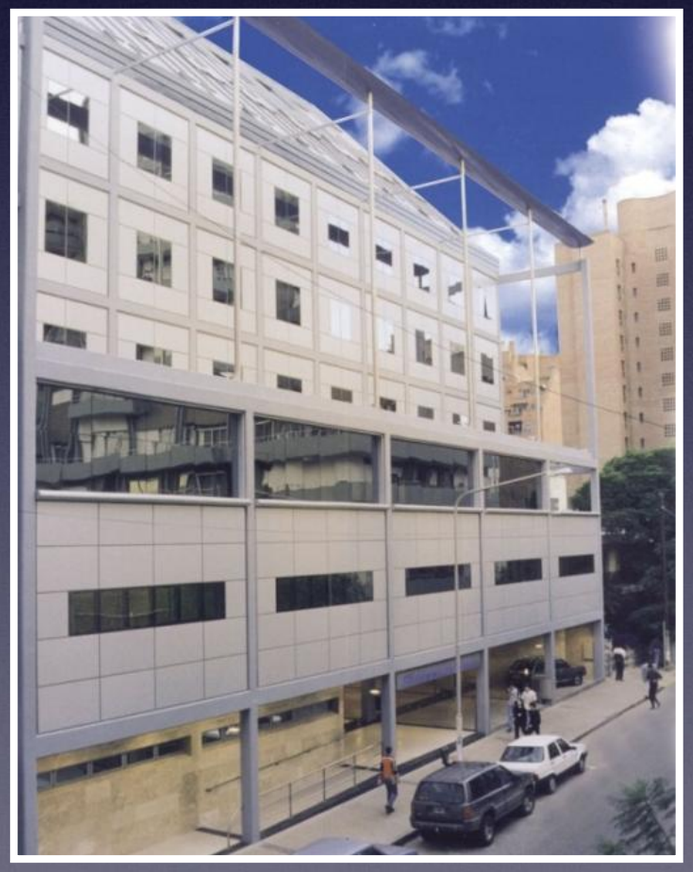
MANEJO QUIRURGICO DE LOS GLIOMAS DE TRONCO

II SIMPOSIO INTERNACIONAL DE RADIOCIRUGIA ESTEREOTACTICA

Dr. Francisco Pueyrredón

HOSPITAL DE NIÑOS DE LA SANTISIMA TRINIDAD



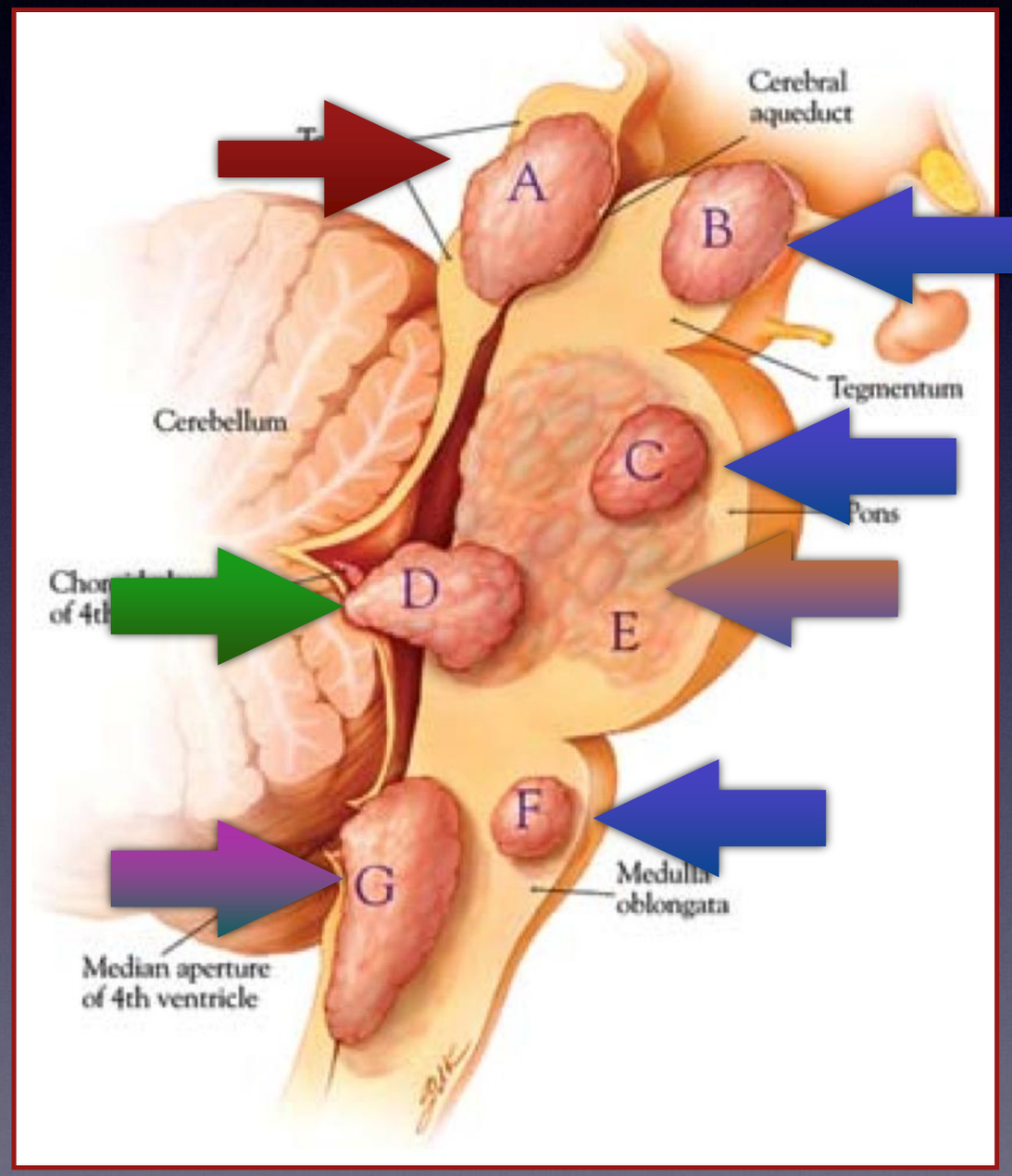
SANATORIO ALLENDE

ESPECIALISTAS EN EL CUIDADO DE LA VIDA

AUTOR	CLASIFIACIÓN	MÉTODO
Epstein (1985)	Intrínisco Difuso Focal Cérvicomedular Exofítico Anterolateral dentro del ángulo pontocerebeloso Pósterolateral dentro del brachium pontis Posterior dentro del cuarto ventrínculo Diseminado Citología positiva Citología negativa	TAC
Epstein y McCleary (1986)	Difuso Focal Lesión circunscripta menor a 2cm sin edema Cérvicomedular	TAC IRM Observación quirúrgica
Choux et al(1999)	Tipo I: Difuso(hipodenso, hipointenso sin refuerzo) Tipo II:Intrínseco y focal (sólido o quístico) Tipo III: Exofítico, tanto dorsal como lateral Tipo IV:bulbomedular	TAC IRM
Guillamo et al (2001)	Infantiles Difuso Intrínseco Focal tectal Posterior exofítico, bulbomedular, otros focales Asociados a neurofibromatosis tipo 1 Adulto Difuso intrínseco de bajo grado Intrínseco maligno Tumores similares a los pediátricos (focal tectal, pilocítico quísitco, posterior exofítico, difuso intrínseco pontino)	IRM

