

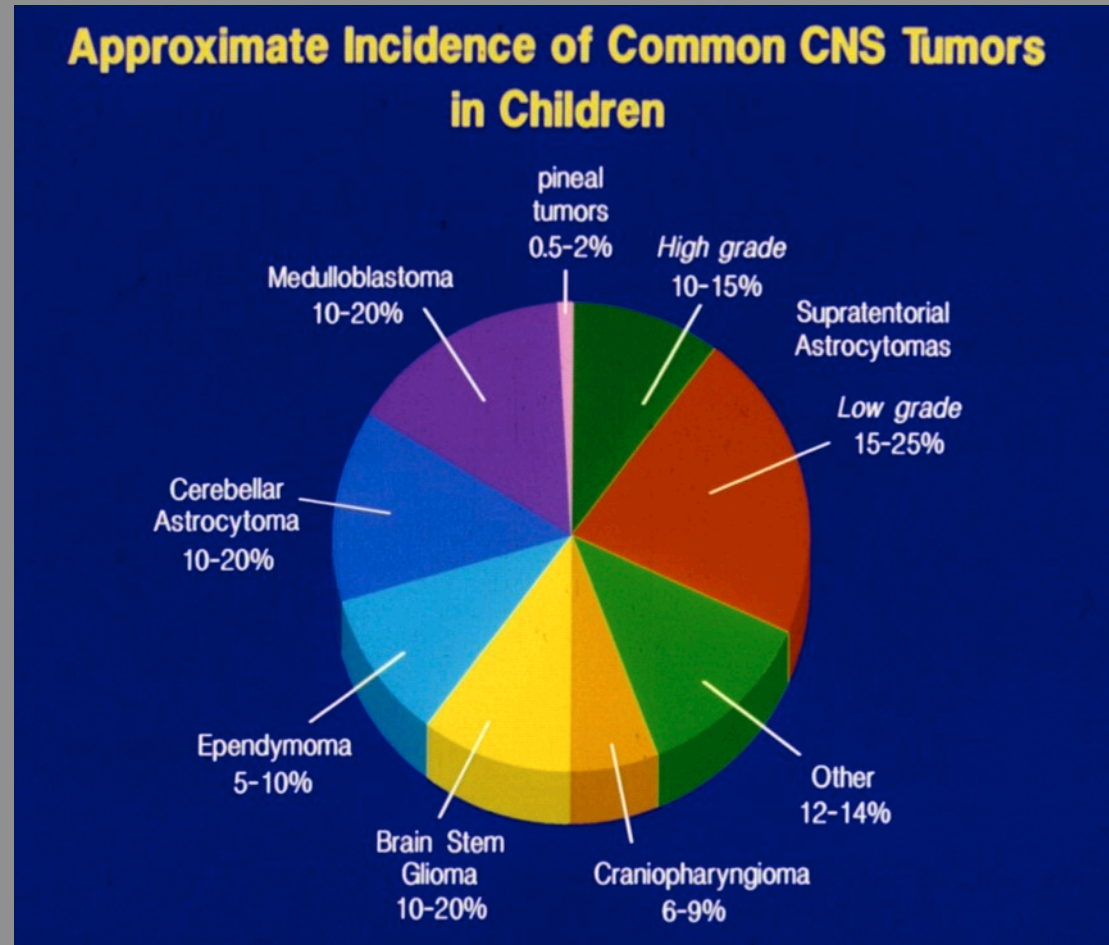
Childhood Posterior Fossa Ependymoma: How I Do It



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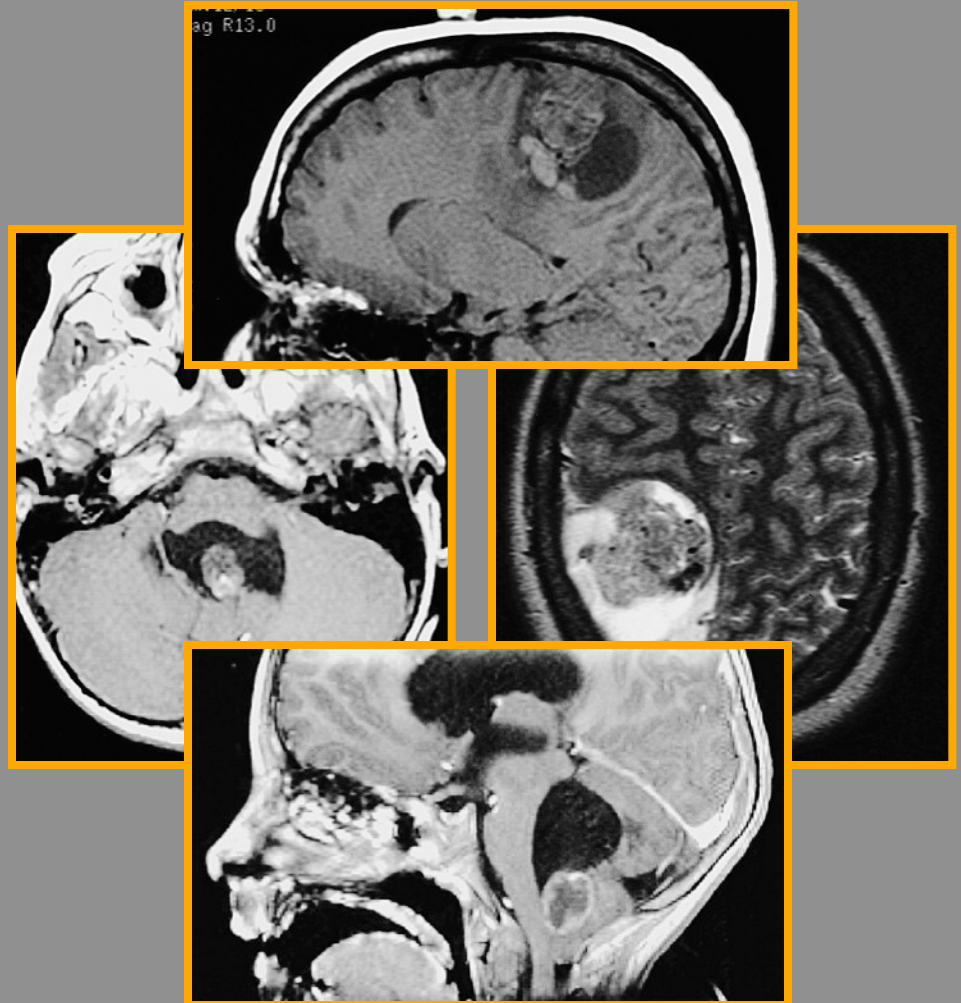
Background

- Ependymoma is the 3rd most common brain tumor of childhood
- Comprises 5-10% of pediatric tumors



Clinical Presentation

- **Tumor Location**
 - 90% intracranial
 - 60% infratentorial
 - 30% supratentorial
- **Natural History**
 - 95% localized
 - 5% disseminated



Extent of Resection

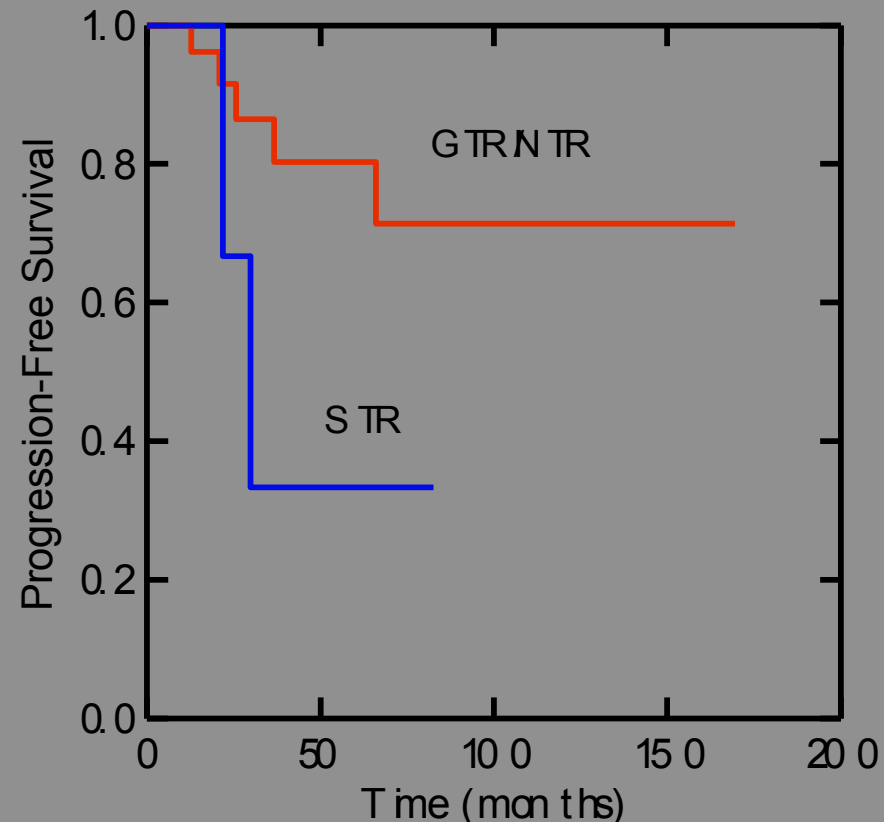
GTR

– PFS 70-80%

< GTR

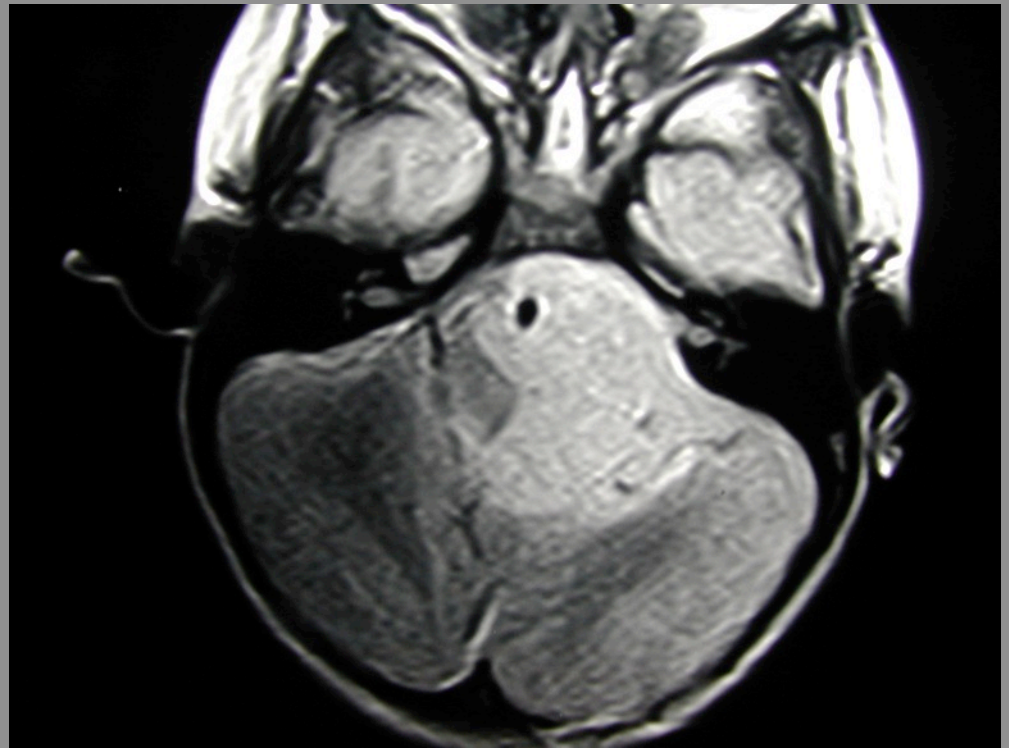
– PFS 30-40%

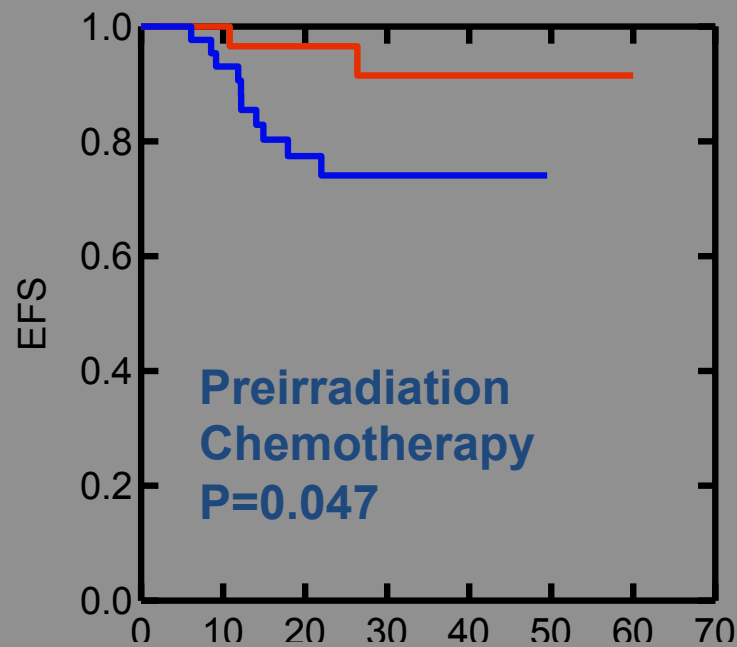
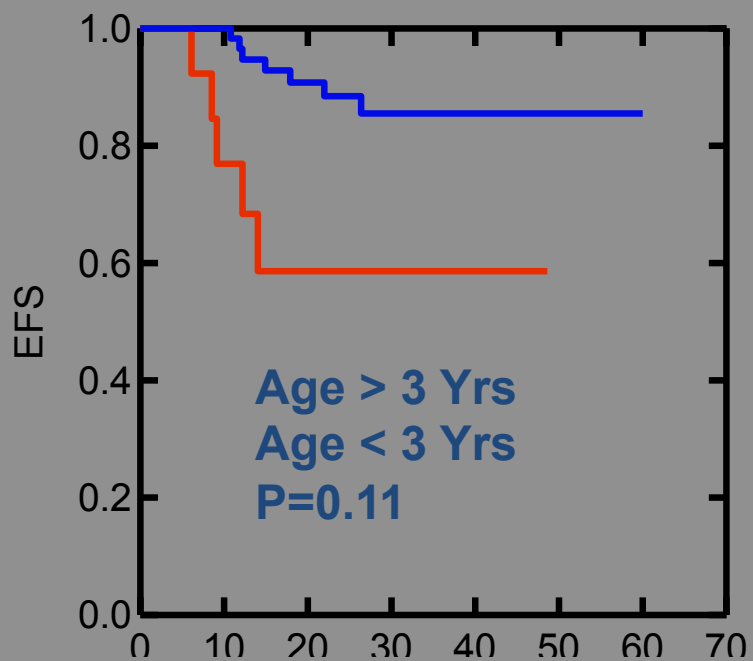
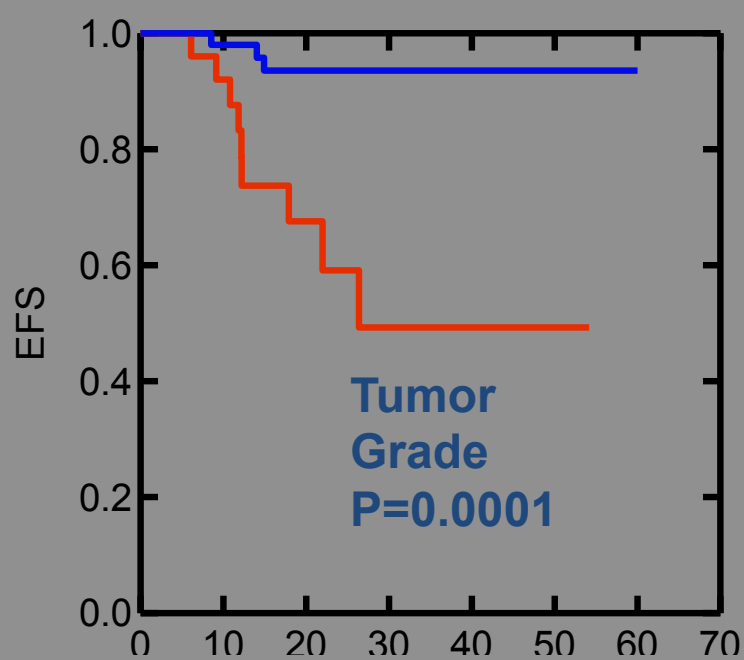
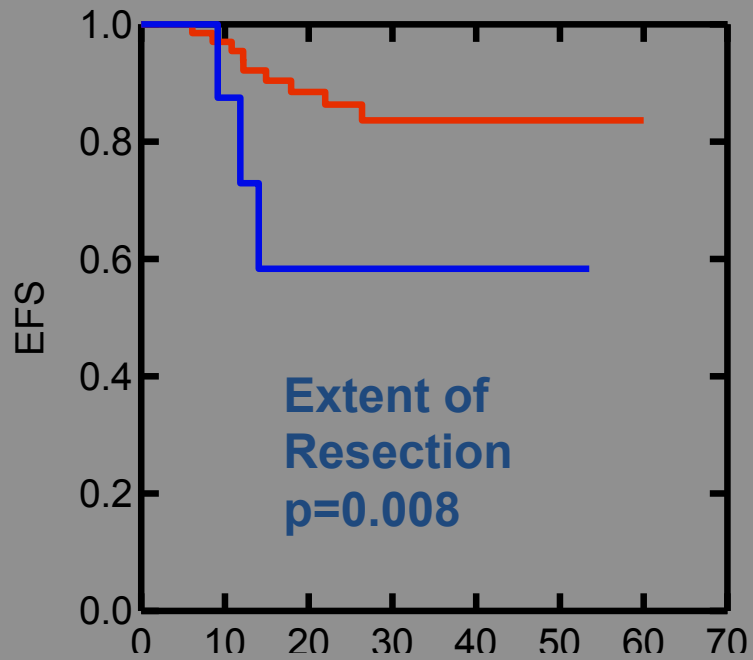
Rate of GTR (USA): 40-50%



