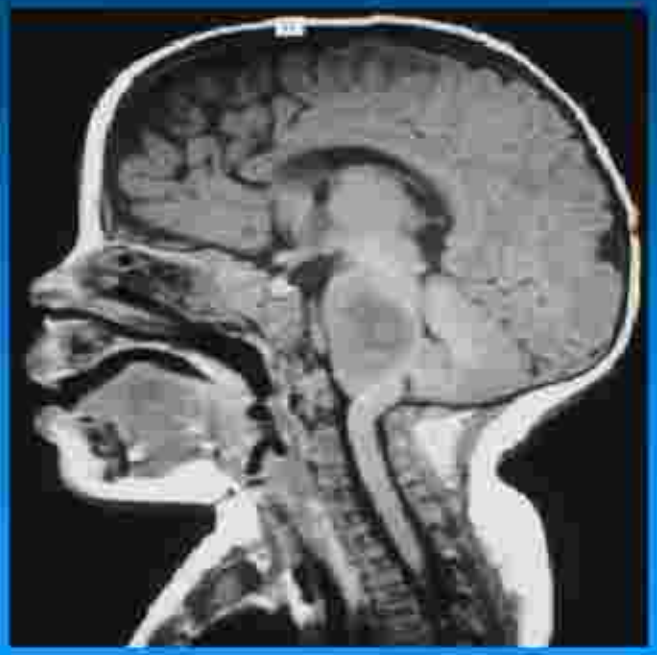
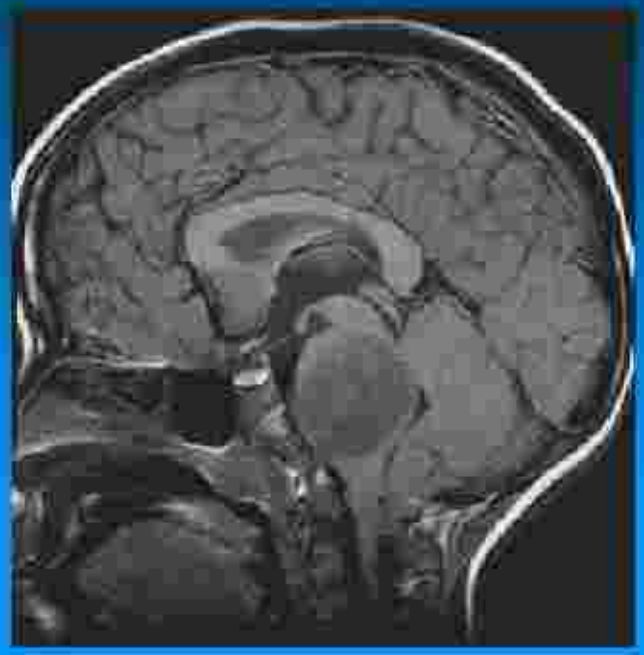
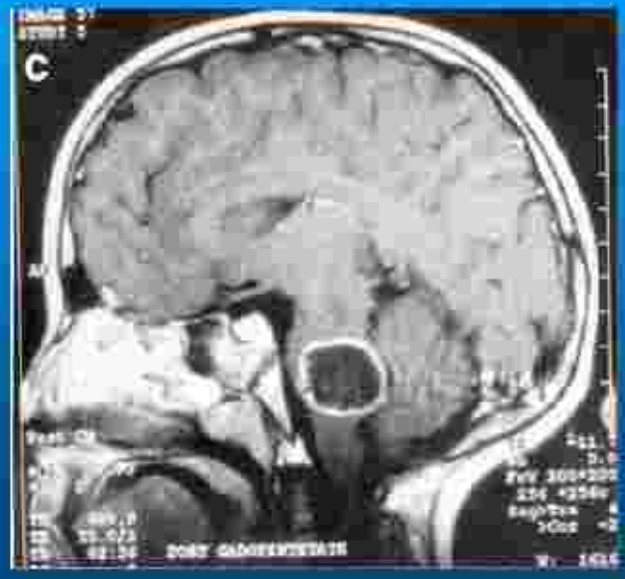