TUMORES DE TRONCO

- Tectales
- Focales
- Exofíticos
- Bulbomedulares
- Difusos



TUMORES DE TRONCO
DIAGNOSTICO

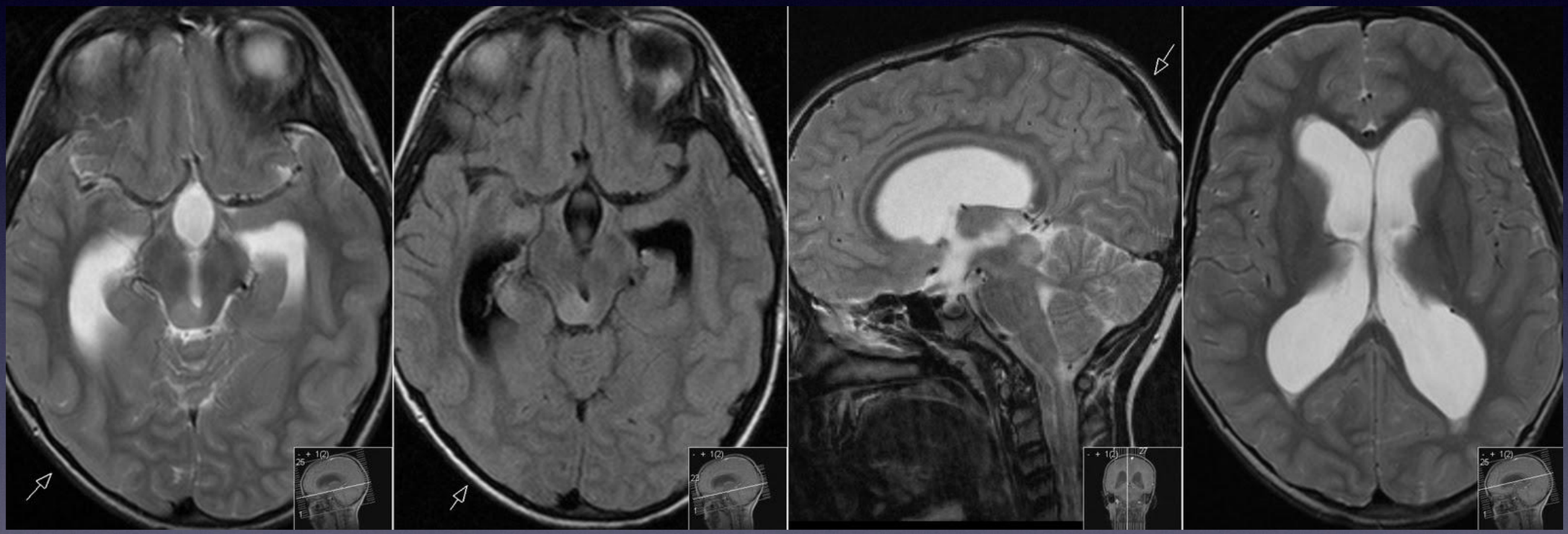
- CLINICA
- RADIOLOGIA

A.Patológica

- Tectales
- Exofíticos
- Focales
- Bulbomedulares

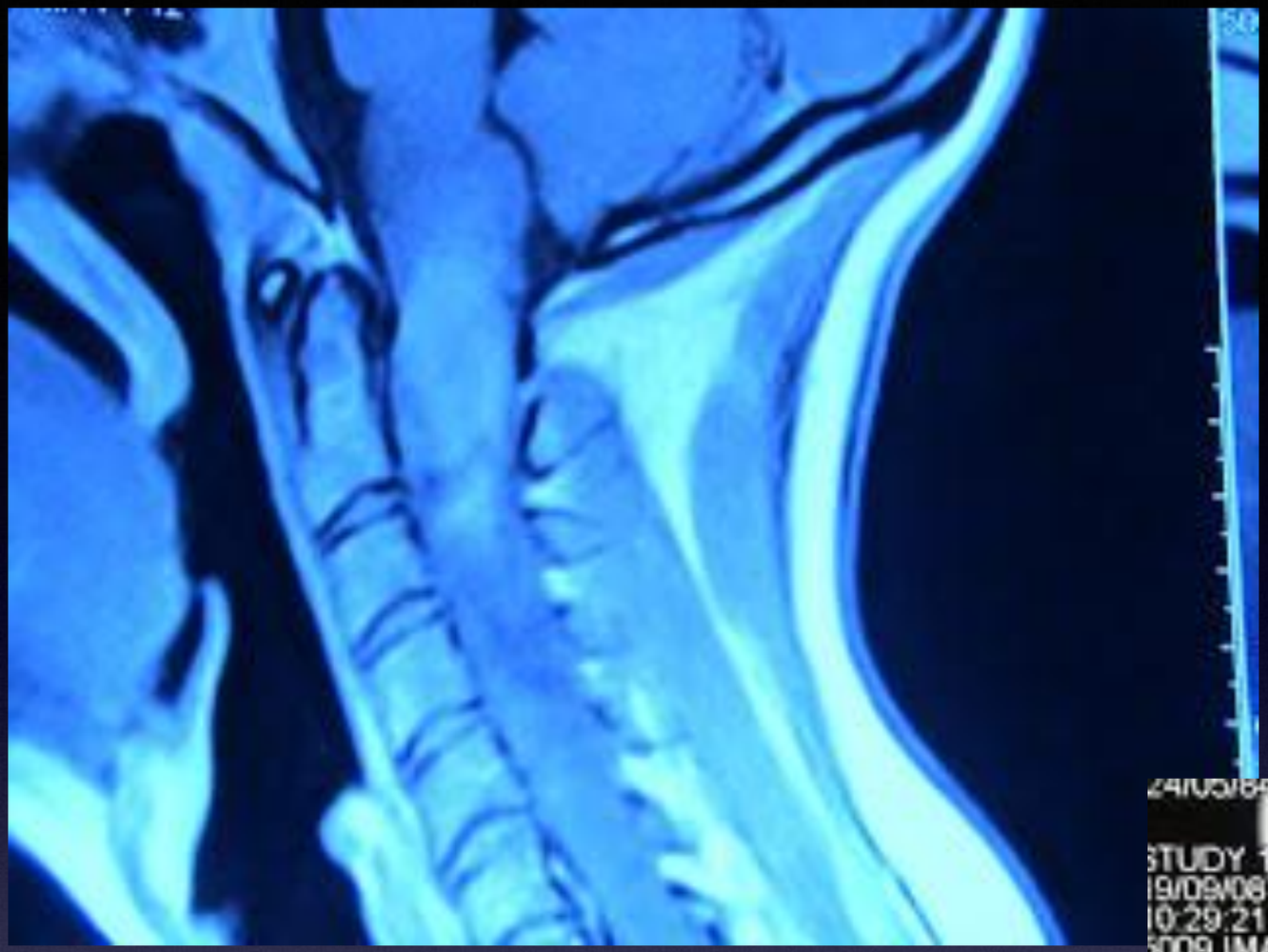
BAJO GRADO

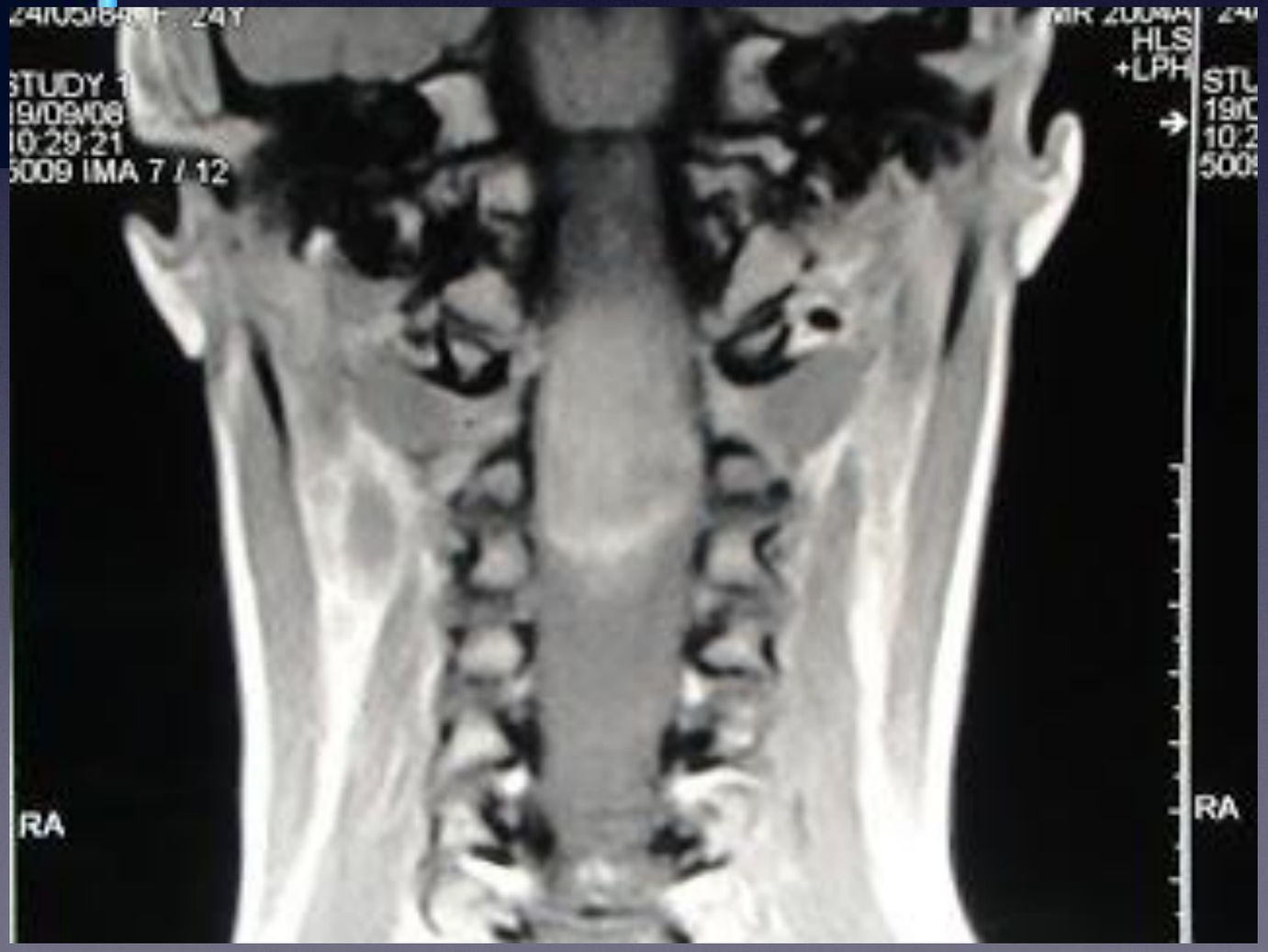
Difusos → ALTO GRADO

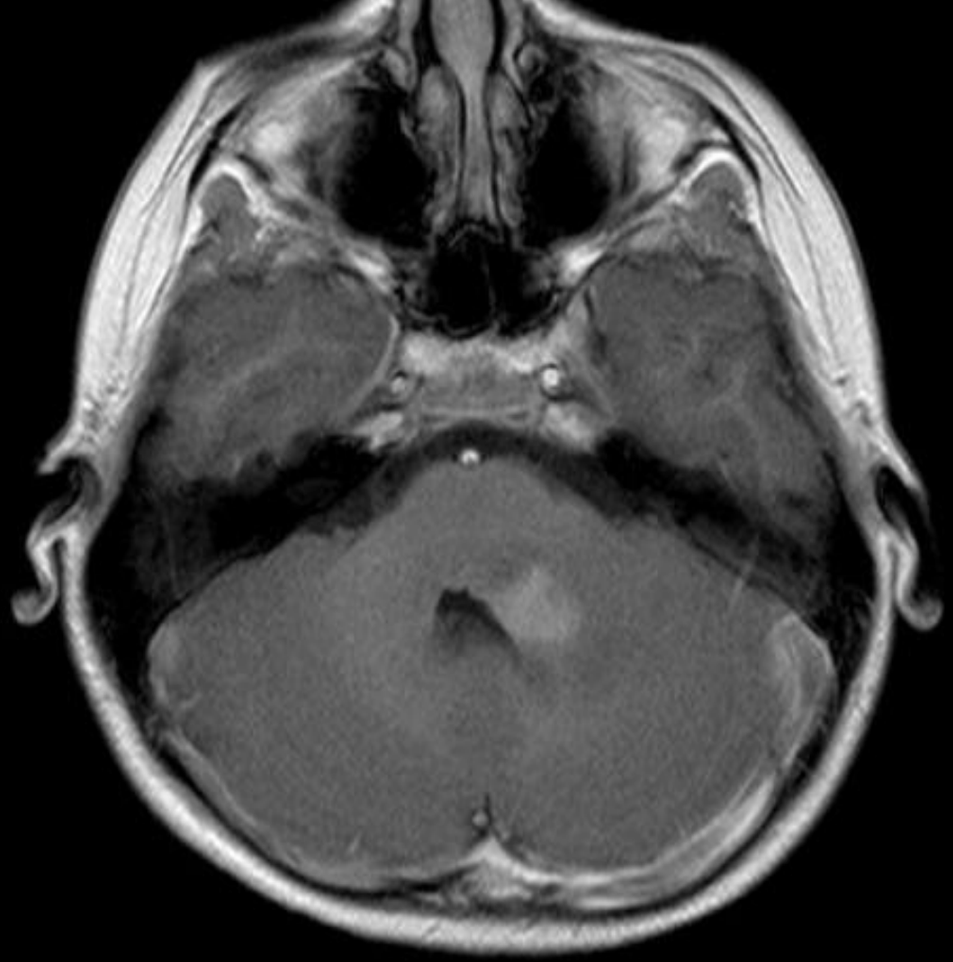


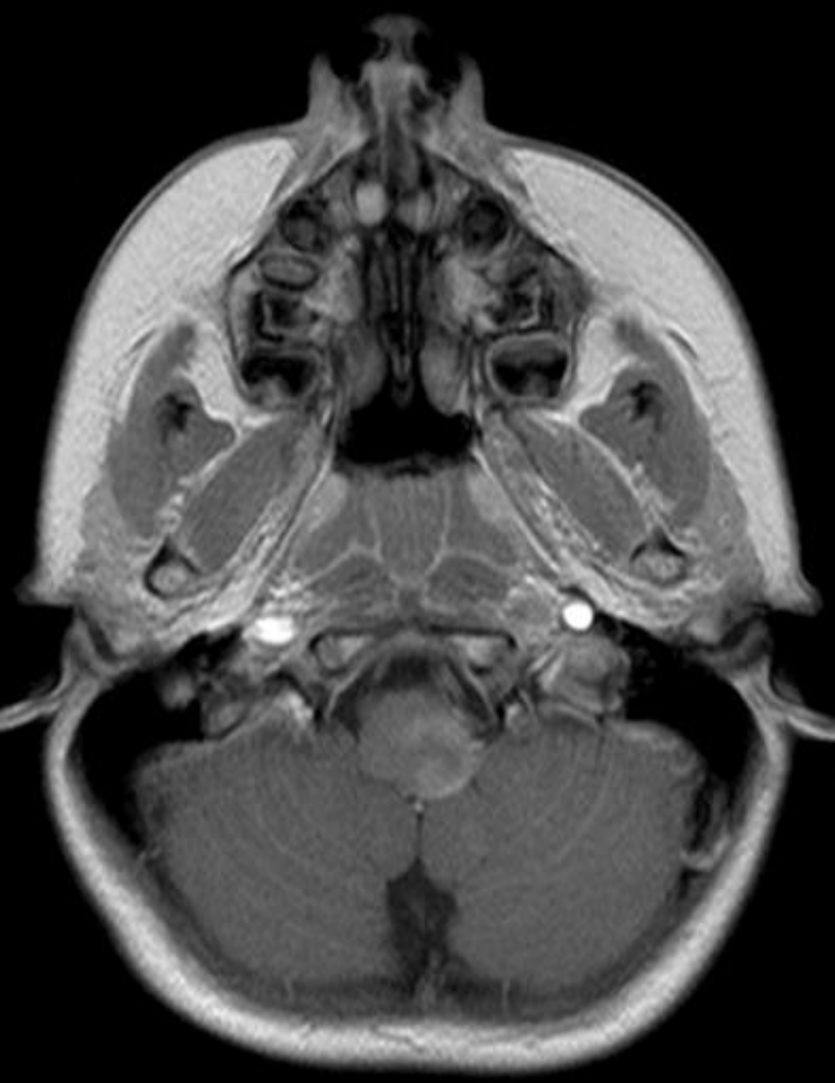
TRATAMIENTO

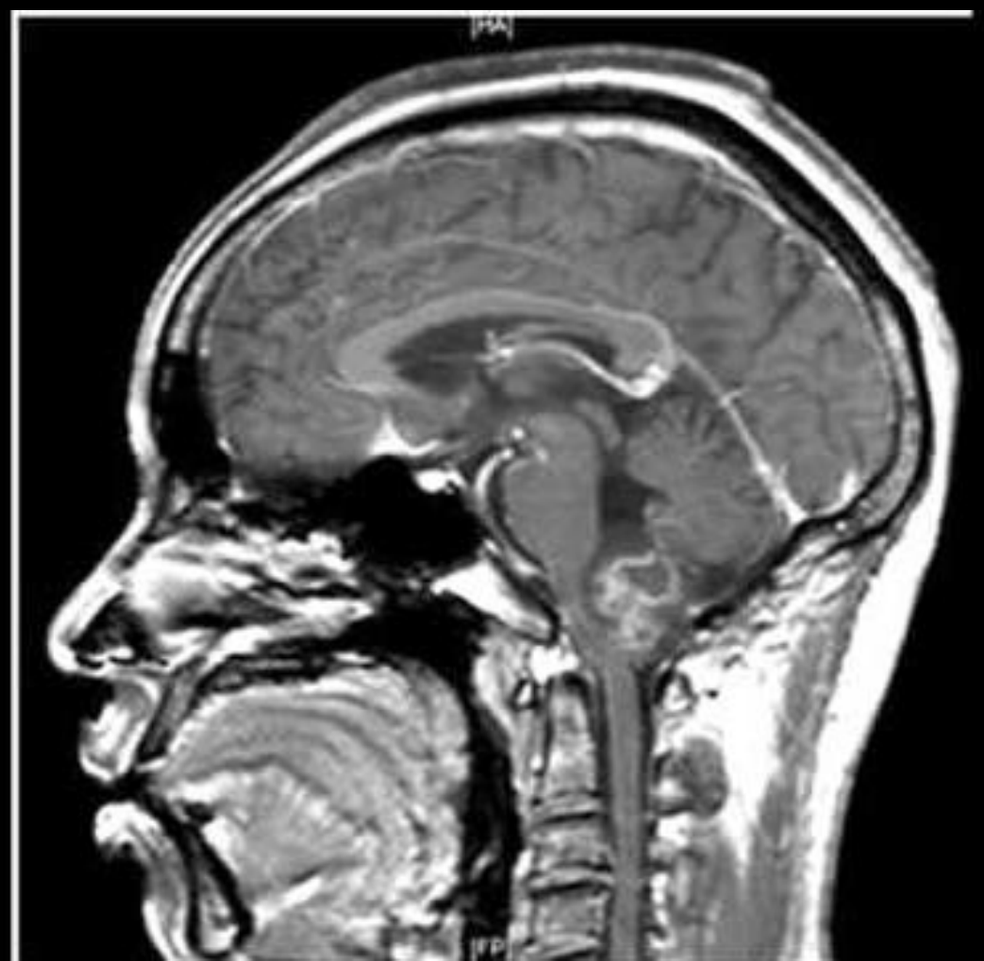
- TUMORES TECTALES:
  - HIDROCEFALIA
  - BIOPSIA?
  - ESPECTANTE




HLS
+LPH
RA
RA

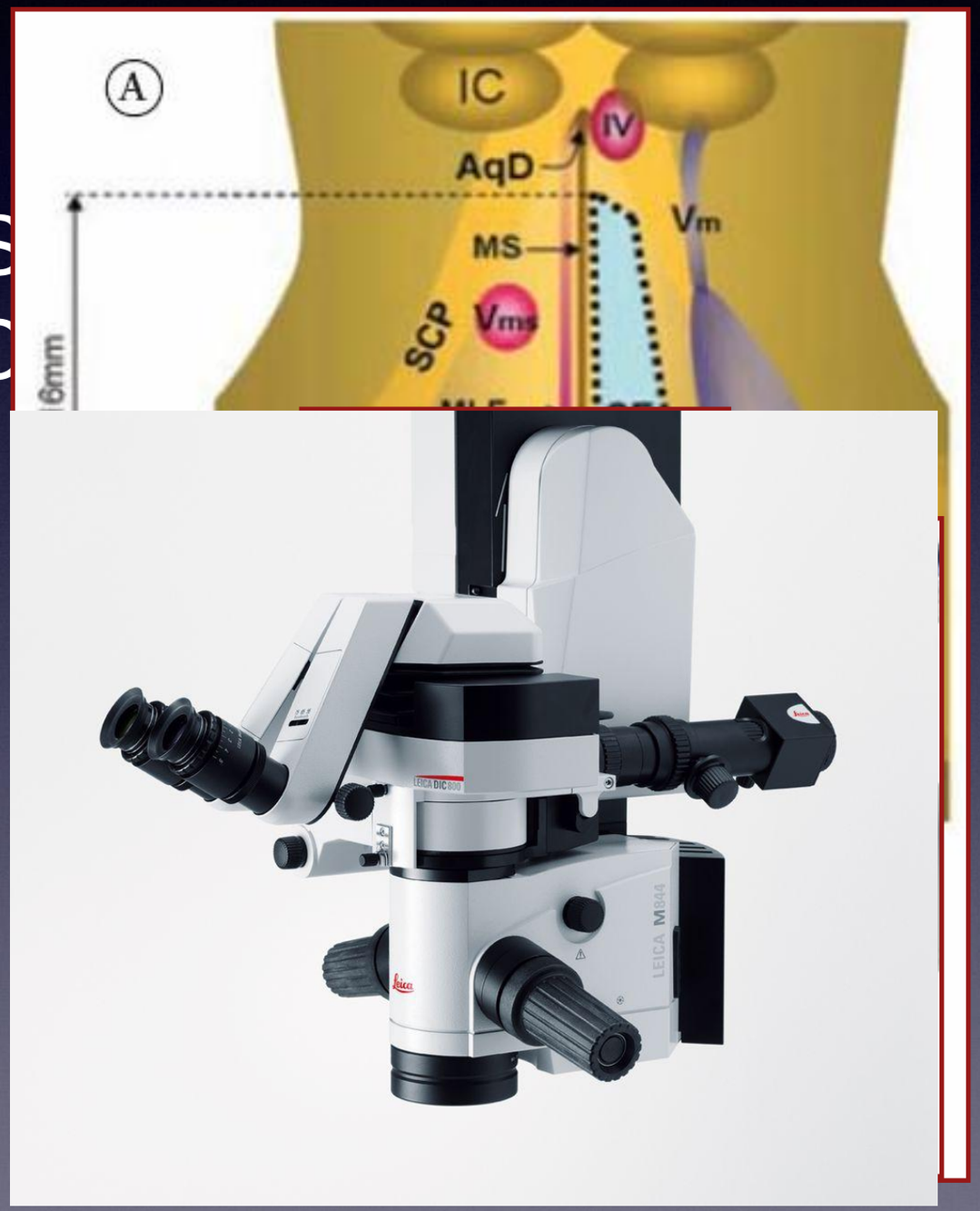






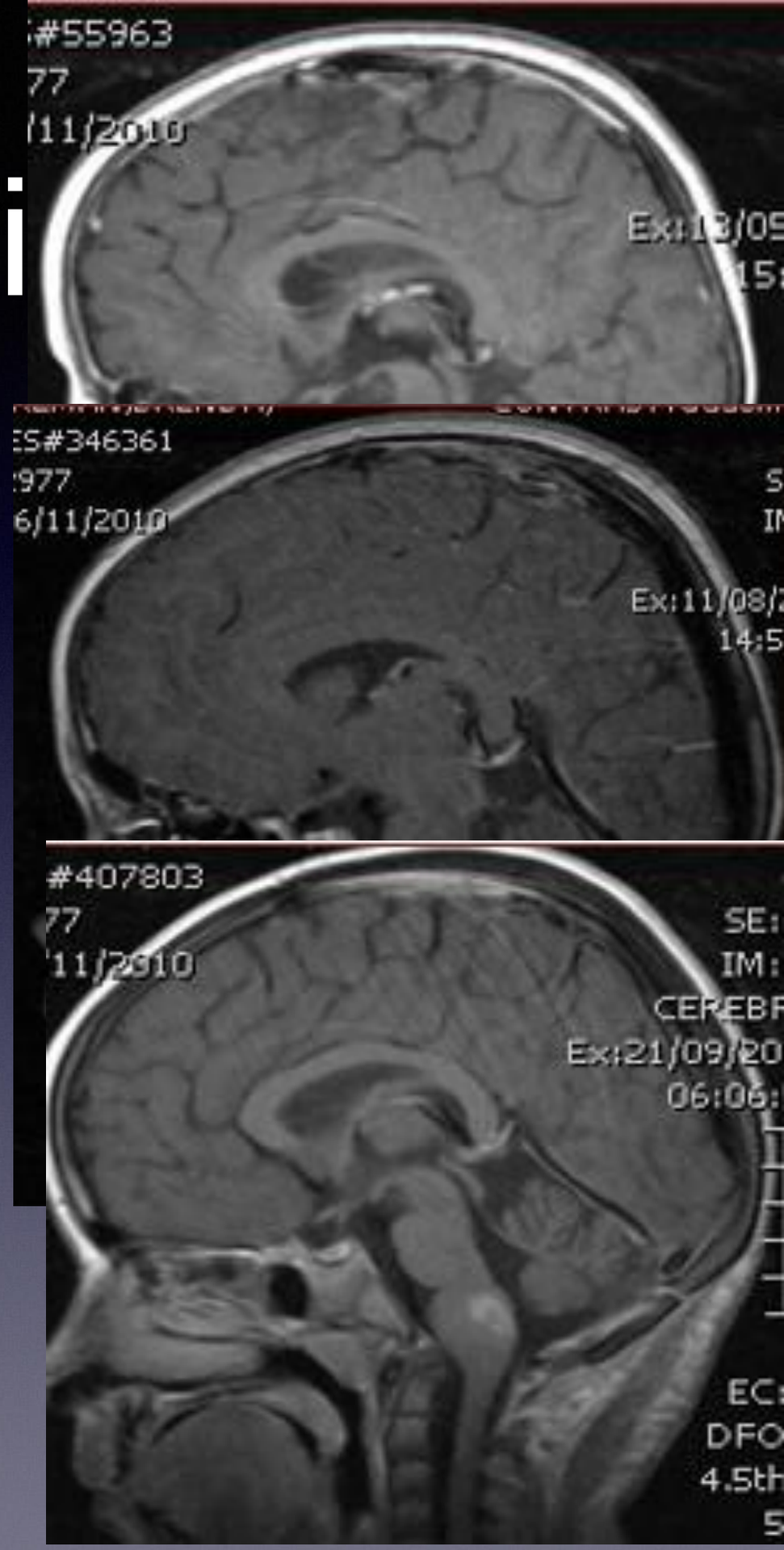
TRATAMIENTO

- EXOFÍTICOS-FOCALES
  BULBOPROTUBERANC
  - BAJO GRADO
  - RESECCIÓN
  - PRESERVACIÓN DE



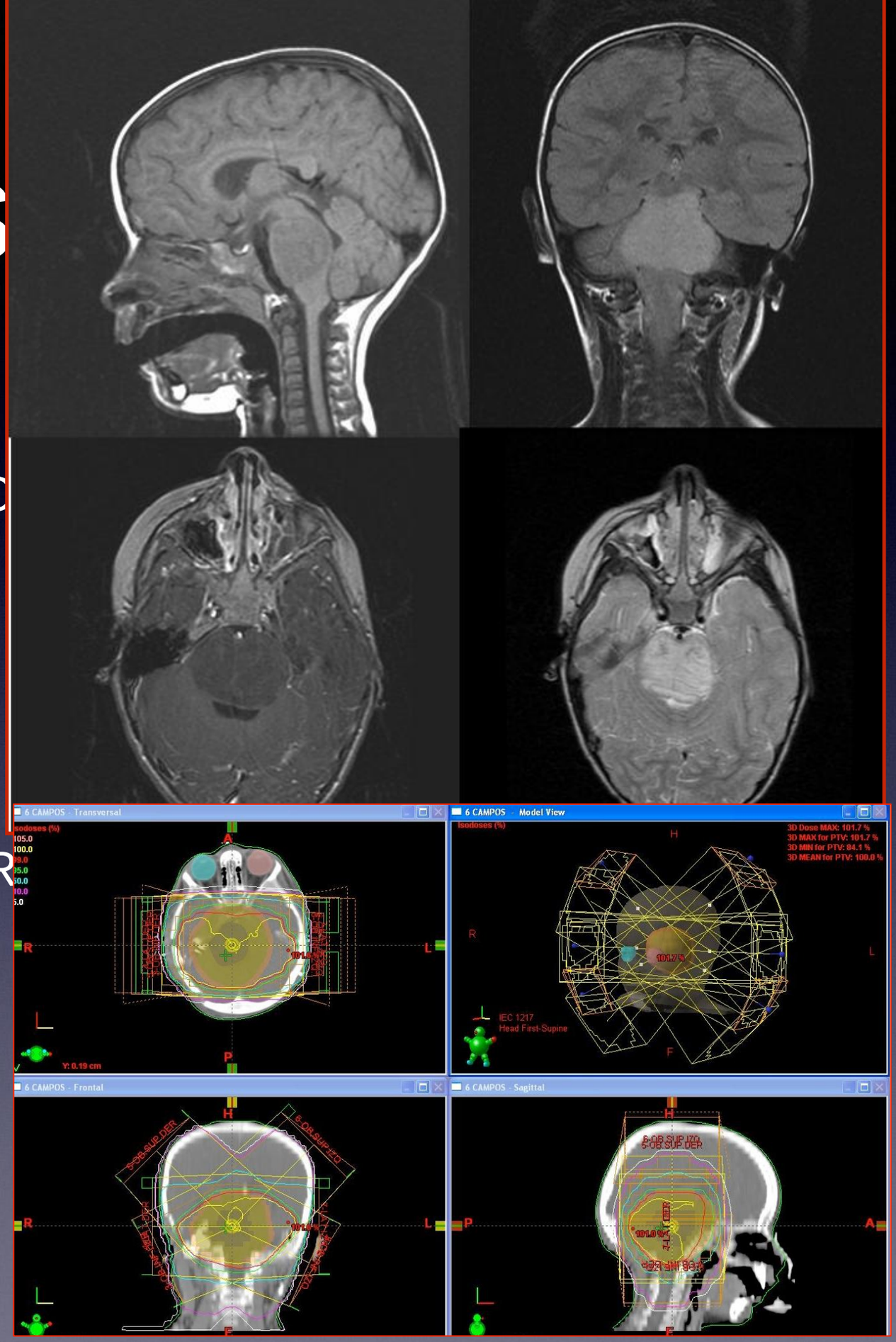
Caso Clíni

- Femenino-8 años
- Tumor focal
- Biopsia astroctima pilocitico
- Transformación quistica
- Cirugía



Tumores

- 75% de los GLIOMAS DE TRONC
- IMÁGENES CLÁSICAS
- EDAD PROMEDIO:7 AÑOS
- CLÍNICA RÁPIDAMENTE PROGR
- GLIOMAS DE ALTO GRADO
- TRATAMIENTO RADIANTE



CONDUCTA

- Neurosurgery 1993