Extent of Resection

Rate of GTR (USA): 40-50%
(one can see why)



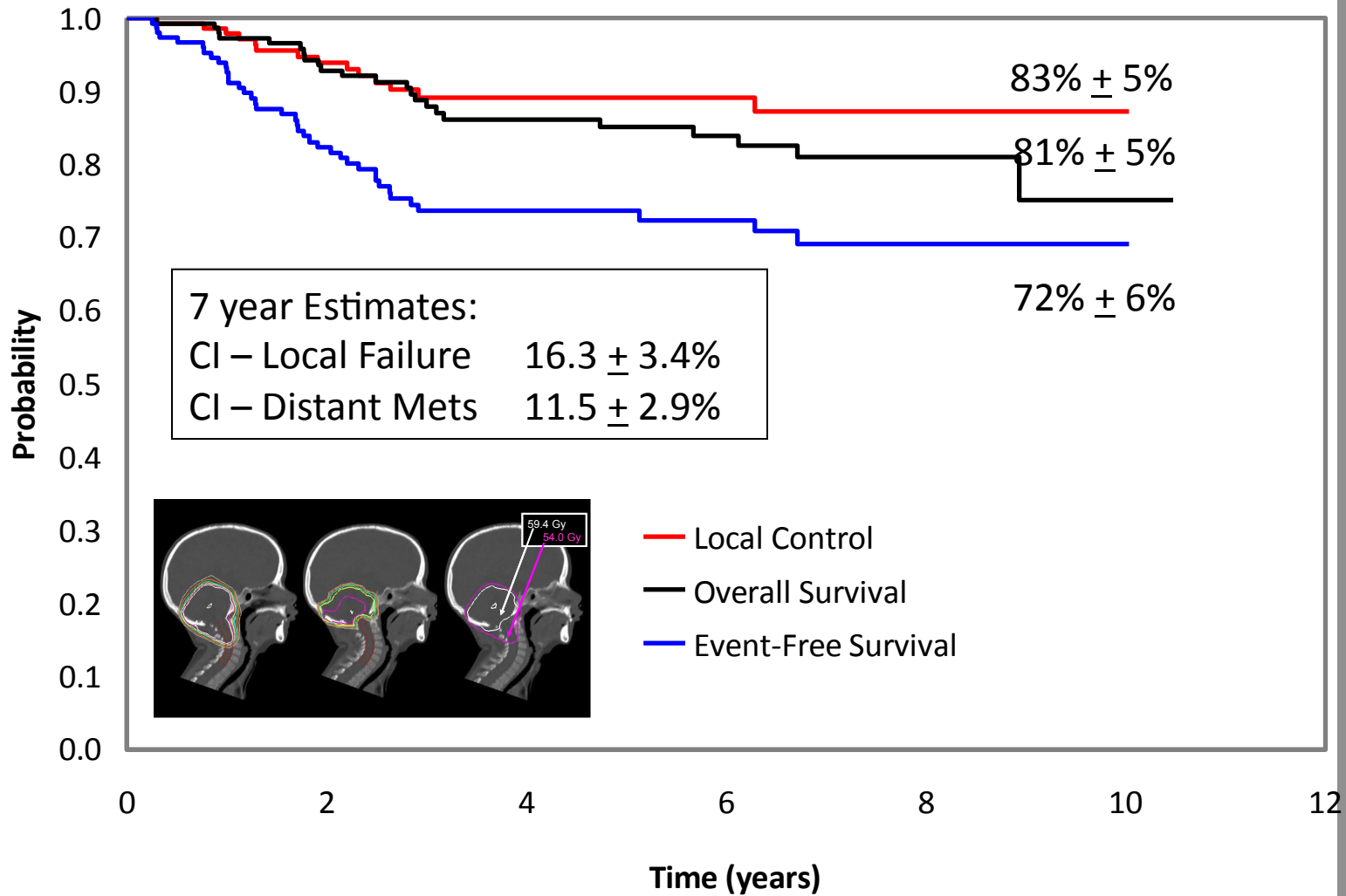


Historical Overview

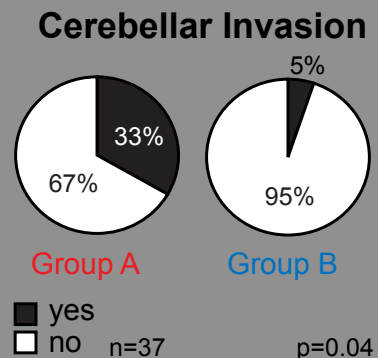
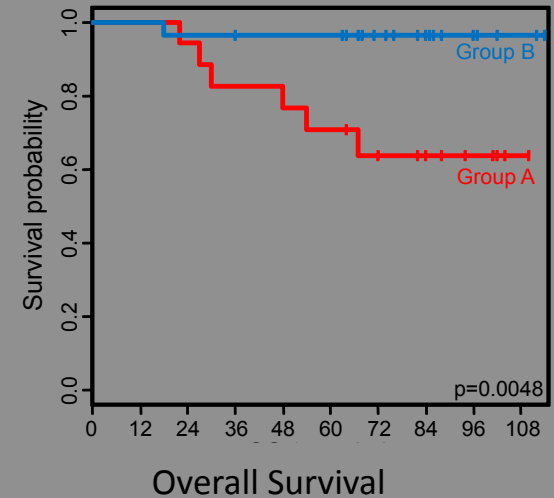
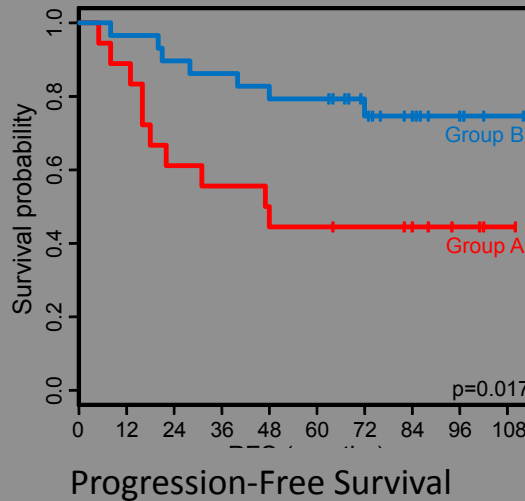
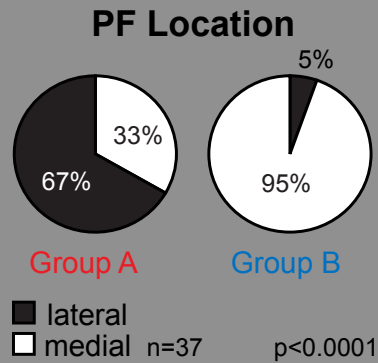
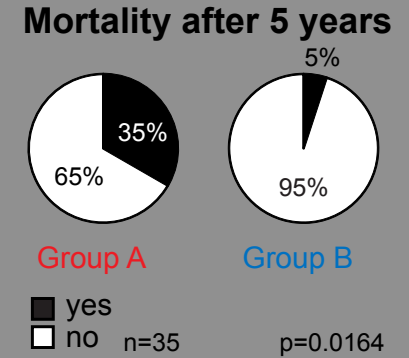
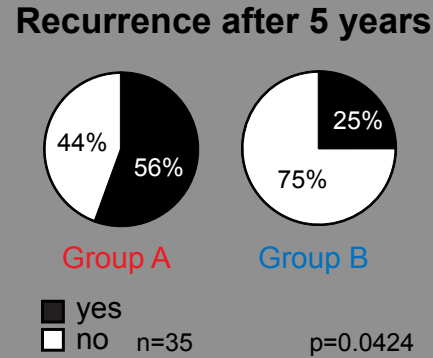
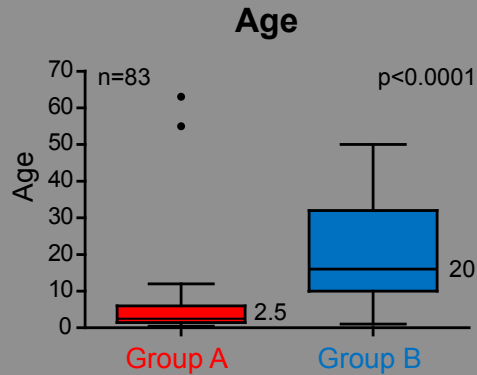
- **Outcome**
 - 5-year Progression-Free Survival 23-45%
 - 5-year Overall Survival 50-64%
- ***Median Time to Recurrence***
 - *13-25 months*
- **Pattern of Failure**
 - 80% Local
 - 20% Distant

Ependymoma: 1997-2007; 153 Kids

St. Jude Children's Research Hospital



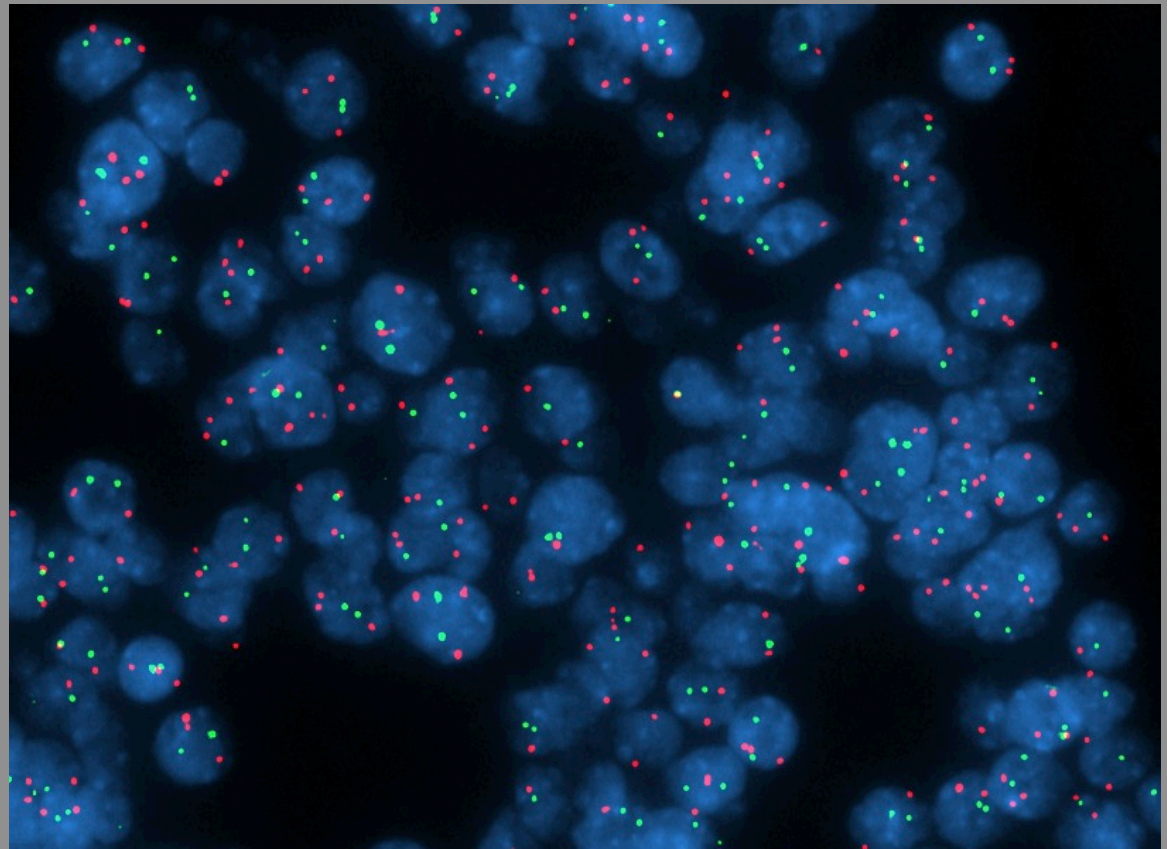
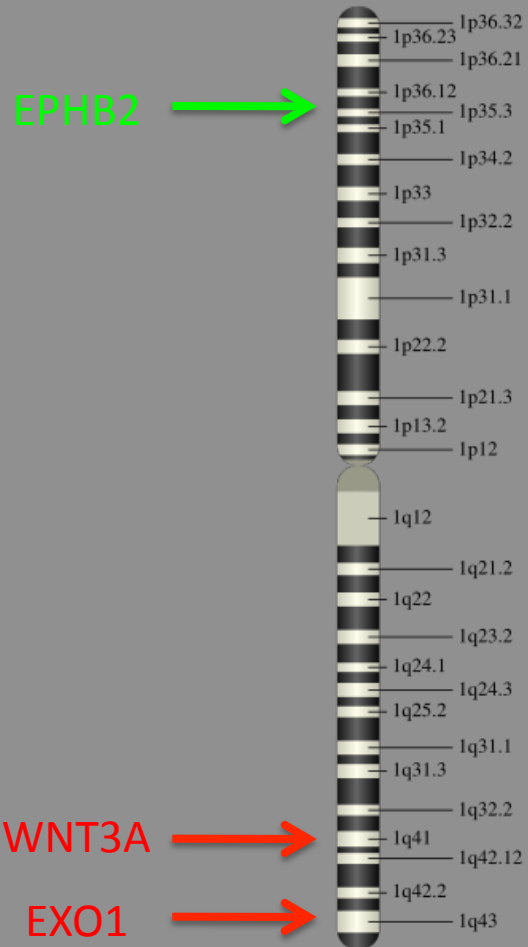
PF-A and PF-B comprised highly distinct clinical entities-CP Angle ependymomas carry a worse prognosis than do 4th ventricular tumors and are molecularly distinct