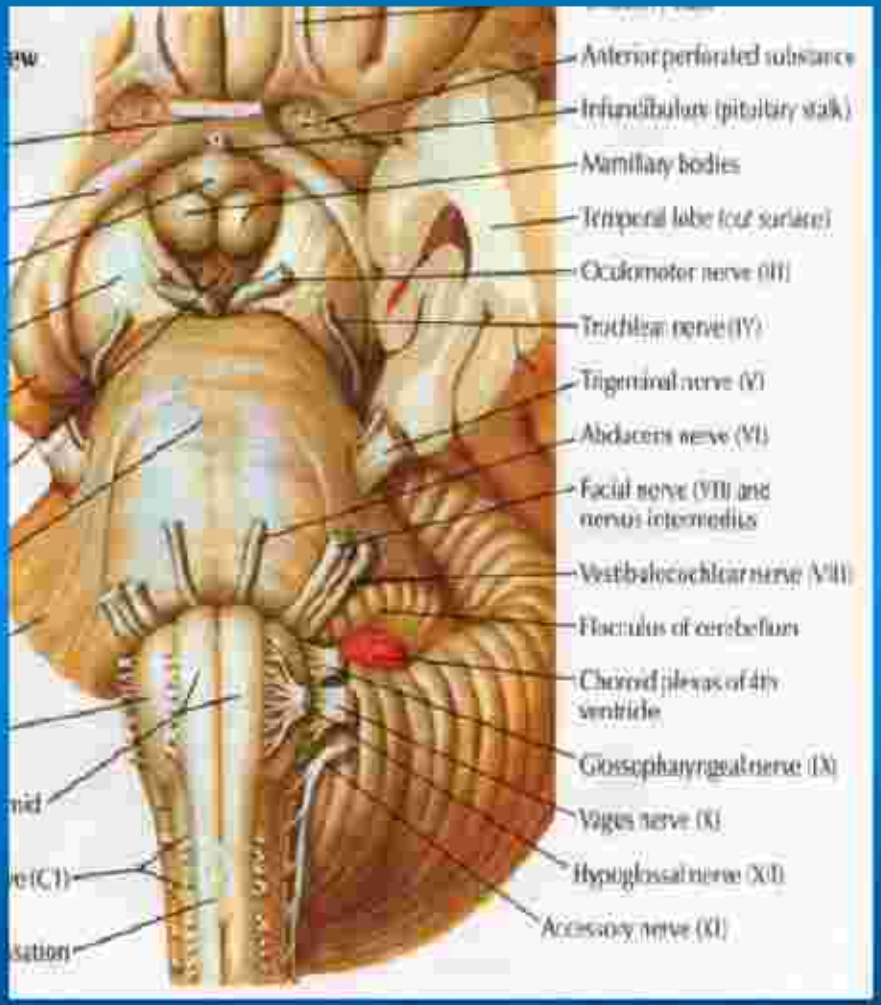



C

Brain stem glioma

- 20% of childhood and 5% of adult CNS tumours.
- Most frequently in children between 3 and 10 years
- Tissue confirmation is frequently not feasible with infiltrating, except in expansile tumors
- 60-80%of patients do not have a histological diagnosis
- Universally associated with dismal prognosis
- Historically, regarded as a single entity

Clinical presentation



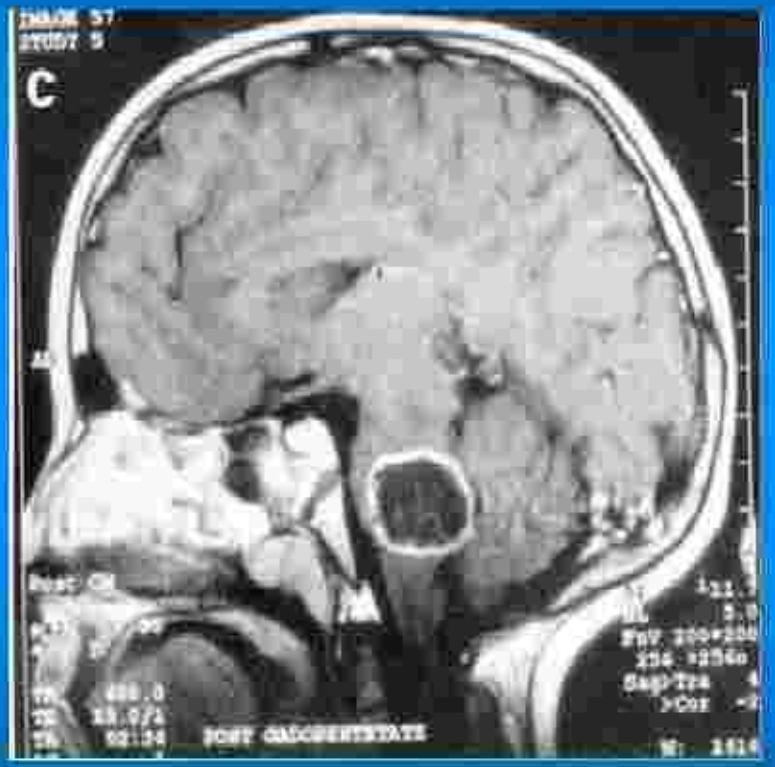
- Insidious/sudden onset
- Cranial nerve palsies
- Long tract signs (hemiparesis)
- Cerebellar signs (ataxia)

- Long history – better prognosis

Types

- Focal 5-10%
- Dorsal exophytic 10-20%
- Cervicomedullary 5-10%
- Diffuse intrinsic 75-85%

Focal tumors



- Surgery should be attempted
- Most are JPA
- If fear of morbidity, RT
- Favourable prognosis