Magnetic Resonance Scans Should Replace Biopsies for the Diagnosis of Diffuse Brain Stem Gliomas: A Report from the Children's Cancer Group

A. Leland Albright, M.D., Roger J. Packer, M.D., Robert Zimmerman, M.D., Lucy B. Rorke, M.D., James Boyett, Ph.D., G. Denman Hammond, M.D.

- DIPG: diagnóstico por resonancia

Cambio de Paradigma

Childs Nerv Syst (2011) 27:1391–1397
DOI 10.1007/s00381-011-1468-z

REVIEW PAPER

Diffuse intrinsic pontine glioma—current status and future strategies

Soumen Khatua · Kevin R. Moore · Tribh S. Vats · John R. W. Kestle

Conclusion A pivotal approach in improving the prognosis of these tumors should include the initiation of biopsy and encouraging families to consider autopsy to study the molecular biology. This will help in redefining this tumor by its molecular signature and profiling targeted therapy. Continued advances should be pursued in neuroimaging technology including identifying surrogate markers of early disease progression. Defining strategies to enhance local

R.Wilkinson & J. Harris

British Journal of Neurosurgery, October 2008; 22(5): 617–618

informa
healthcare

INTRODUCTION AND EDITORIAL

Moral and legal reasons for altruism in the case of brainstem biopsy in diffuse glioma

