglandular Rathke's Cleft Cyst



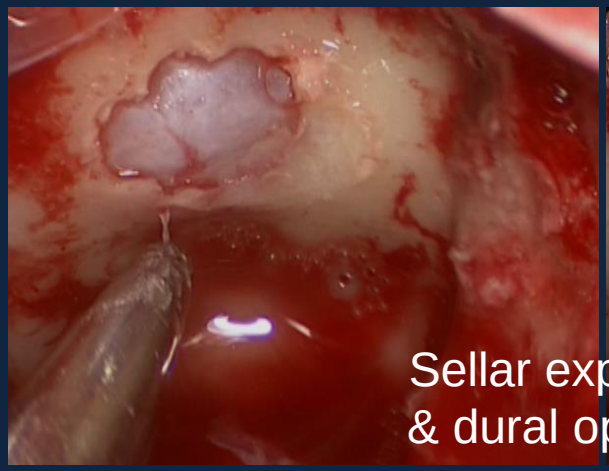




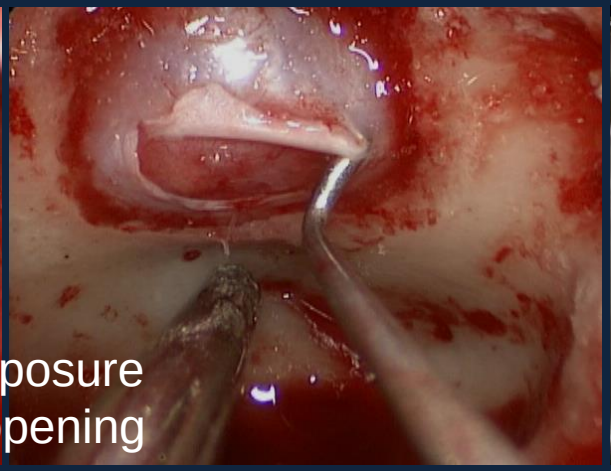
Supraglandular Rathke's Cleft Cyst



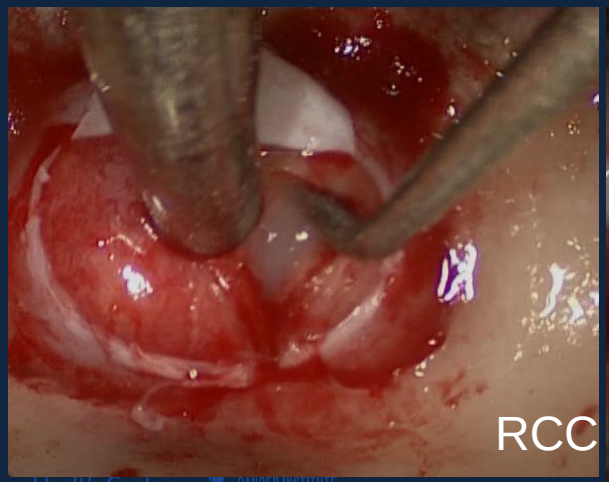
Supraglandular Rathke's Cleft Cyst



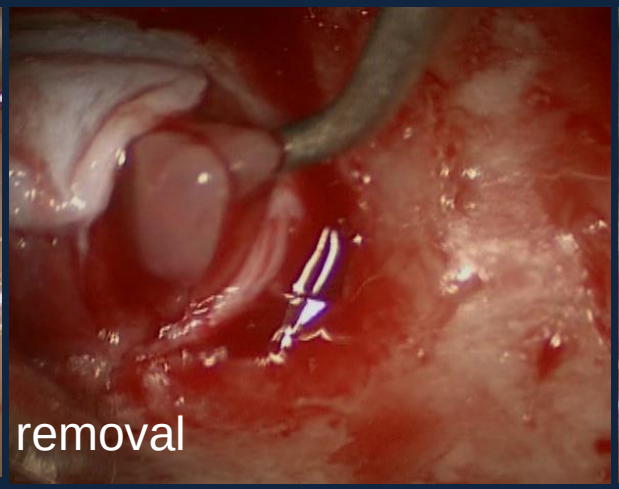
Sellar exposure & dural opening

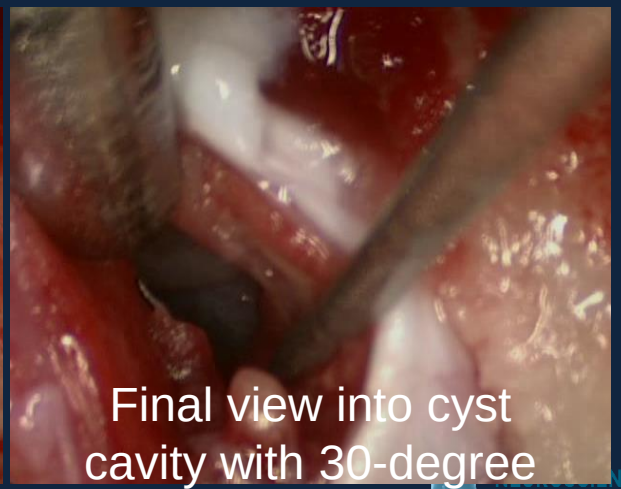


Gland incision to reach RCC



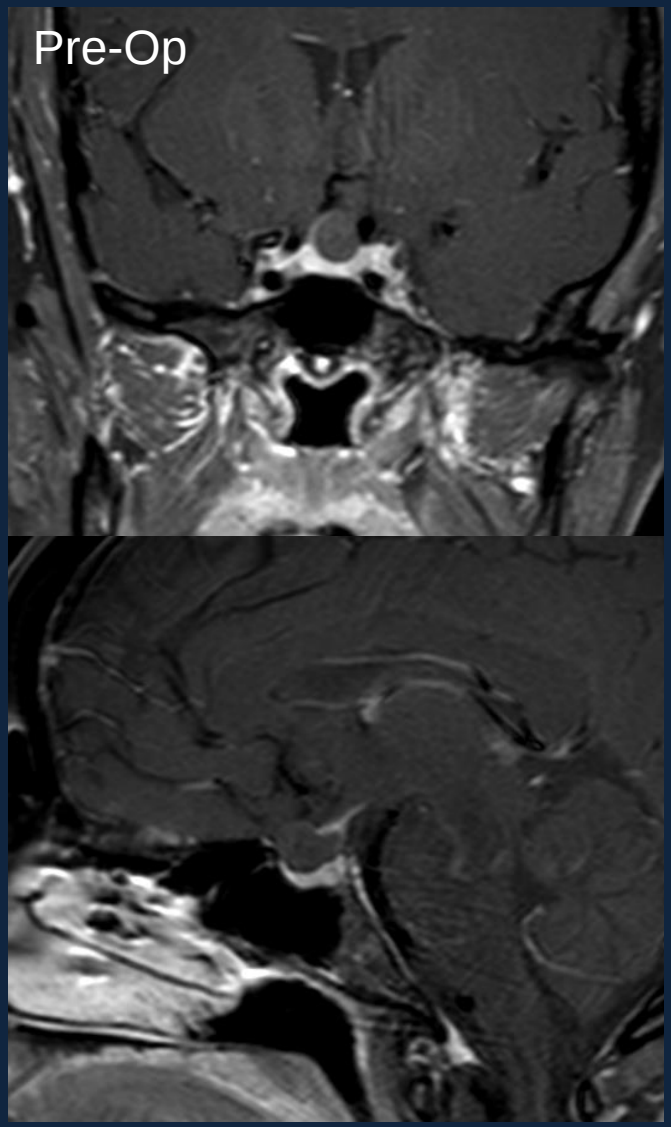
RCC removal

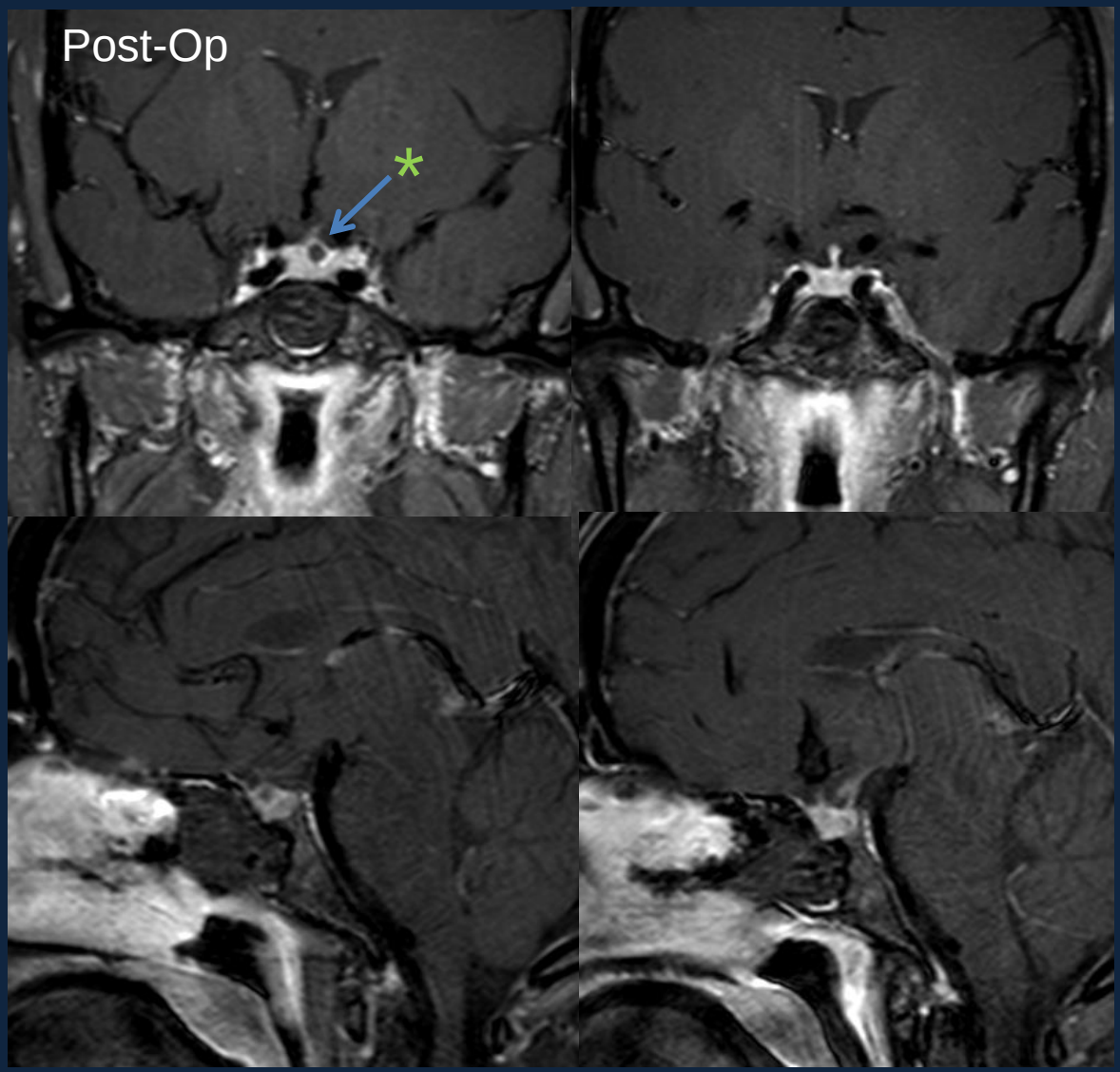




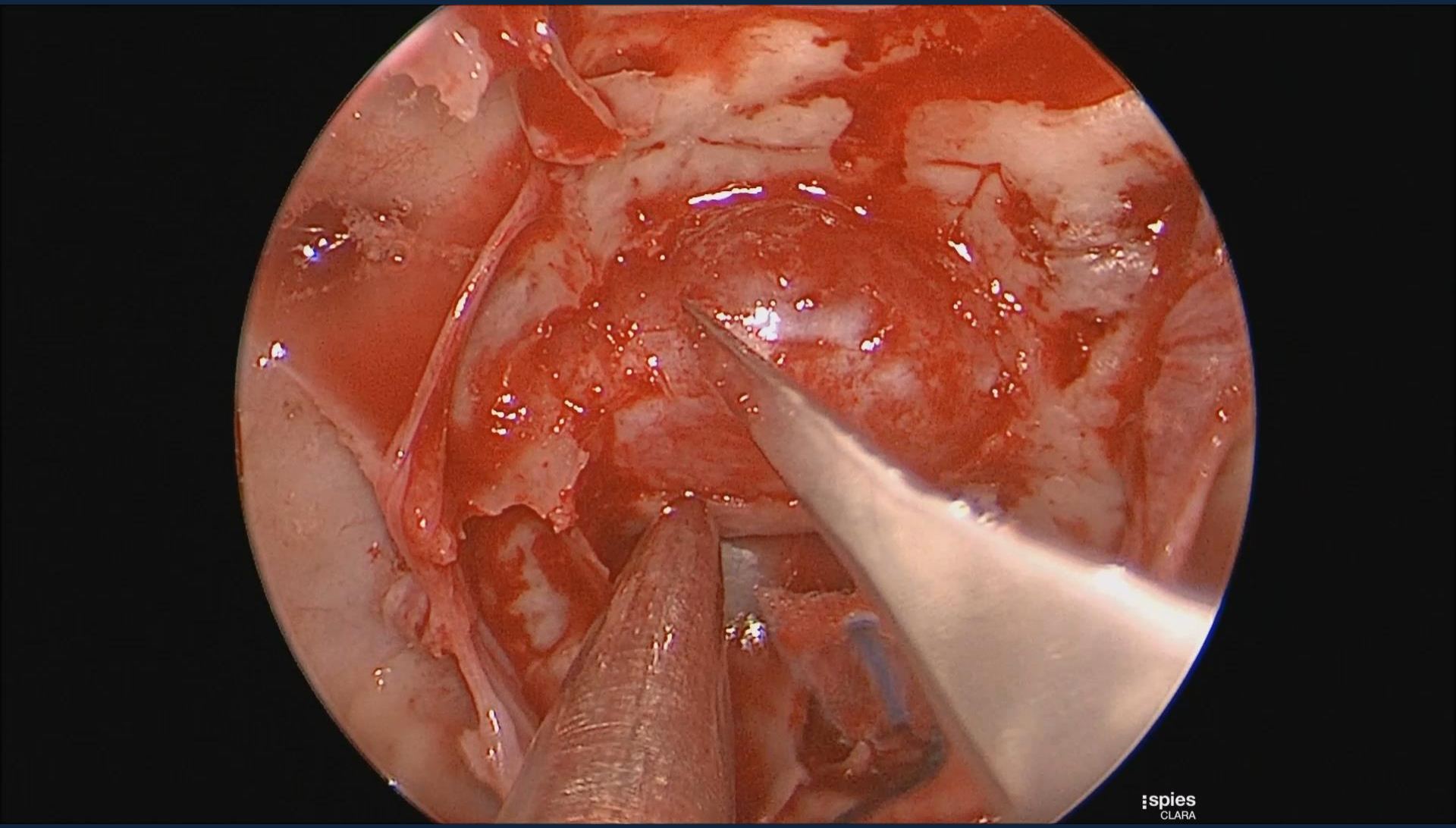
Final view into cyst cavity with 30-degree scope