Abbott Ped Neurosurg 1991

Dorsal exophytic tumors

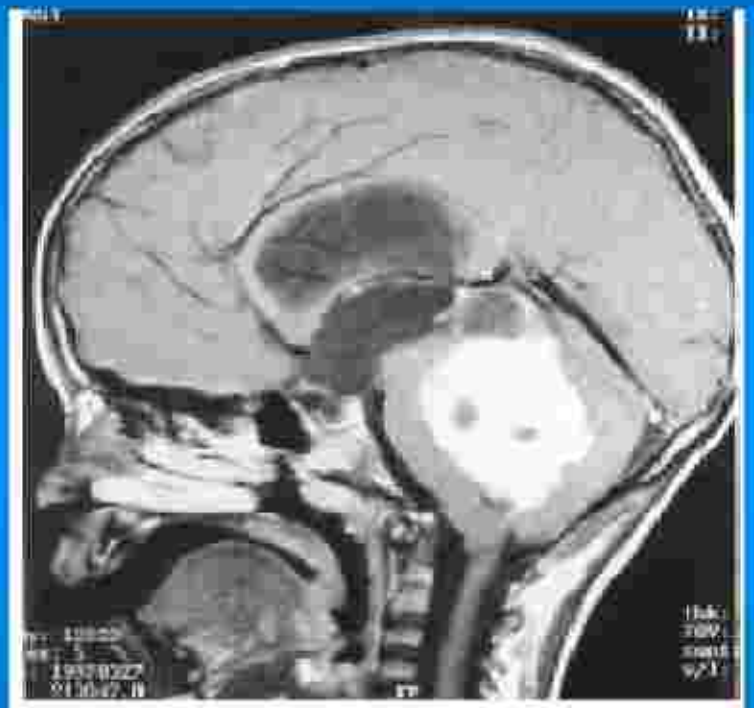


Fig 4.—A large exophytic tumor of the pons in a 6-year-old boy who presented with ataxia as seen on sagital T1 weighted MRI after contrast administration.

- Insidious onset
- Surgery should be attempted
- Most are JPA, low-grade
- Favourable prognosis
- RT for residual/progressive disease