Once emotional and social interests are taken into account there seems little doubt that brain stem biopsy could be lawful even if there was no benefit to the child's medical interests

Am Soc Clin Oncol Edu Book 2012

Is Biopsy Safe in Children with Newly Diagnosed Diffuse Intrinsic Pontine Glioma?

By Stephanie Puget, MD, PhD, Thomas Blauwblomme, MD, and Jacques Grill, MD, PhD

Conclusion

DIPG remains a leading cause of death for children with brain tumors. The role of diagnostic biopsy for patients with these tumors has been controversial because of the high eloquence of the brainstem and the lack of direct benefit for the patient. Based on the literature and our own data, stereotactic biopsy for patients with DIPG is approximately as safe and diagnostic as supratentorial biopsy, and the amount of tissue obtained allows for molecular analysis. This technique should be offered to these patients and opens new perspectives for the characterization of biomarkers that permit children with newly DIPG to enroll in next- generation clinical trials with targeted therapies.[26]

Pediatric RESEARCH January 2014

Children are not just little adults: recent advances in understanding of diffuse intrinsic pontine glioma biology

Kristin M. Schroeder[1], Christine M. Hoeman[1] and Oren J. Becher[1,2]

	DIPG (%)	Pediatric high-grade glioma (non-DIPG) (%)	Adult high-grade glioma (%)	References
ATRX mutation	9	31	14	(28,36)
CDKN2A/B deletion	0–9	8–26	55	(23,25,37–39)
EGFR amplification	0–18	0–19	40–55	(37–44)
H3F3A mutation-K27M	60–71	19	<3	(28,30,36)
H3F3A mutation-G34R/V	0	13–14	<3	(28,30,36)
Hist1H3B (K27M)	18	3	NA	(30)
IDH1/2 mutation	0	10–16.3	42	(28,37,45,46)
TP53 mutation	40–77	21–54	33–43	(27,28,38,47,48)
SETD2 mutation	NA	15	8	(49)
PDGFR-A amplification	13–36	4–10	11	(23–25,29,37,39)
Loss 10q/PTEN	3–64	20–38	42–80	(23,25,27,29,37,39,42)
Gain 1q	23–64	13–43	8–9	(37,39,50)
Gain 2q	26	8	3	(23)
Gain 8q	28	5	5	(23)
Gain 9q	28	10	8	(23)
Gain 7p/7q	14/9	13/15	70/74	(23,37)
Loss 16q	49	18–26	7	(23,37,50)
Loss 17p	31–64	4–25	9	(23,24,39,50)
Loss 20p	26	3	1	(23)
Loss 21q	2	21	3	(23)
Loss 3q	0	21	4	(23)
Loss 4q	7	21–54	2	(23,24,37,43)

ATRX, α-thalassemia/mental retardation syndrome X-linked; CDKN2A/B, cyclin dependent kinase inhibitor 2A/2B; DIPG, diffuse intrinsic pontine glioma; EGFR, epidermal growth factor