Supraglandular Rathke's Cleft Cyst

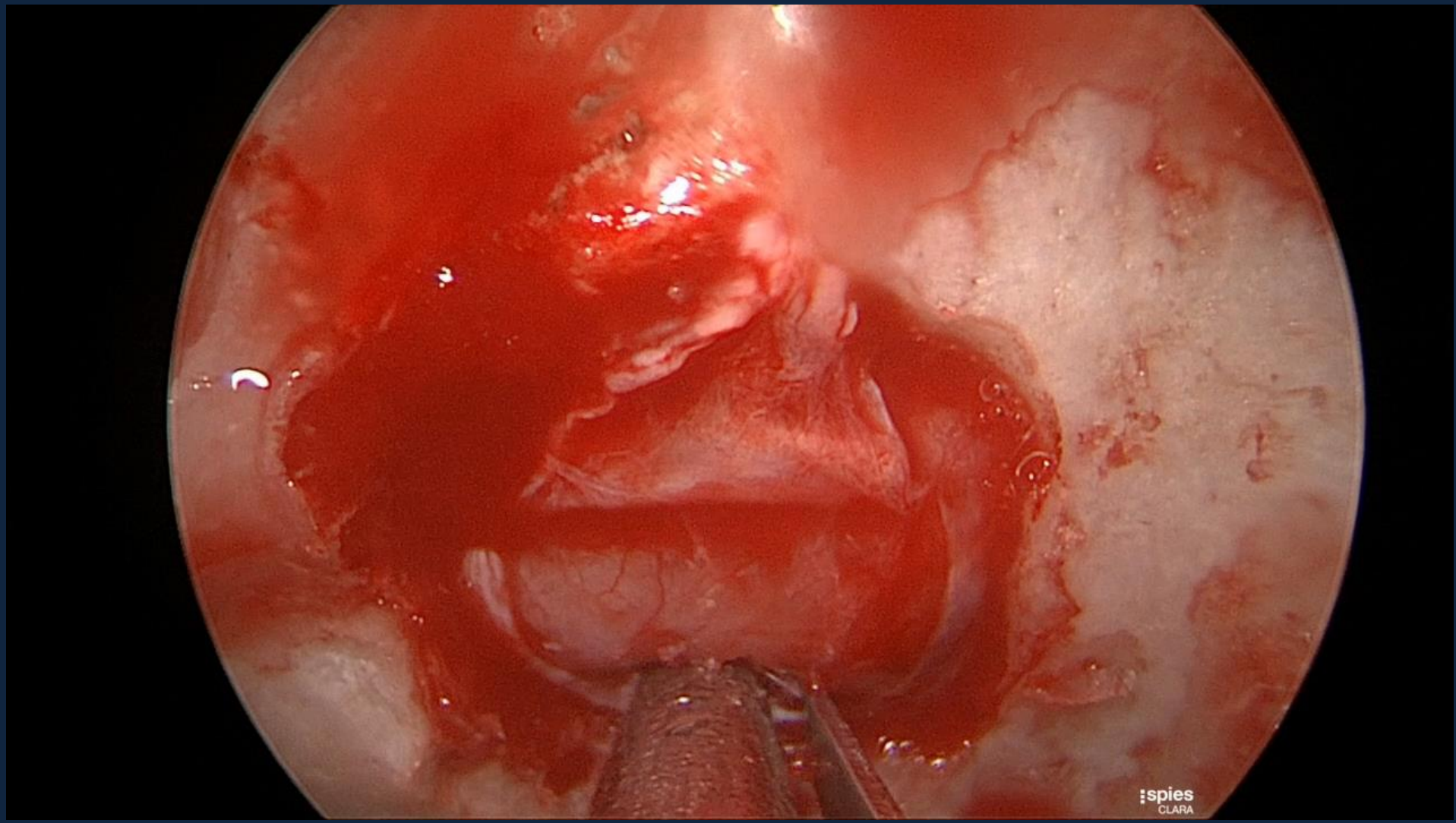




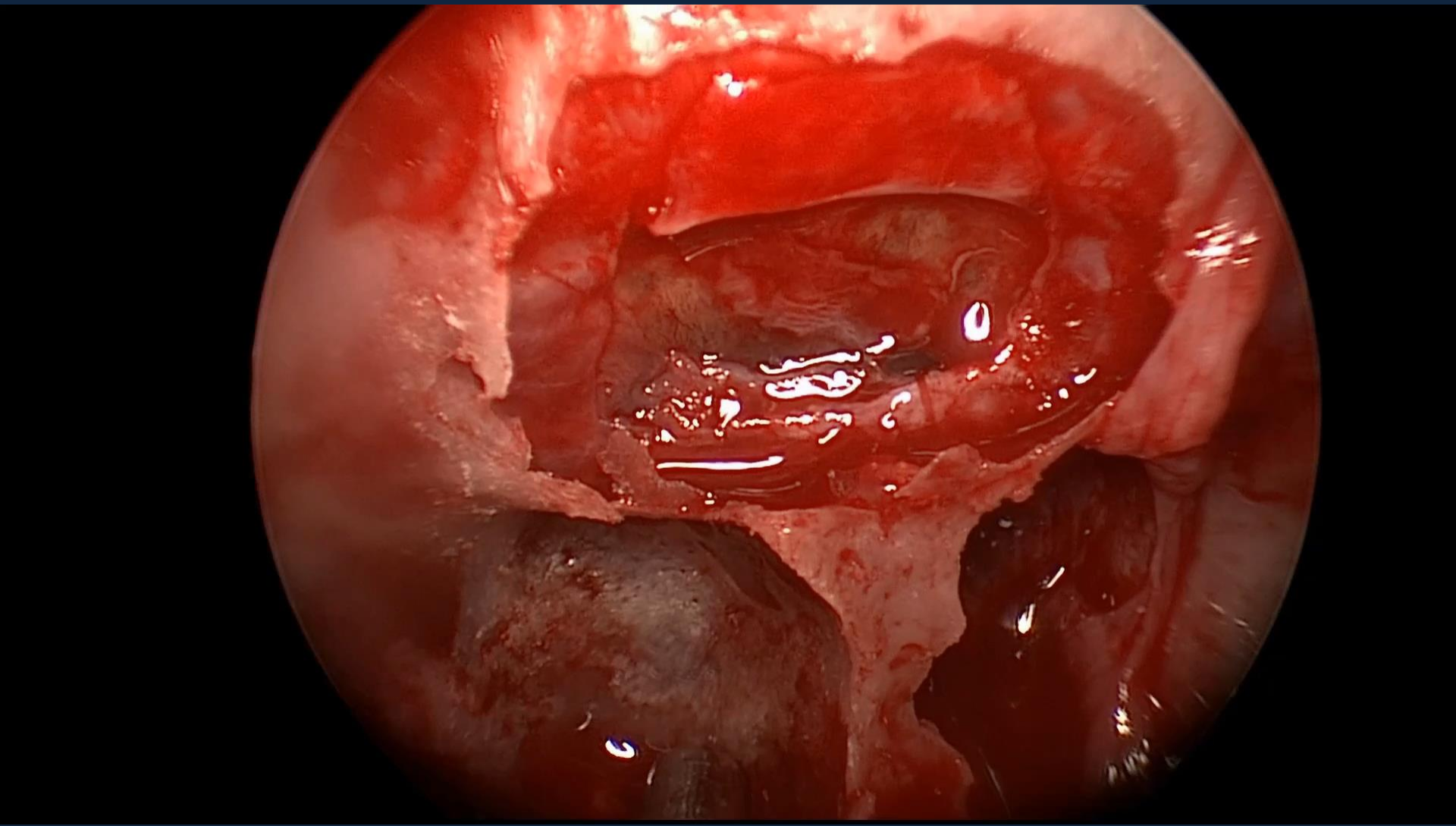
Rathke's Cleft Cyst



Rathke's Cleft Cyst



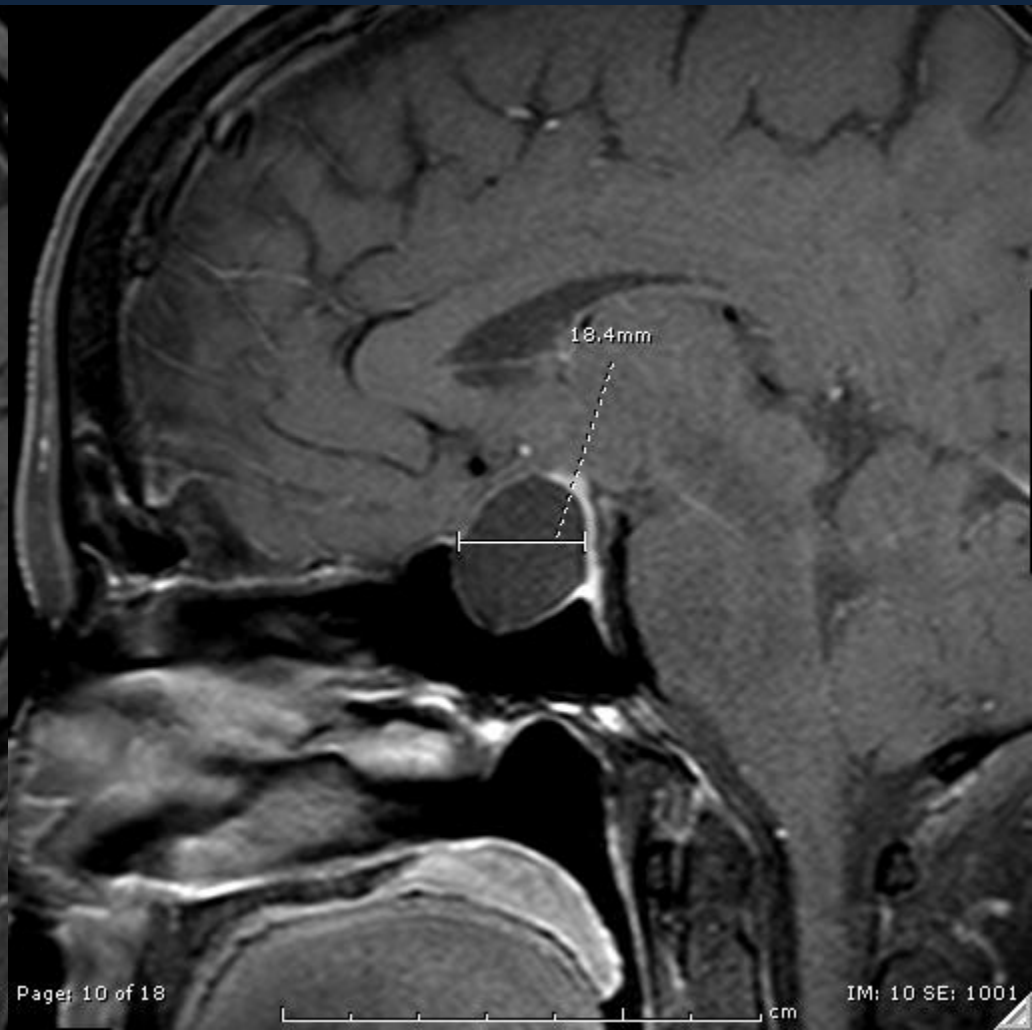
Rathke’s Cleft Cyst

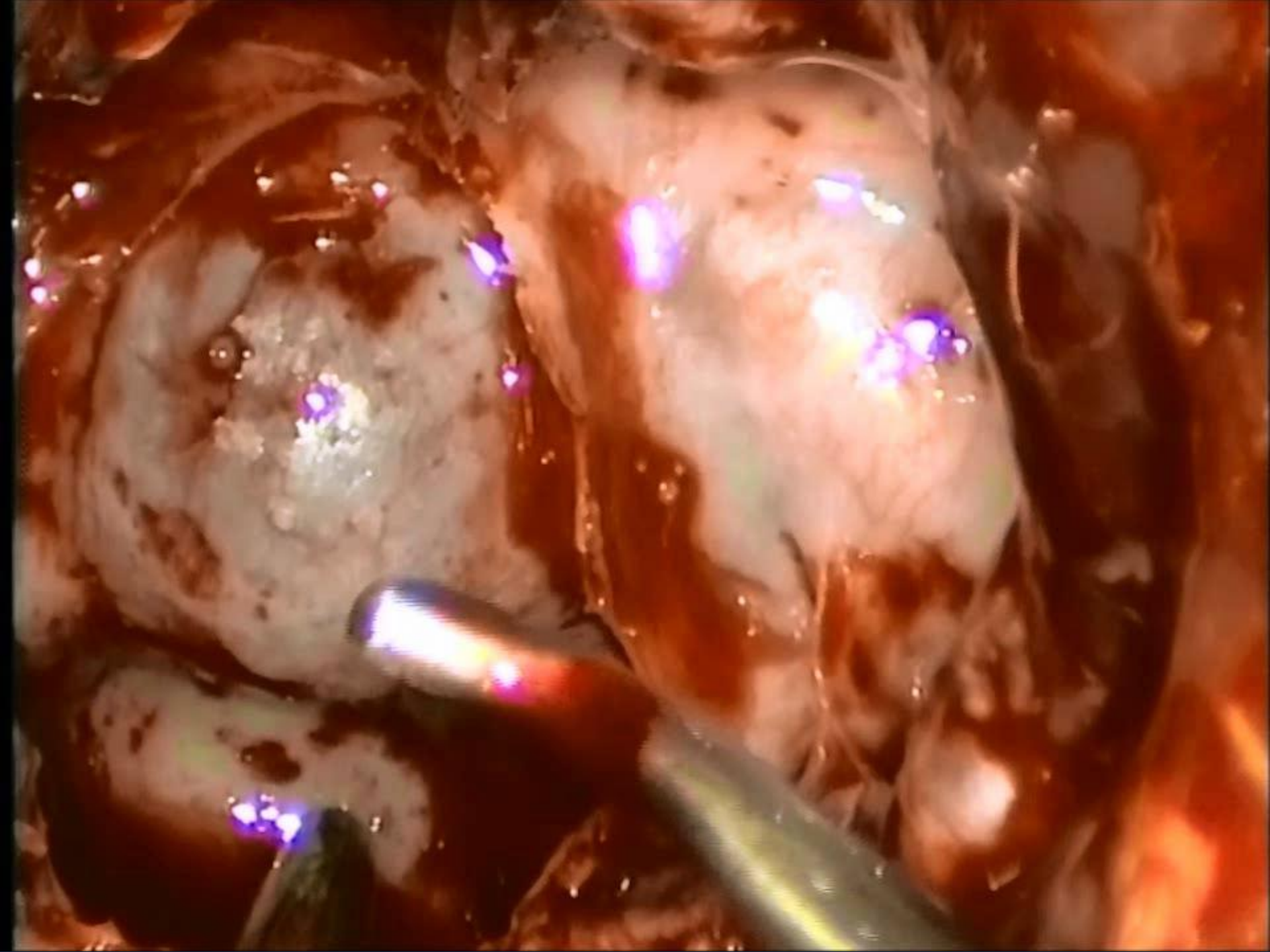


Arachnoid Cyst

- Incompetent diaphragm sella – effectively a contained CSF leak
- Cyst contains cerebrospinal fluid (CSF) and therefore follows CSF signal intensity on all MRI sequences (unlike Rathke's cleft cyst or epidermoid cyst).

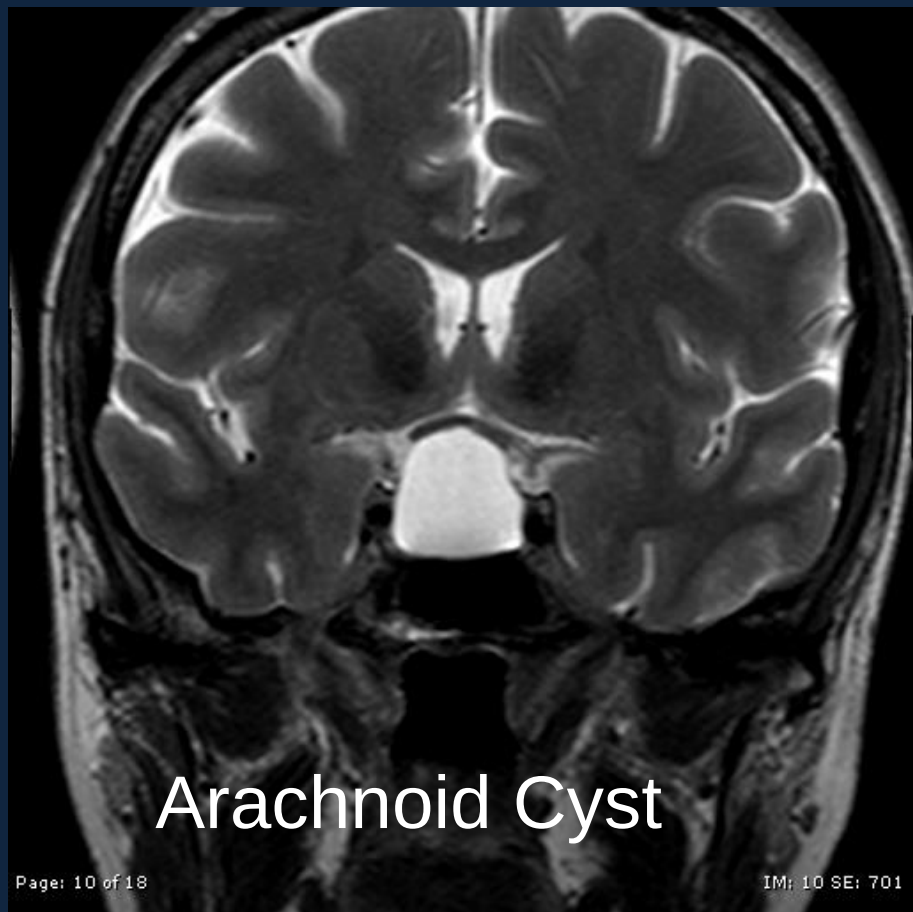
Arachnoid Cyst





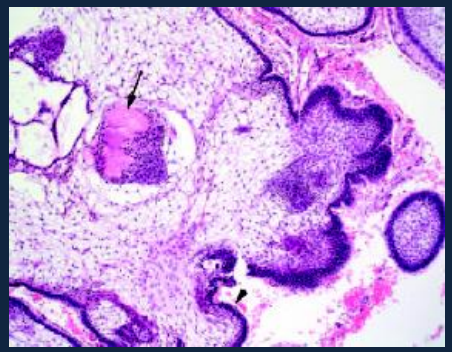
Empty Sella and Chiari I

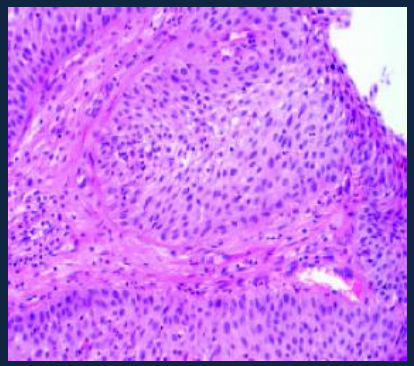
- Empty sella syndrome – non-iatrogenic cause of empty sella with pituitary dysfunction.
- Etiologies including CSF flow abnormalities (Chiari Malformation) or increased intracranial pressure (venous sinus thrombosis)



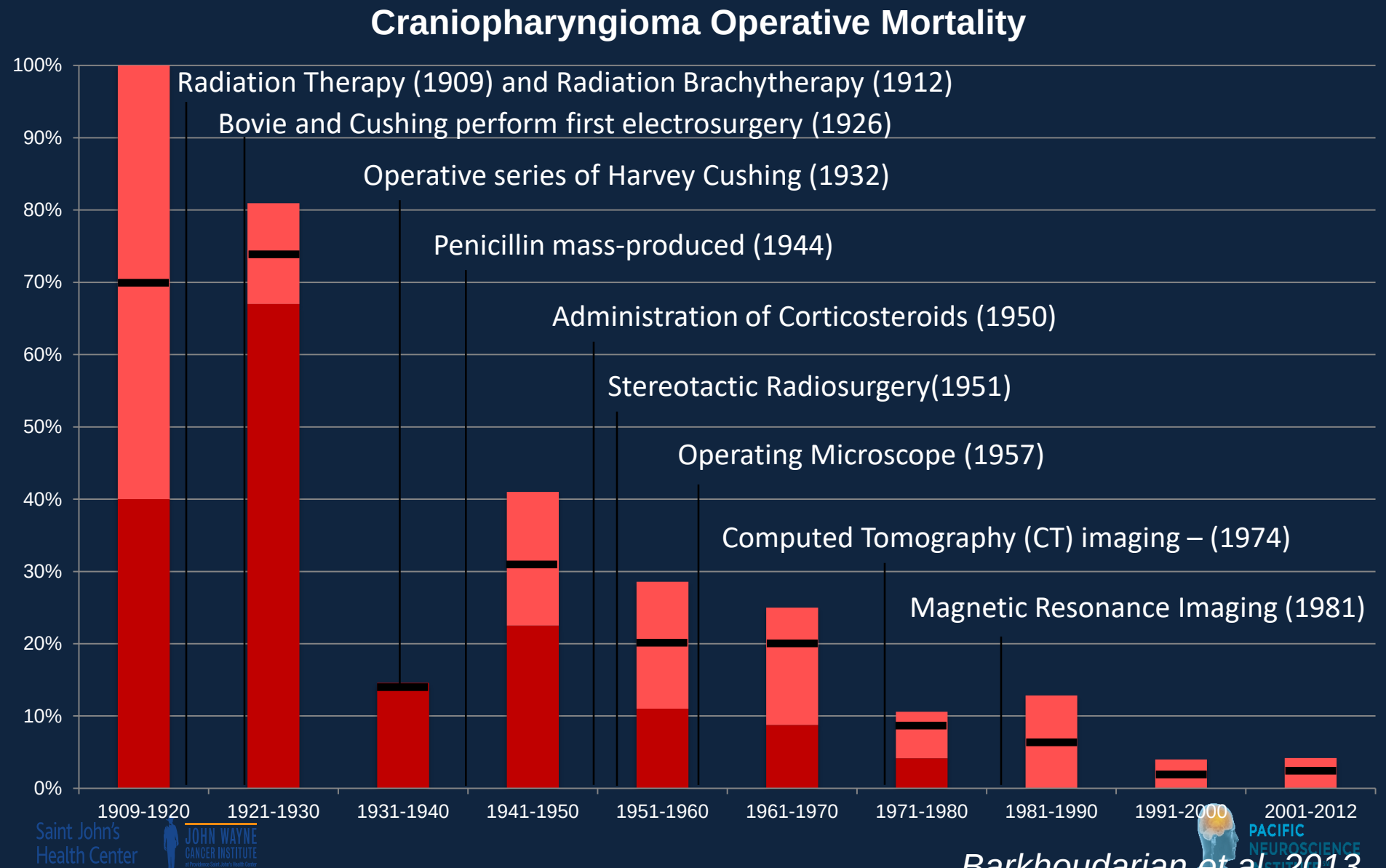
Craniopharyngioma

- 2 - 4% of primary brain tumors
- 10 - 15% of sellar and suprasellar tumors
- Bimodal age distribution: 5 – 15 yrs; 50 – 75 yrs
- Most common non-glial neoplasm in pts under 20 yrs
- Comprise 55% of sellar / suprasellar tumors in children
- Adamantinomatous – more common, younger age, often calcified, more invasive
- Papillary – less common, older age, rarely calcified, less invasive





History



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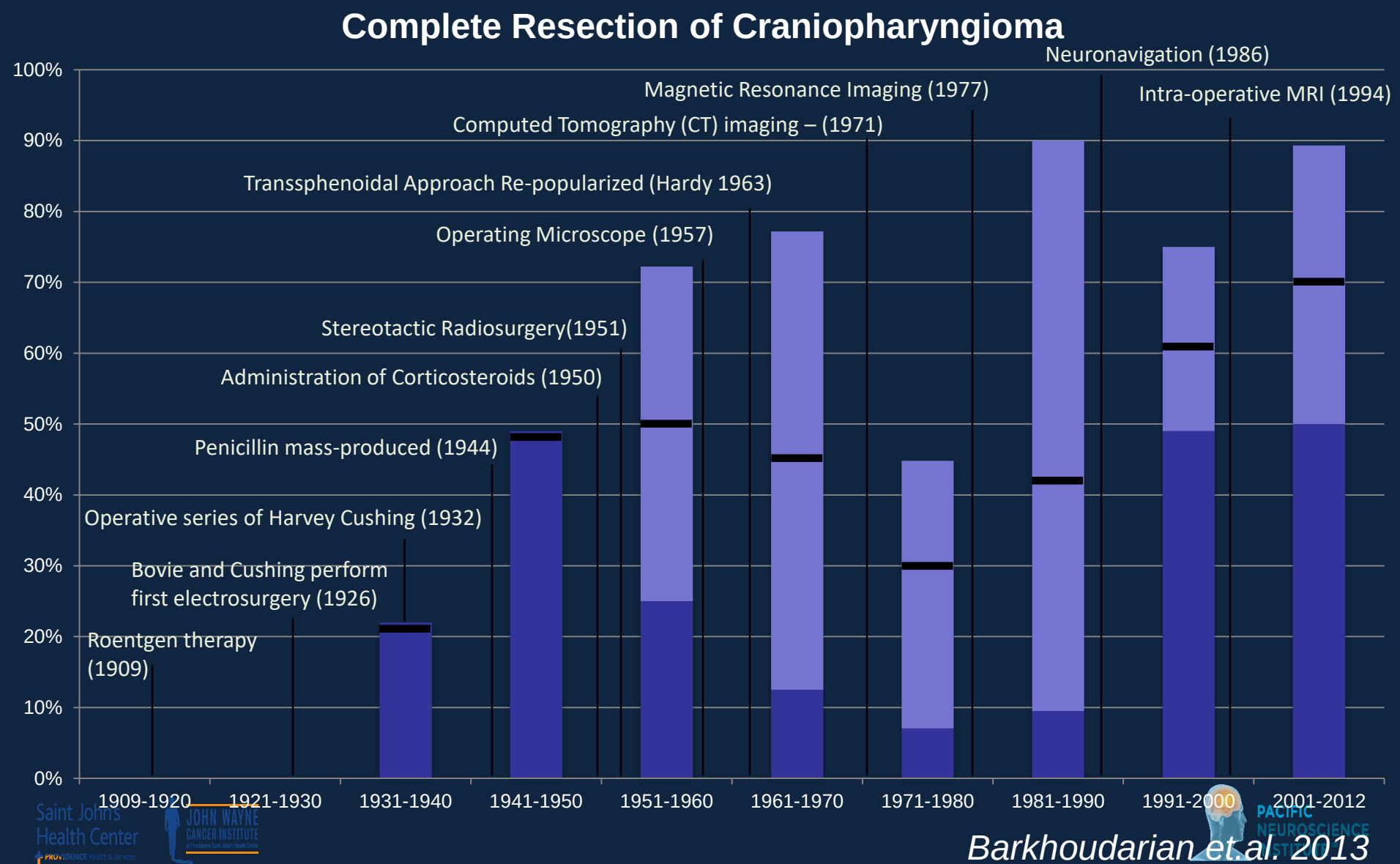
Barkhoudarian et.al. 2013

History



Barkhoudarian et.al. 2013

Wide-ranging Surgical Philosophies

Transsphenoidal approach: 39% Wilson vs 10% Yasargil

Surgical management of craniopharyngiomas

A review of 74 cases

DAVID S. BASKIN, M.D., AND CHARLES B. WILSON, M.D.

Department of Neurosurgery, Baylor College of Medicine, Houston, Texas, and Department of Neurological Surgery, University of California, San Francisco, California

Journal of Neurosurgery, 1986

10% GTR
90% received RT
91% in remission
93% improved vision
2% worsened vision
23% new perm DI
3% mortality

90% GTR
4% received RT
64% good outcome
67% improved vision
15% worsened vision
58% perm DI
17% mortality

Total removal of craniopharyngiomas

Approaches and long-term results in 144 patients

M. GAZI YAŞARGIL, M.D., MARIJAN CURCIC, M.D., MIRJANA KIS, M.D., GERTRUD SIEGENTHALER, M.D., PETER J. TEDDY, F.R.C.S., AND PETER ROTH

Departments of Neurosurgery and Internal Medicine, and Institute of Anesthesiology, University Hospital of Zurich, Zurich, Switzerland

Journal of Neurosurgery, 1990

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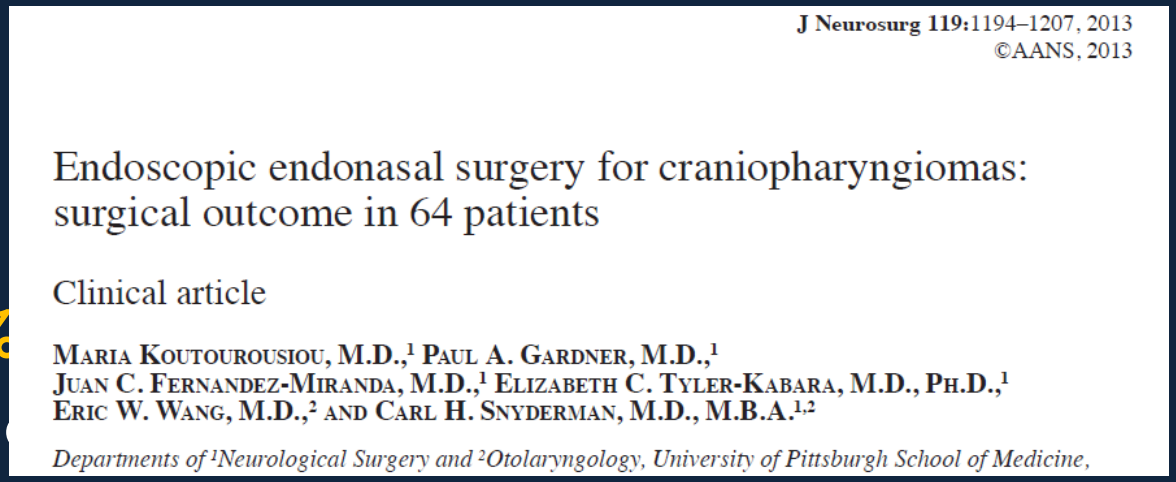
Endoscopic Endonasal vs Microscopic Transsphenoidal and Open Transcranial Resection of Craniopharyngiomas

World Neurg 2012 Komotar et al

- Medline search 1995-2010; 88 studies, 3470 patients
- Endoscopic compared to open cohort:
  - higher GTR (67% vs 48%; P < 0.003)
  - visual improvement (56% vs. 33%; P < 0.003)
- Transsphenoidal cohort similar outcomes to endoscopic.
- CSF leak rate higher in endoscopic (18%) and transsphenoidal (9.0%) than transcranial groups (2.6%; P < 0.003)
- Transcranial group: greater rate of seizure (8.5%), which did not occur in endonasal or transsphenoidal groups (P<0.003).