Pierre-Kahn J Neurosurg 1993;79:845-52

Cervico-medullary tumours

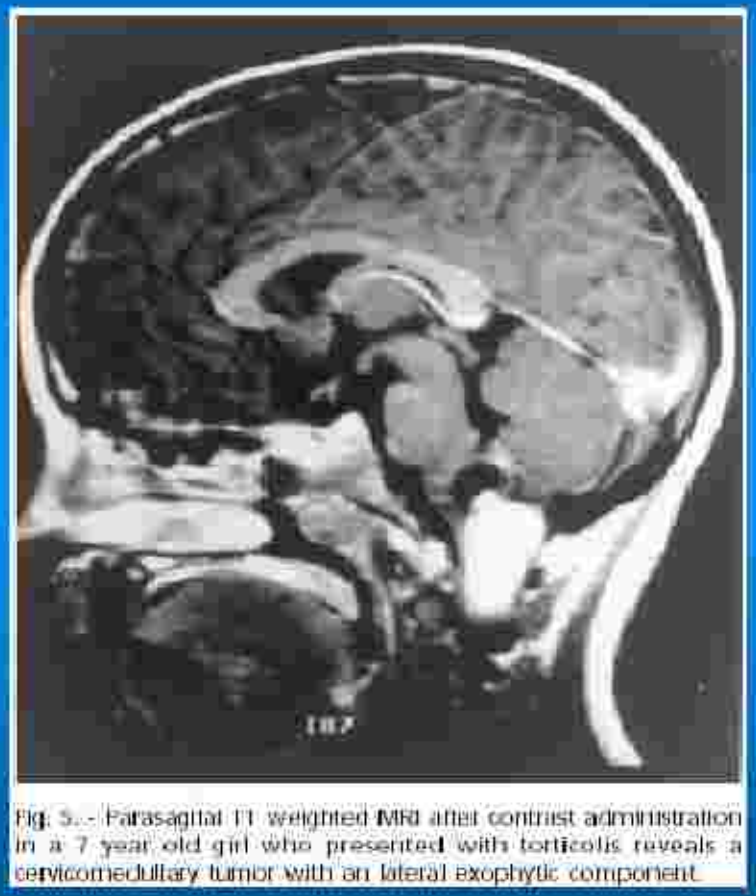


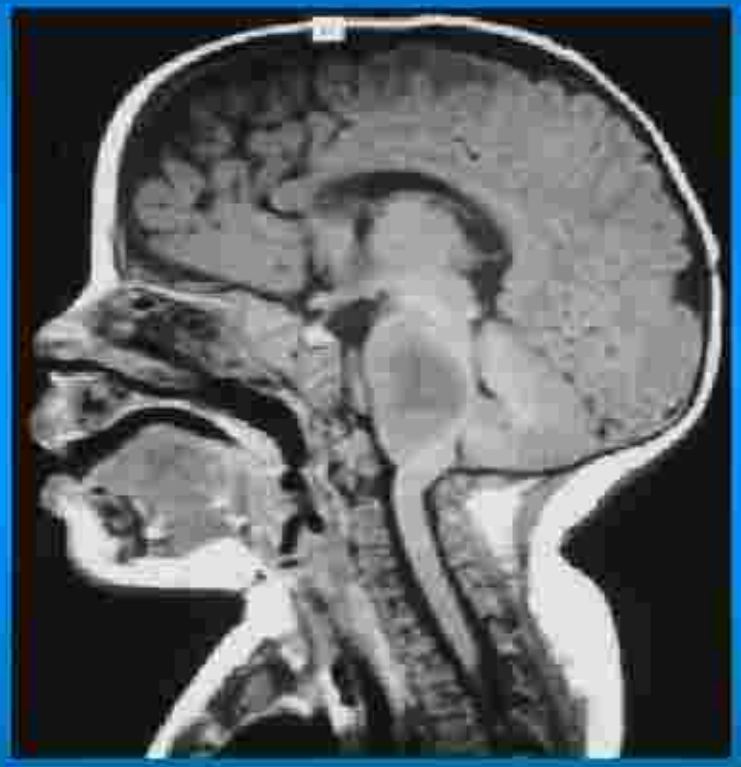
Fig. 5.- Parasagittal T1 weighted MRI after contrast administration in a 7 year old girl who presented with torticolis reveals a cervicomedullary tumor with an lateral exophytic component.

- Typically present with Cr N palsies, long tract signs
- Surgery treatment of choice (GTR achieved in 75% of cases)
- Most are JPA/low-grade
- RT not given routinely except for residual/progressive disease

Epstein J Neurosurg 1986

Diffuse pontine tumours

Major therapeutic challenge



- Typically present with short history
- Surgery (including biopsy) not feasible
- Most are fibrillary, but on autopsy high-grade
- Direct RT in view of typical clinico-radiological picture
- MRS/perfusion/PET could be complementary

Diffuse pontine gliomas

Literally everything tried, but nothing has really changed the outcome of these tumours

Frustrating

RT Dose Escalation/Hyperfractionation

POG# 8495

Group	N	Dose	Median PFS (mths)	Median OS (mths)	1 YS	2 YS
I	34	66Gy/1.1BID	6.5	11	47%	6.3%
II	57	70.2Gy/1.17BID	6	10	39.6%	23%
III	39	75.6Gy/1.26BID	7	10	39.9%	7%