Childs Nerv Syst (2015) 31:1773–1780
DOI 10.1007/s00381-015-2832-1

SPECIAL ANNUAL ISSUE

Biopsy in a series of 130 pediatric diffuse intrinsic Pontine gliomas

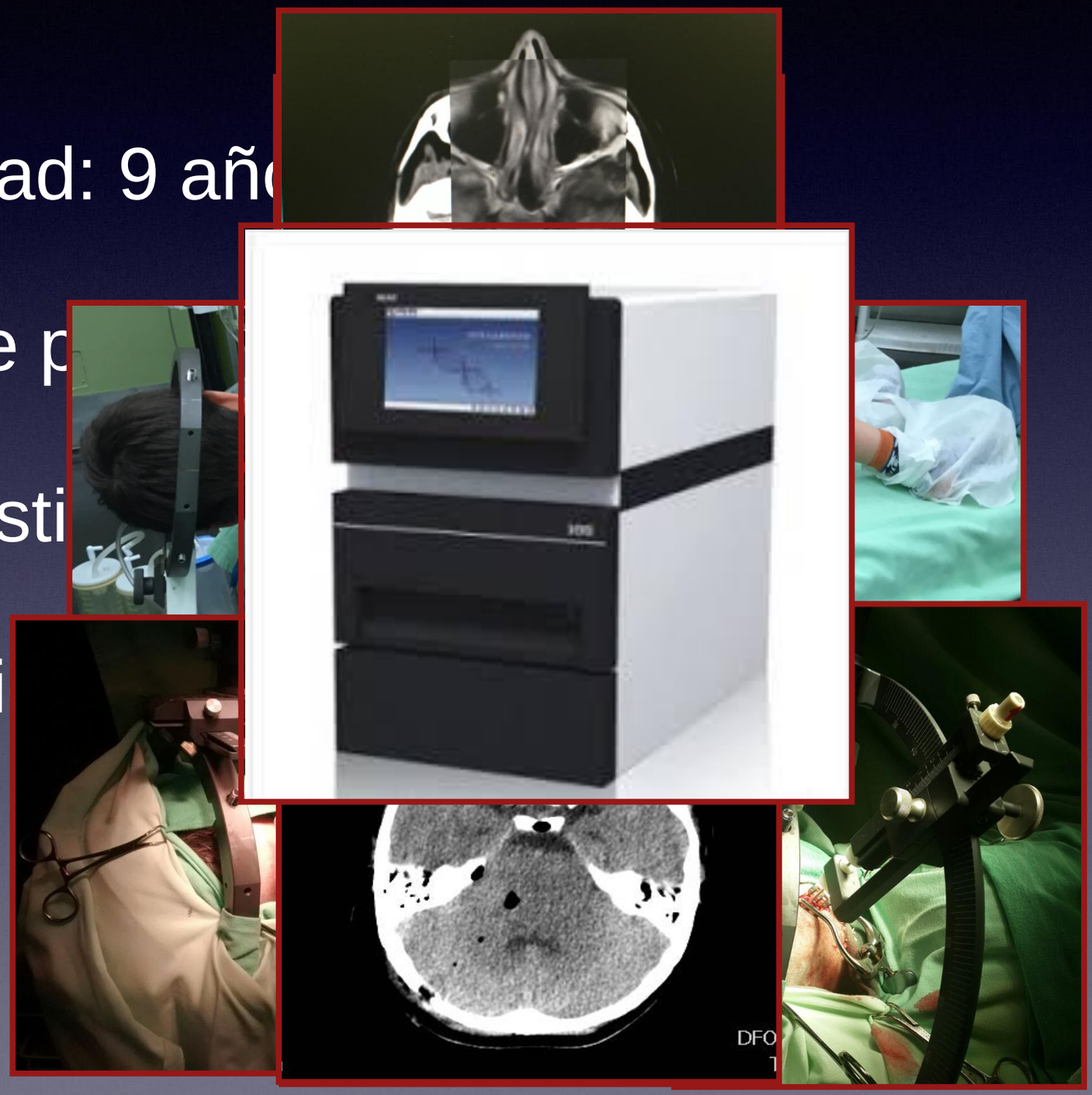
Stephanie Puget[1,2,5] · Kevin Beccaria[1,2] · Thomas Blauwblomme[1,2] · Thomas Roujeau[1,2] · Syril James[1,2] · Jacques Grill[3] · Michel Zerah[1,2] · Pascale Varlet[4] · Christian Sainte-Rose[1,2]

There is a growing body of evidence that up-front biopsy in DIPG is now considered rational for the majority as it may alter treatment with targeted therapy and may help in correlate biology with response with appropriate biomarkers

This worldwide realization will probably lead in the near future to the introduction of up-front stereotactic biopsies as a standard healthcare intervention to stimulate translational research and development of individualized treatment for DIPG and to establish stereotactic biopsies as a standard diagnostic tool for all children suffering from DIPG.

Caso Clínico

- Sexo Femenino-Edad: 9 añ
- Clínica rápidamente p
- Imágenes caracterísi
- Biopsia estereotácti
- Histona 3.3 K27M



Acta Neuropathol (2016) 131:803–820
DOI 10.1007/s00401-016-1545-1

REVIEW

The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary

David N. Louis[1] · Arie Perry[2] · Guido Reifenberger[3,4] · Andreas von Deimling[4,5] · Dominique Figarella-Branger[6] · Webster K. Cavenee[7] · Hiroko Ohgaki[8] · Otmar D. Wiestler[9] · Paul Kleihues[10] · David W. Ellison[11]

Pediatric diffuse gliomas

In the past, pediatric diffuse gliomas were grouped with their adult counterparts, despite known differences in behavior between pediatric and adult gliomas with similar histological appearances. Information on the distinct underlying genetic abnormalities in pediatric diffuse gliomas is beginning to allow the separation of some entities from histologically similar adult counterparts [24, 37, 52]. One narrowly defined group of tumors primarily occurring in children (but sometimes in adults too) is characterized by K27M mutations in the histone H3 gene *H3F3A*, or less commonly in the related *HIST1H3B* gene, a diffuse growth pattern, and a midline location (e.g., thalamus, brain stem, and spinal cord) (Fig. 4) [19, 51]. This newly defined entity is termed *diffuse midline glioma, H3 K27M–mutant* and includes tumors previously referred to as diffuse intrinsic pontine glioma (DIPG). The identification of this phenotypically and molecularly defined set of tumors provides a rationale for therapies directed against the effects of these mutations.

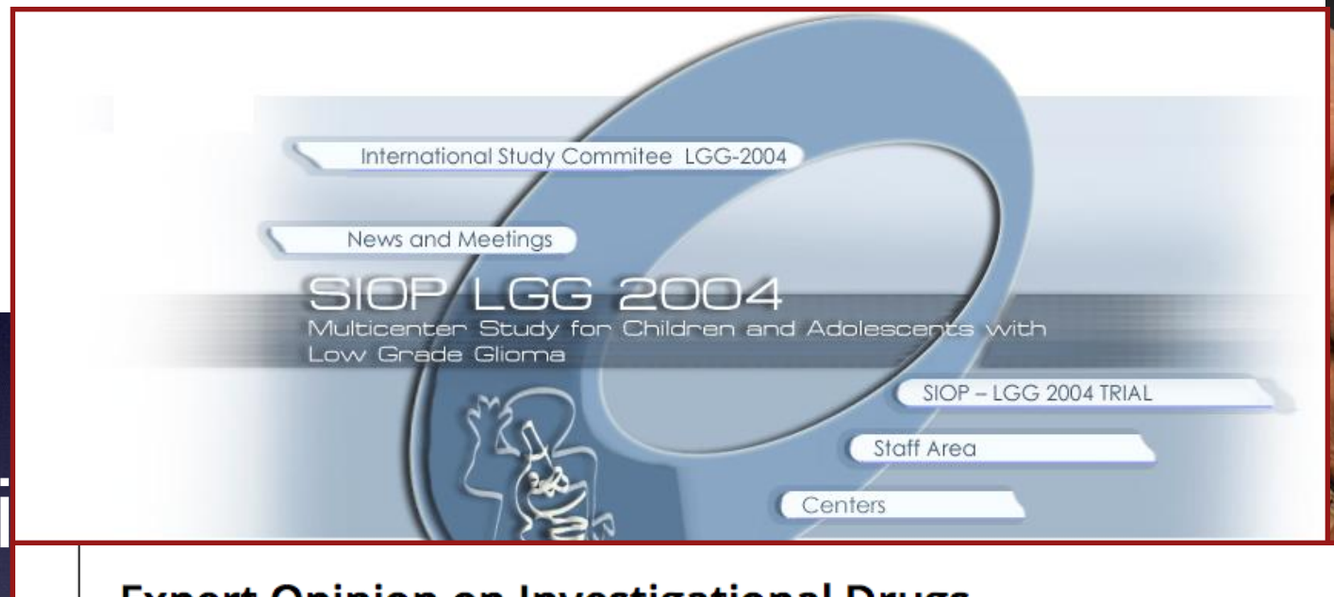
Biología M

- Diferencias con glion
- Protocolos de tratami
- Nuevos Marcadores
- Nuevas perspectivas

Acta Neuropathol (2011) 121:397–405
DOI 10.1007/s00401-011-0802-6

ORIGINAL PAPER

Analysis of *BRAF* V600E mutation in 1,320 nervous system tumors



Expert Opinion on Investigational Drugs

ISSN: 1354-3784 (Print) 1744-7658 (Online) Journal homepage: http://www.tandfonline.com/loi/ieid20

BRAF inhibitors in BRAF-V600 mutated primary neuroepithelial brain tumors

Matthias Preusser, Michal Bienkowski & Peter Birner

To cite this article: Matthias Preusser, Michal Bienkowski & Peter Birner (2015): BRAF inhibitors in BRAF-V600 mutated primary neuroepithelial brain tumors, Expert Opinion on Investigational Drugs, DOI: 10.1517/13543784.2016.1110143