J Neurosurg 119:1194–1207, 2013
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Endoscopic endonasal surgery for craniopharyngiomas: surgical outcome in 64 patients

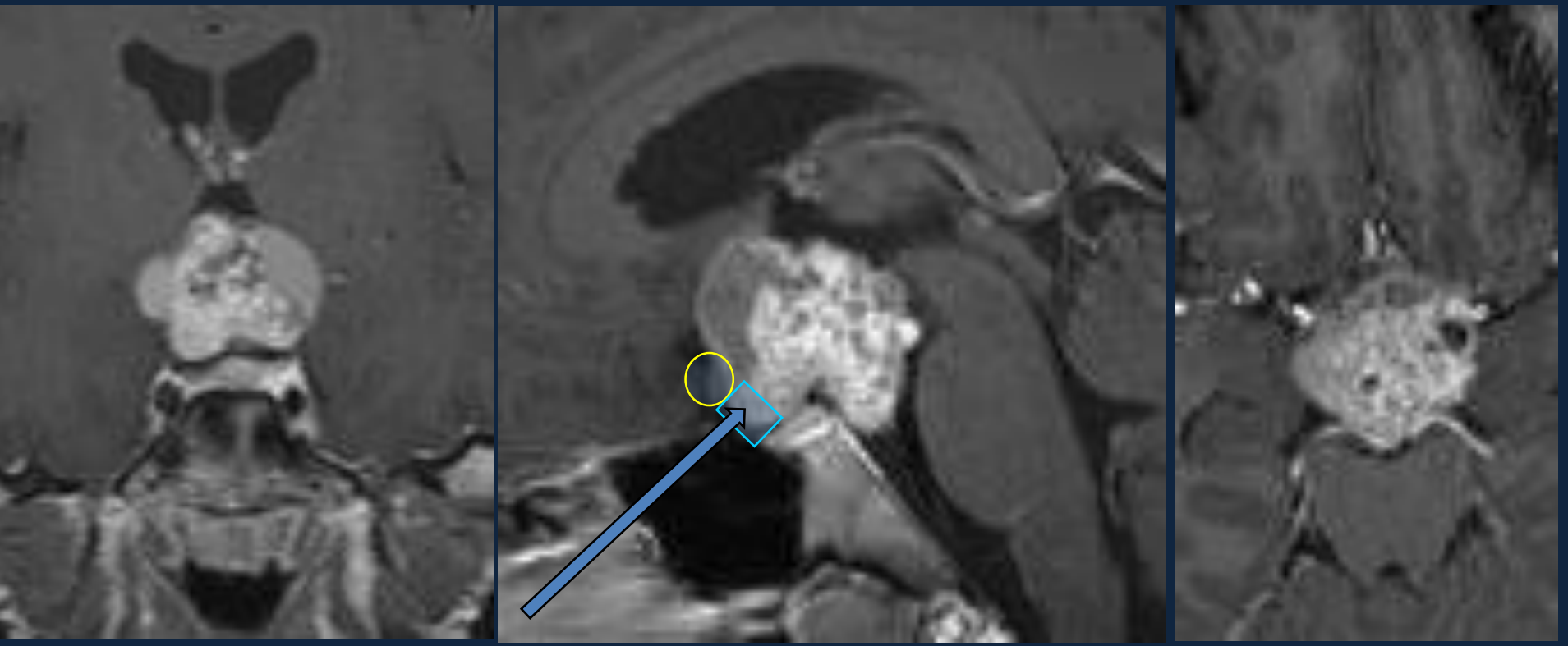
Clinical article

Maria Koutourousiou, M.D.,[1] Paul A. Gardner, M.D.,[1]
Juan C. Fernandez-Miranda, M.D.,[1] Elizabeth C. Tyler-Kabara, M.D., Ph.D.,[1]
Eric W. Wang, M.D.,[2] and Carl H. Snyderman, M.D., M.B.A.[1,2]

Departments of [1]Neurological Surgery and [2]Otolaryngology, University of Pittsburgh School of Medicine,

- 64 pts (1
- **GTR 38%**
- Hormon
  - Improved in 20%, worsened in 32.5%
  - In 24 with normal preop endocrine - 58% worsened;
  - DI developed in 47%
- CSF leak rate 23% (decreased to 10.6% in recent cases)
- Meningitis 8%
- No visual worsening or mortality
- Tumor recurrence in 34%

Craniopharyngioma



Retro-chiasmal Location

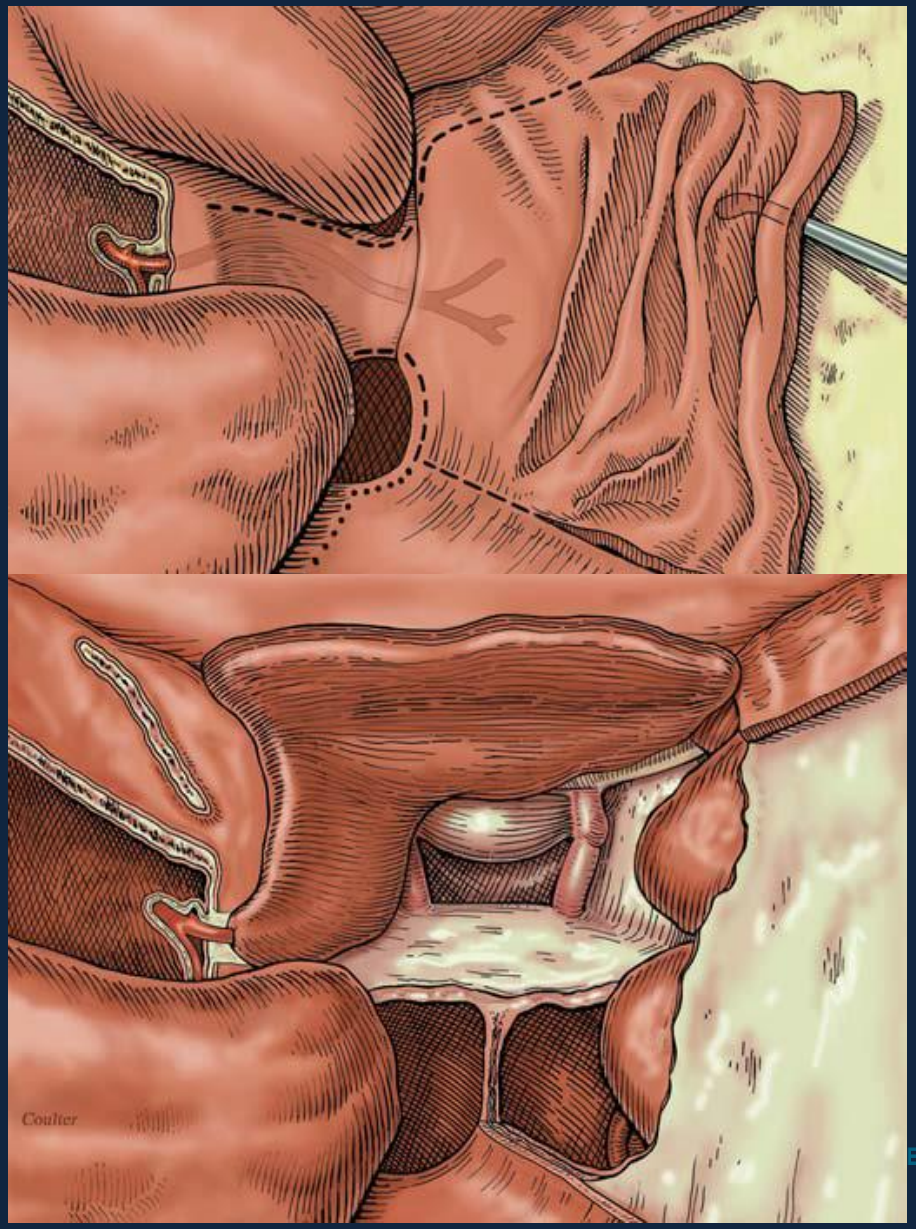
Pedicled Flap Closure

Pedicled vascular mucosal flaps have improved CSF leak rates

- ~15% to ~3-5% (0% at one institution)

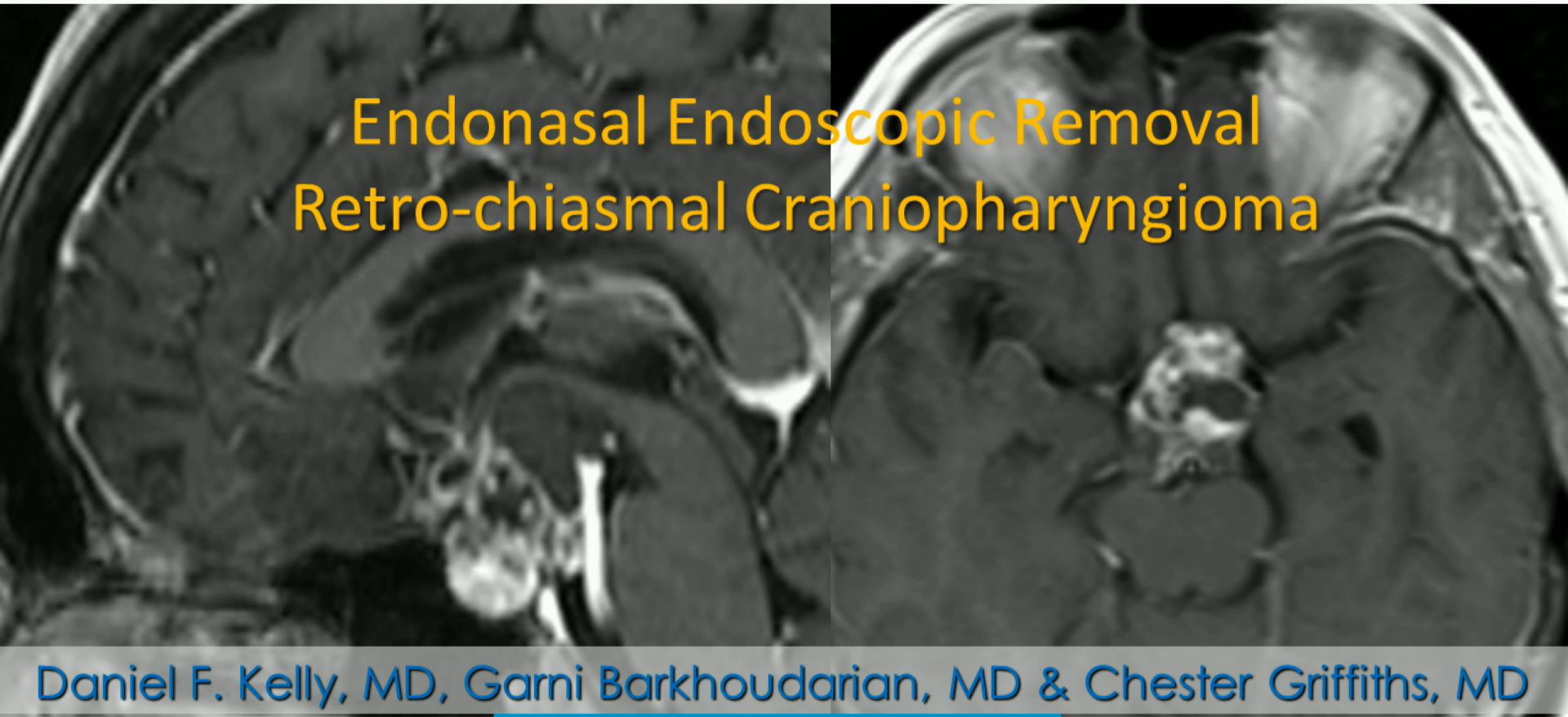
Flap Options:

- Nasoseptal Flap
- Middle Turbinate Flap
- Trap Door Flap
- Pericranial Flap
- Temporalis transposition Flap



Kassam et.al. 2008

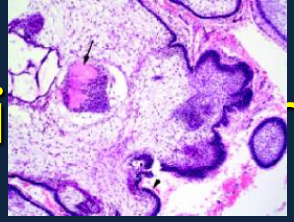
Extended Transplanar Approach

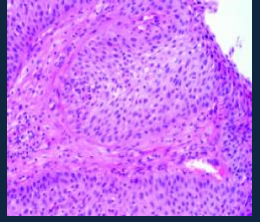


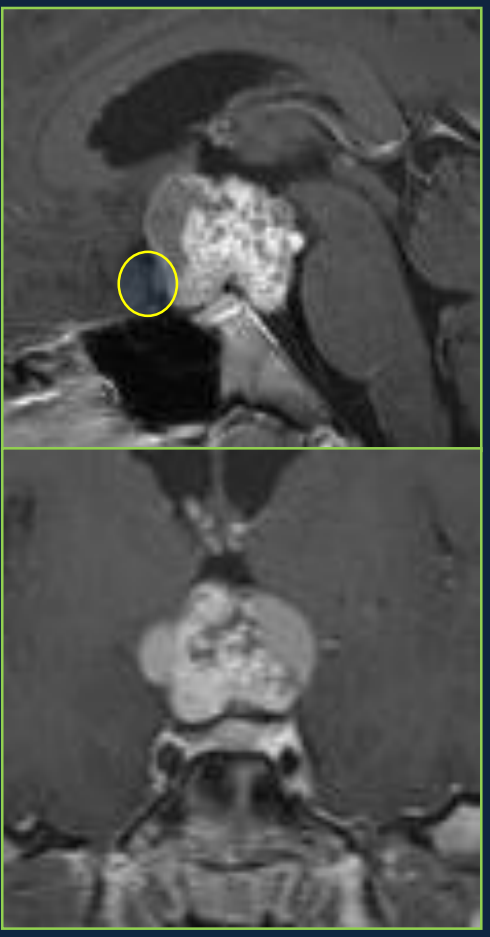
Daniel F. Kelly, MD, Garni Barkhoudarian, MD & Chester Griffiths, MD

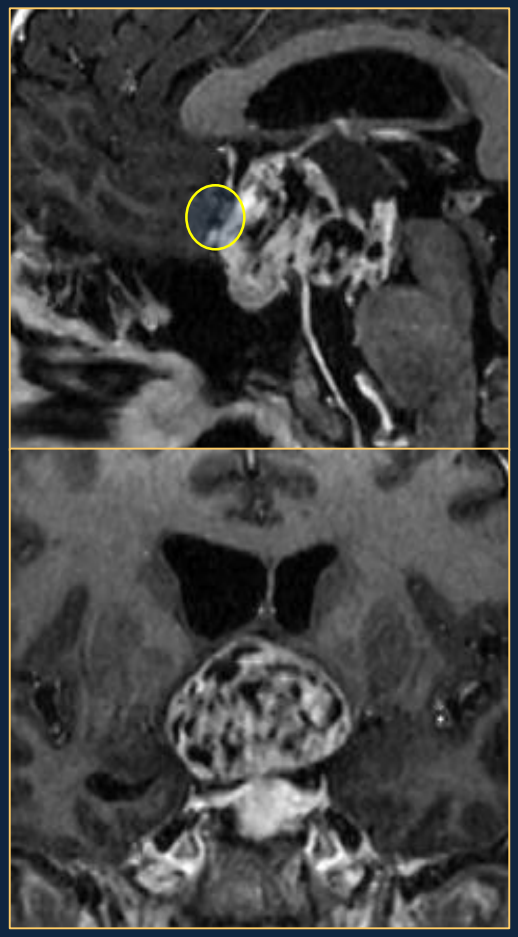
PACIFIC
BRAIN TUMOR CENTER
Pituitary Disorders Program

Crani ngioma









Endonasal

Endonasal

Endonasal

Either Approach

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Endonasal versus Supraorbital Keyhole Removal of Craniopharyngiomas and Tuberculum Sellae Meningiomas

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OBJECTIVE: Endonasal and supraorbital "eyebrow" craniotomies are increasingly being used to remove craniopharyngiomas and tuberculum sellae meningiomas. Herein, we assess the relative advantages, disadvantages, and selection criteria of these 2 keyhole approaches.

METHODS: All consecutive patients who had endonasal or supraorbital removal of a craniopharyngioma or tuberculum sellae meningioma were analyzed.

RESULTS: Of 43 patients, 22 had a craniopharyngioma (18 endonasal, 4 supraorbital), and 21 had a meningioma (12 endonasal, 7 supraorbital, 2 both routes); 33% had prior surgery. Craniopharyngiomas were primarily retrochiasmal in location in 78% of endonasal cases versus 25% of supraorbital cases ($P = 0.08$). Meningiomas were larger when approached by the supraorbital route versus the endonasal route (33 ± 10 versus 25 ± 8 mm, respectively; $P = 0.008$). Endoscopy was used in 84% of endonasal approaches and in 31% of supraorbital approaches ($P = 0.001$). Of patients having first-time surgery for a craniopharyngioma (n = 14) or meningioma (n = 15), total/near total removal was achieved in 83% and 80% of patients by the endonasal route and in 50% and 80% of patients by the supraorbital route, respectively. Vision improved in

Endonasal route preferred for most retrochiasmal craniopharyngiomas; Supraorbital route recommended for meningiomas > 30-35 mm or with growth beyond supraclinoid carotids.

For smaller midline tumors, either approach may be used

is a narrow surgical corridor. The endonasal approach has the added challenges of

Endonasal approach has the added challenges of restricted lateral suprasellar access, an essential need for endoscopy and a more demanding skull base repair.

Neurosurgery 64[ONS Suppl 2]:ons000–ons000, 2009 DOI: 10.1227/01.NEU.0000327857.22221.53

Received, April 14, 2008.

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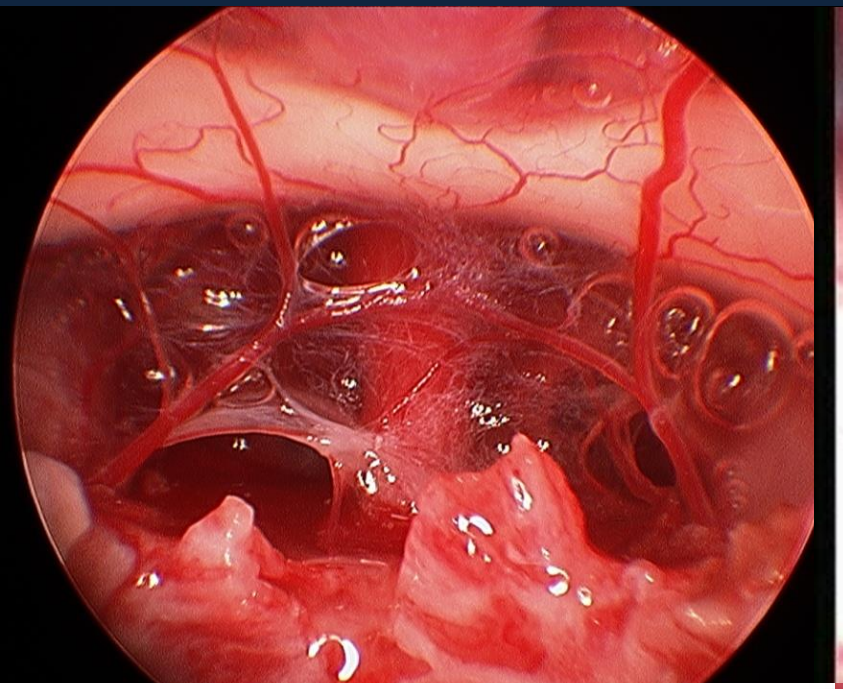