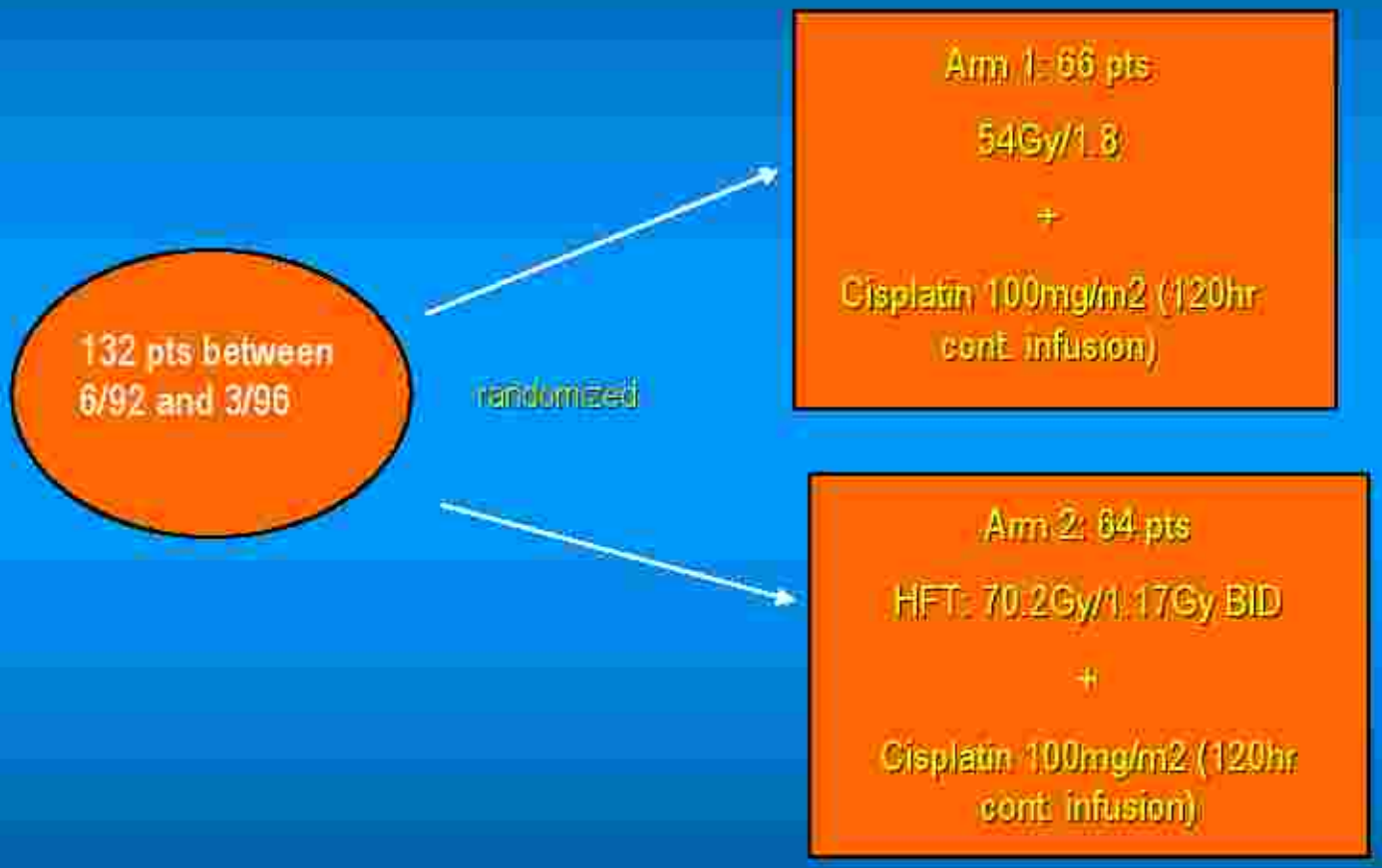
Increased toxicities with 75.6 Gy

Toxicities	%
Steroid use > 3 mths	62
Intralesional necrosis	45
Otitis media/externa	26
Skin reaction	21

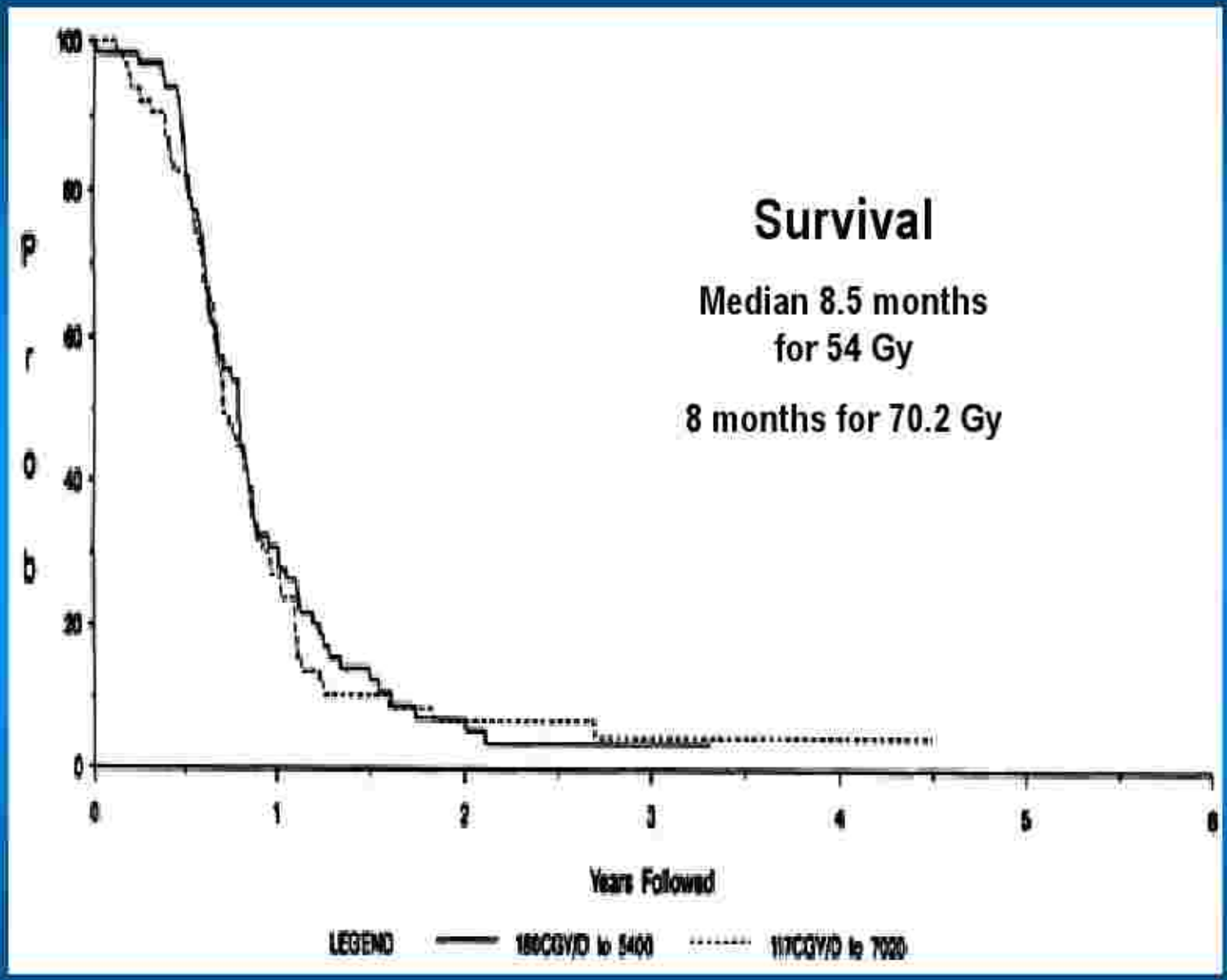
Freeman et al., IJROBP, 1993: 27(2)