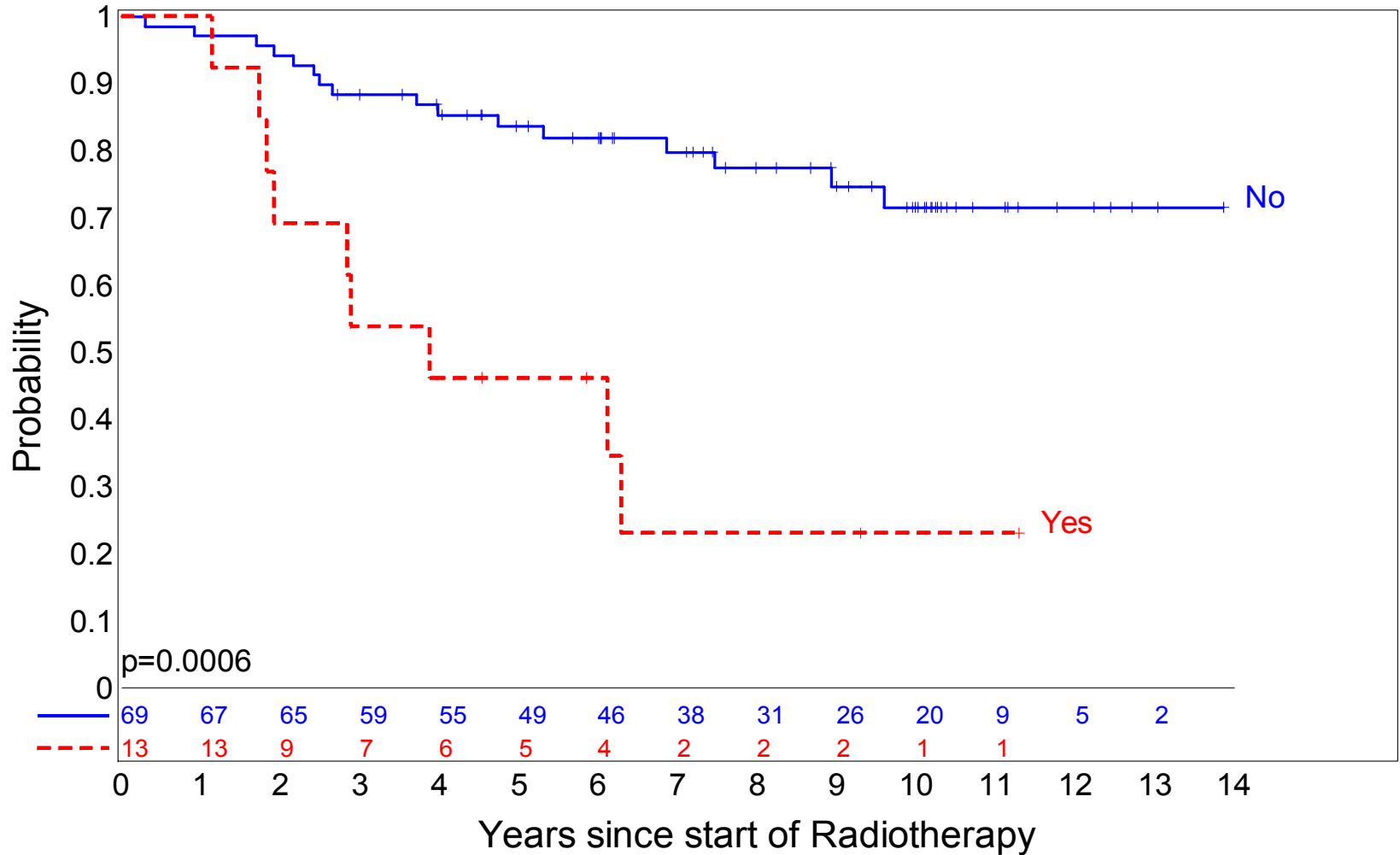
Witt H, Mack SC, et al., Cancer Cell 20, August 16, 2011, p143-157

iFISH probes – chromosome 1

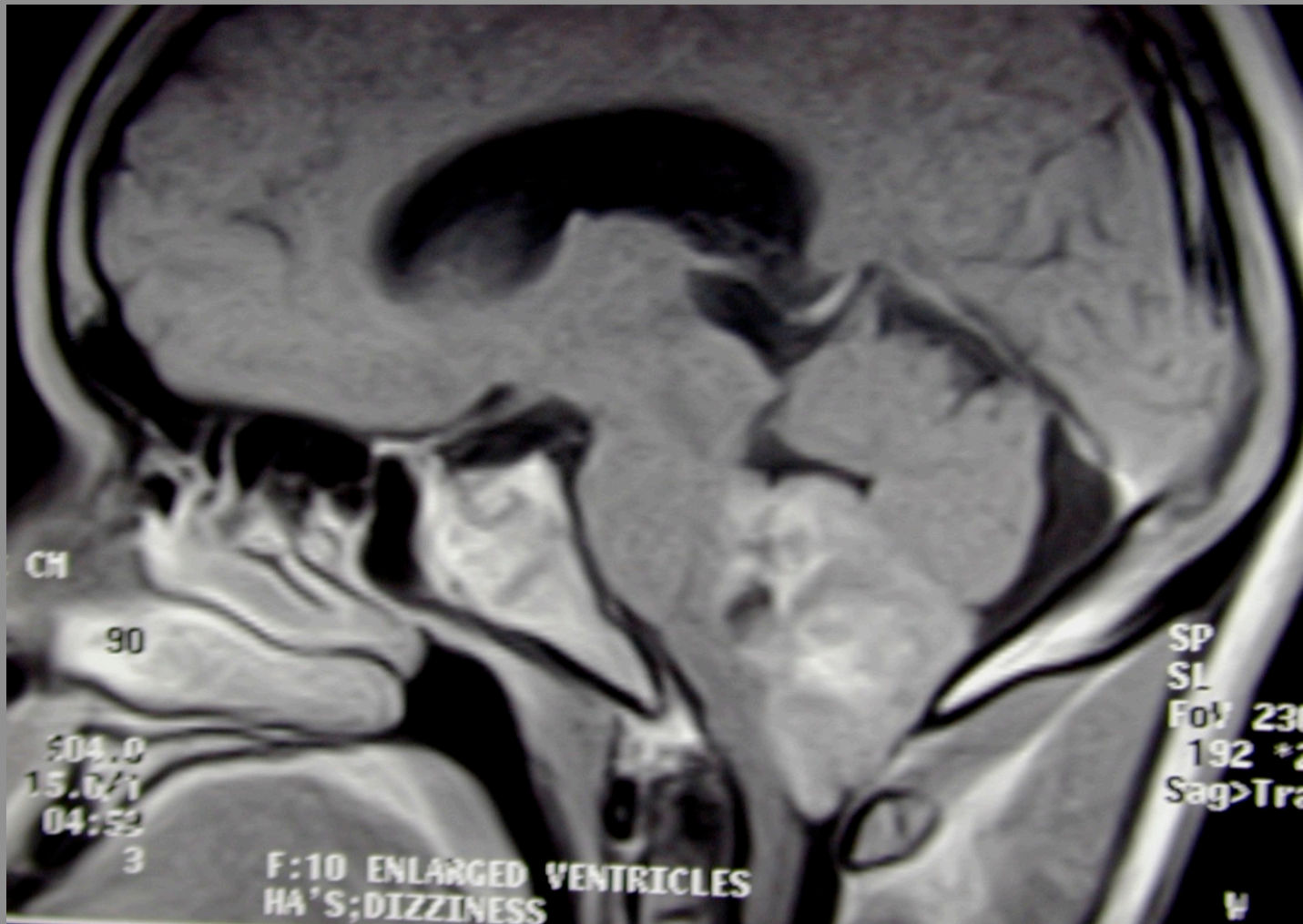
q probe – *WNT3A* or *EXO1* / p probe – *EPHB2*

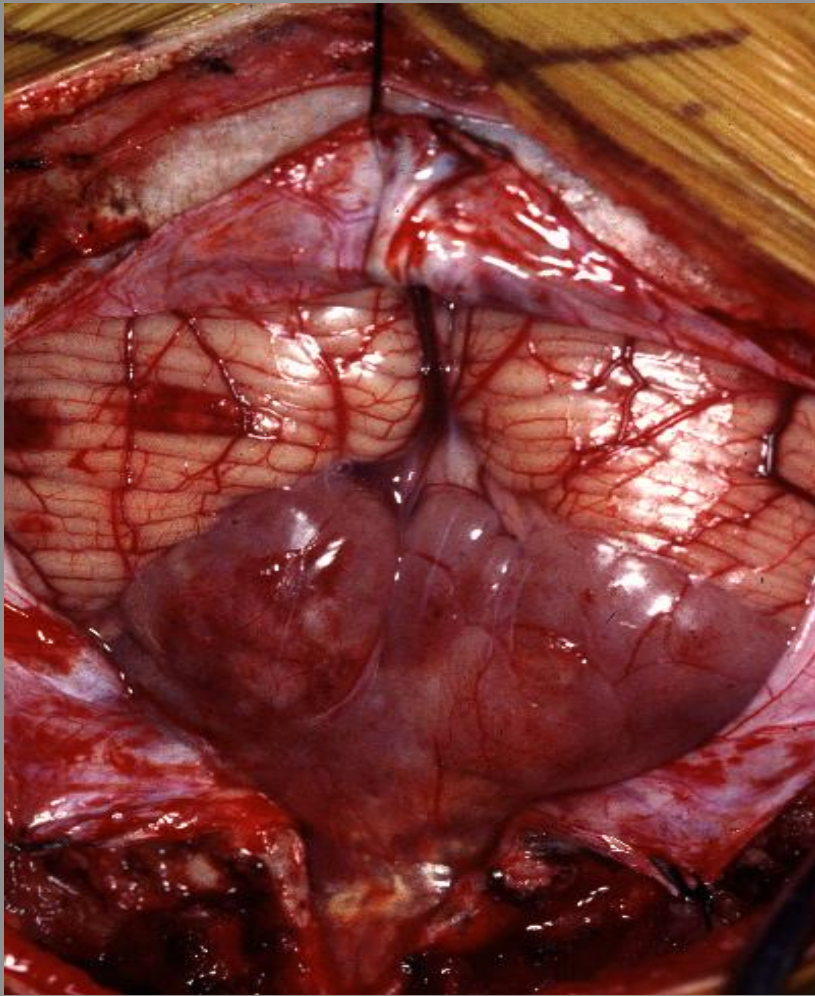


Progression Free Survival by gain of chromosome 1q



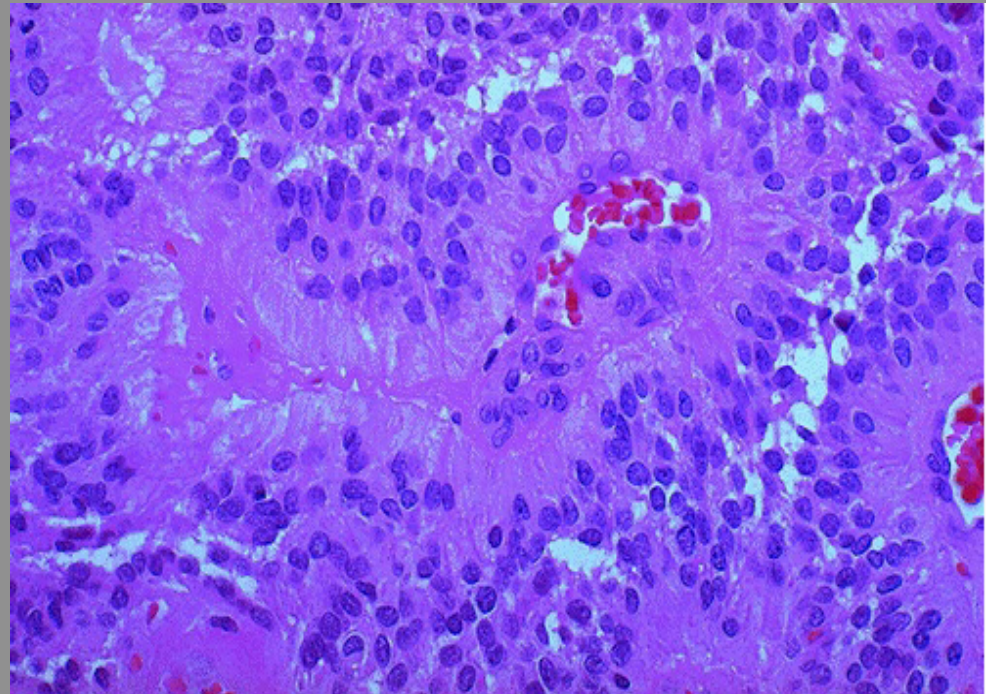
Surgical Technique for 4th ventricular tumors