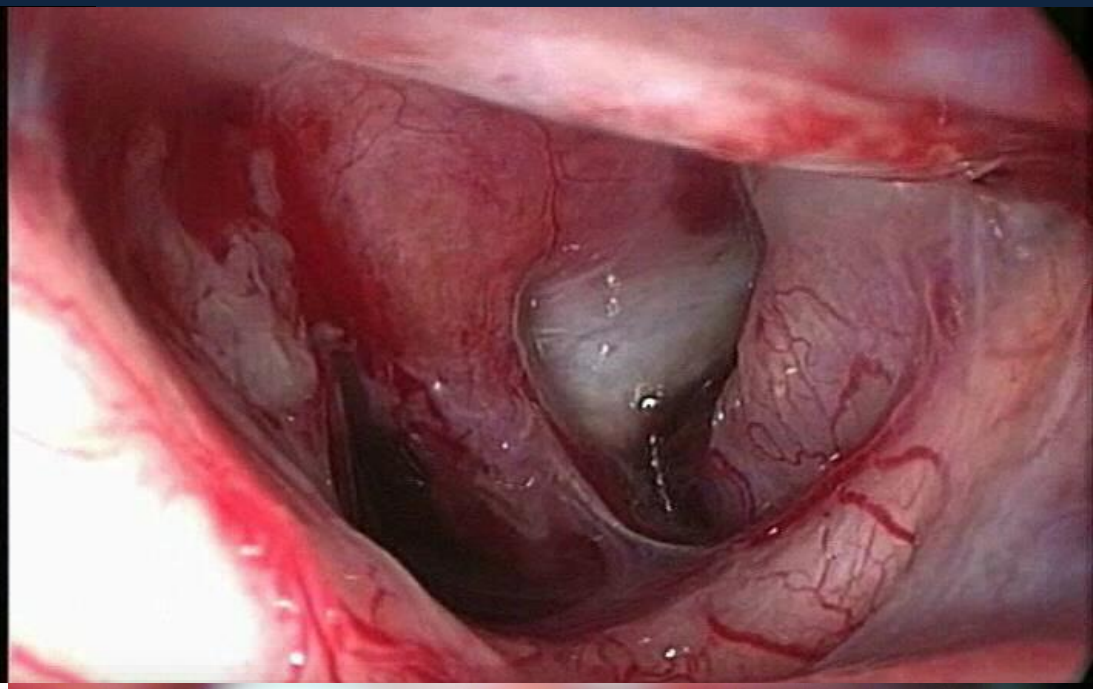

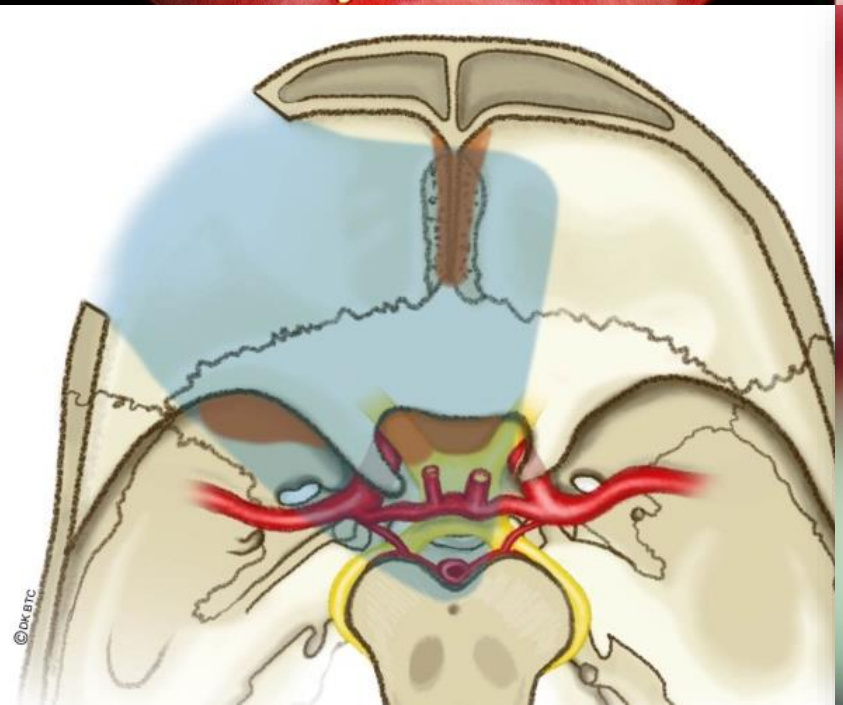
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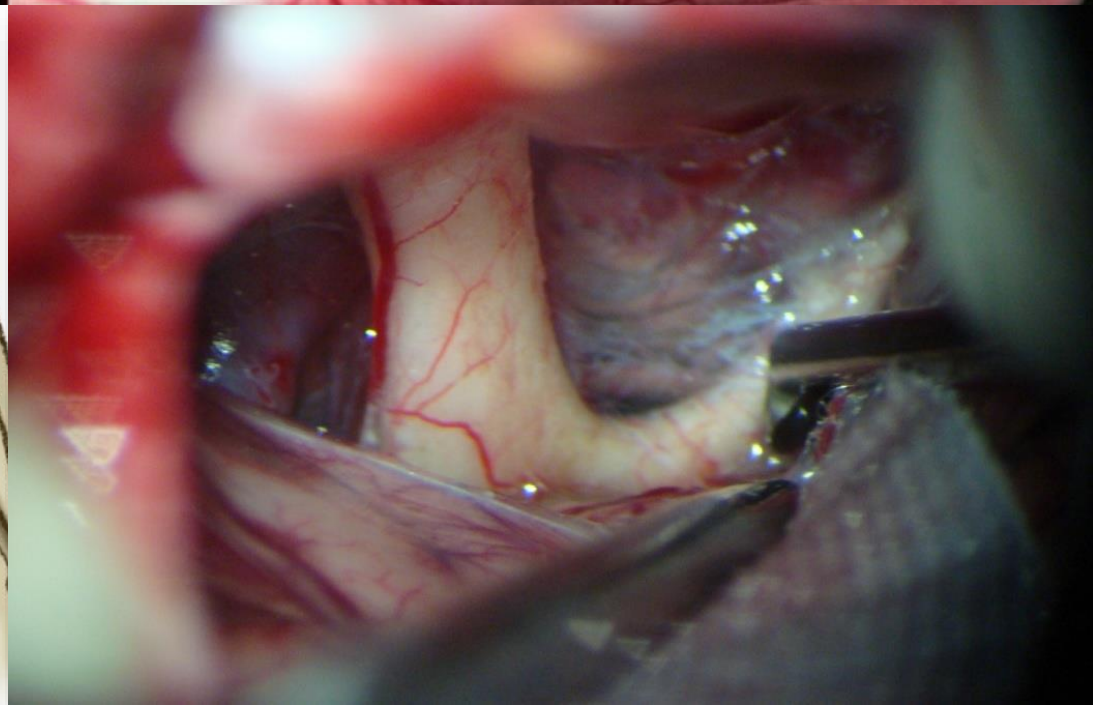
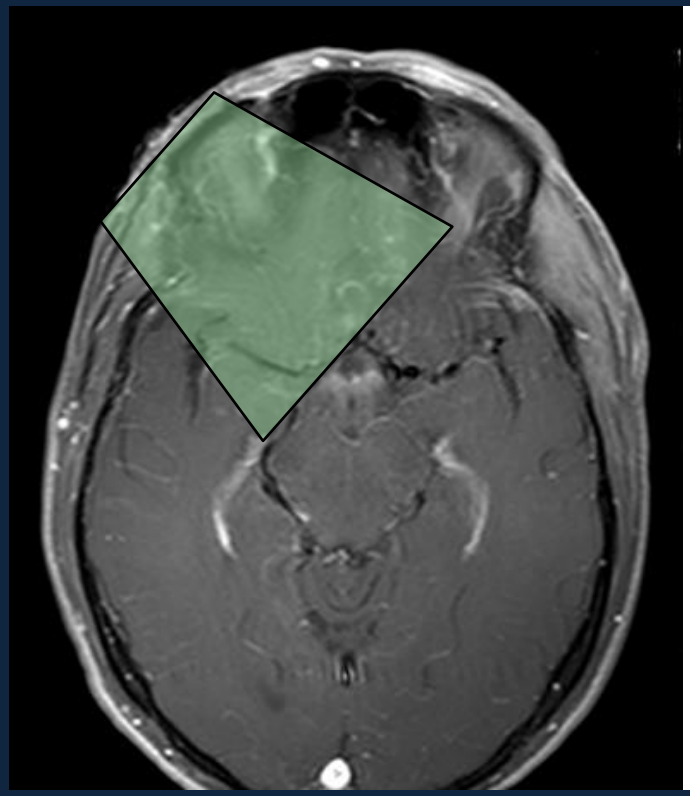
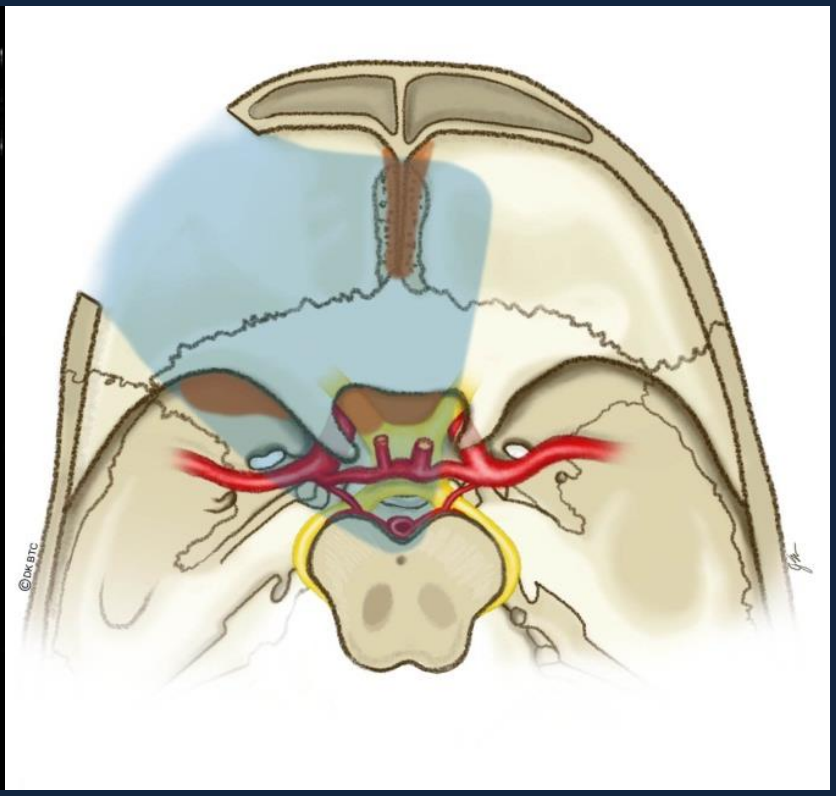


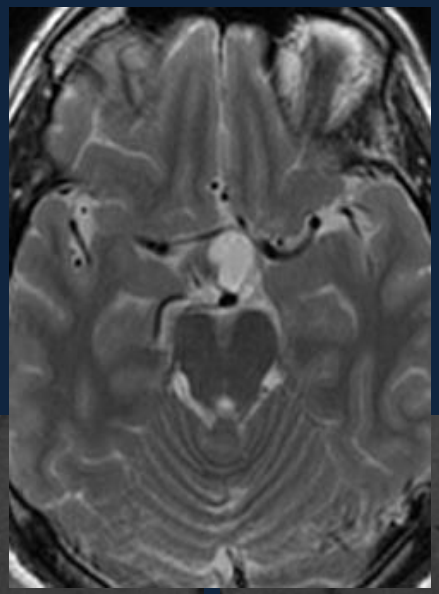
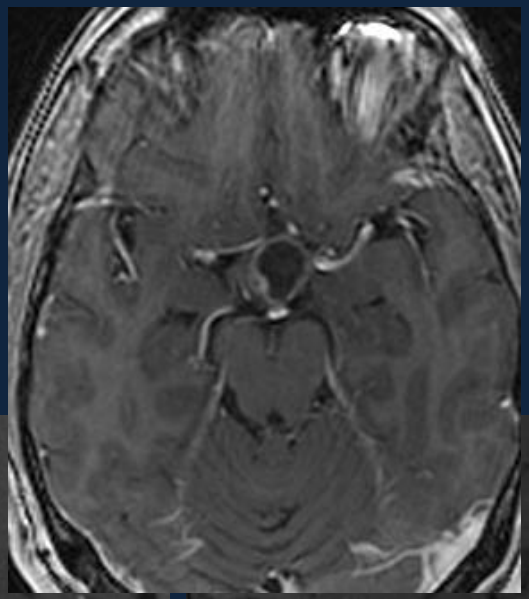
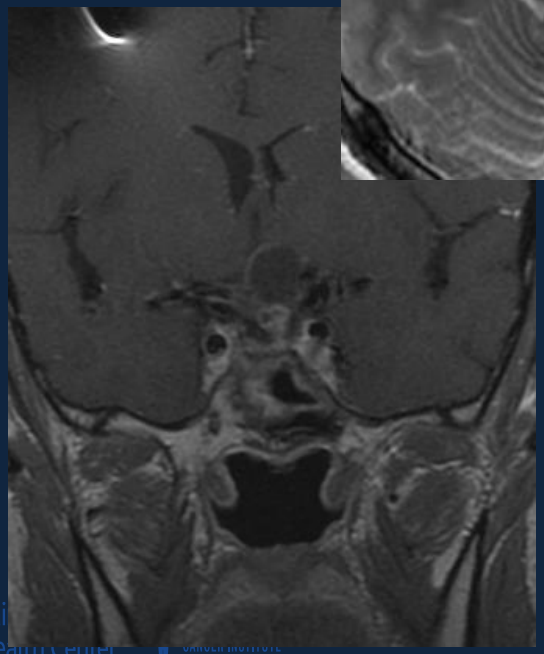
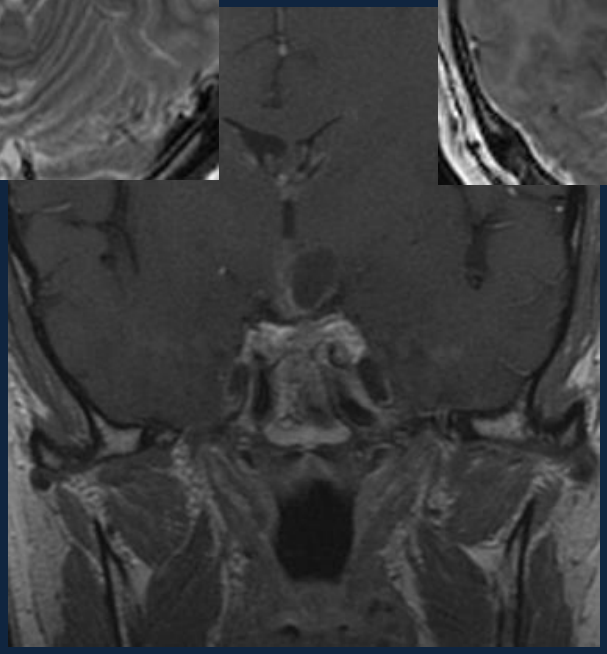
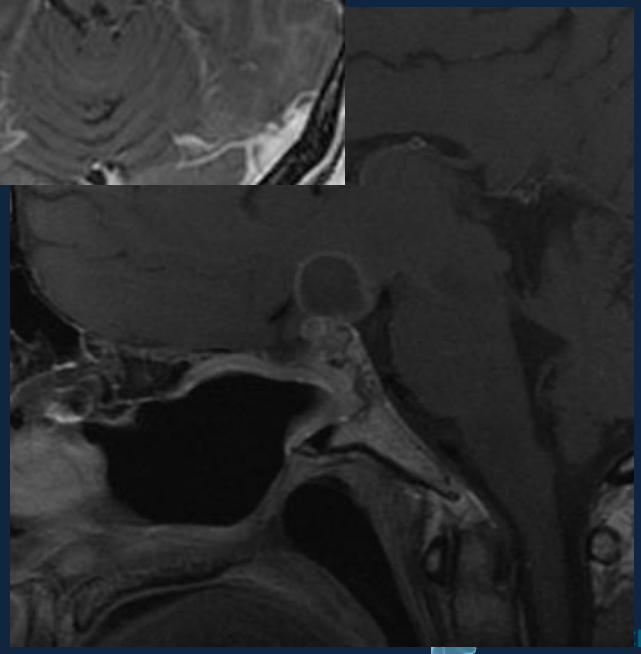
Supraorbital Eyebrow Craniotomy

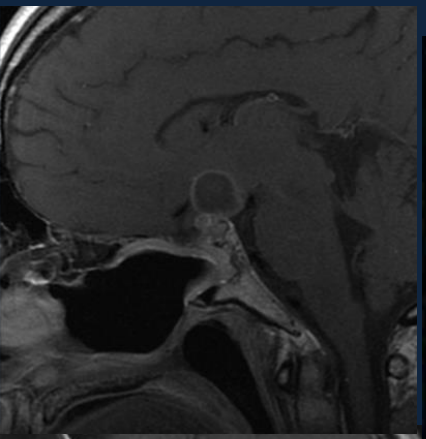


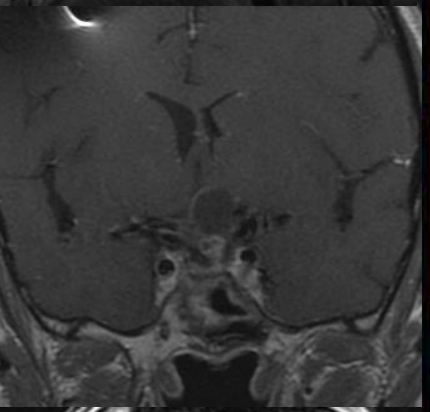


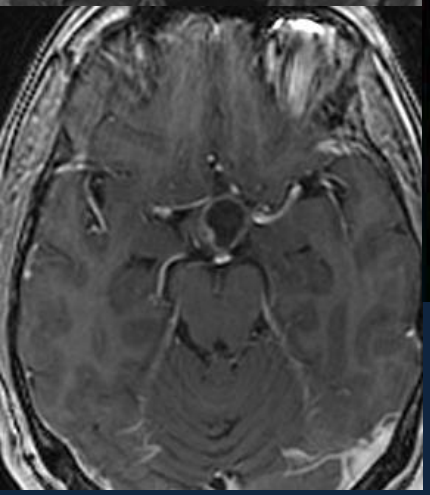
- "Sweet-spot" of fronto-temporal craniotomy
- Entry point on floor of frontal fossa
- Exposure of frontal fossae, parasellar & perisylvian regions
- Ideal for craniopharyngiomas with lateral parasellar and prechiasmal extension, and some reoperative cases

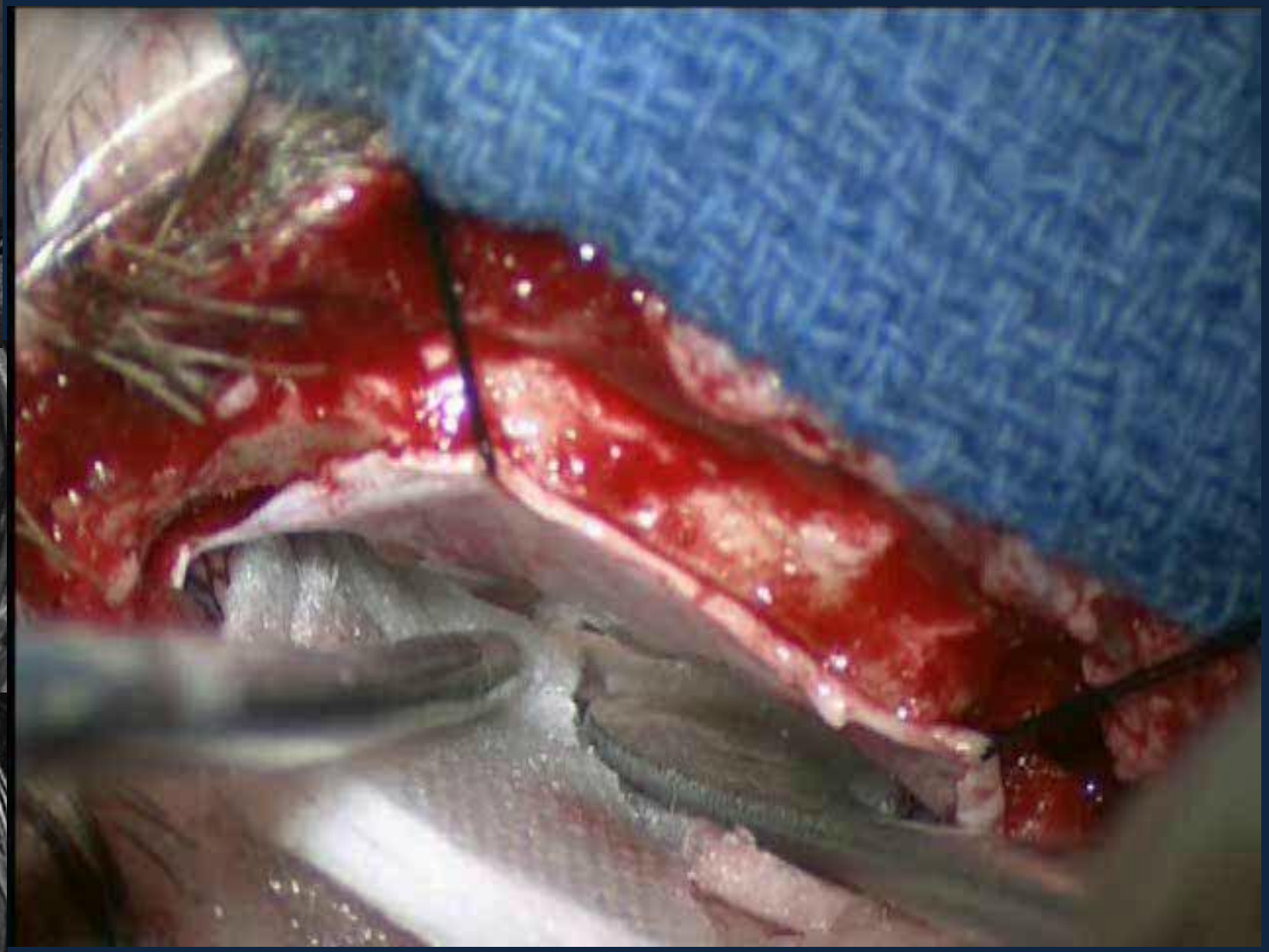
- 51 yr old man with recurrent craniopharyngioma
- Multiple EEAs and intra-cavitary radiotherapy
- Progressive visual loss with increased cyst size









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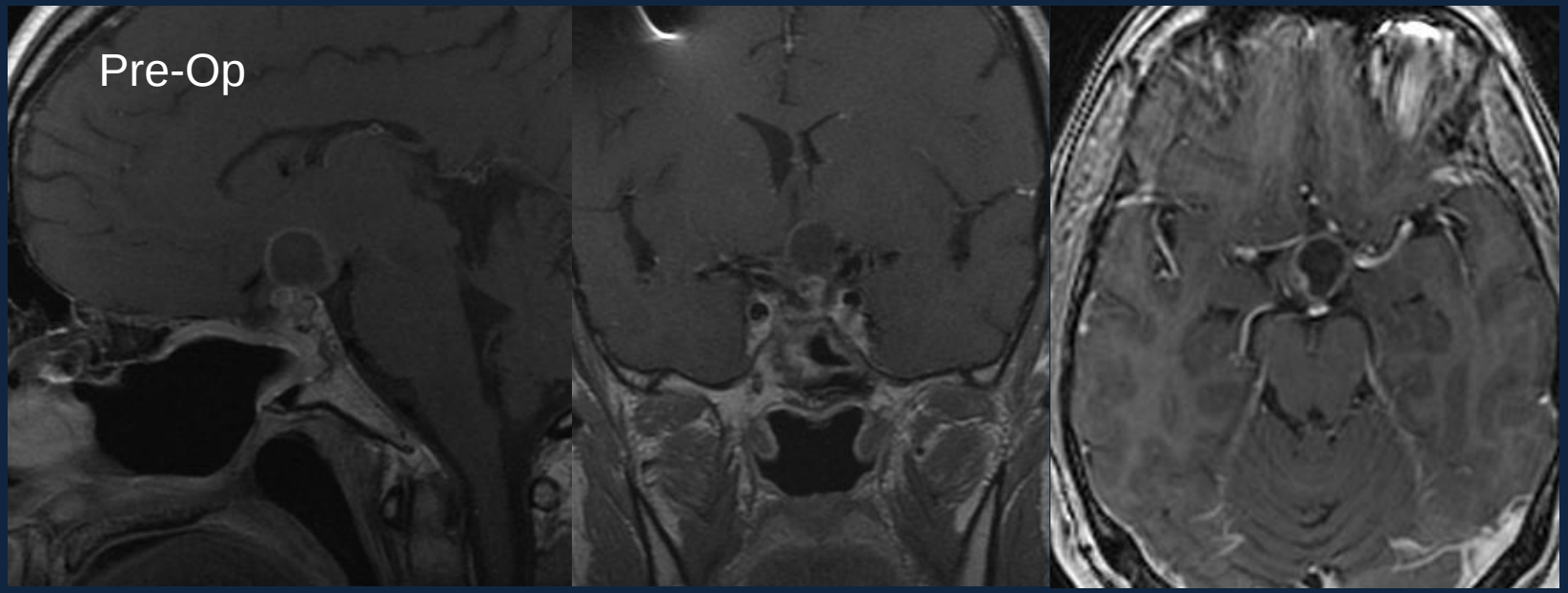
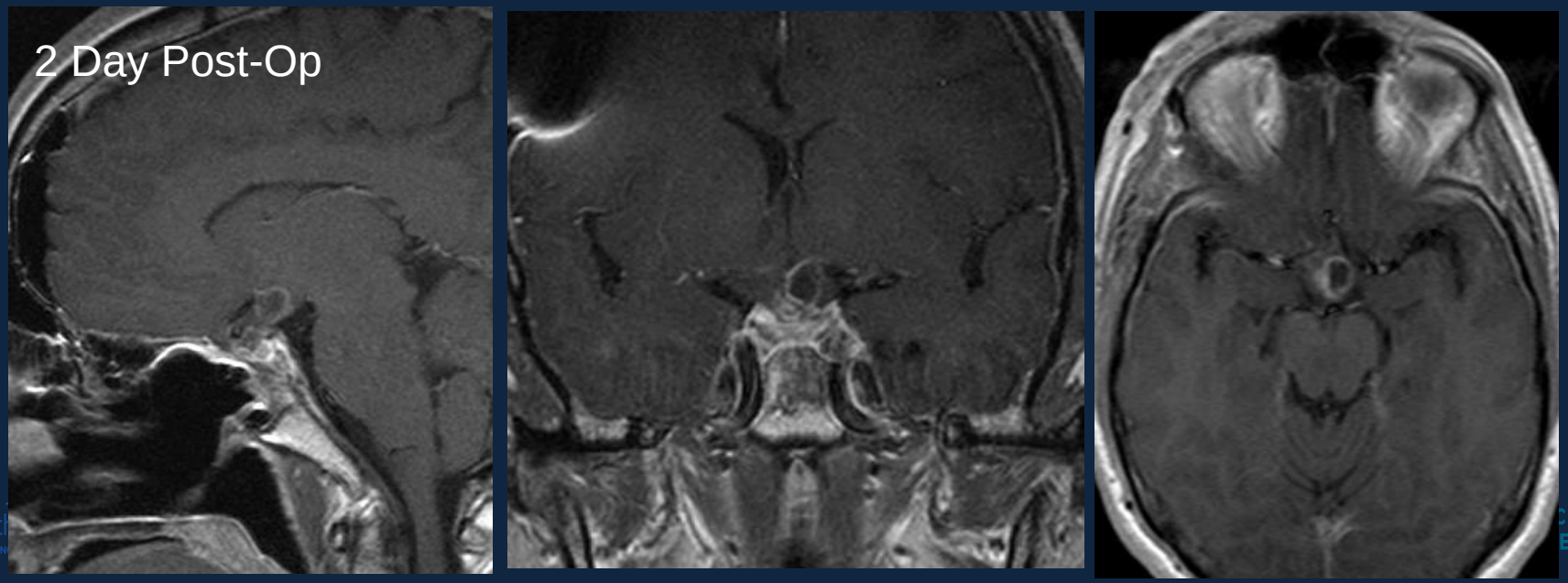
Recurrent Craniopharyngioma





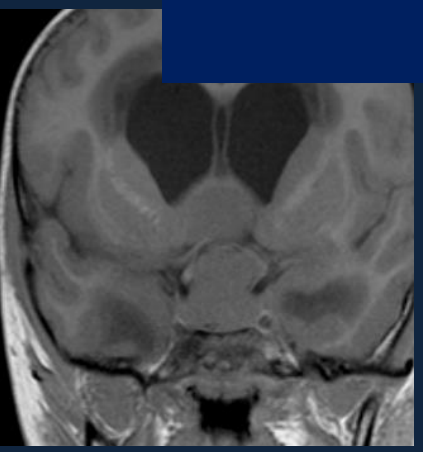
Supraorbital Eyebrow Craniotomy

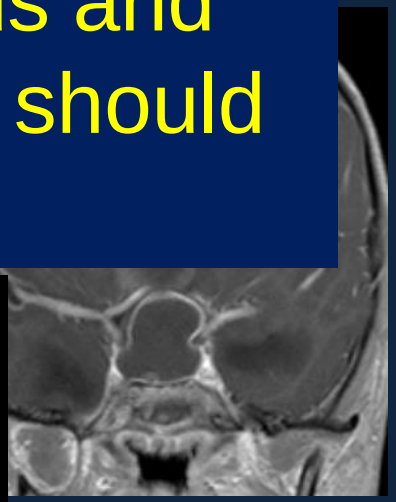
15 days after surgery

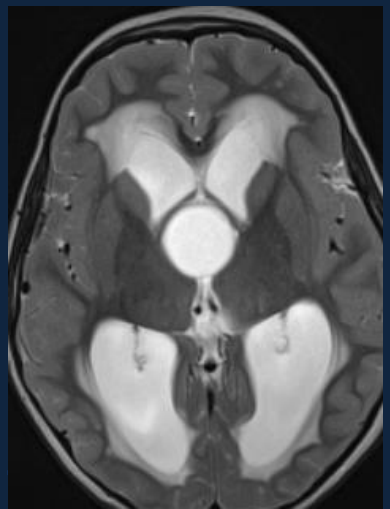
20 months after surgery

Craniopharyngioma in 6 yr old boy with progressive visual loss and pituitary gland failure

Management of hydrocephalus and elevated intracranial pressures should always be a priority!