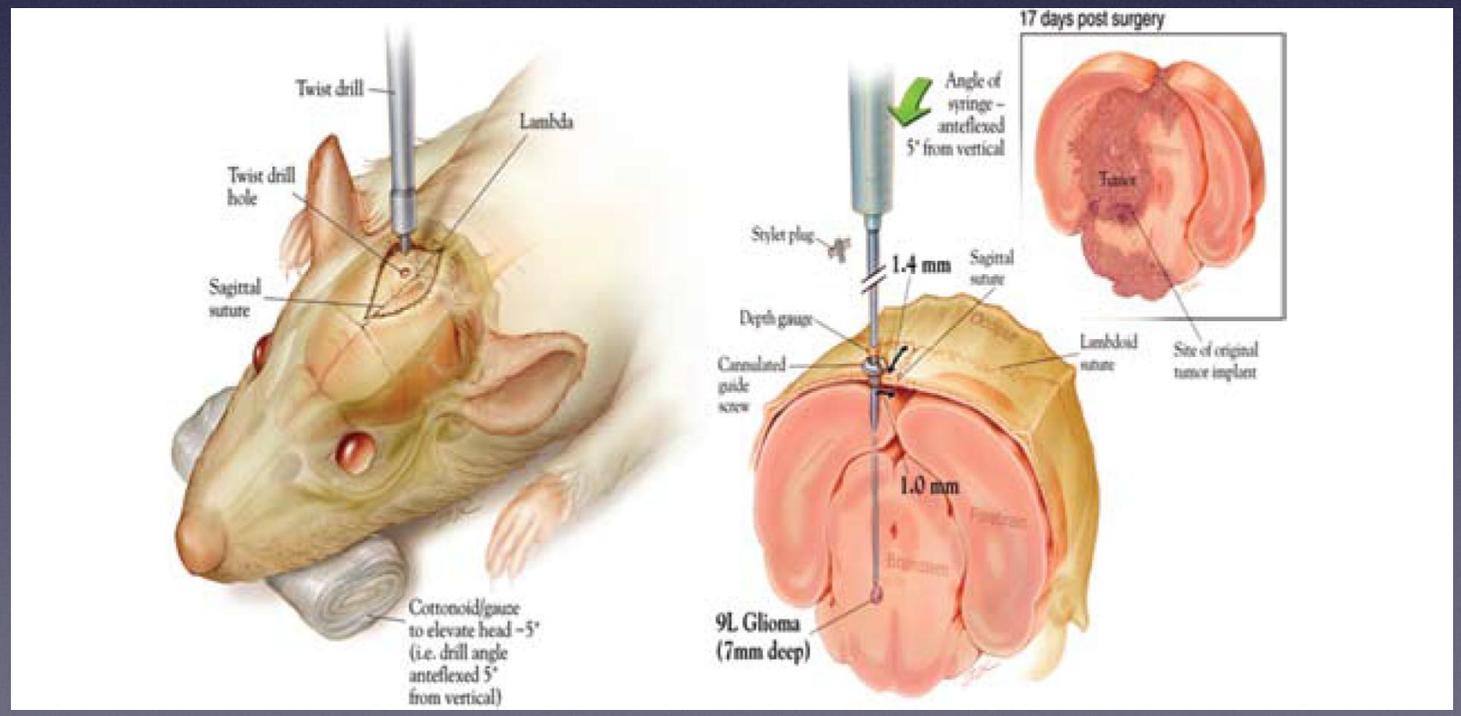
J Neurosurg Pediatrics 3:259–269, 2009

Childs Nerv Syst (2015) 31:557–562
DOI 10.1007/s00381-015-2640-7

ORIGINAL PAPER

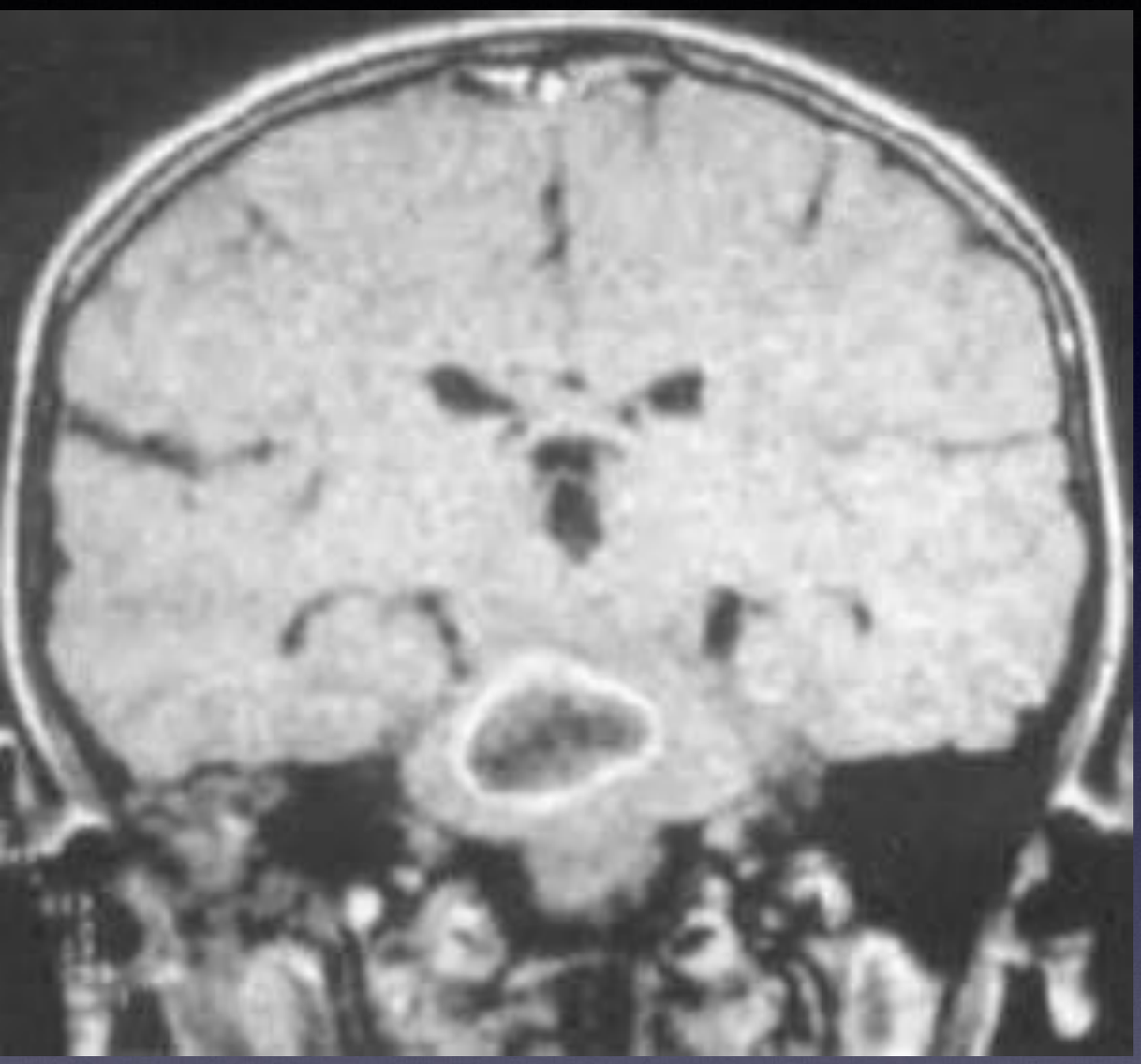
Toxicity evaluation of convection-enhanced delivery of small-molecule kinase inhibitors in naïve mouse brainstem

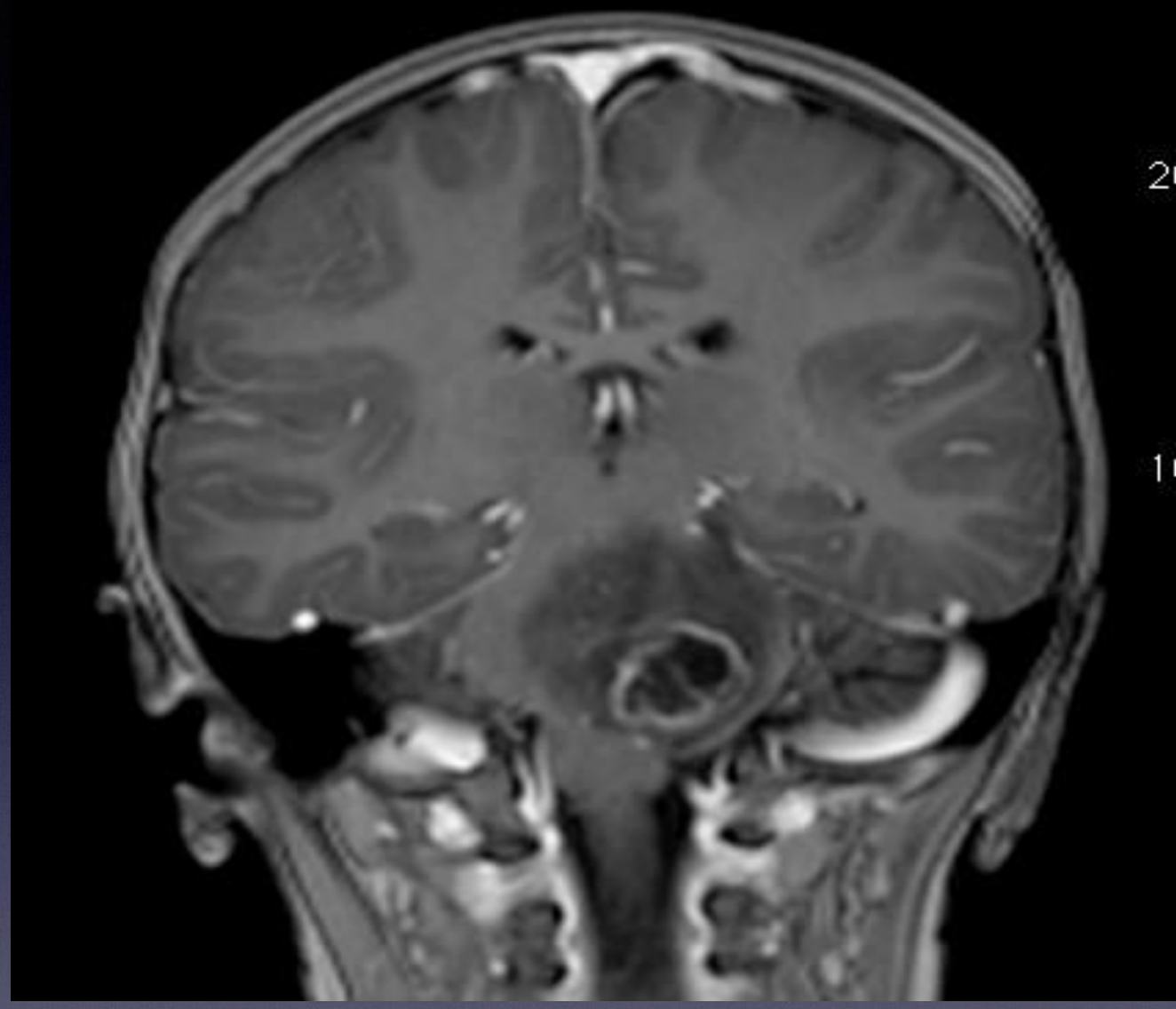
Zhiping Zhou · Sharon L. Ho · Ranjodh Singh · David J. Pisapia · Mark M. Souweidane