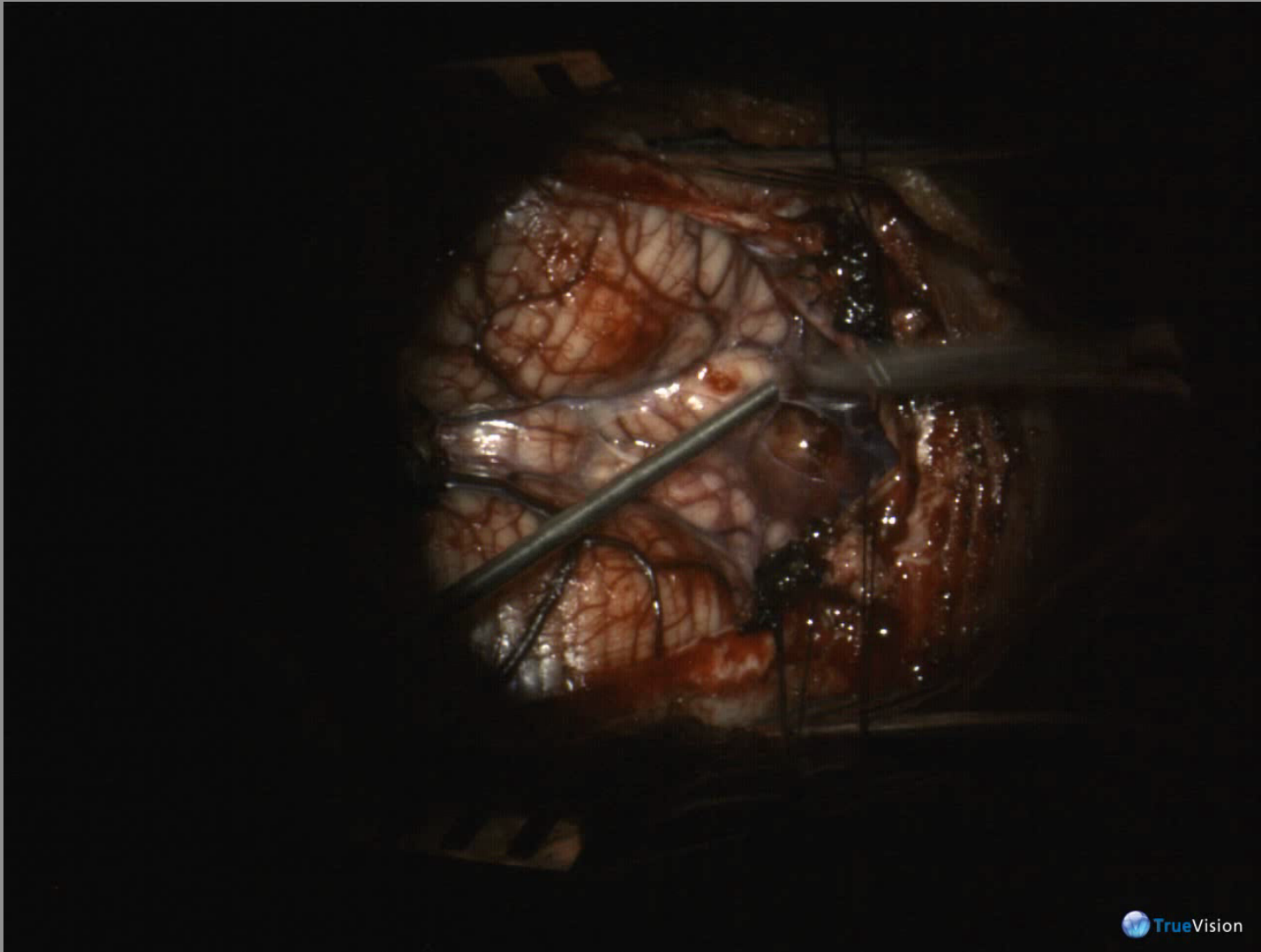


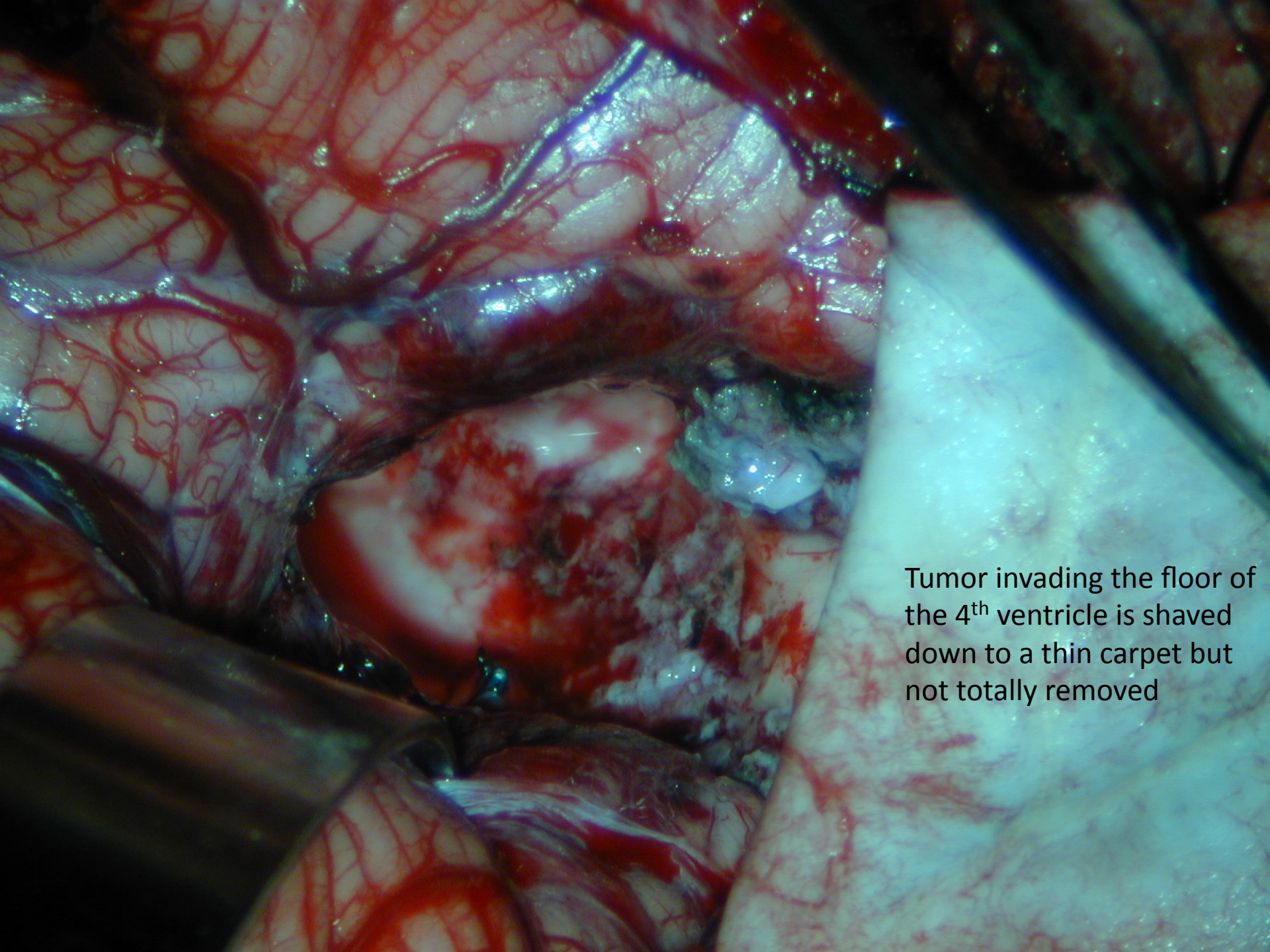
***Prone position
Craniotomy with bone
replacement***

***Do not attempt to remove all
tumor if invading the floor of the
4th ventricle but rather leave a
thin carpet on the floor as shown
in the next slides***

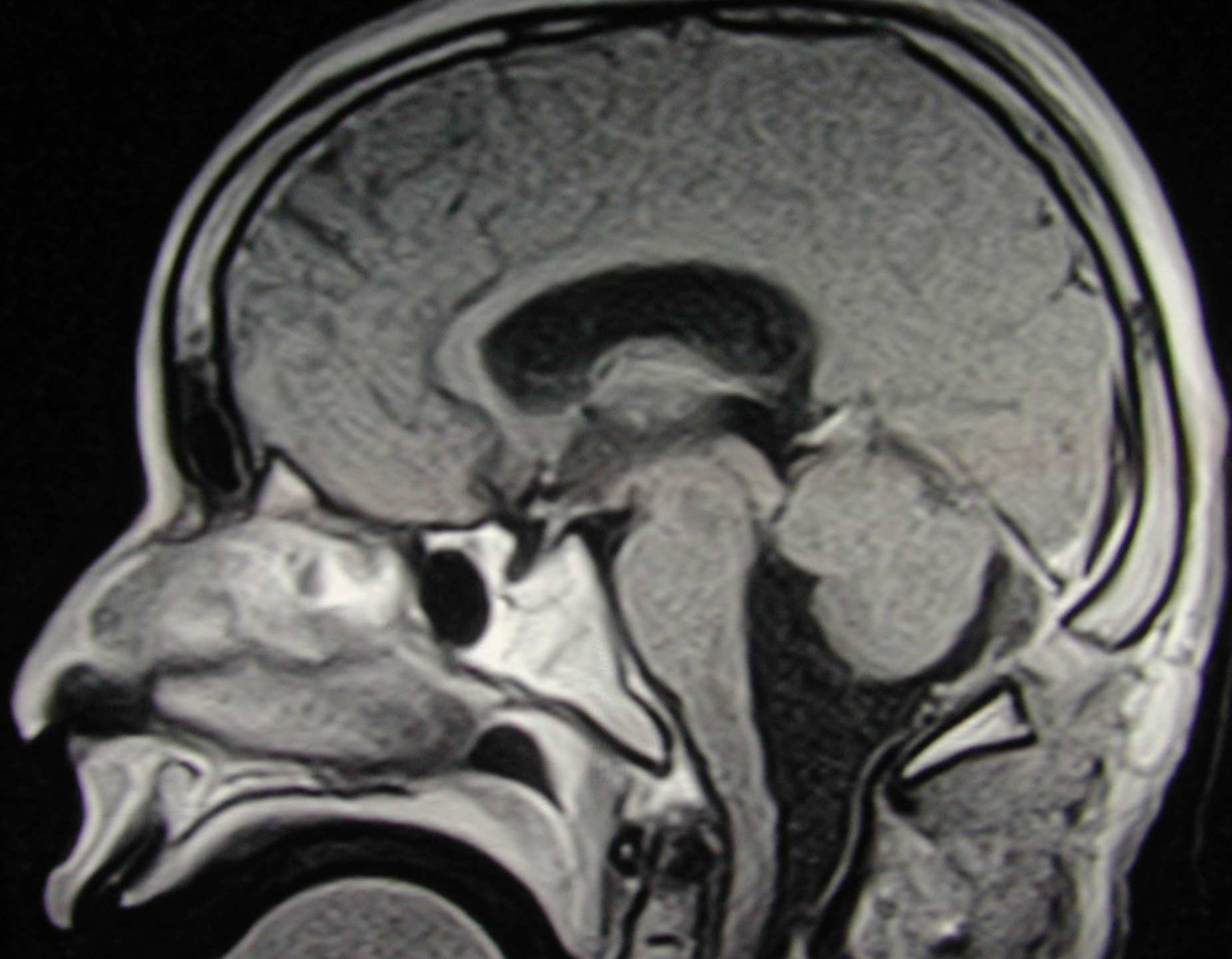


Resection of 4th ventricular tumor

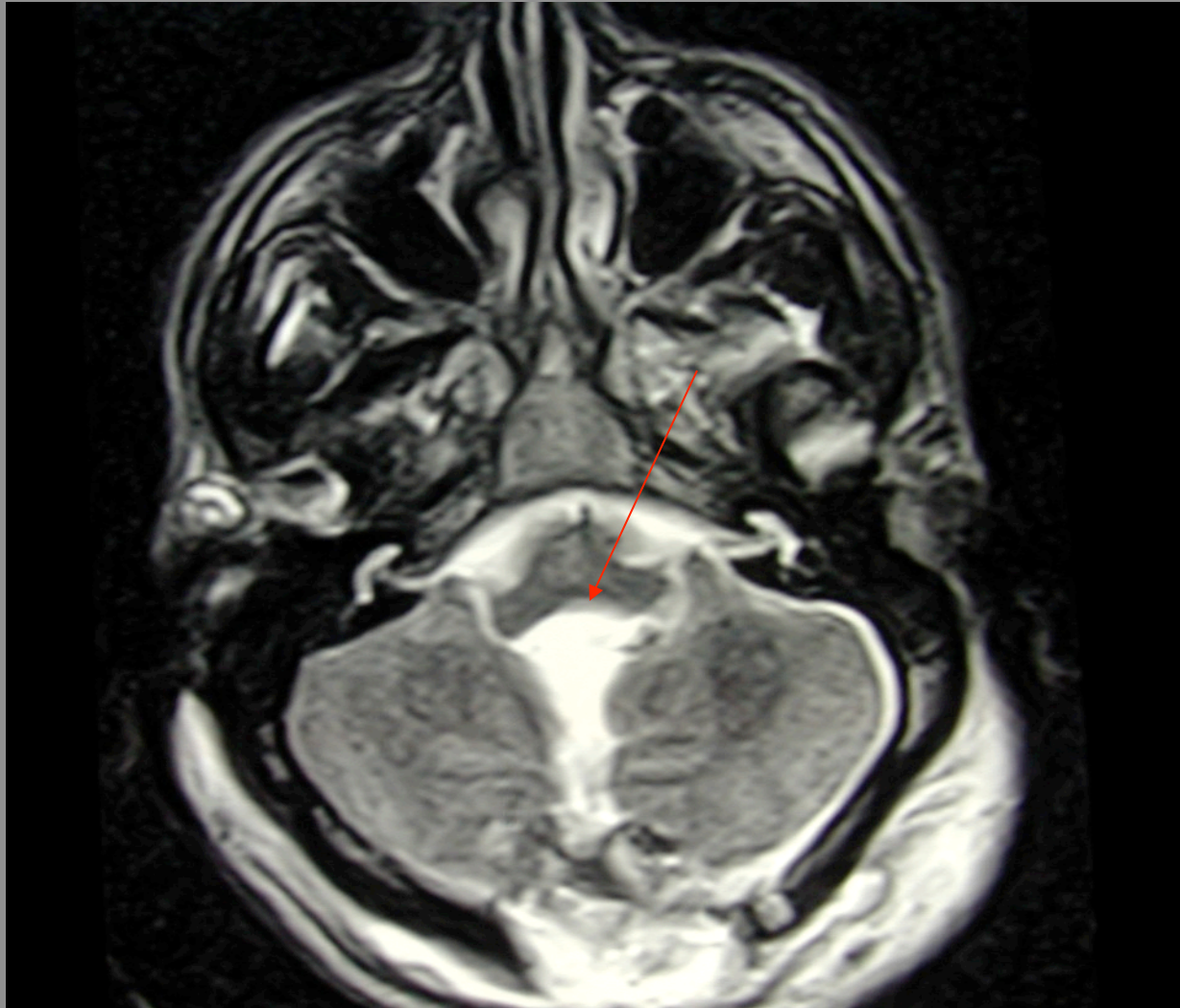


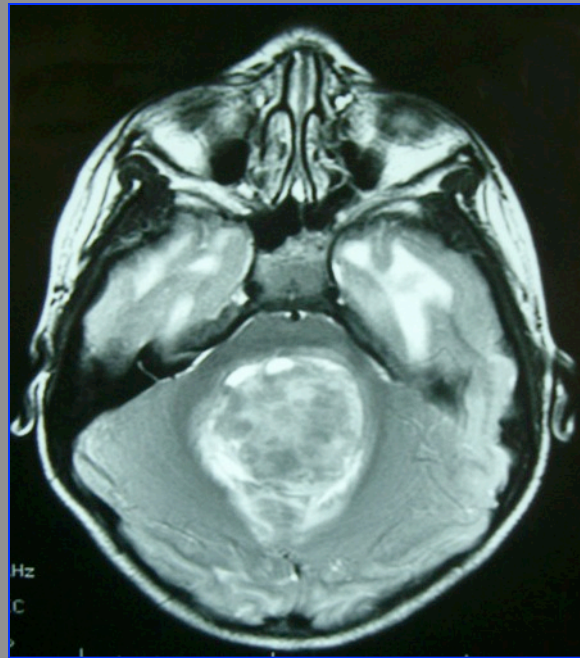
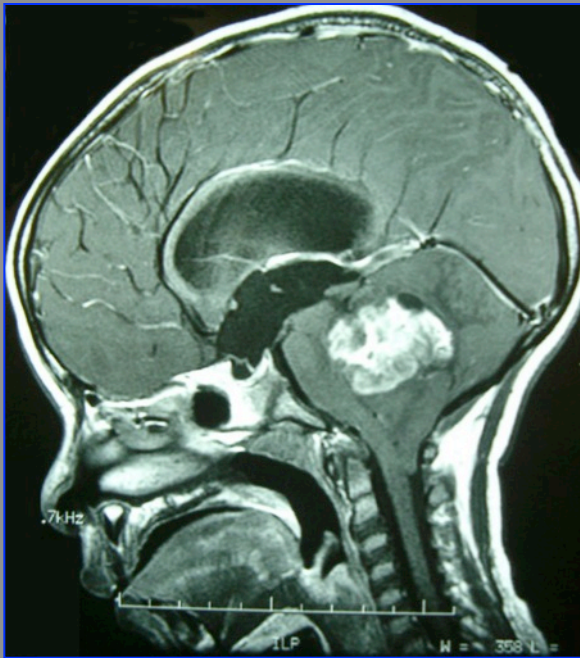


Tumor invading the floor of the 4th ventricle is shaved down to a thin carpet but not totally removed