Randomised trial

POG #9239:



Mandell IJORBP; 1999: 43(5)



Mandell IJROBP 1999

Chemotherapy
Randomised trial (n=74)

- RT alone (50-60Gy)
- RT + chemo (CCNU, vincristine, prednisone)

- RT alone → 5 yr survival was 17%; median time to relapse - 8 ms
- RT + chemo → 5 yr survival was 23% (p=0.56); median time to relapse 7 mths.

J. Neurosurgery 66:1987

Chemotherapy
cipslatin based

Compared 57 patients treated with 70.2Gy (POG #8495)
to
64 pts treated with identical RT + cisplatinum (POG 9239)

"Identical cohort, non-randomised"

No difference in outcome

Freeman IJORBP 2000, 47(3).

Int. J. Radiation Oncology Biol. Phys., Vol. 47, No. 3, pp. 561–564, 2000

0360-3016/00/$ see front matter

PII S0360-3016(00)00471-5

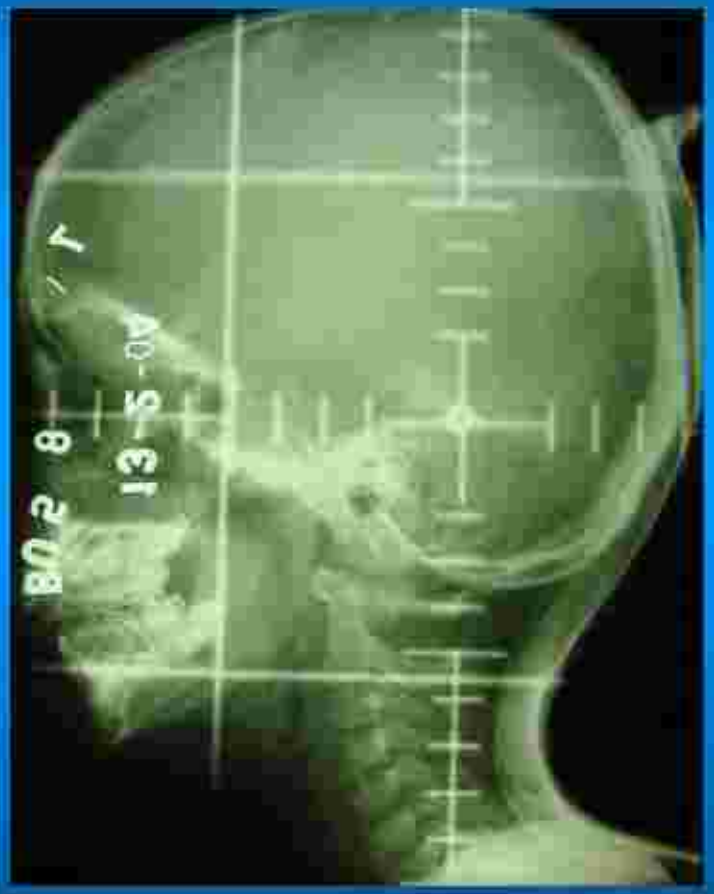
CLINICAL INVESTIGATION **Brain**

A DETRIMENTAL EFFECT OF A COMBINED CHEMOTHERAPY–RADIOTHERAPY APPROACH IN CHILDREN WITH DIFFUSE INTRINSIC BRAIN STEM GLIOMAS?