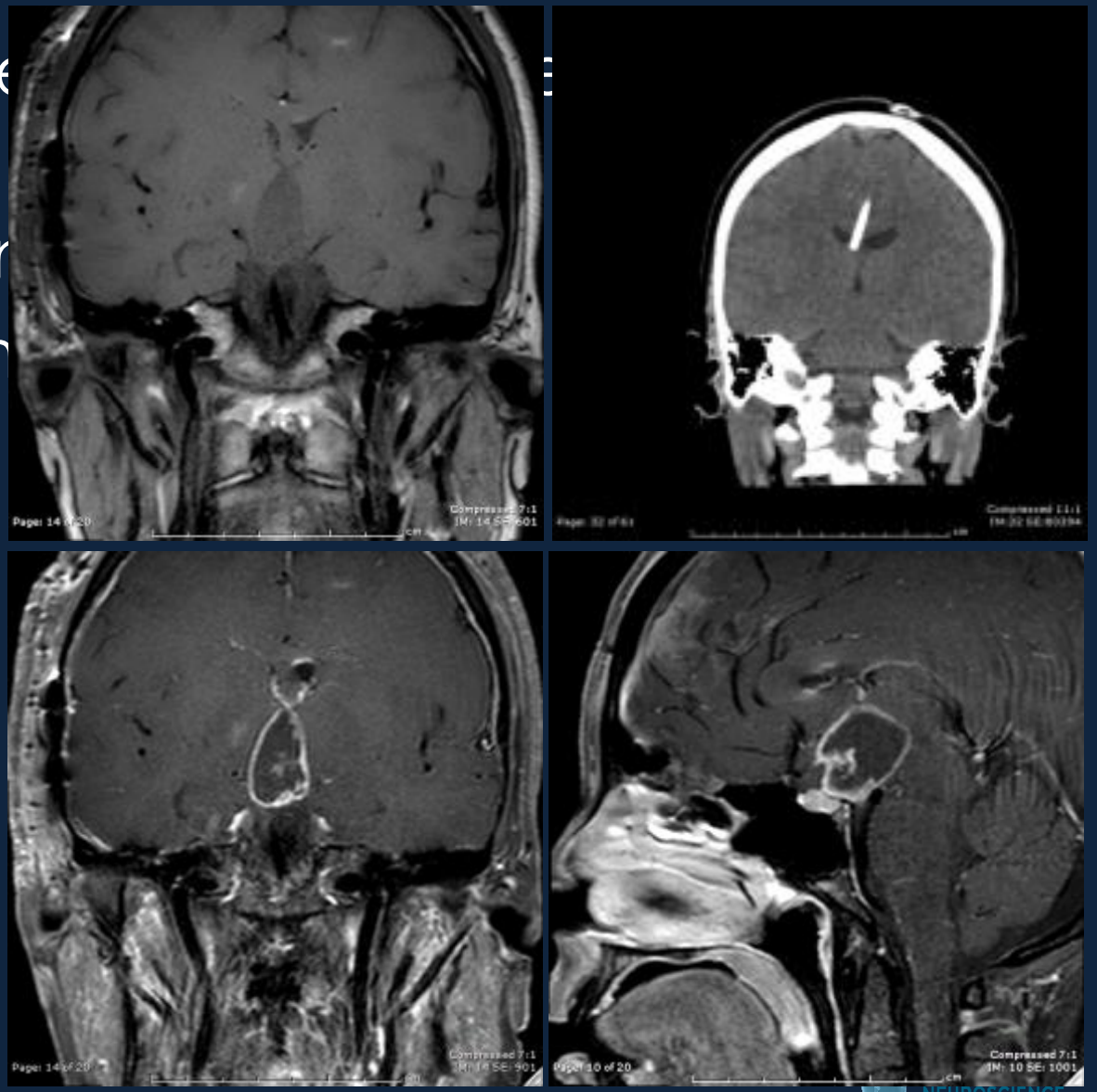




Obstructive Hydrocephalus

31F with headache
difficulties

- COZ and VP Shur
- Biopsy non-diagn



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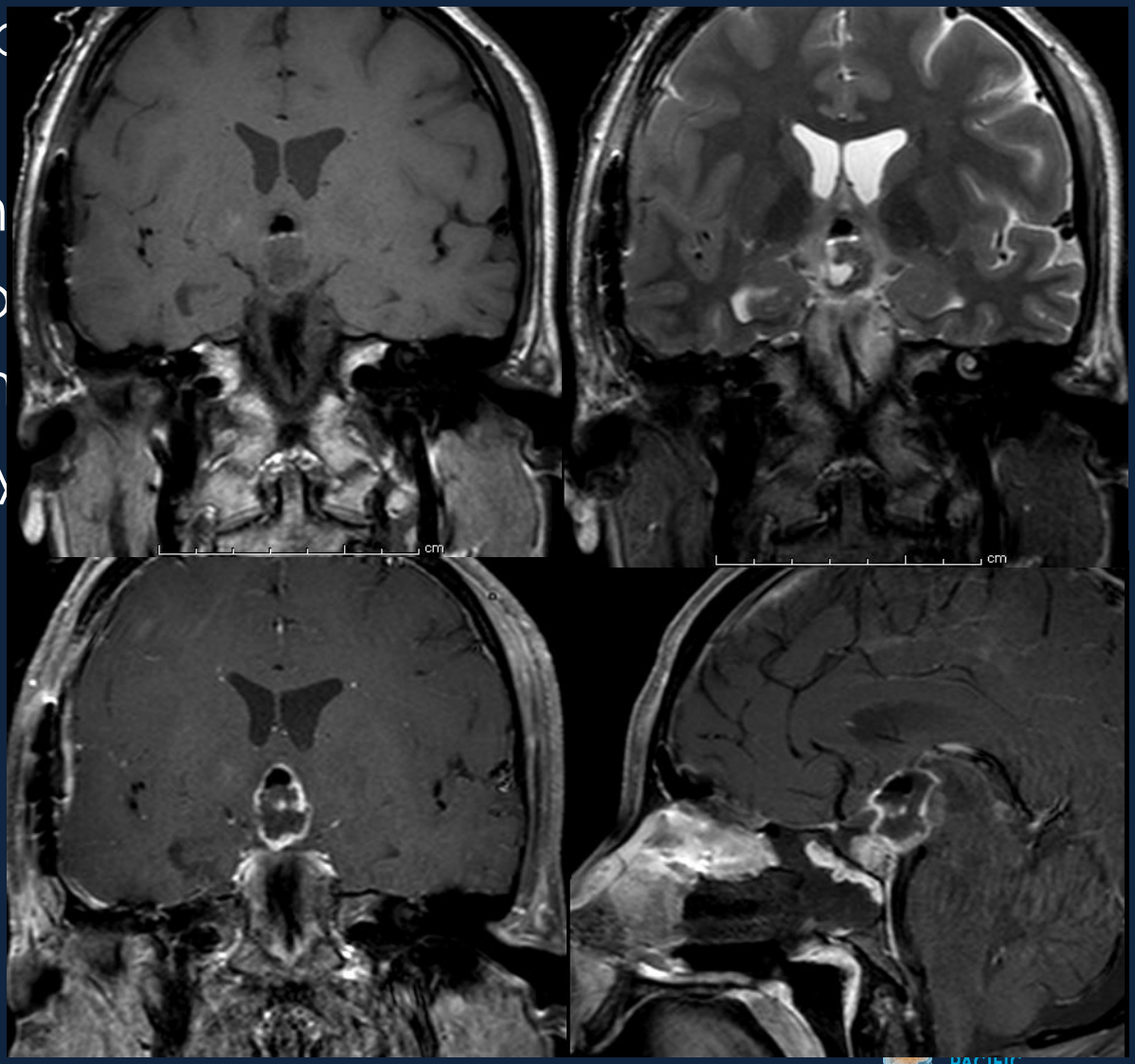
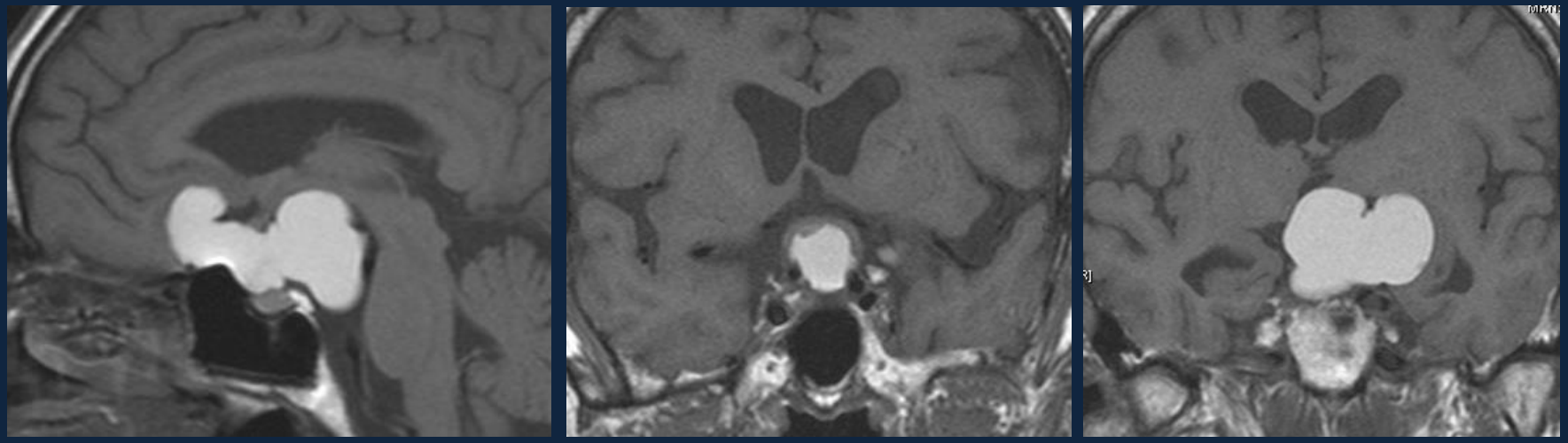
Obstructive Hydrocephalus

- Shunt removed (exp
- EVD placed
- Endonasal debulkin
- EVD weaned off po
- FSRT with tumor cor
- No recurrence of hy

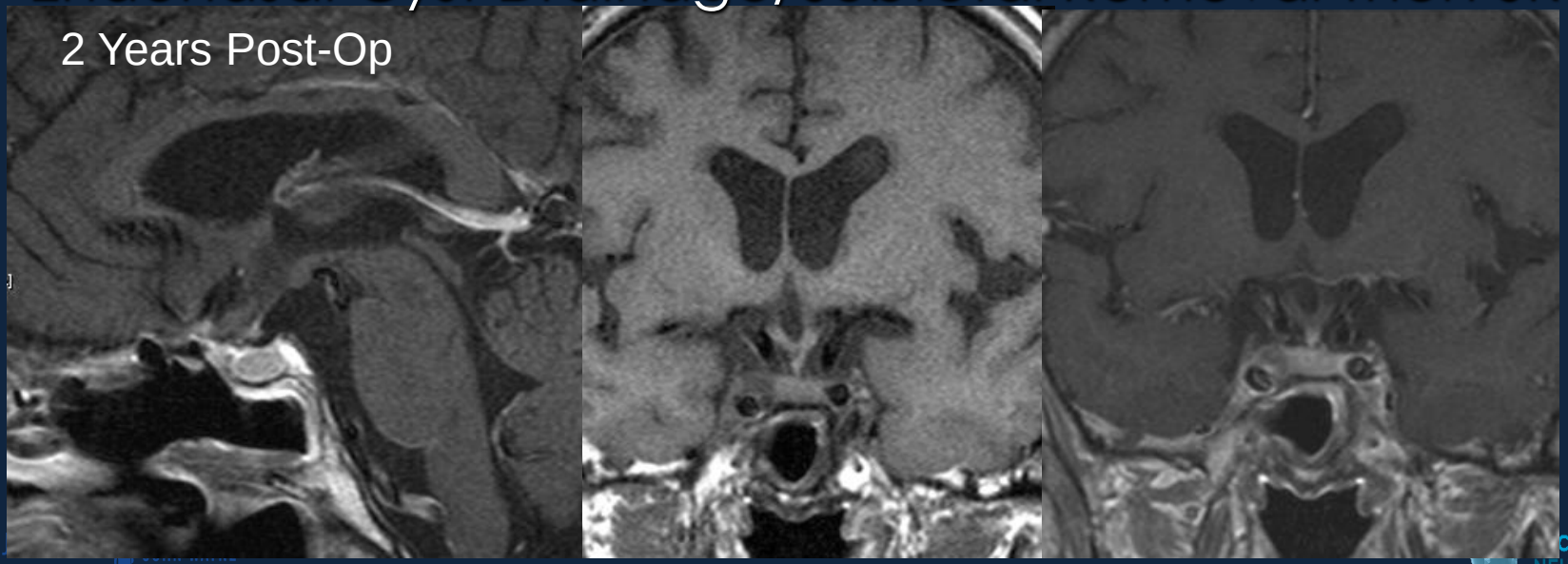


Craniopharyngioma: 79 yr old man with visual loss



Endonasal Cyst Drainage/Subtotal Removal Then SRT

2 Years Post-Op



Cyst Management

- Cystic recurrence of craniopharyngiomas can be rapidly symptomatic and difficult to manage
- Intracystic catheter placement (aka ommaya reservoir) is mainstay of management
- Cyst control options include:
  - Serial aspiration of cyst fluid
  - Instillation of radioactive isotopes (brachytherapy)
  - Instillation of Interferon-α
  - Aspiration and fractionated stereotatic radiation therapy

Cyst Management

Serial Aspiration:

- Can be useful to manage symptoms in patients who are not candidates for further intervention
- Can be used to delay radiation in pediatric population
- May be associated with increased complications:
  - Meningitis: 2.5%
  - Obstruction: 5%
  - *Srikandarajah et.al. 2014*

Cyst Management

Brachytherapy:

- One of the oldest treatment modalities (Hirsch 1912)
  - Yttrium-90
  - Phosphorous-32
- Julow et.al. report 10 year survival: 61% (^{90}Y)
  - Julow et.al. 2007
- Hasegawa et.al. report 10 year Tumor Free Survival 70% (^{32}P)
  - Hasegawa et.al. 2004

Cyst Management

Intracystic Interferon-α:

- Interferon-α can induce apoptosis via JAK-STAT signal cascade
- Has been efficacious in squamous cell carcinoma
- Jakacki et.al. reported 15 patients, of which 3 had cystic components. 1/3 had response
  - *Jakacki et.al. JNS, 2000*
- Cavalheiro et.al. report 7 of 9 patients with intracystic IFN-a had complete response (at 20 months).
  - *Cavalheiro et.al., Child's nervous system, 2005*
- Toxicity well tolerated – usually flu-like symptoms

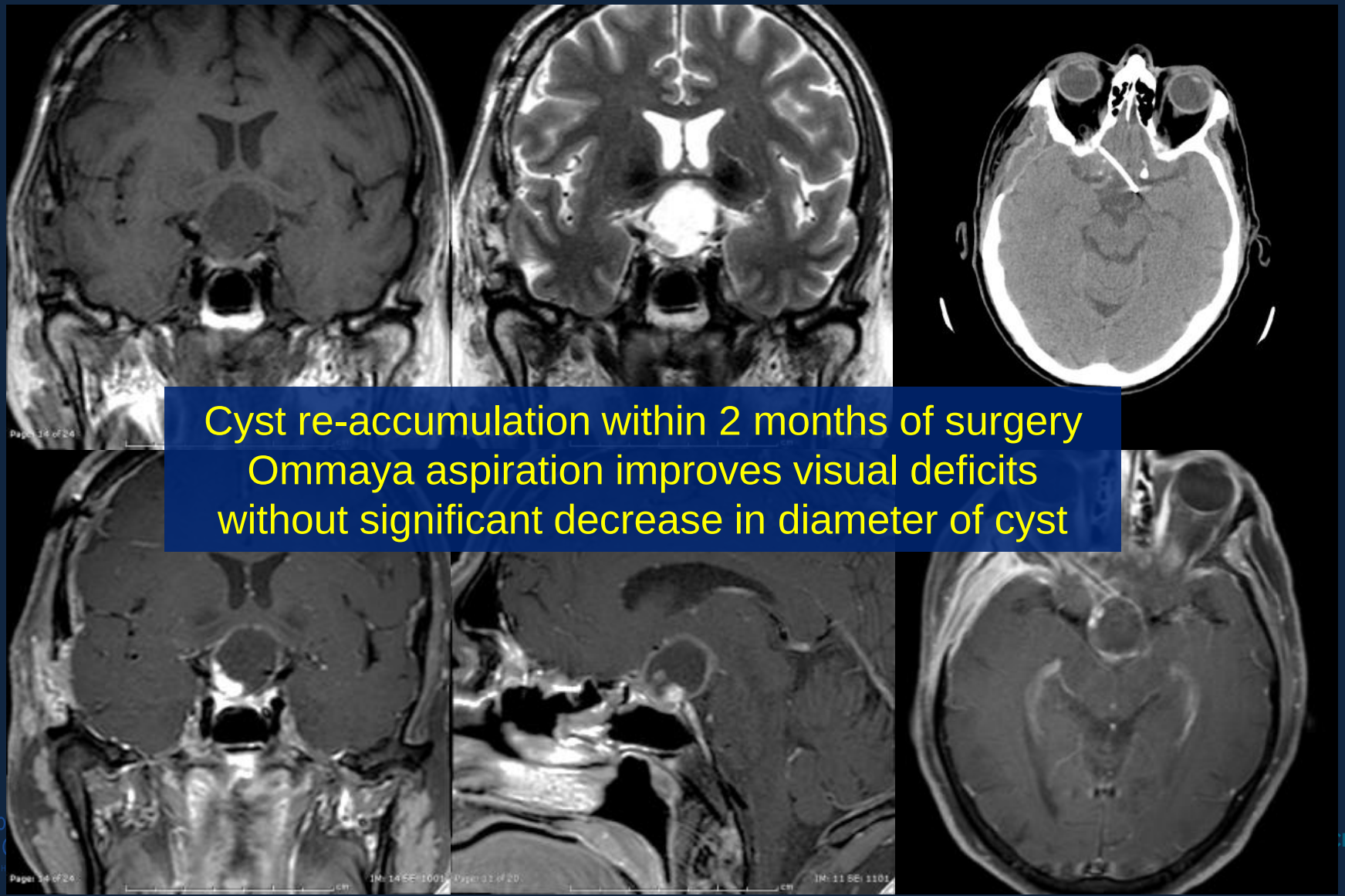
Cyst Management

Cyst Aspiration and FSRT

- Concept: Decrease cyst size, then immediately radiate
- May need to continue to aspirate as radiation takes effect
  - up to 5 months – Constine et.al. 1989.
- Kanesaka et.al. – 17 patients, 30Gy (6 fx)
  - 82.4% local control at 3 years
  - *Kanesaka et.al. IJROBP 2012*
- Need to monitor cyst during radiation with frequent radiation
  - 6/17 patients demonstrated cyst growth during radiation therapy
  - 1 had re-aspiration, 4 had increased size of radiation field.
  - *Winkfield et.al. IJROBP 2009*