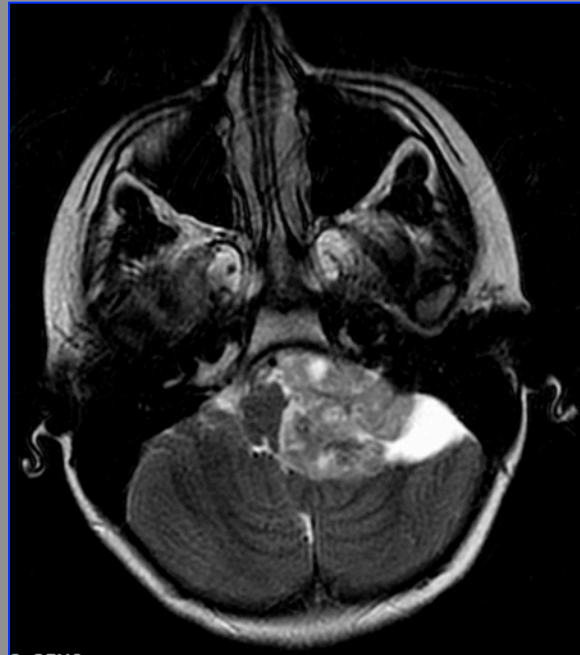
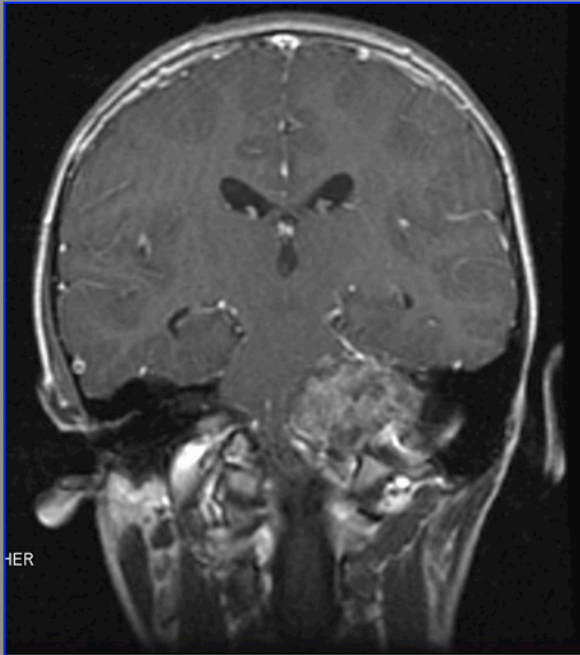
Minimal Radiographic Residual



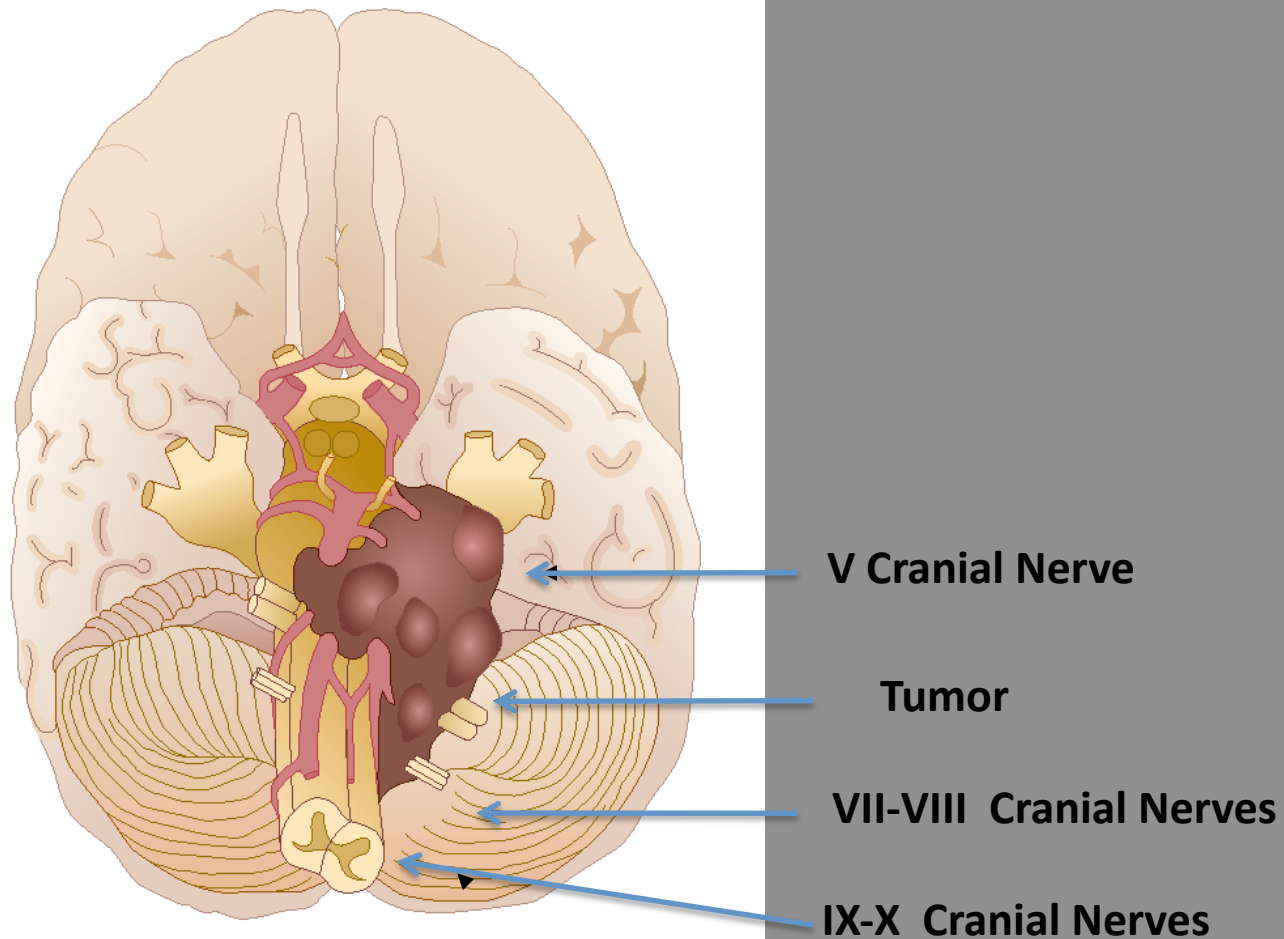


Conventional tumor
of fourth ventricle

Our data so far show
that CPA tumors are
totally resected less
often than tumors in
the fourth ventricle.



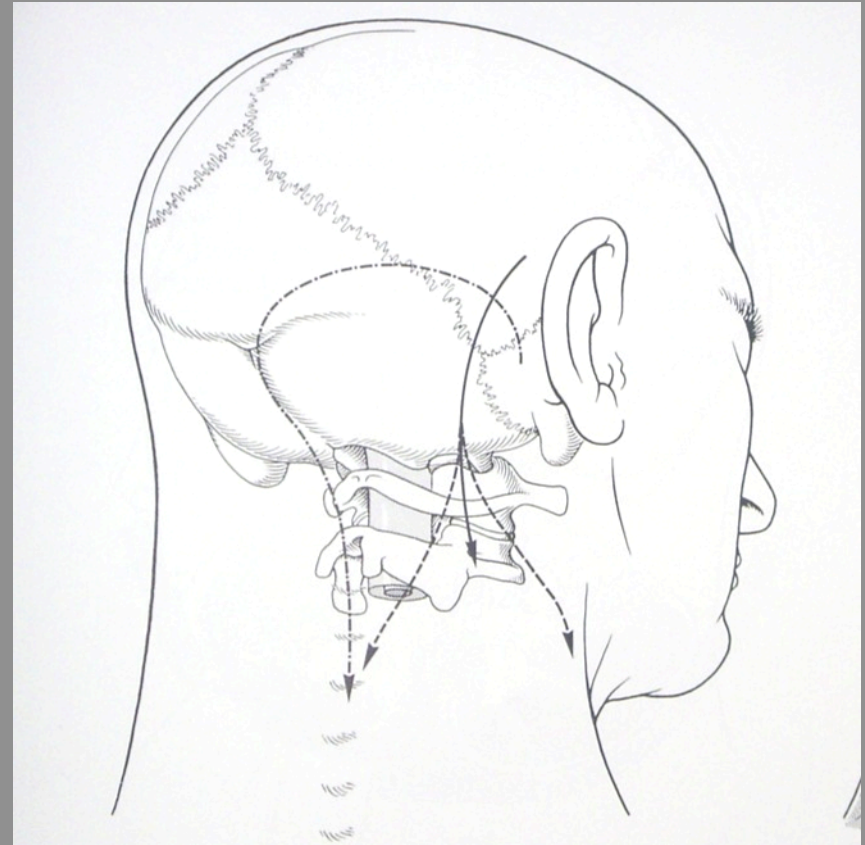
CPA tumor



Anterior view of brain demonstrating rotation of brain stem produced by slow growing CPA ependymoma . Demonstrates encasement of arteries and lower cranial nerves by tumor.

Patient Positioning

- Prone on bolsters
- Chin is turned to the shoulder
- Head is flexed
- Strapped and padded to allow maximal table rotation
- Craniotomy crosses the midline for 4th ventricular access
- Bed rotation one way allows 4th ventricle tumor resection and the other allows telovelar resection of CP angel component

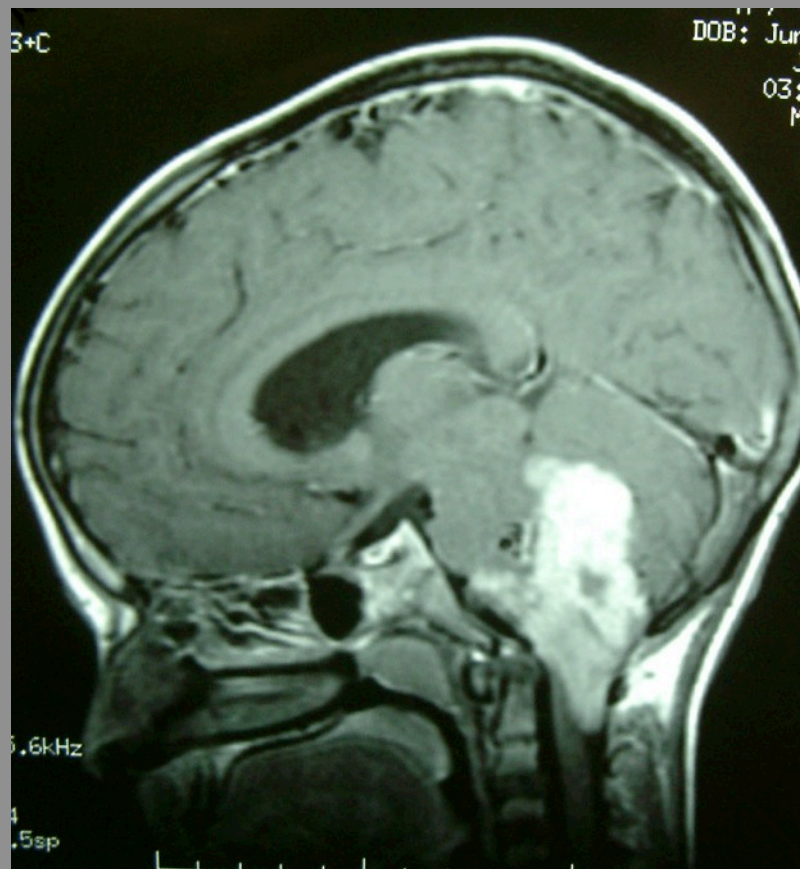


Patient Positioning



Operative Technique

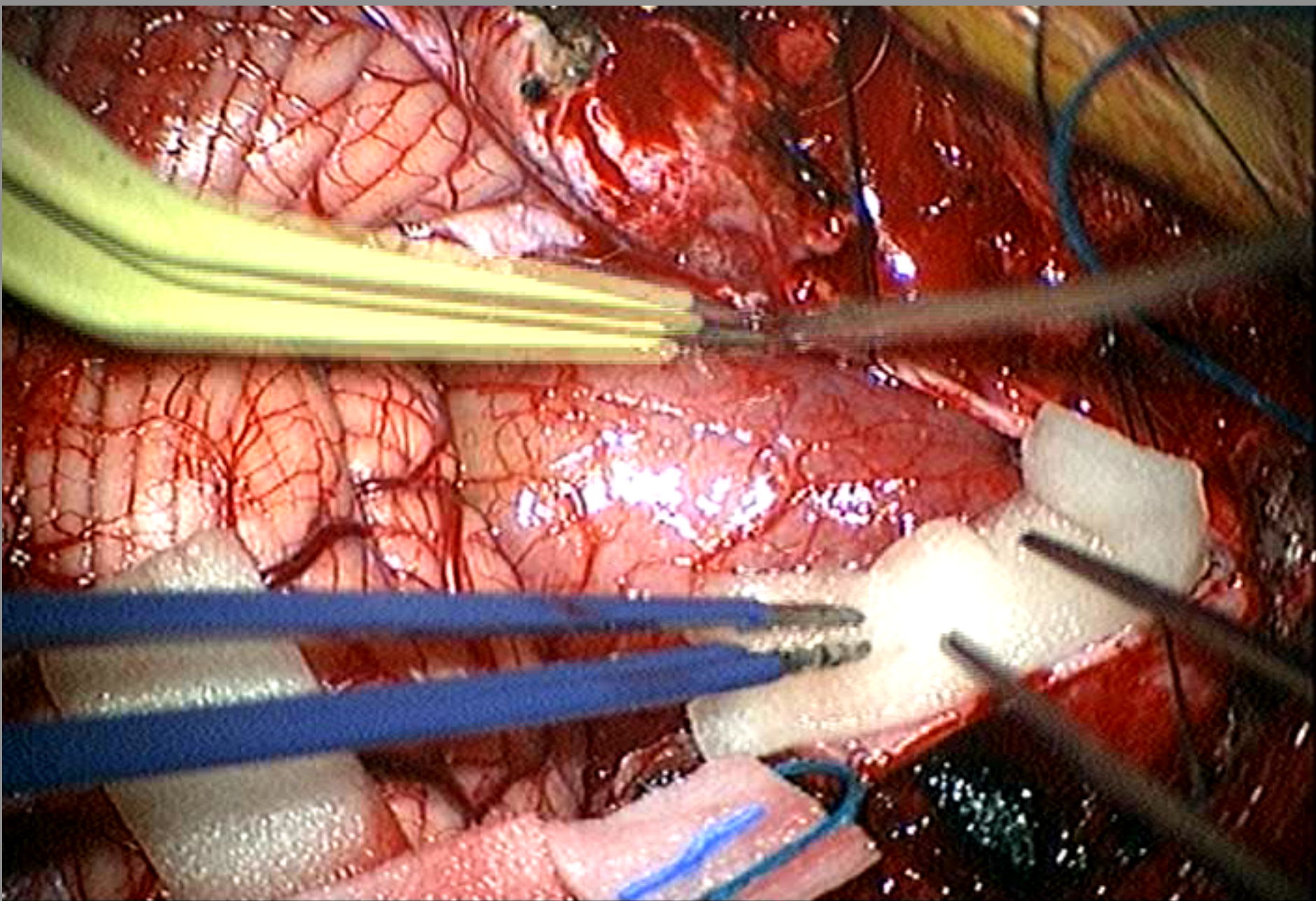
- 8 y/o male presents with 2 month history of progressive gait disturbance and headaches
- PE Ataxia and papilledema