DIFUSOS
INDICACIONES BIOPSIA

- DUDA DIAGNOSTICA
- BIOLOGIA MOLECULAR





TUMORES DE TRONCO

PRONOSTICO

- DIFUSOS: PROMEDIO DE SOBRE VIDA MENOR A UN AÑO (Cohen KJ, Pollack IF, Zhou T, et al.: Temozolomide in the treatment of high-grade gliomas in children: a report from the Children's Oncology Group. Neuro Oncol 13 (3): 317-23, 2011)

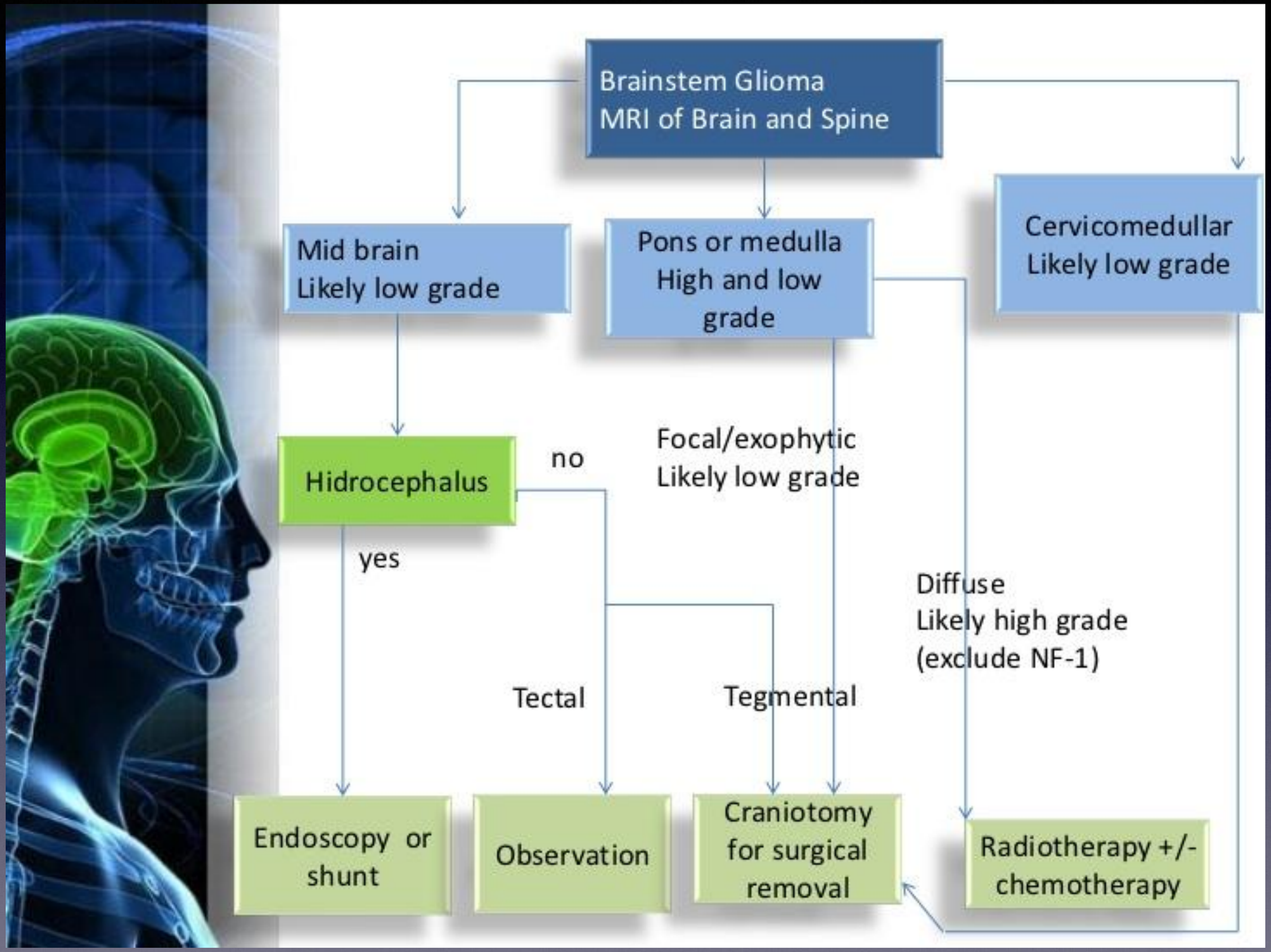
- FOCALES: PROMEDIO DE SOBRE VIDA MAYOR A 90% A 5 AÑOS (Klimo P Jr, Pai Panandiker AS, Thompson CJ, et al.: Management and outcome of focal low-grade brainstem tumors in pediatric patients: the St. Jude experience. J Neurosurg Pediatr 11 (3): 274-81, 2013)

TUMORES DE TRONCO
FACTORES PRONOSTICO

- HISTOLOGIA/GRADO DEL TUMOR (Ballester LY, Wang Z, Shandilya S, et al.: Morphologic characteristics and immunohistochemical profile of diffuse intrinsic pontine gliomas. Am J Surg Pathol 37 (9): 1357-64, 2013)

- EDAD (Broniscer A, Laningham FH, Sanders RP, et al.: Young age may predict a better outcome for children with diffuse pontine glioma. Cancer 113 (3): 566-72, 2008)

- NF1 (Albers AC, Gutmann DH: Gliomas in patients with neurofibromatosis type 1. Expert Rev Neurother 9 (4): 535-9, 2009)


Brainstem Glioma
MRI of Brain and Spine
Mid brain
Likely low grade
Pons or medulla
High and low
grade
Cervicomedullar
Likely low grade
Hidrocephalus
no
yes
Focal/exophytic
Likely low grade
Diffuse
Likely high grade
(exclude NF-1)
Tectal
Tegmental
Endoscopy or
shunt
Observation
Craniotomy
for surgical
removal
Radiotherapy +/-
chemotherapy

Treatment Group	Standard Treatment Options
Newly diagnosed childhood brain stem gliomas:	
Diffuse intrinsic pontine gliomas	Radiation therapy
Focal brain stem gliomas	Surgical resection (with or without chemotherapy and/or radiation therapy)
	Observation (with or without cerebrospinal fluid diversion)
	Radiation therapy, chemotherapy, or alternative approaches for unresectable tumors
Recurrent/progressive childhood brain stem gliomas:	
Diffuse intrinsic pontine gliomas	There is no standard treatment
Focal brain stem gliomas	Repeat surgical resection
	Radiation therapy
	Chemotherapy

Conclusiones

- Variables anatómicas y Patológicas
- Tratamiento adecuado a cada paciente (Quirúrgico vs Médico)
- Biología Molecular (DIPG)
- Perspectivas Futuras

- En la mayoría de los casos la decisión de una intervención quirúrgica se basa en la premisa de que cualquier beneficio proporcionado en términos de resultados no se compensa con la morbilidad del procedimiento quirúrgico

CALIDAD DE VIDA

Primum Non Nocere

It was a law in old Egypt that all inventions in handicrafts had to be judged by an assembly educated men and be written on pillars in a sacred place. Likewise, we should have an assembly just and equally well-educated men. They should scrutinize all that has been written, and deposit a public place only what appears worthwhile, destroy what is worthless.

Galen, Against the Opinions of Julian Concerning the Aphorisms of Hippocrates Trans. R.E. Siegel, quoted by P. Prioreschi Roman Medicine, p. 327.

http://www.nlm.nih.gov/news/Galen.jpg

MUCHAS GRACIAS