Cyst Management

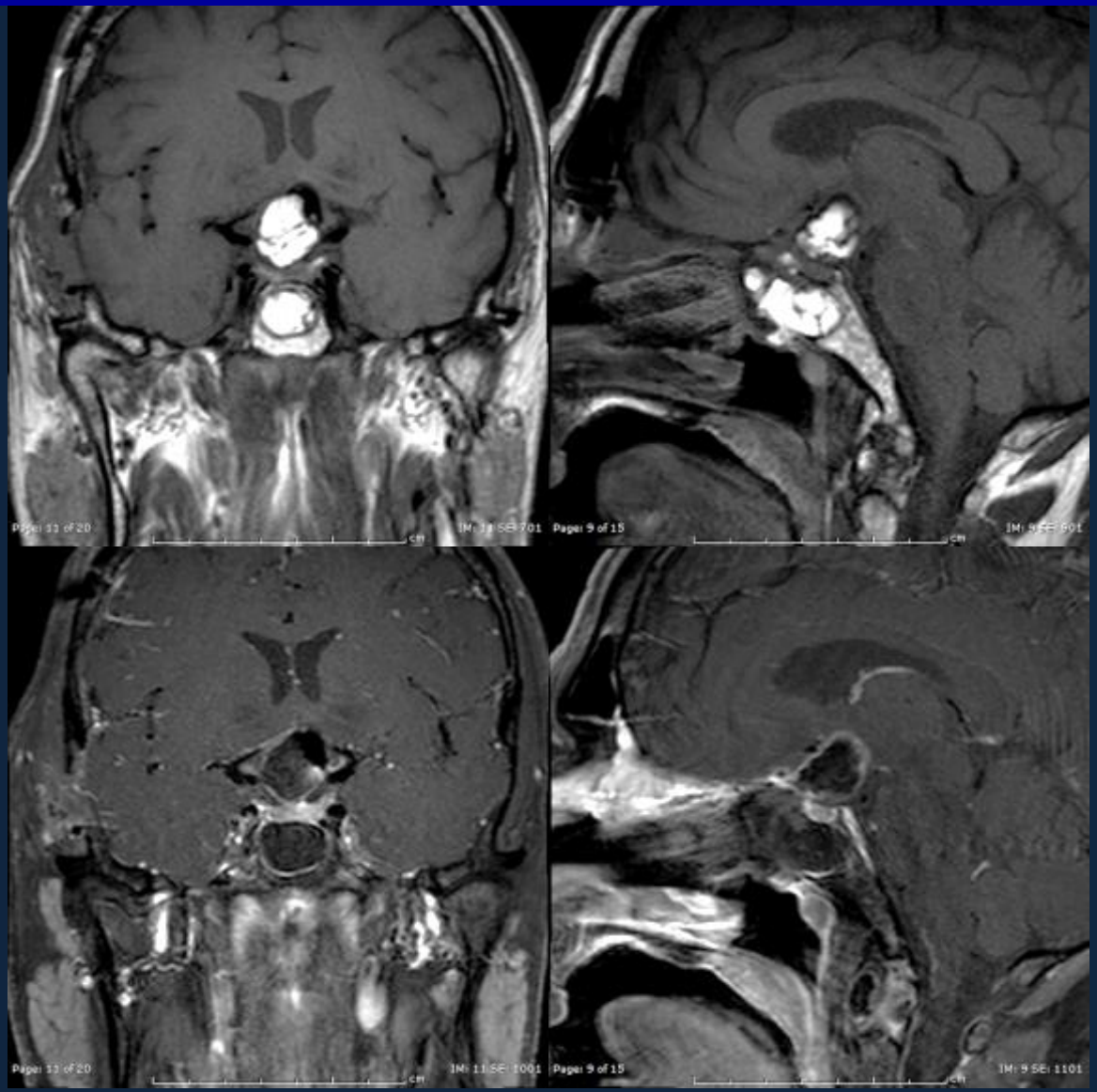
57 year old man with progressive vision loss, s/p craniotomy



Cyst re-accumulation within 2 months of surgery
Ommaya aspiration improves visual deficits
without significant decrease in diameter of cyst

Cyst Management

S/P endonasal debulking, fenestration of cyst and immediate FSRT



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Radiation Therapy

- Well accepted adjunct to surgical resection
- Harrabi et.al. – Long term outcomes with FSRT
  - 50-58Gy over 30 fx
  - 10-year PFS 92.1%; 20-year PFS 88.1%
  - 10-year OS 83.3%; 20-year OS 67.8%

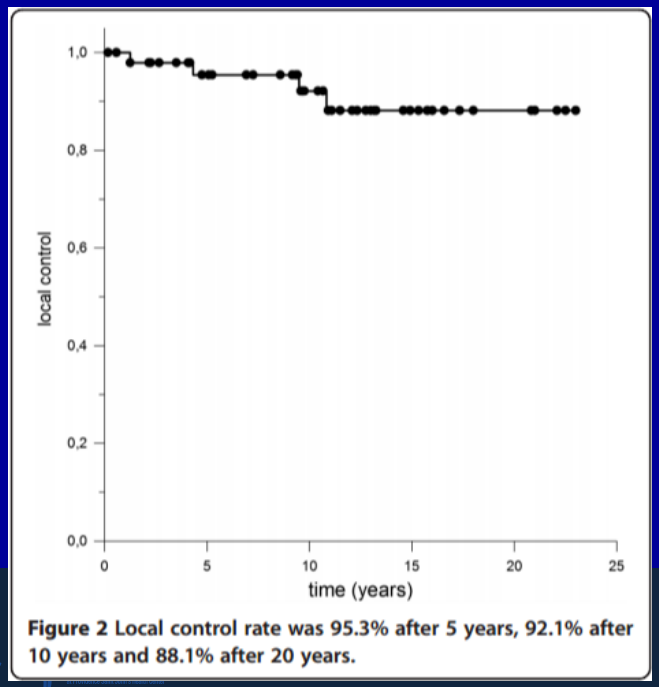


Figure 2 Local control rate was 95.3% after 5 years, 92.1% after 10 years and 88.1% after 20 years.

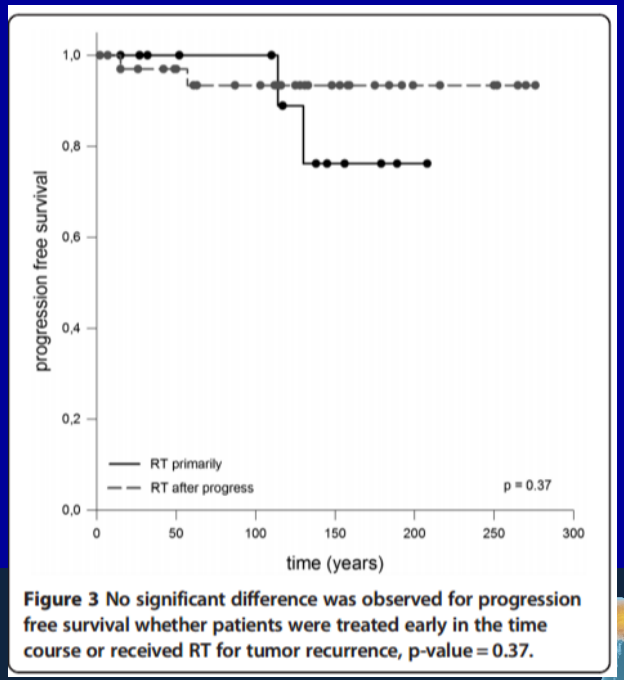


Figure 3 No significant difference was observed for progression free survival whether patients were treated early in the time course or received RT for tumor recurrence, p-value = 0.37.

Harrabi et.al. Rad Onc 2014

NATURE GENETICS VOLUME 46 | NUMBER 2 | FEBRUARY 2014

Exome sequencing identifies *BRAF* mutations in papillary craniopharyngiomas

Priscilla K Brastianos[1–5,22], Amaro Taylor-Weiner[5,22], Peter E Manley[6,22], Robert T Jones[4,7], Dora Dias-Santagata[3,8], Aaron R Thorner[4,7], Michael S Lawrence[5], Fausto J Rodriguez[9], Lindsay A Bernardo[8], Laura Schubert[7], Ashwini Sunkavalli[7], Nick Shillingford[10], Monica L Calicchio[10], Hart G W Lidov[3,10,11], Hala Taha[12], Maria Martinez-Lage[13], Mariarita Santi[14], Phillip B Storm[15,16], John Y K Lee[15], James N Palmer[15,17], Nithin D Adappa[17], R Michael Scott[3,18], Ian F Dunn[3,19], Edward R Laws Jr[3,19], Chip Stewart[5], Keith L Ligon[3,4,10,11], Mai P Hoang[3,8], Paul Van Hummelen[4,7], William C Hahn[3–5,7], David N Louis[3,8], Adam C Resnick[15,16], Mark W Kieran[3,6,20,23], Gad Getz[3,5,8,23] & Sandro Santagata[3,10,11,21,23]

Craniopharyngiomas of Adamantinomatous Type Harbor β-*Catenin* Gene Mutations

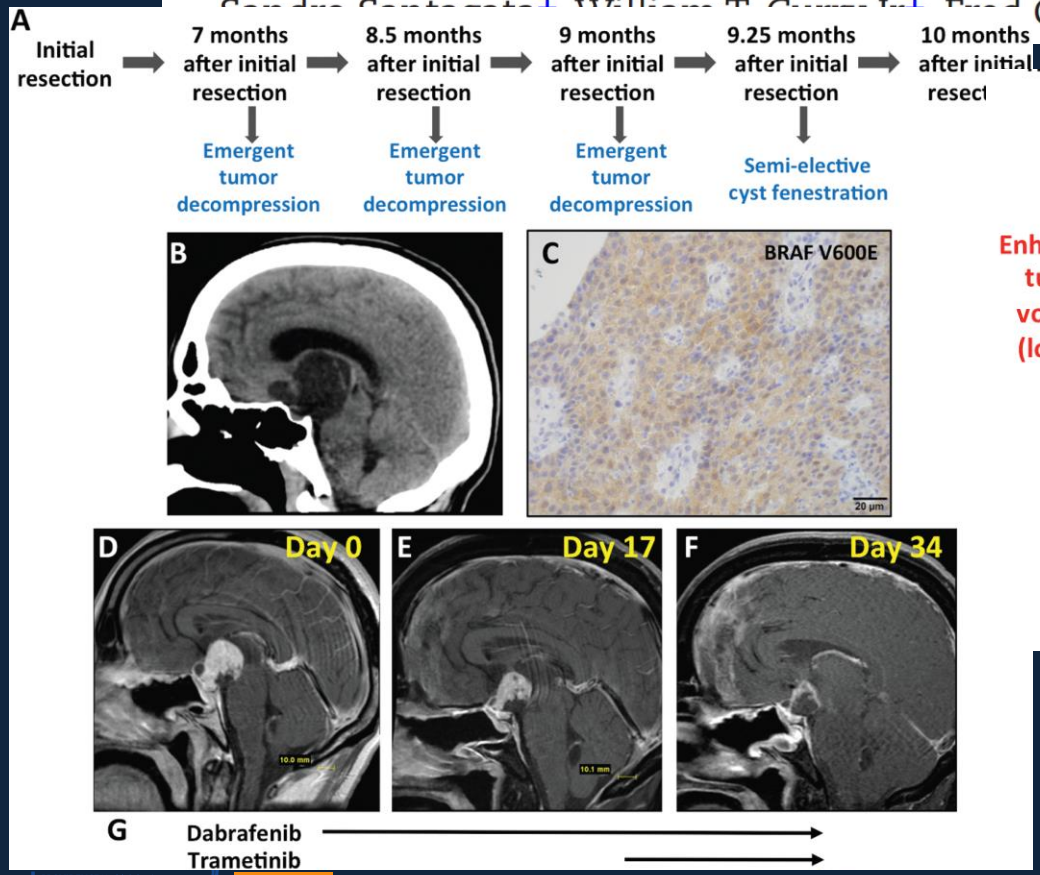
Shigeki Sekine, Tatsuhiro Shibata, Akiko Kokubu, Yukio Morishita, Masayuki Noguchi, Yukihiro Nakanishi, Michiie Sakamoto, Setsuo Hirohashi

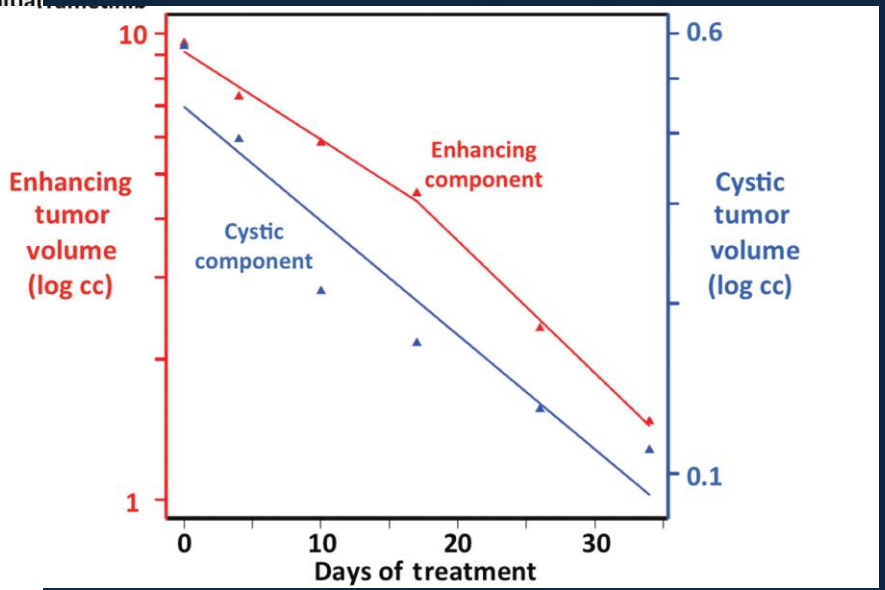
BRIEF COMMUNICATION

Dramatic Response of BRAF V600E Mutant Papillary Craniopharyngioma to Targeted Therapy

Priscilla K. Brastianos*, Ganesh M. Shankar *, Corey M. Gill*, Amaro Taylor-Weiner, Naema Nayyar, David J. Panka, Ryan J. Sullivan, Dennie T. Frederick, Malak Abedalthagafi, Pamela S. Jones, Ian F. Dunn, Brian V. Nahed, Javier M. Romero, David N. Louis, Gad Getz, Daniel P. Cahill†, [illegible] G. Barker II†

JNCI 2016





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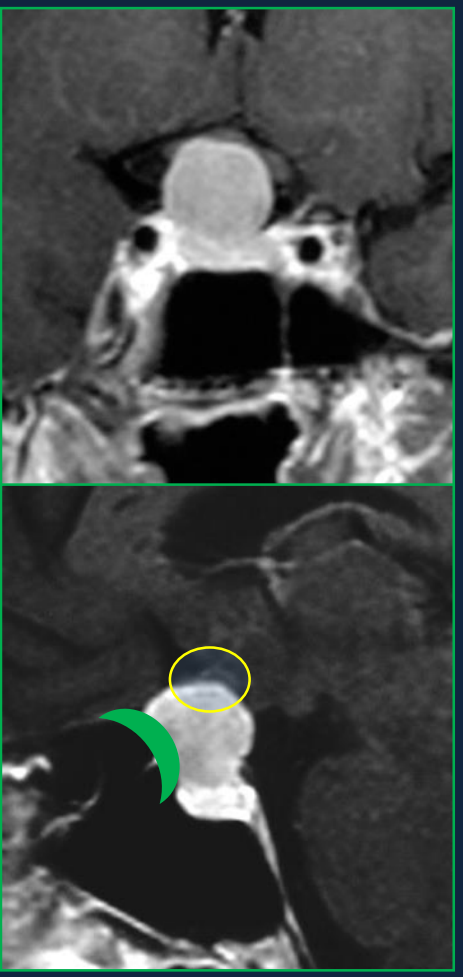
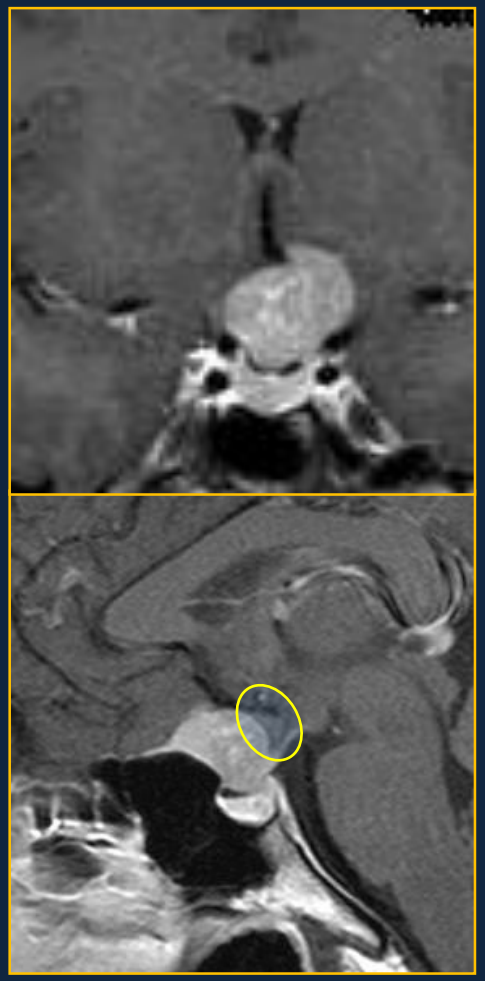
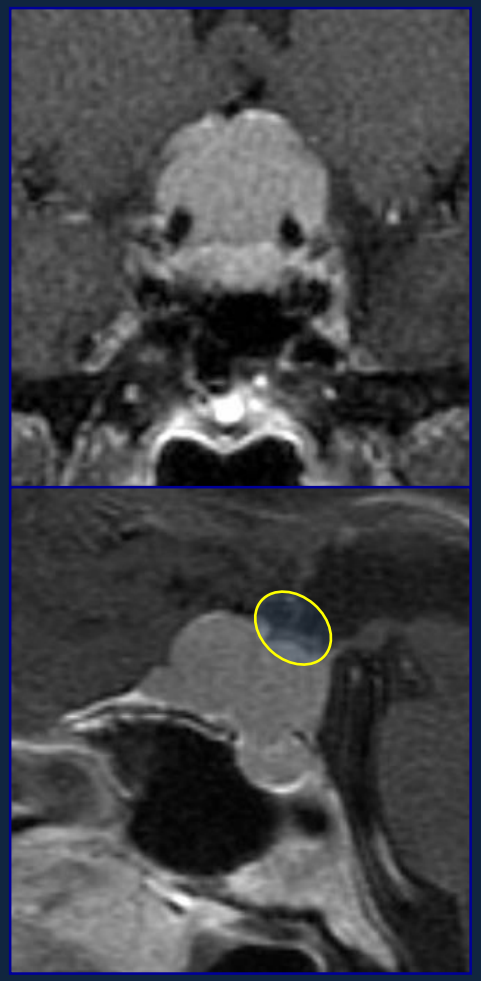
Tuberculum Sellae Meningioma



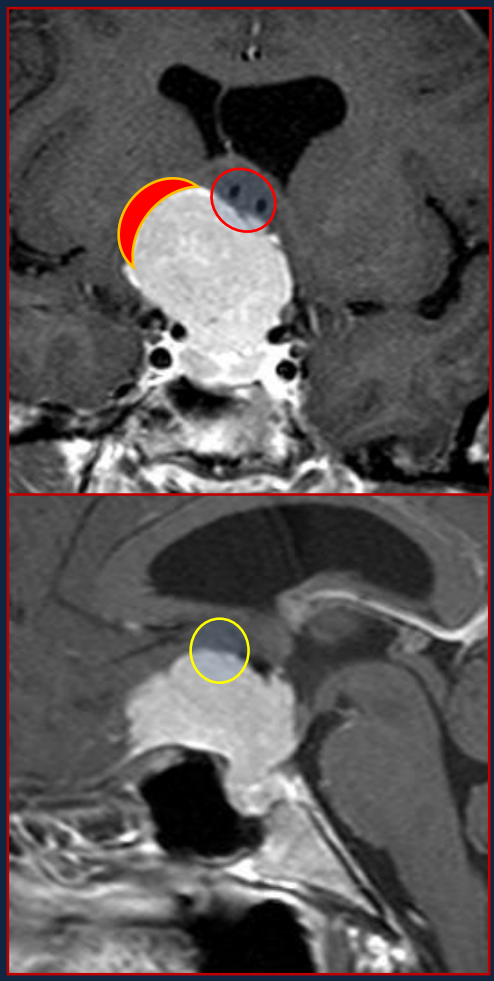
Endonasal



Endonasal



Endo or SO



Supraorbital or conventional

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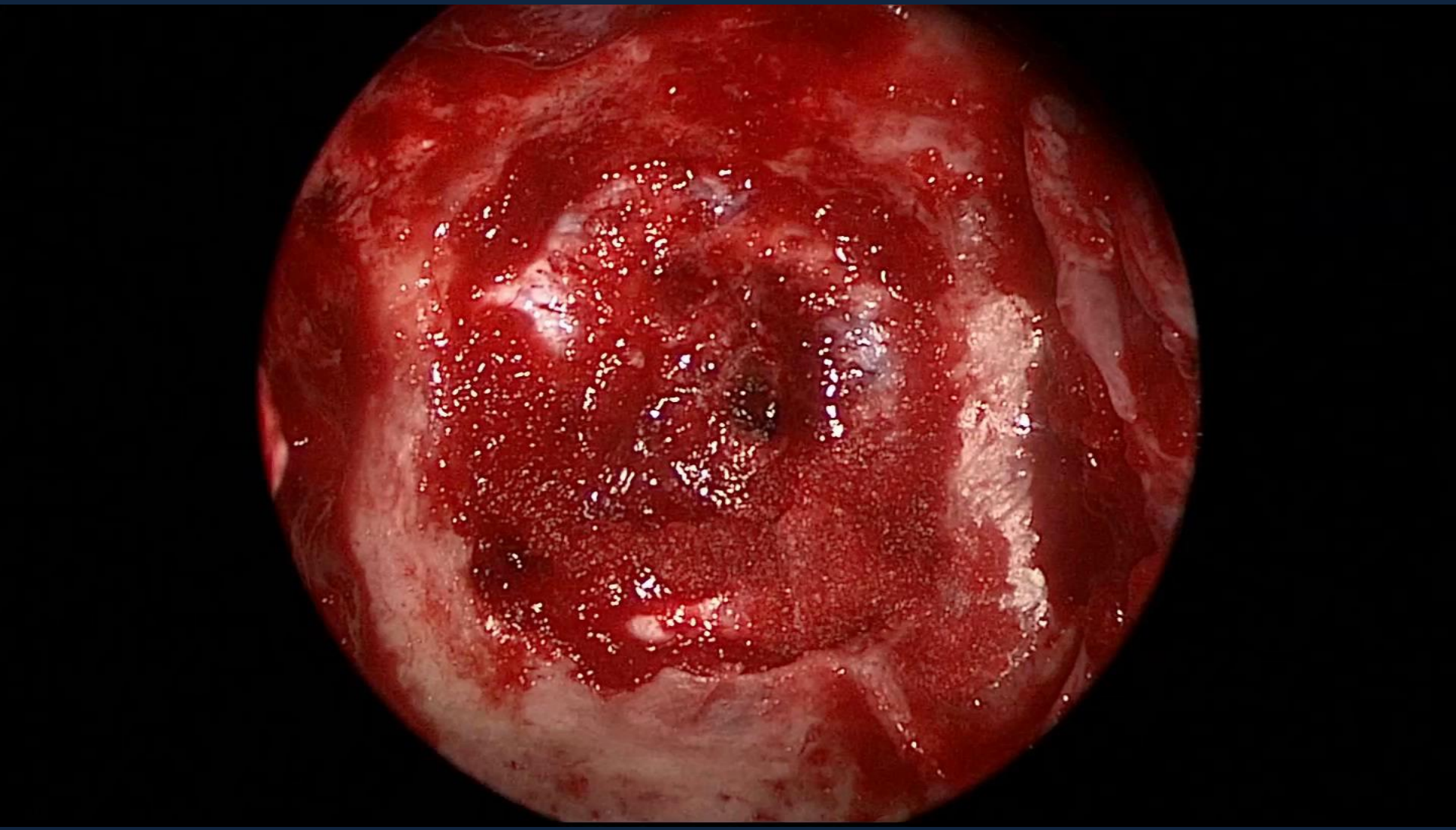
Tuberculum Sellae Meningioma