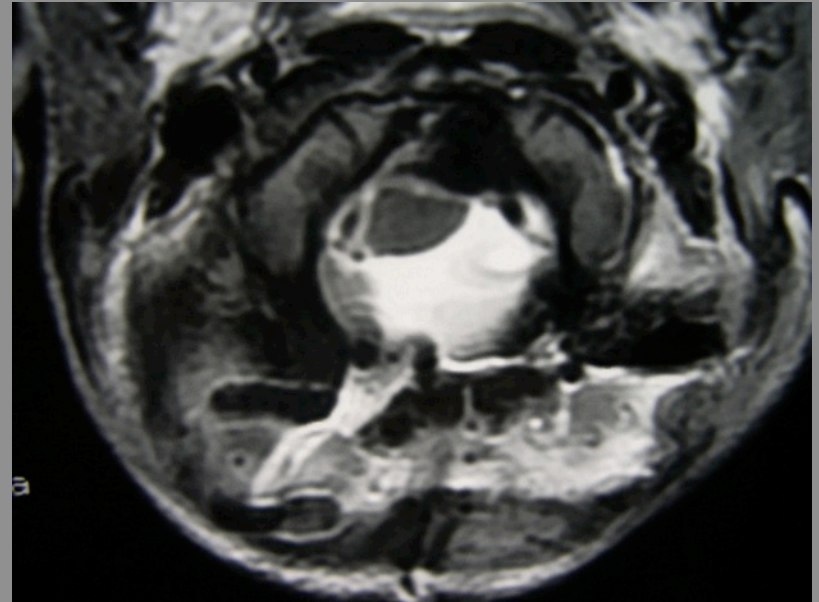
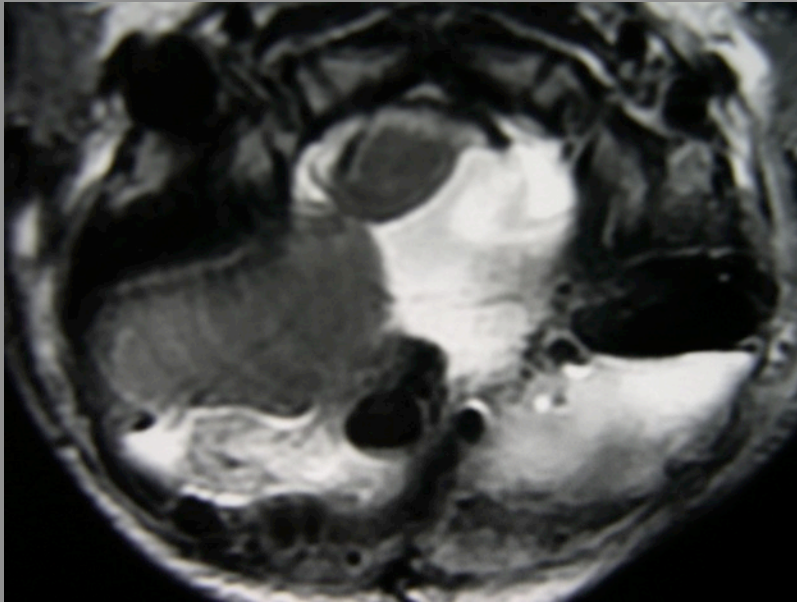
Operative Technique

Surgeons stand across from one another

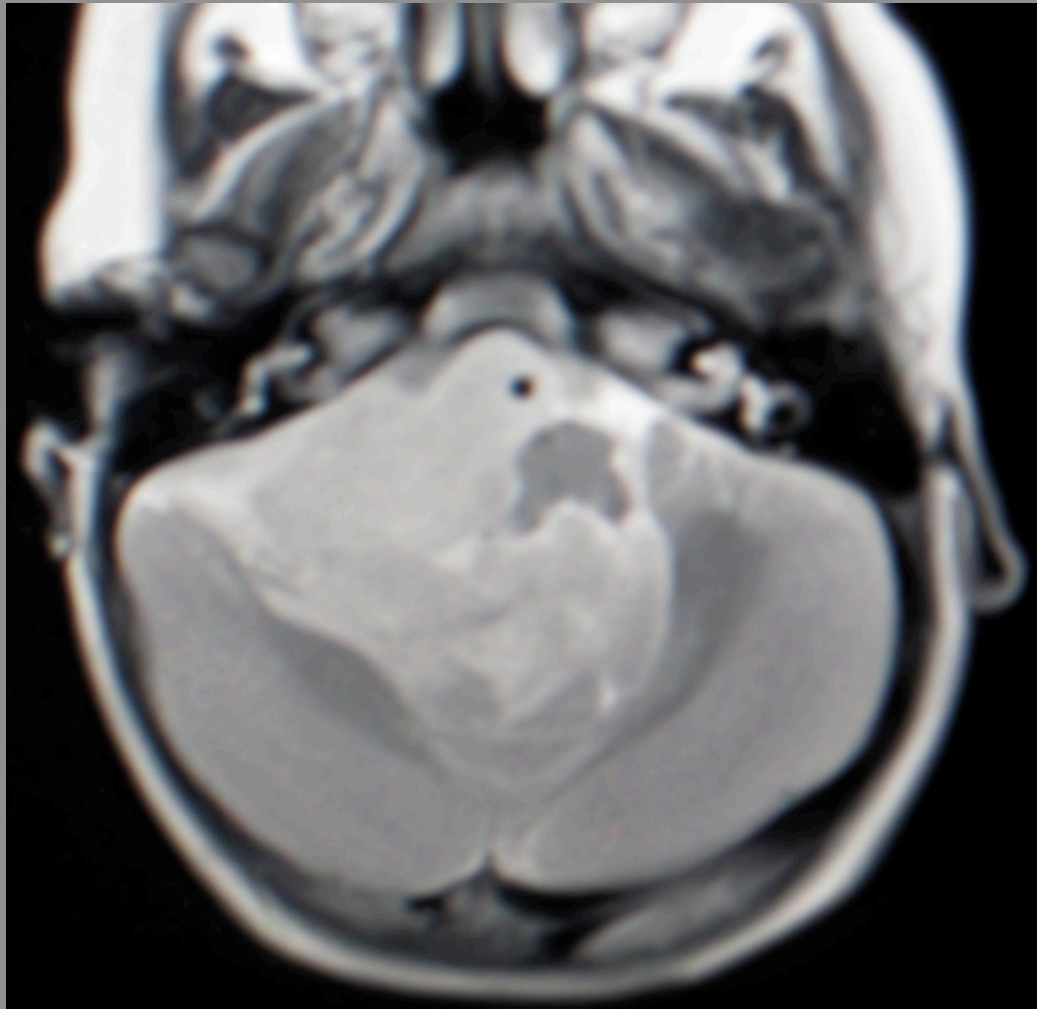


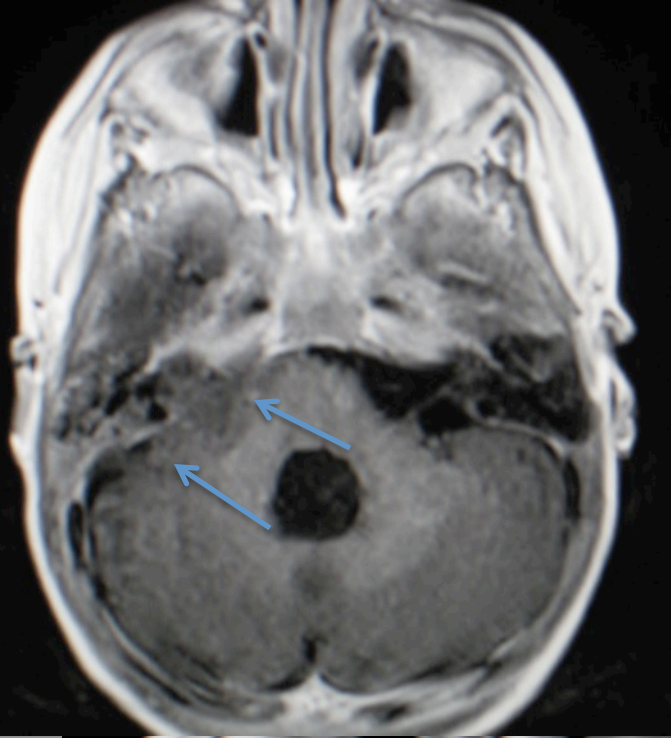


Early Post-operative Imaging

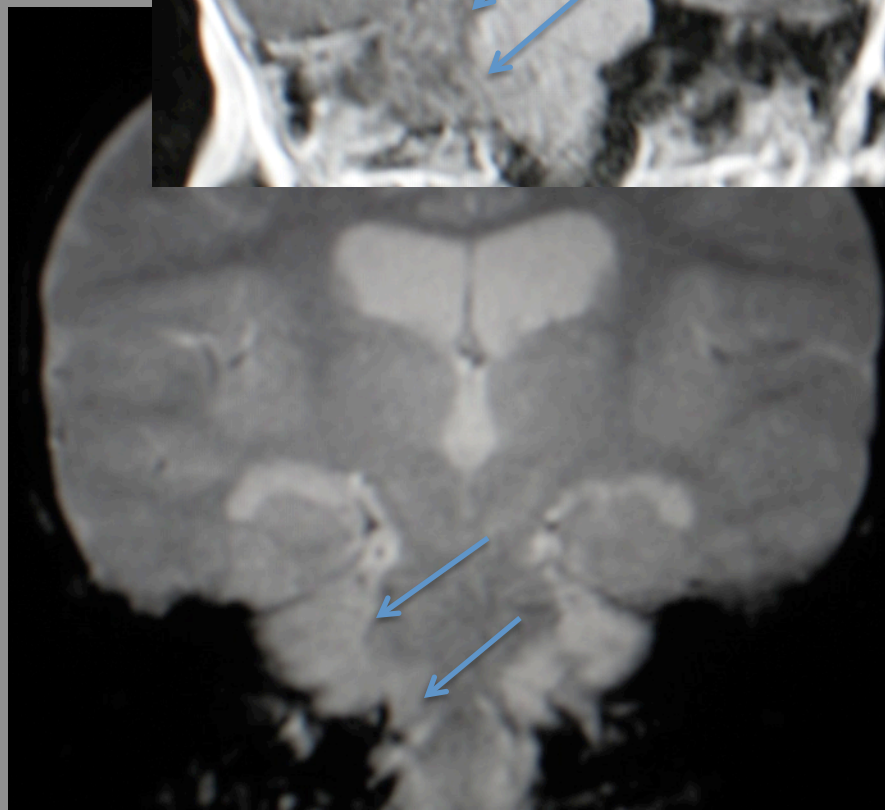
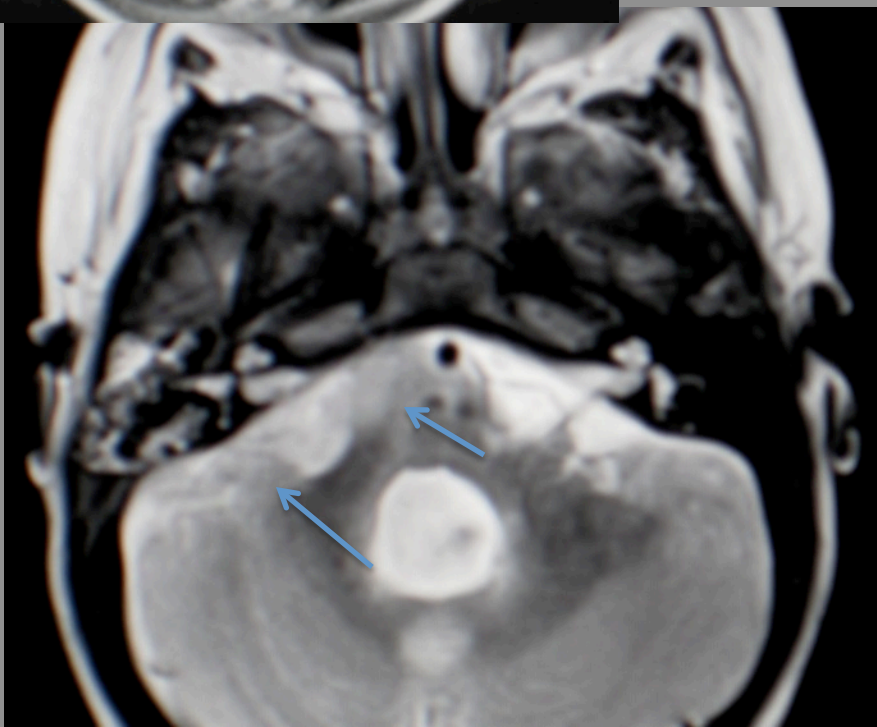
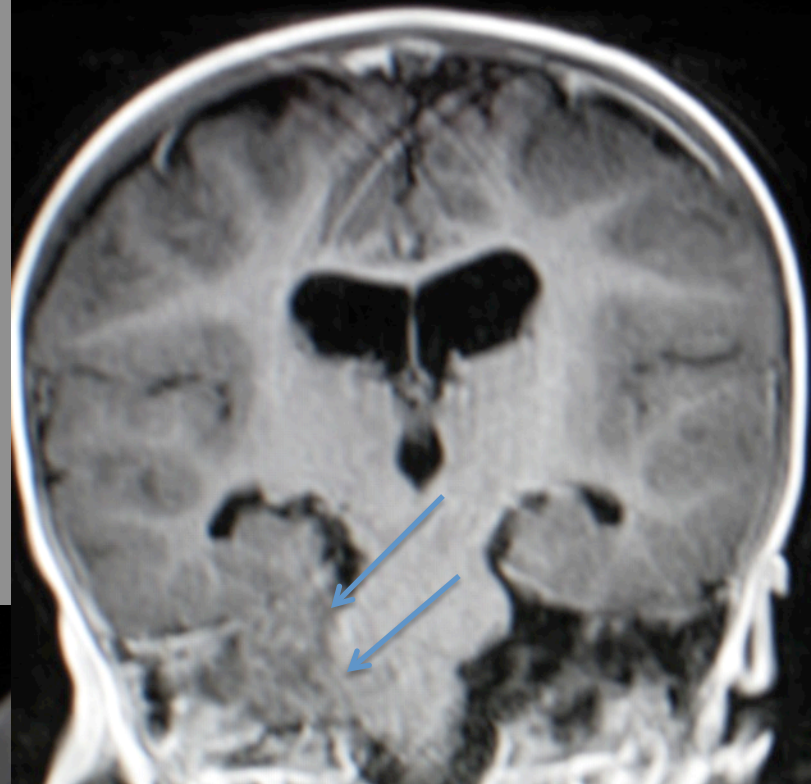