Cavernous Sinus Lesion

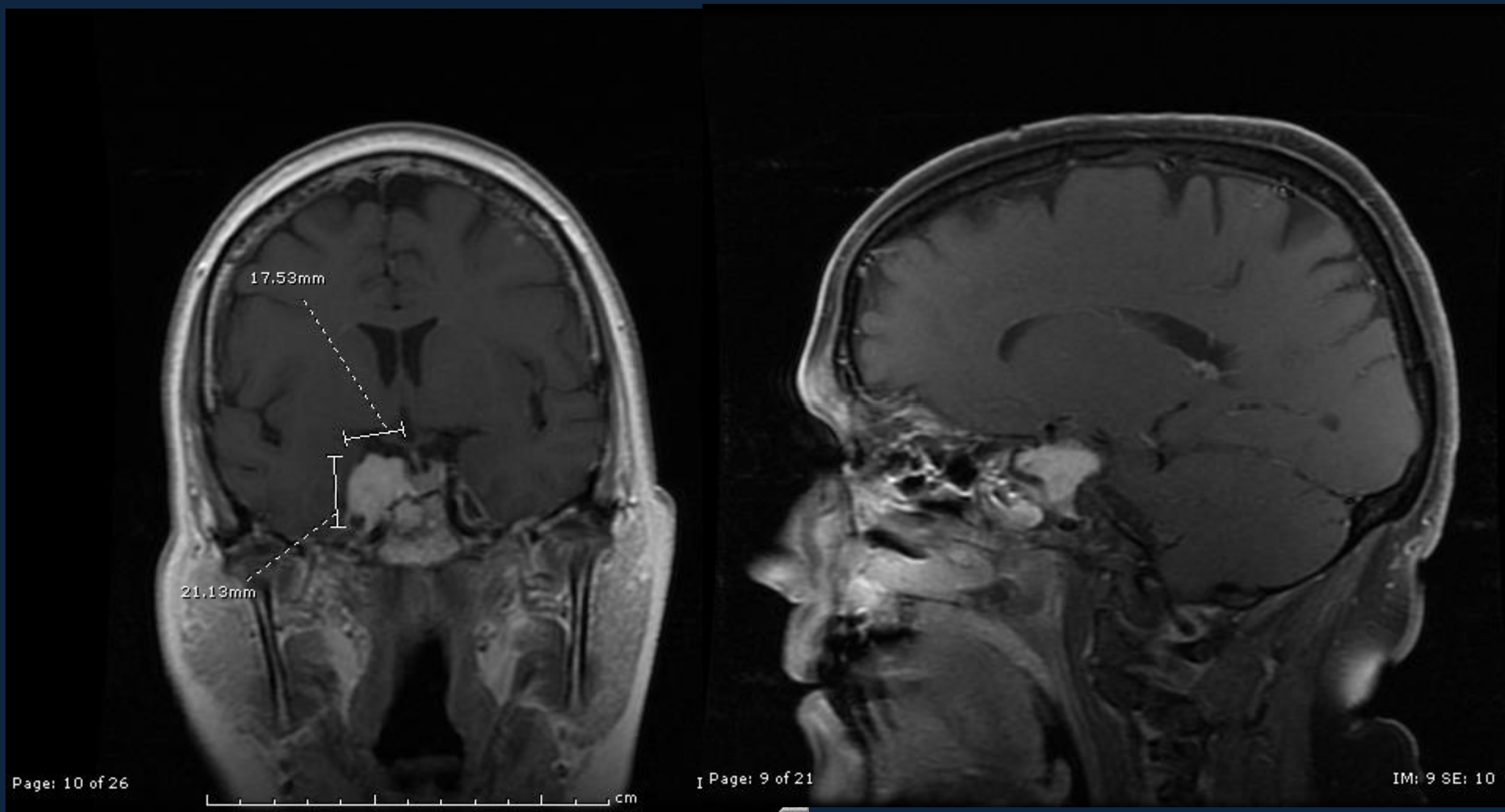
Sarcoidosis

Cavernous Sinus Lesion

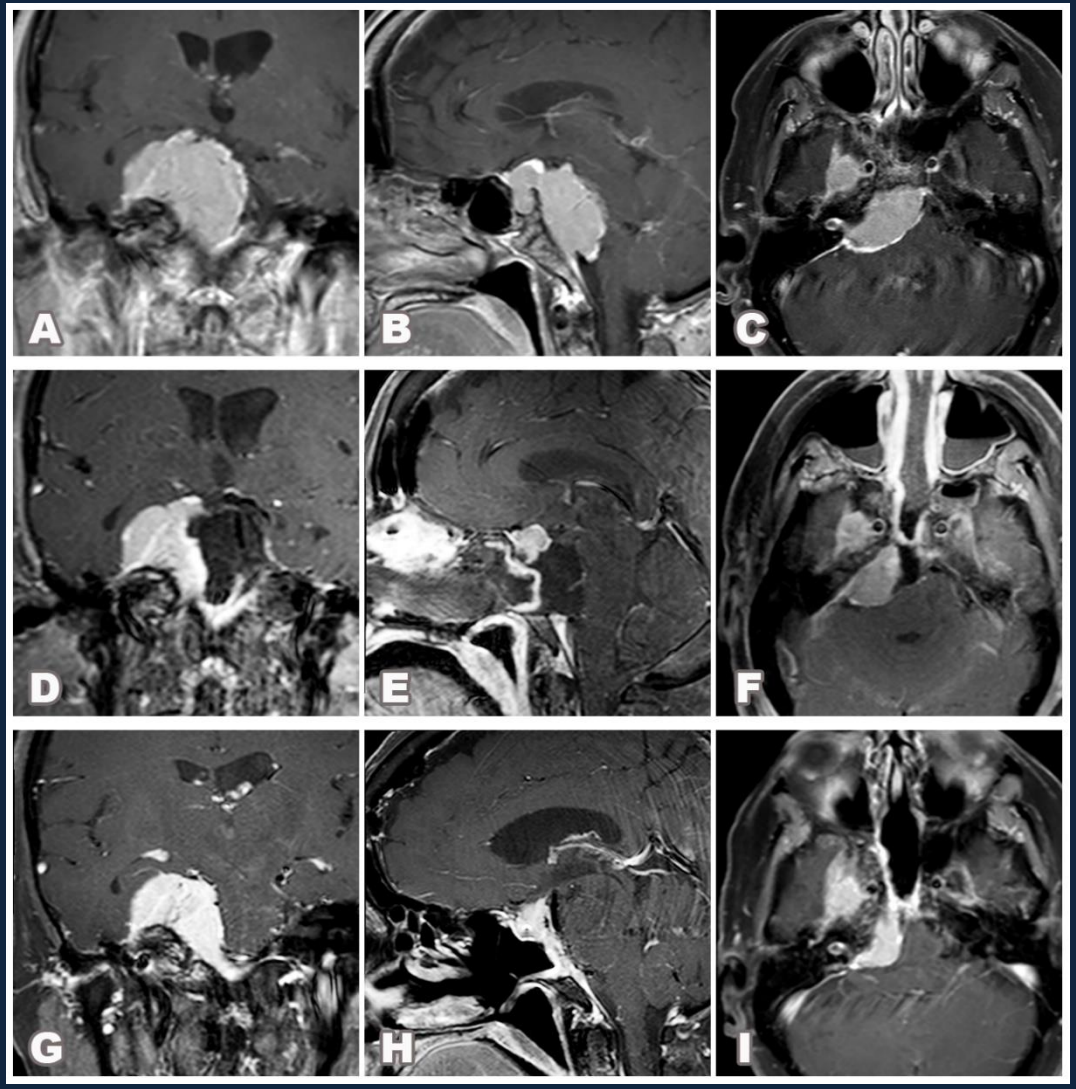
Lymphoma

Cavernous Sinus Lesion

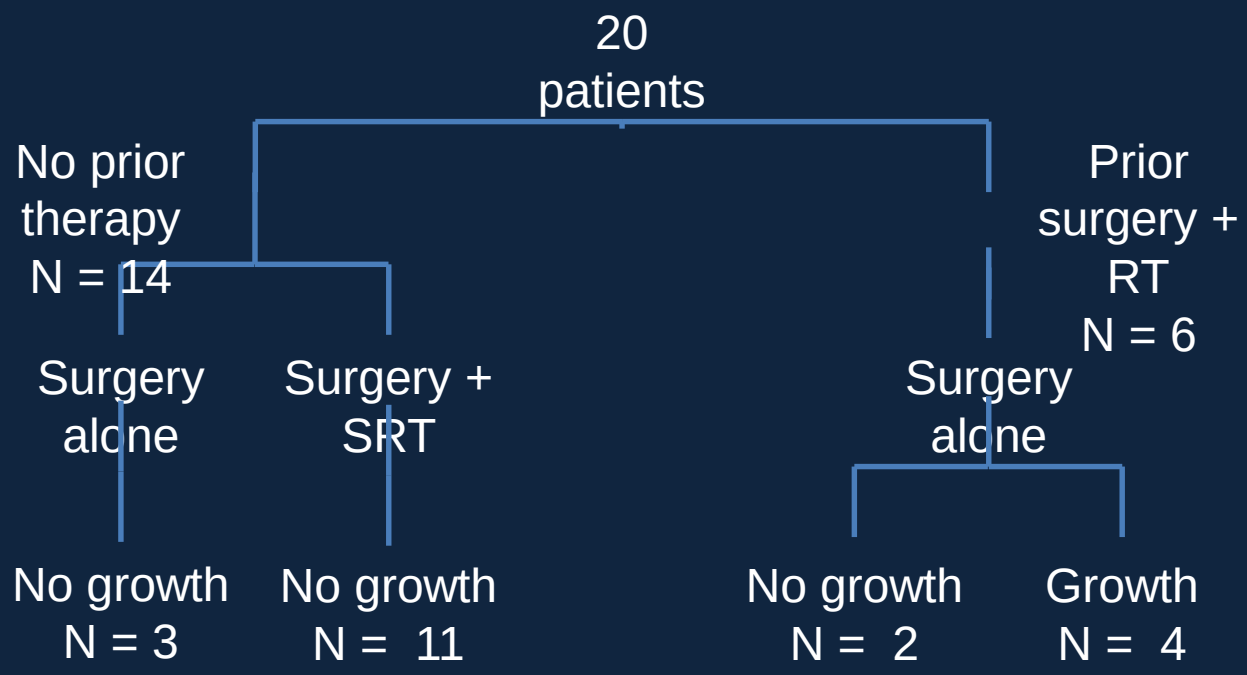
Meningioma



Cavernous Sinus Lesion



Cavernous Sinus Lesion



	Improved	Stable	Worsened	New
Cranial neuropathy N = 16	9/16 (56.2%)	7/16 (43.8%)	NA	3
Endocrinopathy N = 7	5/7 (71.4%)	2/7 (28.6%)	NA	NA

	Improved	Stable	Worsened	New
Cranial neuropathy N = 13	1/13 (7.7%)	9/13 (69.2%)	3/13 (23.1%)	3
Endocrinopathy N = 13	6/13 (46.2%)	7/13 (53.8%)	NA	NA

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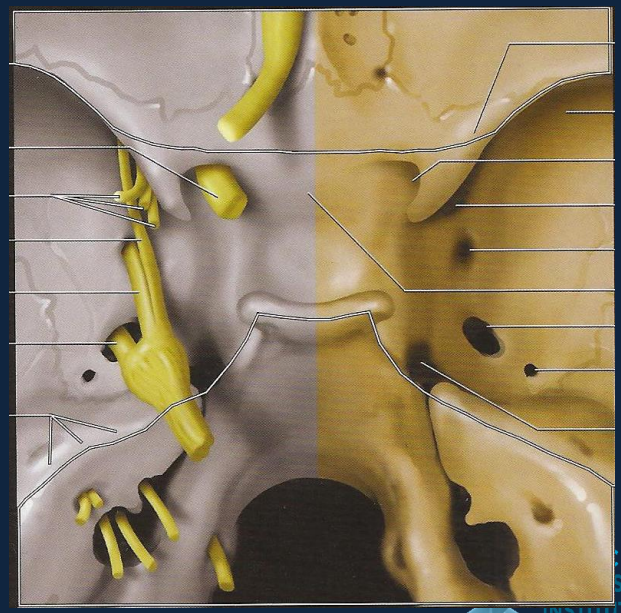
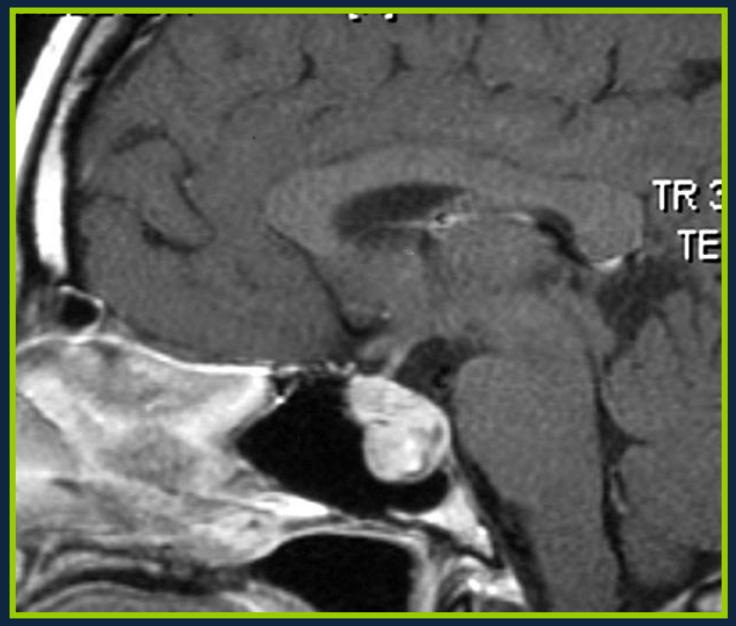
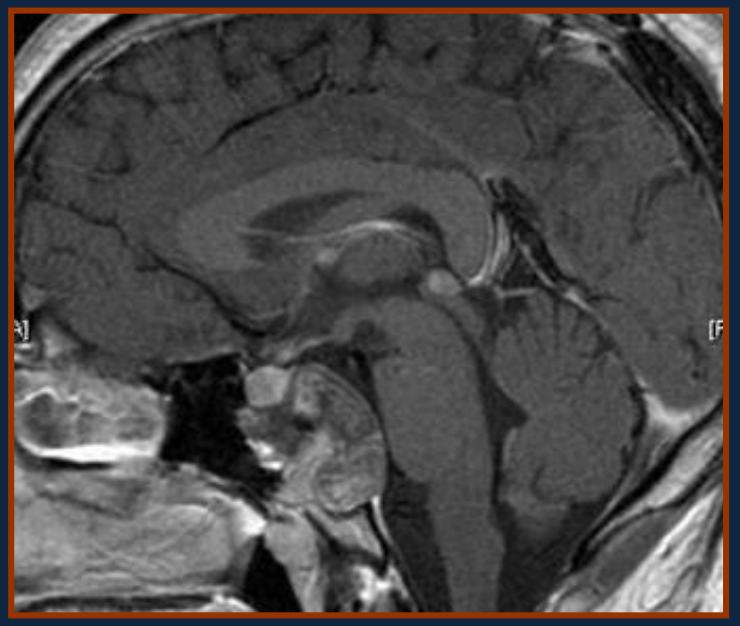
Chordoma

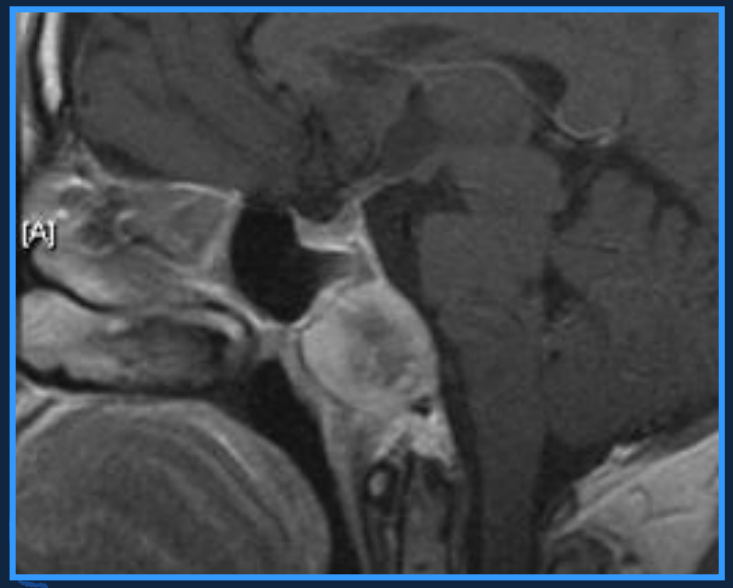
- Incidence: extremely rare
  - 0.2/100,000 person-years
  - 0.1% of all brain tumors in USA (CBTRUS 2011)
- Pathophysiology: transformation of notochord rests
  - Sella, clivus, foramen magnum, C1, nasopharynx, nucleus pulposus
- Locations:
  - 35% skull base
  - 50% sacrum
  - 15% vertebral bodies
- Ecchondrosis physaliphora:
  - Also composed of notochord rests
  - Present in 2% of autopsies
  - Possible precursor to chordoma

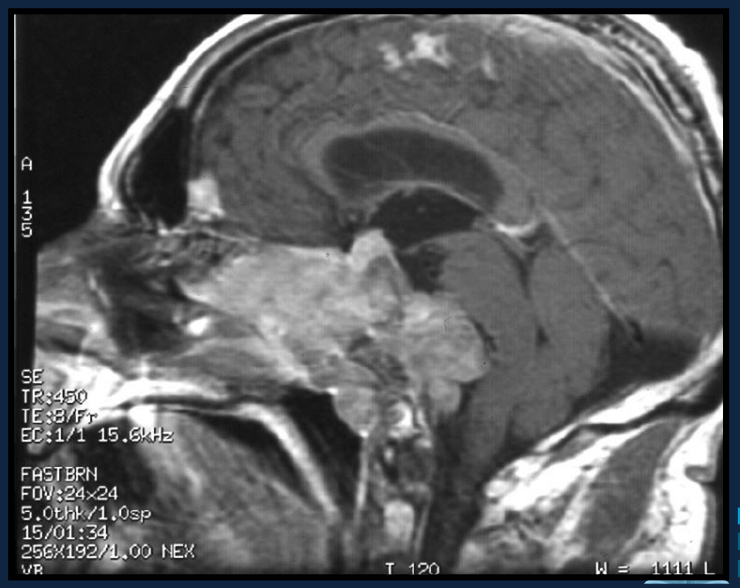


Clival Chordoma









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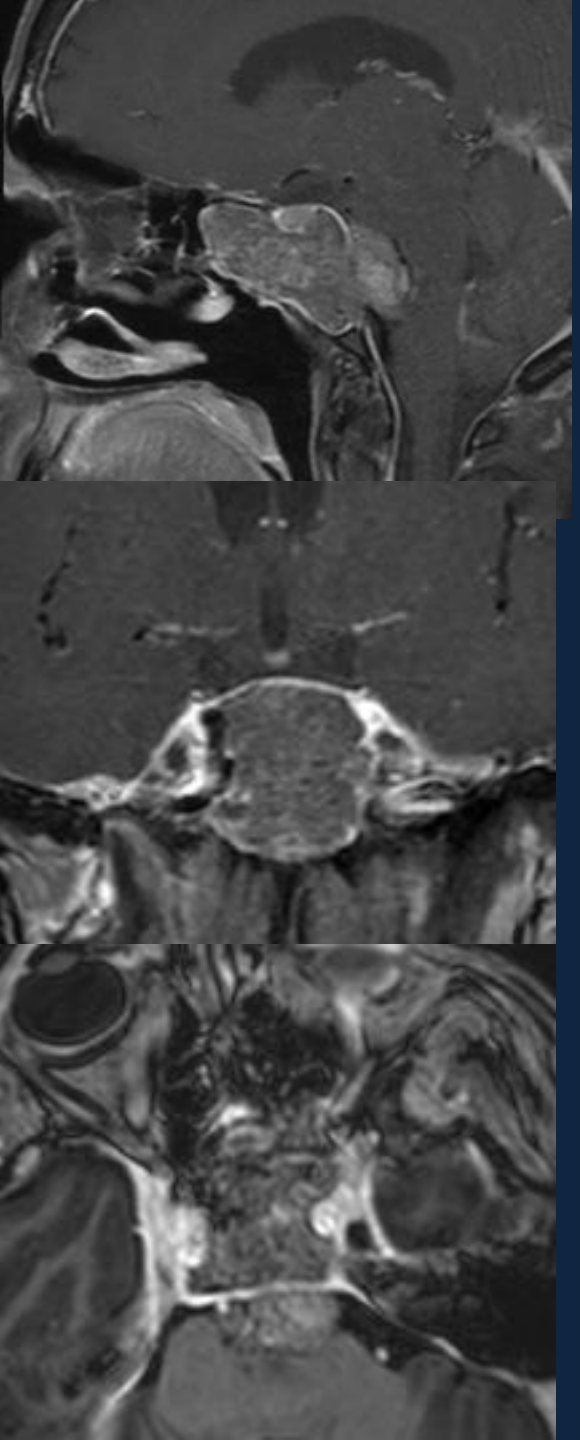
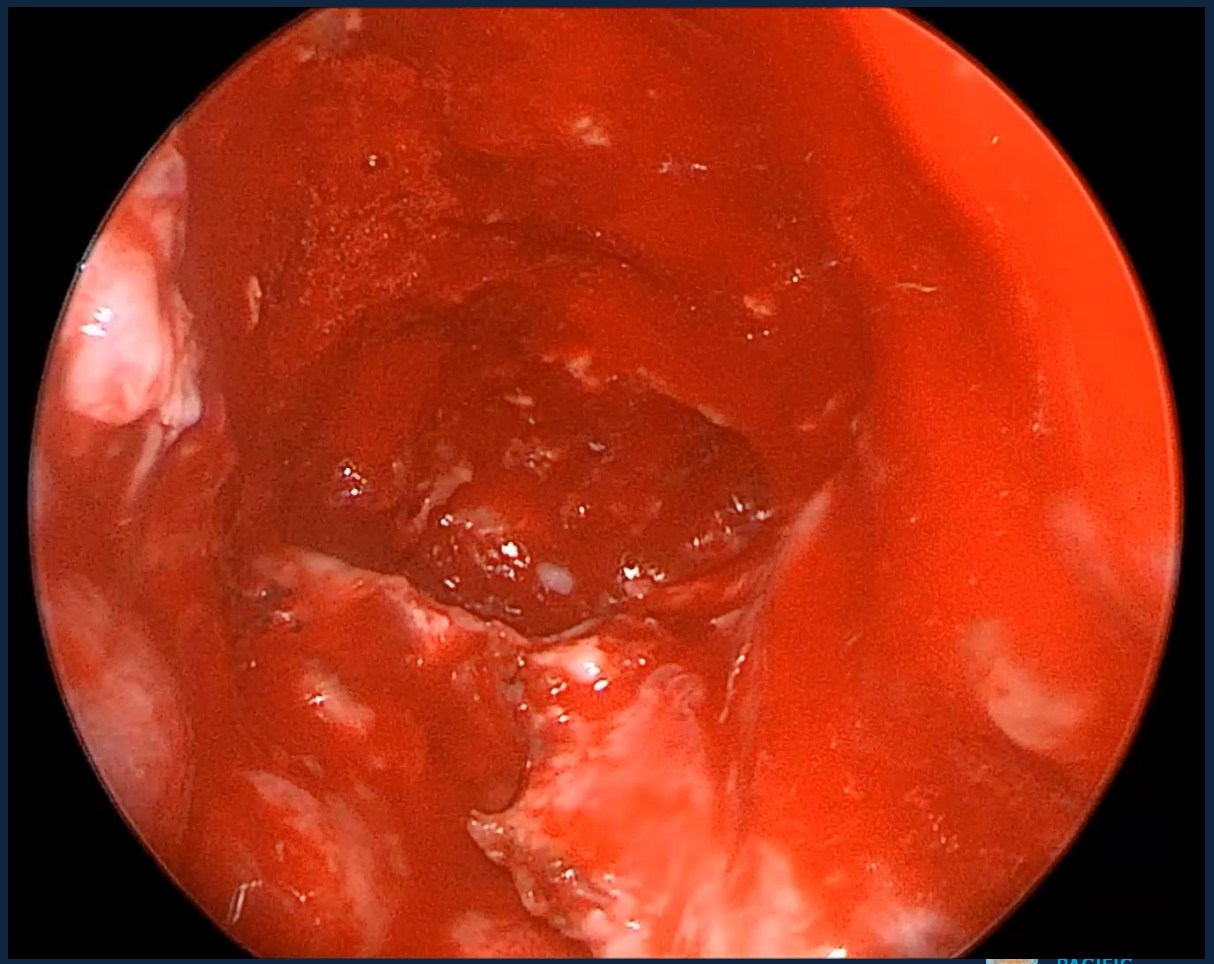


Hemorrhagic chordoma

62 yr old woman with headache & meningitis



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Endoscopic Endonasal Approach for Resection of Cranial Base Chordomas: Outcomes and Learning Curve

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BACKGROUND: Gross total resection (GTR) of cranial base chordomas represents a surgical challenge because of the location, invasiveness, and tumor extension. In the past decade, the endoscopic endonasal approach (EEA) has been used with notable outcomes.

OBJECTIVE: To present the endoscopic endonasal experience in the treatment of cranial base chordomas at our institution.

METHODS: From April 2003 to March 2011, 60 patients underwent an EEA for primary (n = 35) or previously treated (n = 25) cranial base chordomas. We evaluated the degree of GTR and complications. We studied the factors that influenced outcomes and compared our surgical results in the early and late years of our experience.

RESULTS: The [illegible] GTR [illegible] (82.9% in primary and 44% in previously treated patients). The most important limitations for GTR were tumor [illegible] cm^3 ($P = .042$), tumor location in the lower clivus with lateral extension ($P = .022$), and previously treated disease ($P = .002$). The learning curve had a [illegible] GTR, increasing the success rate to 88.9% (92.6% in primary patients and 63.6% in previously treated patients) during recent years ($P < .0001$). The most frequent complication was cerebrospinal fluid leak (20%) resulting in meningitis in 3.3%. Carotid injuries occurred in 2 patients without any resulting deficit. Neurological complications [illegible] (3.7%) and long tract deficits (1.7%). There was no operative mortality in our series.

CONCLUSION: For the treatment of cranial base chordomas, the EEA is a competitive alternative to transcranial approaches with minimal morbidity and high success rates of GTR when performed by experienced cranial base surgeons.

KEY WORDS: Chordoma, Clivus, Endoscopic cranial base surgery, Endoscopic endonasal approach, Learning curve

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N=60; 35 de novo; 25 prev rx
- GTR 67%
- CSF leaks 20%
- Meningitis 3%
- Carotid artery injury 3%

Factors Predicting Recurrence After Resection of Clival Chordoma Using Variable Surgical Approaches and Radiation Modalities

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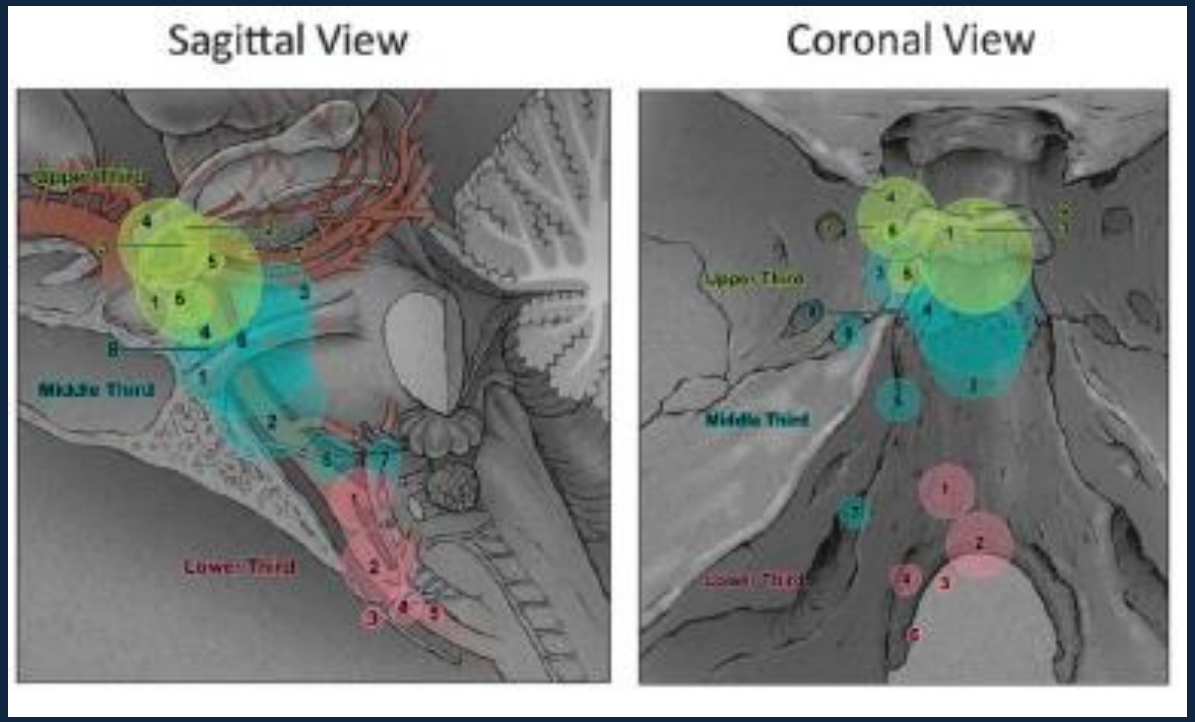
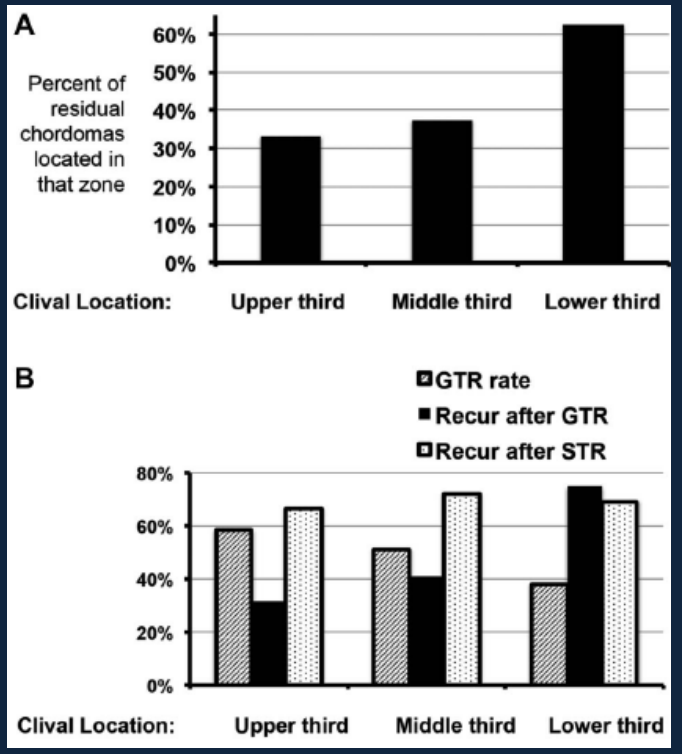
BACKGROUND: Clival chordomas frequently recur because of their location and invasiveness.
OBJECTIVE: To investigate clinical, operative, and anatomic factors associated with clival chordoma recurrence.
METHODS: Retrospective review of clival chordomas treated at our center from 1993 to 2013.
RESULTS: Fifty patients (56% male) with median age of 59 years (range, 8-76) were newly diagnosed with clival chordoma of mean diameter 3.3 cm (range, 1.5-6.7). Symptoms included headaches (38%), diplopia (36%), and dysphagia (14%). Procedures included transsphenoidal (n = 34), transoral (n = 4), craniotomy (n = 5), and staged approaches (n = 7). Gross total resection (GTR) rate was 52%, with 83% mean volumetric reduction, values that improved over time. While the lower third of the clivus was the least likely superoinferior zone to contain tumor (upper third = 72%/middle third = 82%/lower third = 42%), it most frequently contained residual tumor [illegible] rates were 61% (diplopia) and 53% (headache). Postoperative radiation included proton beam [illegible] tensity-modulated radiation therapy (n = 6), external beam (n = 10), and none (n = 4). At last follow-up of 47 patients, 23 (49%) remain disease-free or have stable residu[illegible] after GTR (upper/mid/lower third = 32%/41%/75%). In a multivariate Cox proportional hazards model, male gender (hazard ratio [HR] = 1.2/P [illegible] presence of tumor in the middle third (HR = 1.2/P = .02) and lower third (HR = 1.8/P = .02) of the clivus increased further growth, while radiation modality did not.
CONCLUSION: Our findings underscore lo[illegible] support for GTR as reducing chordoma recurrence. The lower third of the clivus frequently harbored residual or recurrent tumor, despite staged approaches providing mediolateral (transcranial + endonasal) or superoinferior (endonasal + transoral) breadth. There was no benefit of proton-based over photon-based radiation, contradicting conventional presumptions.

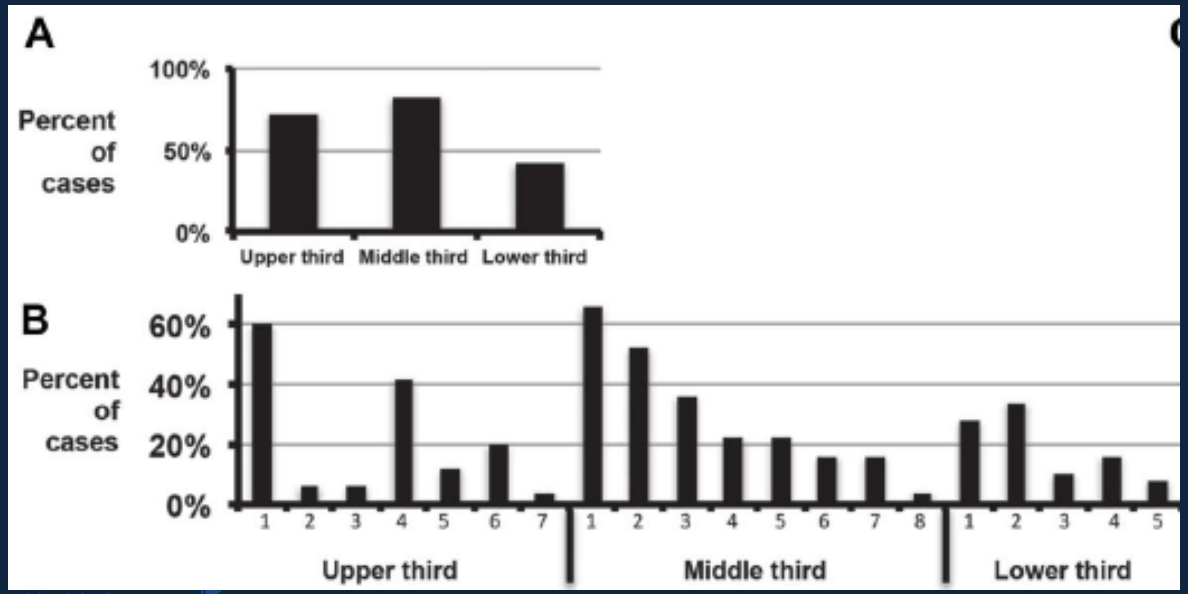
KEY WORDS: Chordoma, Cyberknife, Endoscopic, Proton beam, Recurrence

Neurosurgery 76:179–186, 2015 DOI: 10.1227/NEU.0000000000000611 www.neurosurgery-online.com

N=50; all de novo (1993-2013), 34 TSph
- GTR 52%
- Radiotherapy in 92%
- Disease-free at last F/U 49%
- 51% recurrence/progression







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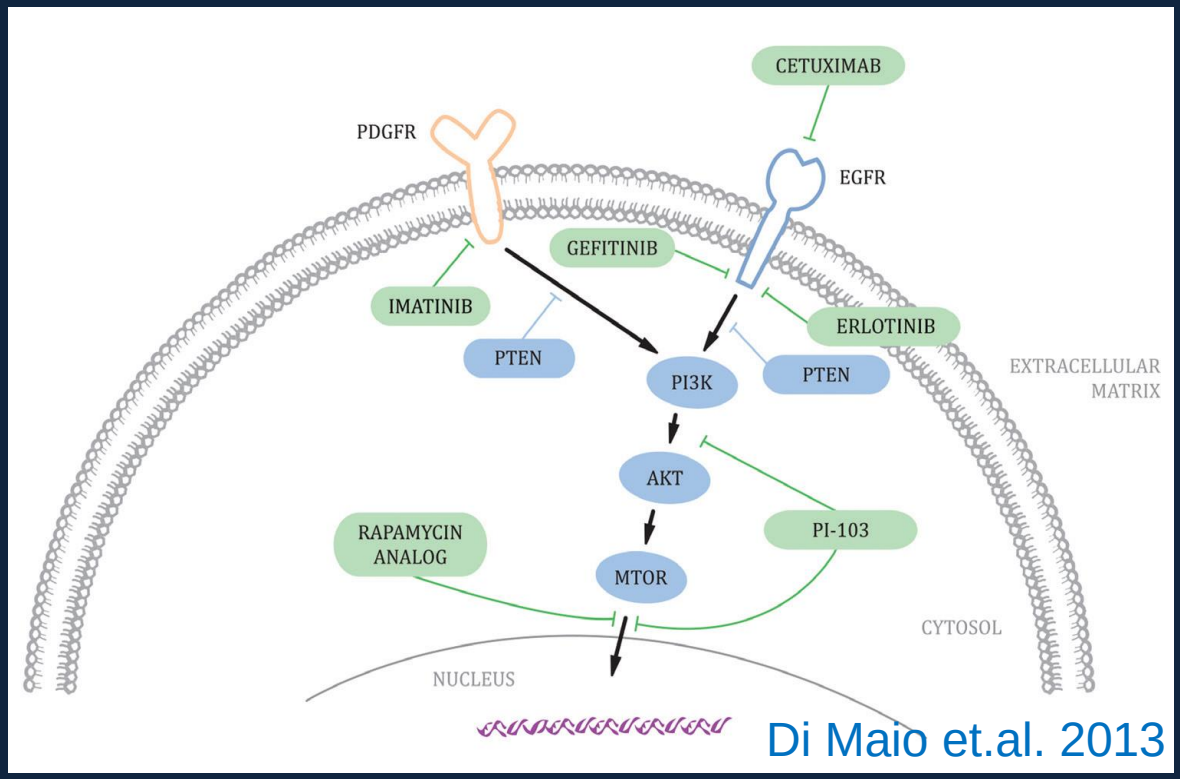
Molecular Markers and Therapy



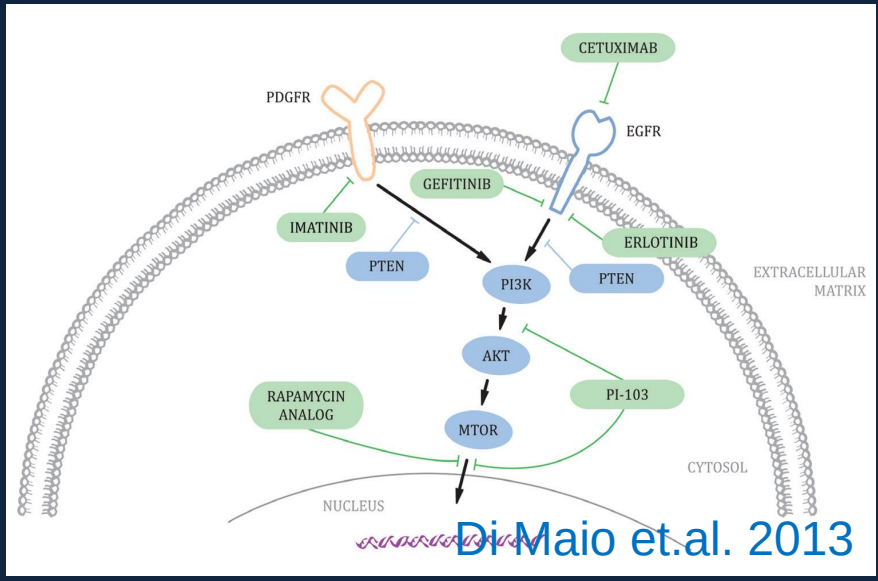
- Brachyury (T) gene
  - Copy Number Gains (CNG)
  - Single Nucleotide Polymorphisms (SNP)
    - (rs2305089)

Molecular Markers and Therapy

Imatinib:
- Phase II – 64-70% stable tumor
- Minimal decrease in tumor size

EGFR (Erlotinib / Cetuximab / gefitinib)
- Case reports

mTOR (Sirolimus)
- cell-line and expression data
- Combination study for imatinib refractory chordoma



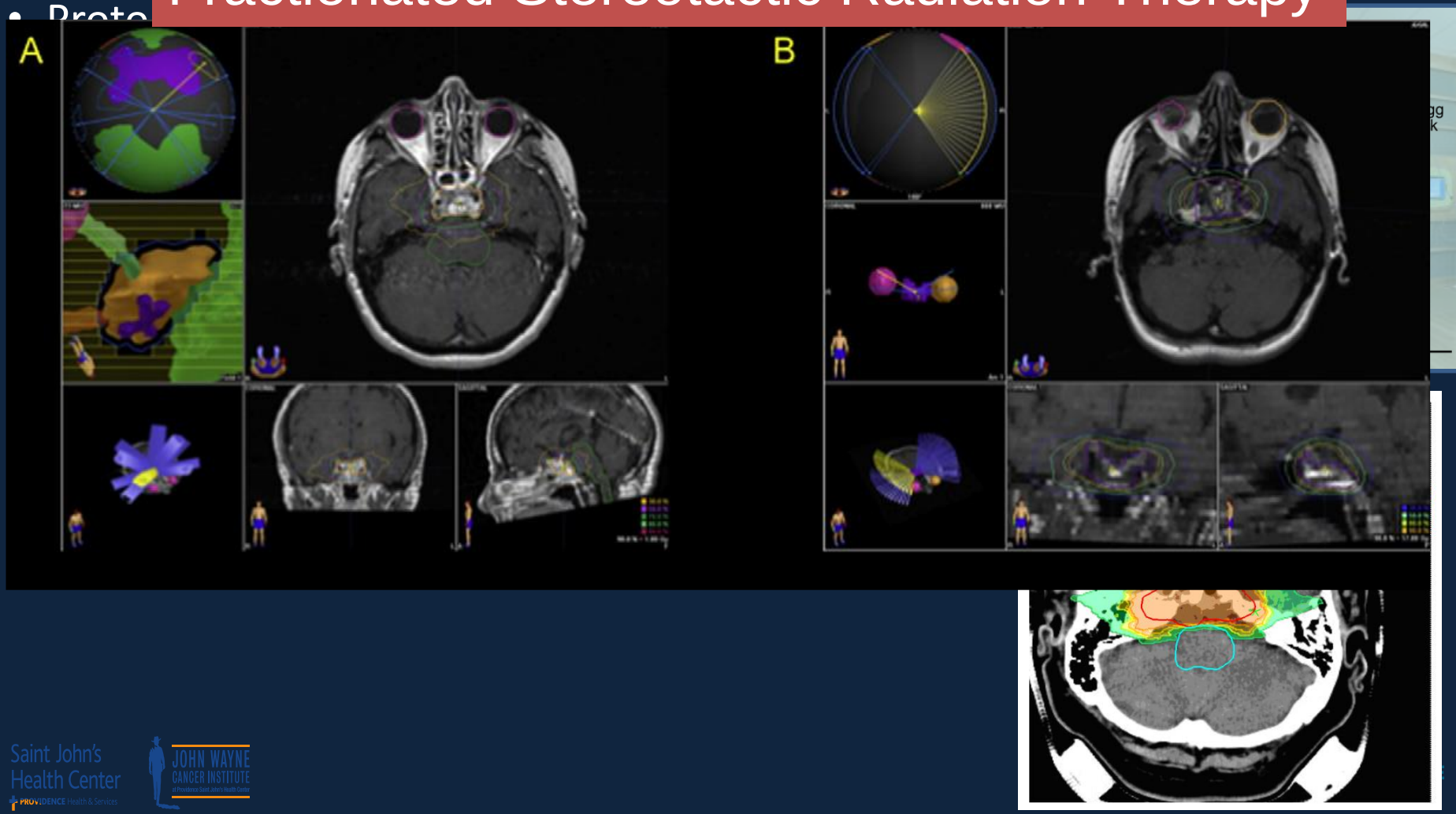
Di Maio et.al. 2013

Variable expression of biomarkers in chordomas suggests role of individualized regimens

Radiation Therapy

- Proto

Fractionated Stereotactic Radiation Therapy



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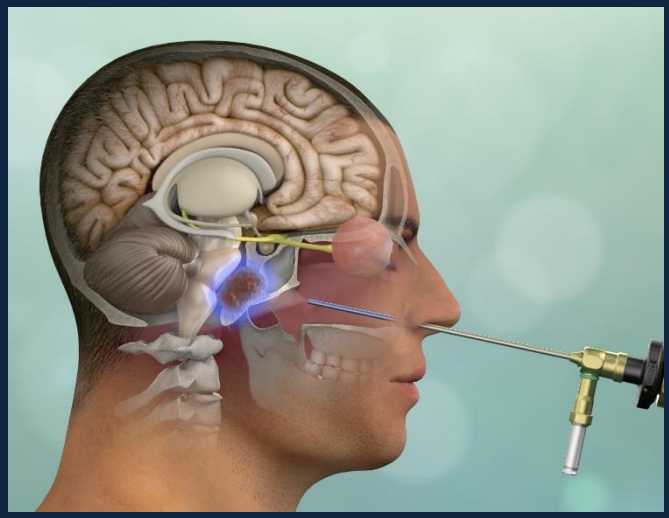
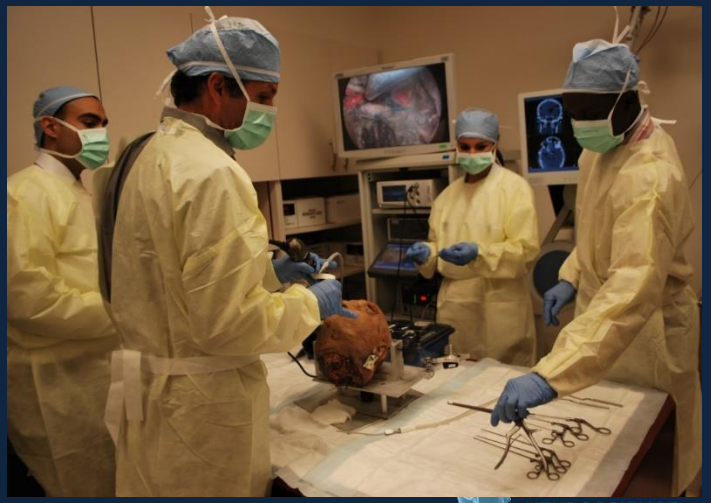
Thank You





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