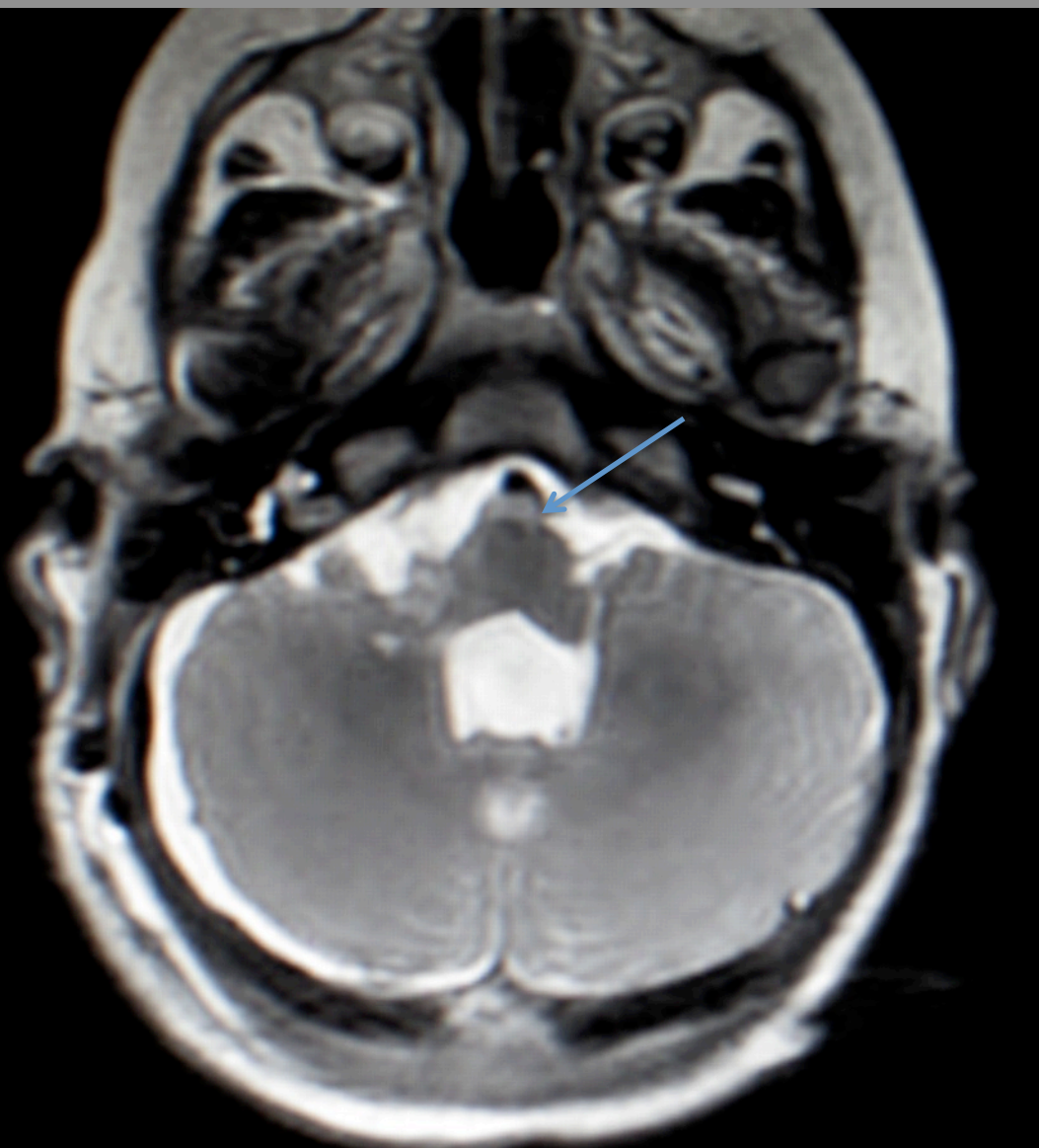
Case MK-2 y/o



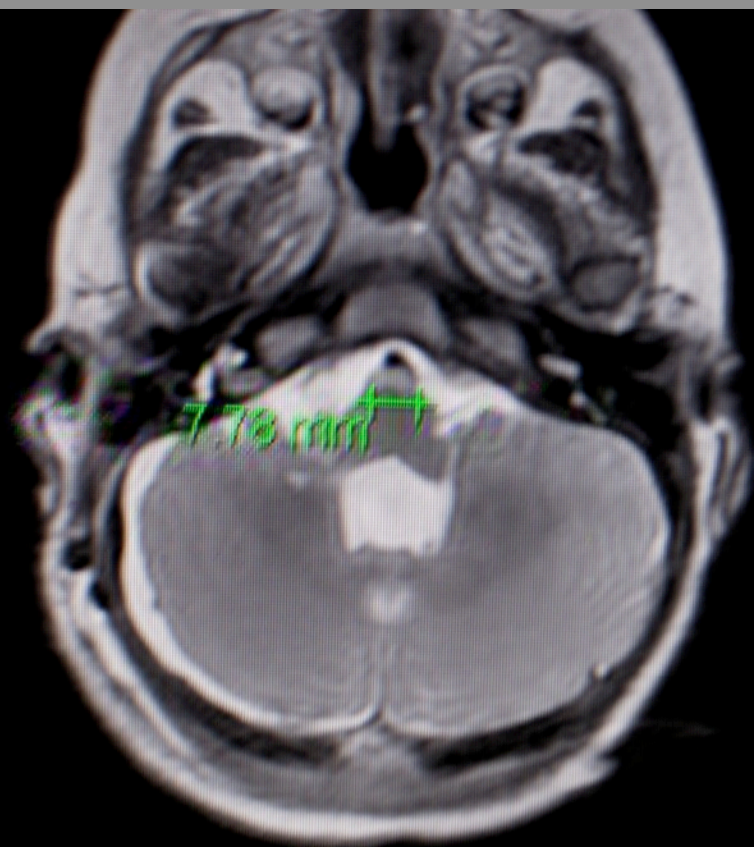


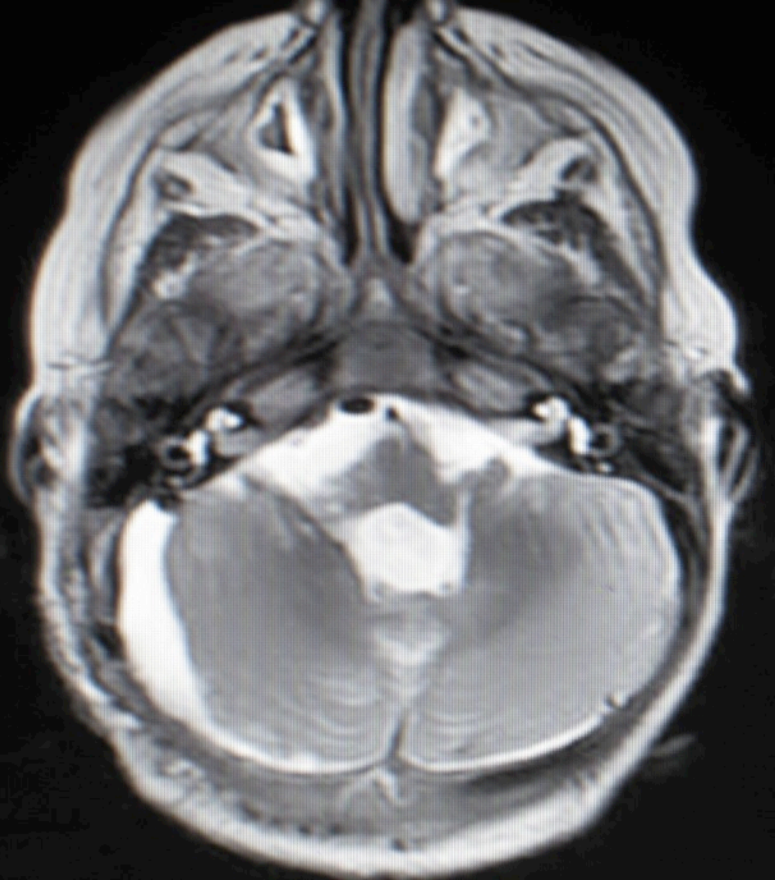
Subtotal resection
elsewhere
Residual grew on
chemotherapy
Referred for re-
resection





Early post-op MRI showed residual tumor
Patient taken back to OR for resection of remaining tumor
Today Intra-operative MRI would prevent return to OR





Two days post op
Pt has right 6th and partial 7th
cranial nerve palsies



Post-Operative Care

- All patients are kept intubated overnight
- ENT scopes patients at extubation
- None are fed per orum until video-swallowing test is passed
- Mild CN manipulation – re-test in a week
- Others get early trach and g-tube
 - 1/3 have trach/g-tube or both
 - All but one have been decannulated by a year (one presented with central sleep apnea and Ondine's Curse persists)
 - With greater experience none have required a tracheostomy in the past 4 years

Facial Re-Animation

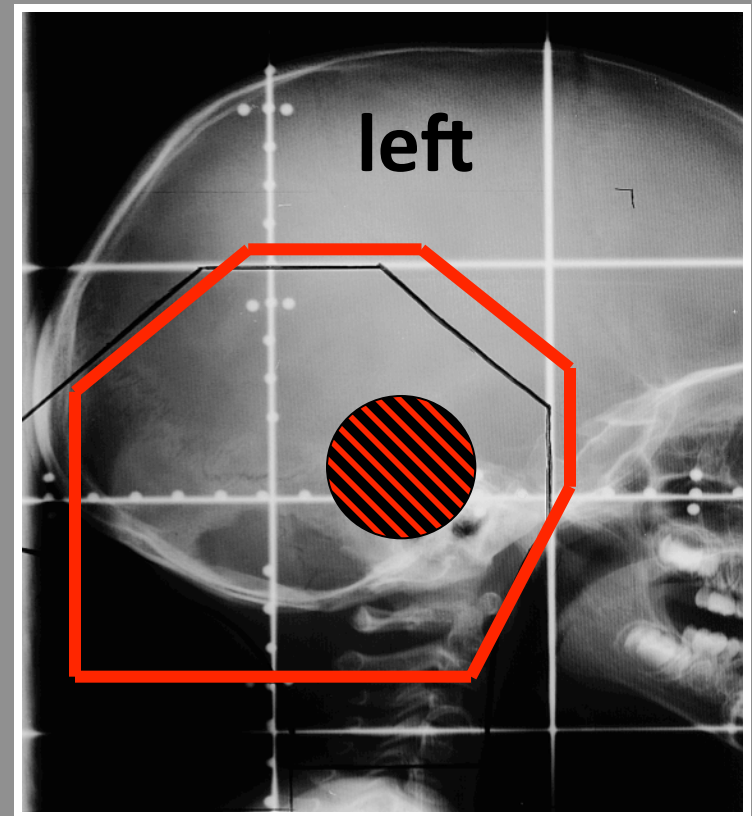
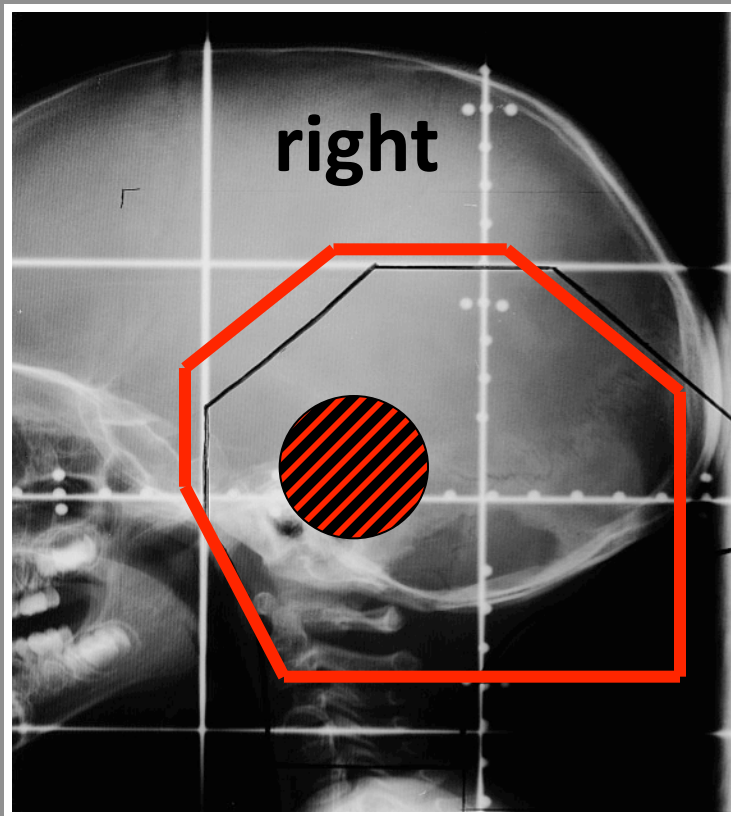


Background-Radiation Therapy

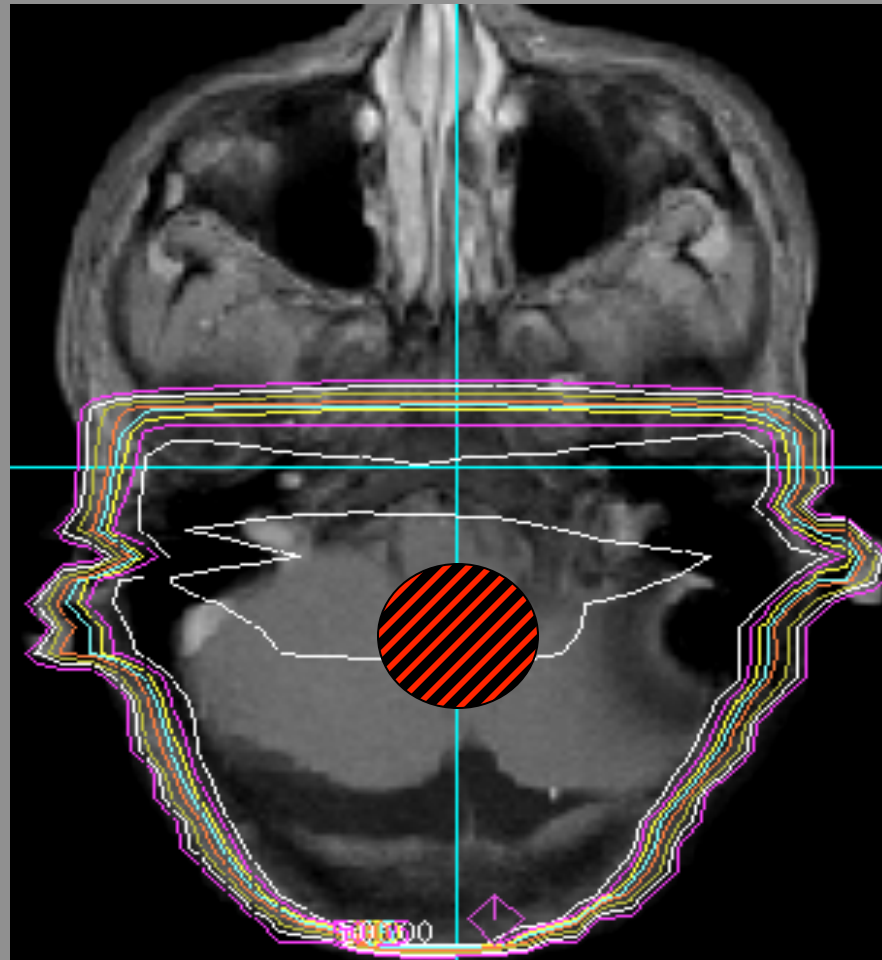
- **1970s and 1980s**
 - **Craniospinal RT improved survival**
 - **>4500 Gy was better**
- **1980s and 1990s**
 - **Conformal RT**
- **The new millenium**
 - **3 Dimensional Conformal RT**
 - **Proton Beam Therapy**

Radiation Therapy for Ependymoma

conventional radiation therapy includes radiation to cochlea, both posterior temporal lobes and hypothalamus

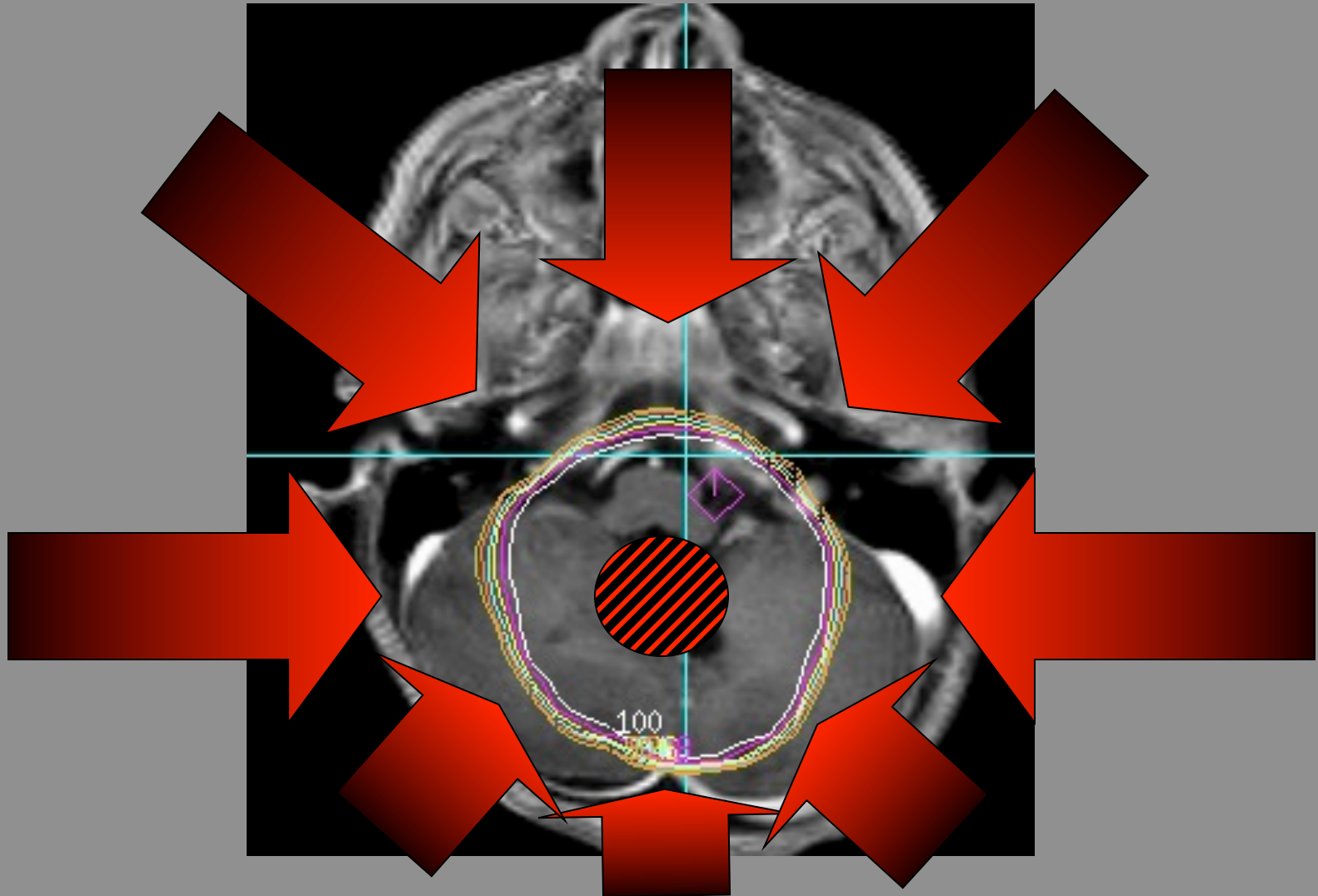


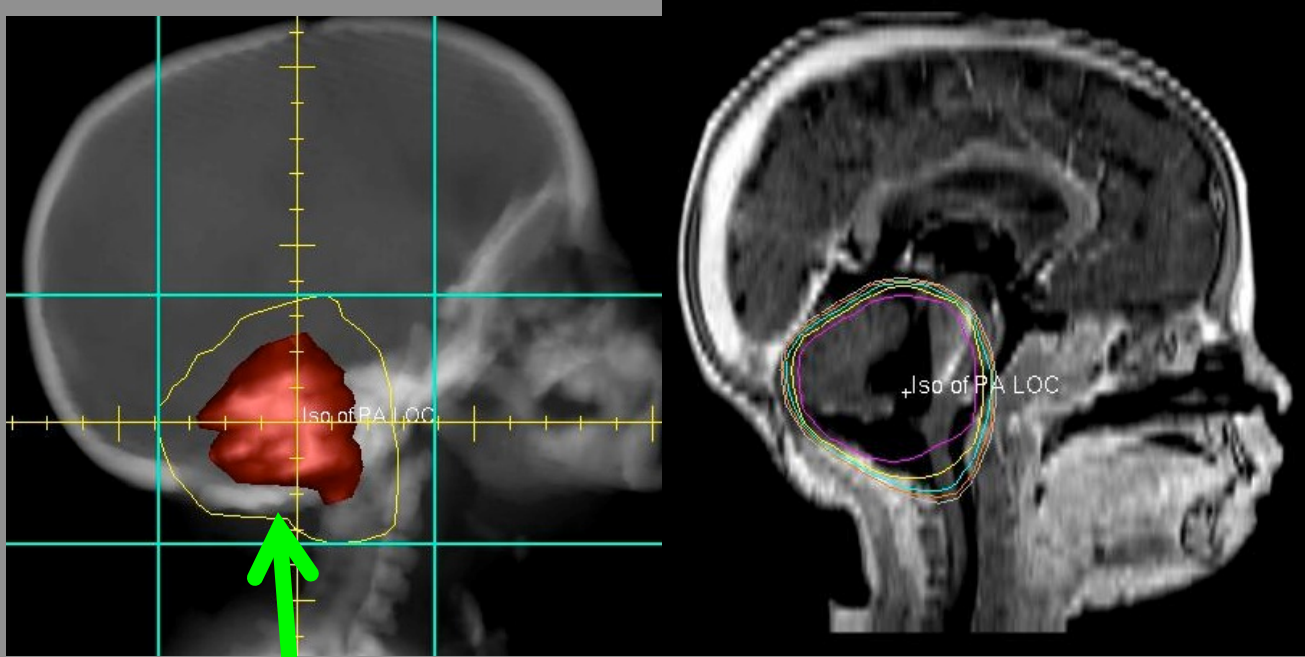
Radiation Therapy for Ependymoma **conventional radiation therapy**



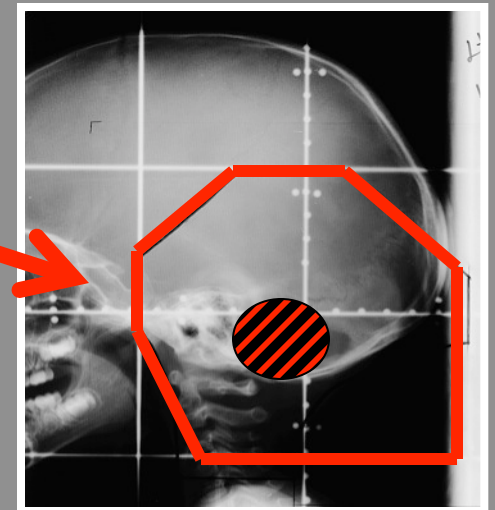
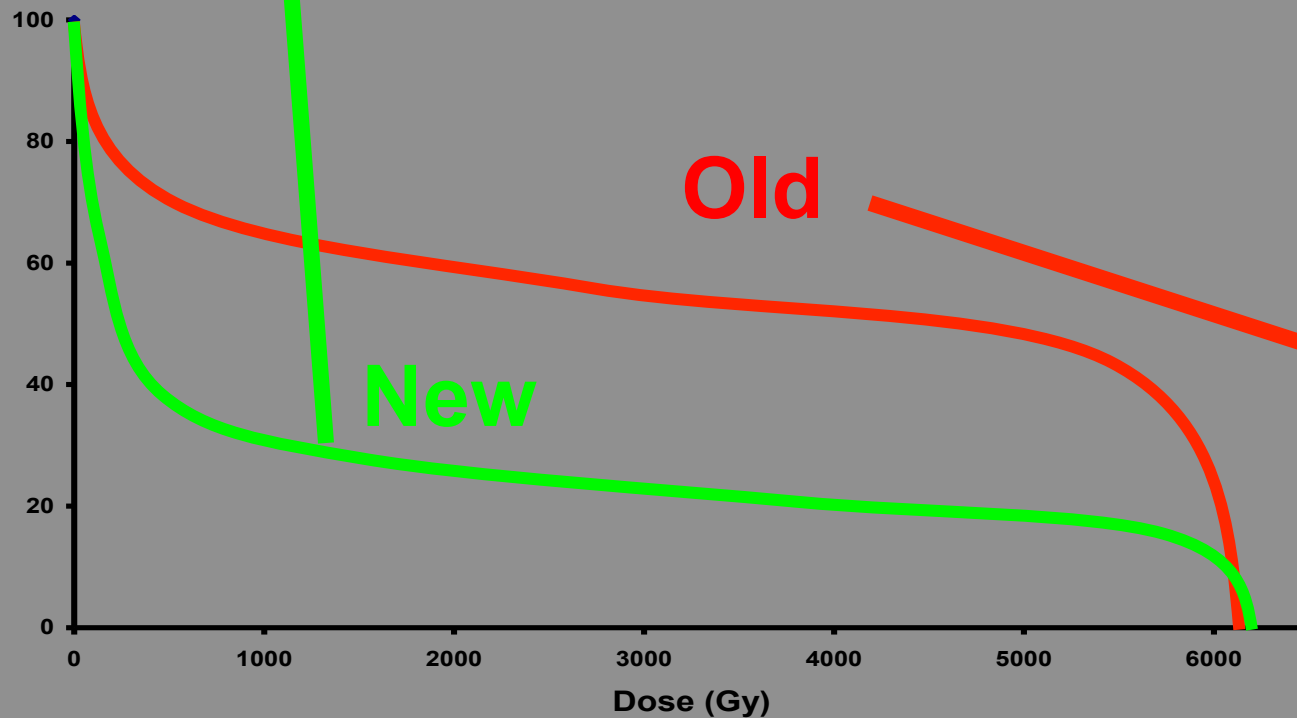
Radiation Therapy for Ependymoma

conformal radiation therapy spares those structures and their function



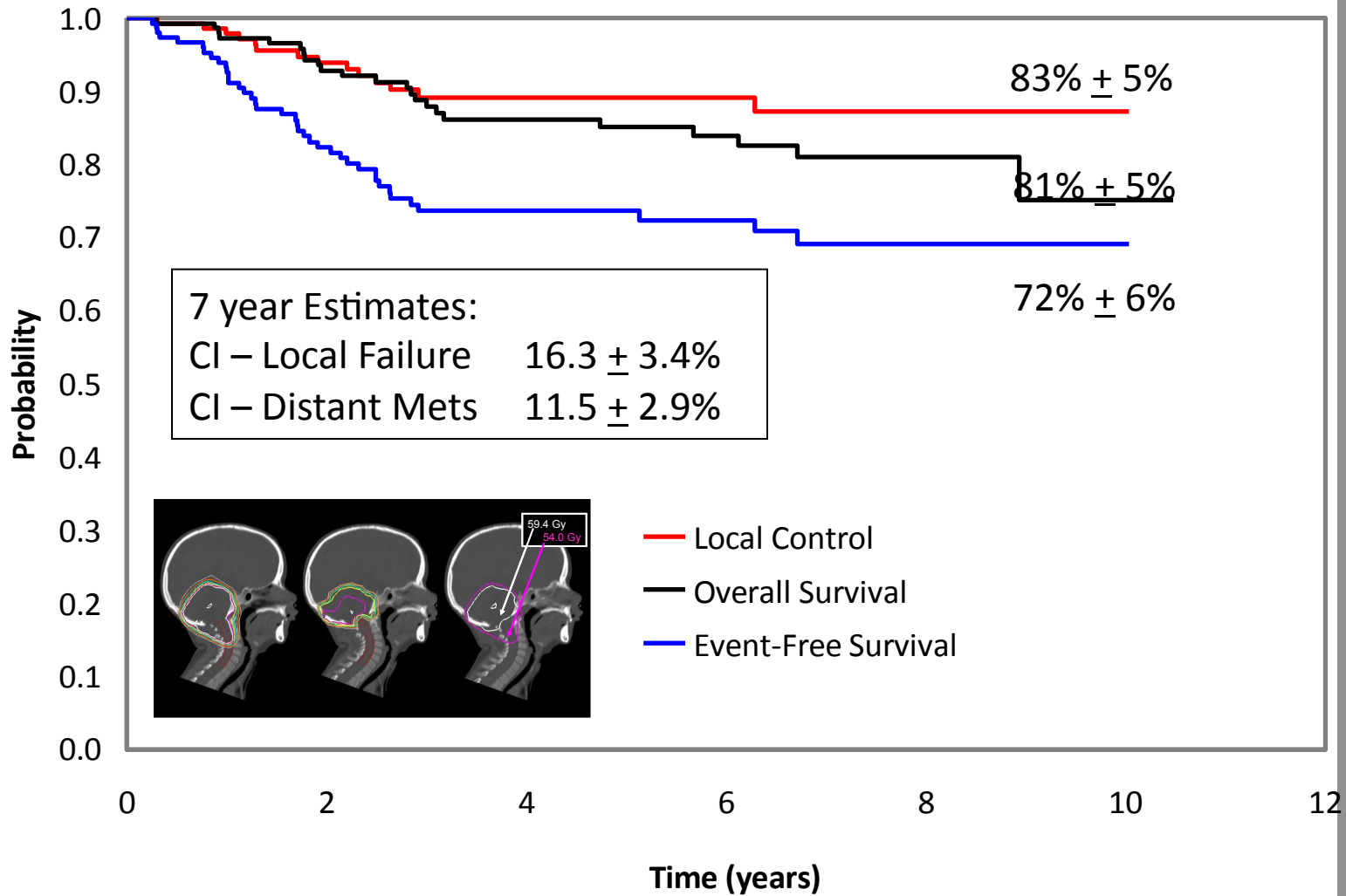


*Temporal
Lobe
Dosimetry*



Ependymoma: 1997-2007; 153 Kids

St. Jude Children's Research Hospital



153 Patients 7/97-12/07

Age at RT	2.6 years	0.9-22.9 years
Tumor Location	Infratentorial	122 (80%) ←
	Supratentorial	31 (20%)
Tumor Grade	WHO II	68 (44%)
	WHO III	85 (56%) ←
Race	White	126 (82%)
	Non-White	27 (18%)
Gender	Female	58 (38%)
	Male	95 (62%) ←

Treatment

RT Dose	54.0Gy	22 (14%)
	59.4Gy	131 (86%) ←
Surgery Extent	GTR	125 (82%) ←
	NTR	17 (11%)
	STR	11 (7%)
Surgery Number	1	87 (57%)
	2-4	66 (43%) ←
Pre-RT	Yes	35 (23%) ←
Chemotherapy	No	118 (77%)

Univariate Analysis

			Overall Survival (SE)%			Event-Free Survival (SE)%		
Factors	Sub-Group	N	5-Year	7-Year	P-value	5-Year	7-Year	P-value
Tumor Grade	Differentiated	68	0.919 ± 0.039	0.894 ± 0.050	0.006	0.875 ± 0.048	0.827 ± 0.064	0.0031
	Anaplastic	85	0.783 ± 0.061	0.718 ± 0.098		0.621 ± 0.076	0.621 ± 0.115	
Race	White	126	0.877 ± 0.036	0.845 ± 0.050	0.0590	0.753 ± 0.048	0.721 ± 0.064	0.683
	Black	19	0.742 ± 0.154	0.594 ± 0.189		0.662 ± 0.192	0.662 ± 0.192	
	Hispanic	6	0.625 ± 0.271	0.625 ± 0.271		0.667 ± 0.272	0.667 ± 0.272	
	Asian	2	NA	NA		NA	NA	
Gender	Female	58	0.918 ± 0.041	0.886 ± 0.060	0.091	0.844 ± 0.056	0.844 ± 0.056	0.0218
	Male	95	0.811 ± 0.056	0.761 ± 0.076		0.682 ± 0.068	0.624 ± 0.090	
Surgery Group	GTR	125	0.930 ± 0.029	0.880 ± 0.047	0.00000	0.821 ± 0.045	0.800 ± 0.061	0.00000
	NTR	17	0.583 ± 0.188	0.583 ± 0.188		0.448 ± 0.166	0.448 ± 0.166	
	STR	11	0.436 ± 0.164	0.436 ± 0.164		0.375 ± 0.148	0.250 ± 0.217	
Pre-RT Chemotherapy	Yes	35	0.736 ± 0.092	0.690 ± 0.122	0.038	0.580 ± 0.104	0.532 ± 0.121	0.0053
	No	118	0.886 ± 0.037	0.853 ± 0.052		0.795 ± 0.049	0.773 ± 0.066	

Event-free and Overall Survival

Series	Time Period	Patients	5yr PFS	10yr PFS	5yr OS	10yr OS
Akyuz	1972-1991	62	-	36%	-	50%
Perilongo	1977-1993	92	-	35%	-	56%
Shu	1980-2000	49	41%	31%	66%	56%
Oya	1961-1999	48	42%	42%	62%	47%
Pollack	1975-1993	40	46%	36%	57%	45%
Jaing	1985-2002	43	46%	-	54%	-
V. Veelan	1980-1999	83	48%	46%	73%	51%
Robertson	1986-1992	32	50%	-	64%	-
Mansur	1964-2000	60	58%	46%	71%	55%
Merchant	1997-2007	153	74%	69%	85%	75%

Conclusions

- A Gross Total Resection doubles the chances of the child surviving this cancer compared to anything less
- Highly vascular tumors are devascularized by a round or two of chemotherapy, facilitating surgical resection
- Conventional chemotherapy does not extend survival for incompletely resected ependymomas
- Delaying radiotherapy to give chemotherapy portends a worse prognosis compared to early referral for irradiation