CAROLYN R. FREEMAN, M.B., B.S., FRCP(C),* JIM KEPNER, PH.D.,† LARRY E. KUN, M.D.,‡ ROBERT A. SANFORD, M.D.,§ RICHARD KADOTA, M.D.,‖ LYNDA MANDELL, M.D.,¶ AND HENRY FRIEDMAN, M.D.#

*McGill University, Montreal, PQ, Canada; †Pediatric Oncology Group Statistical Office, Gainesville, FL; ‡St. Jude Children's Research Hospital and the University of Tennessee College of Medicine, Memphis, TN; §Semmes Murphy Clinic, Memphis, TN; ‖Children's Hospital and Health Center, University of California, San Diego Medical Center, San Diego, CA; ¶Mount Sinai, School of Medicine, New York, NY; and #Duke University Medical Center, Durham, NC

Radiotherapy



FS a little generous as kids could be uncooperative

Conventional Cobalt/6 MV

No great benefit of hi-fi techniques

Beneficial in focal tumours (conformal/stereotactic/IMRT)

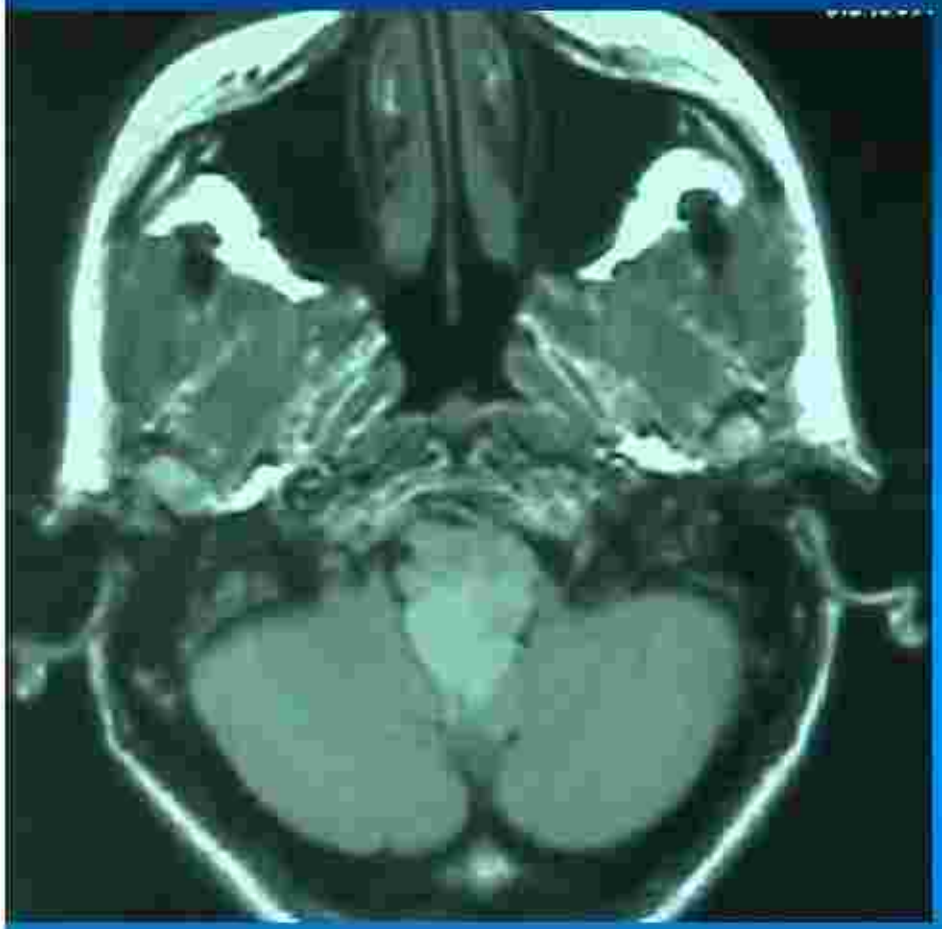
54-60 Gy/30#

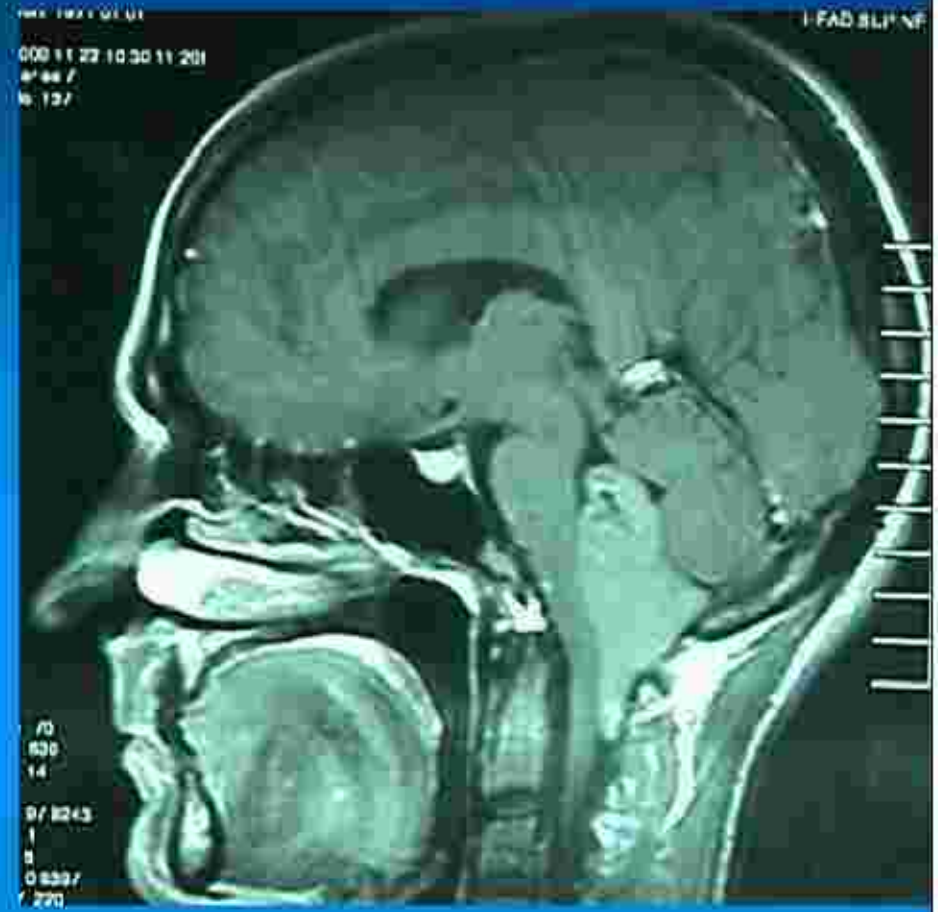
Recurrent brain stem gliomas

- Individualise, symptomatic care/steriods
- Re-irradiation rarely ever possible/helpful
- Chemo largely ineffective
- Temozolomide, Tamoxifen, interferons, Iressa, etc – several small phase II studies - investigational

Large study material – learnt what does not work

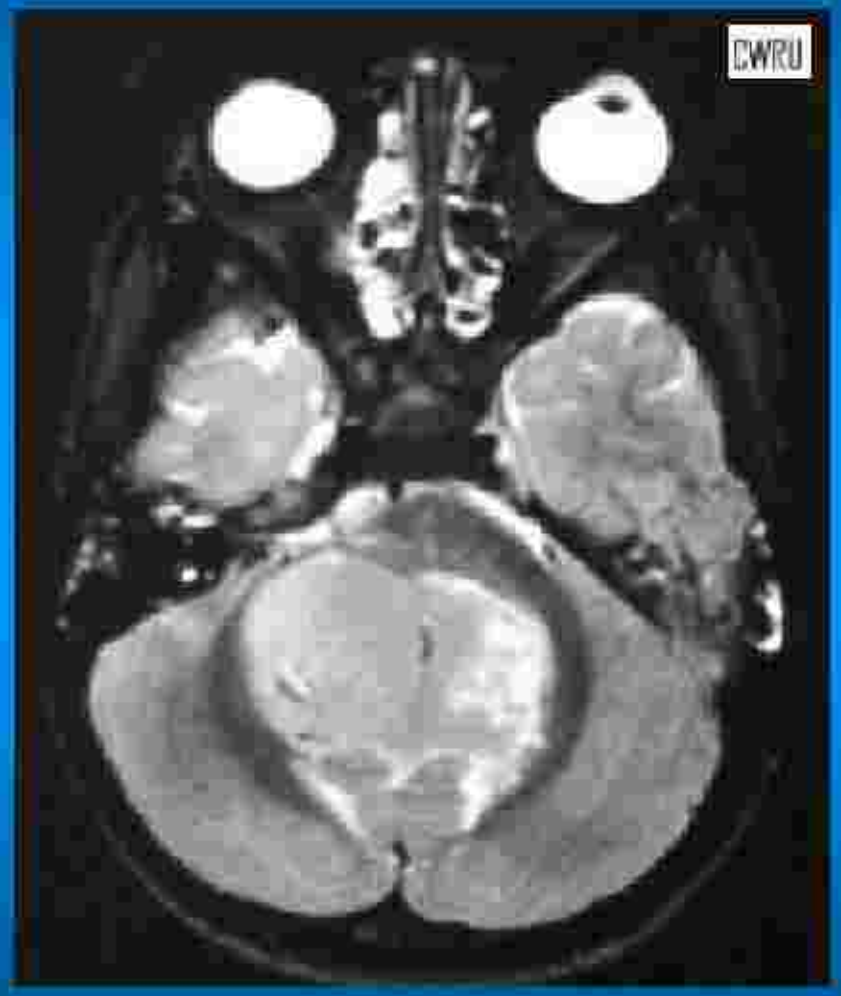
Something very original/innovative needed





10% of all childhood CNS tumours
90% are intracranial; 2/3 within the posterior fossa
50% of pts are < 5yrs old, 25% are less than 2
Difficult to treat, perplexing tumours

Ependymoma



Haemorrhage, calcification

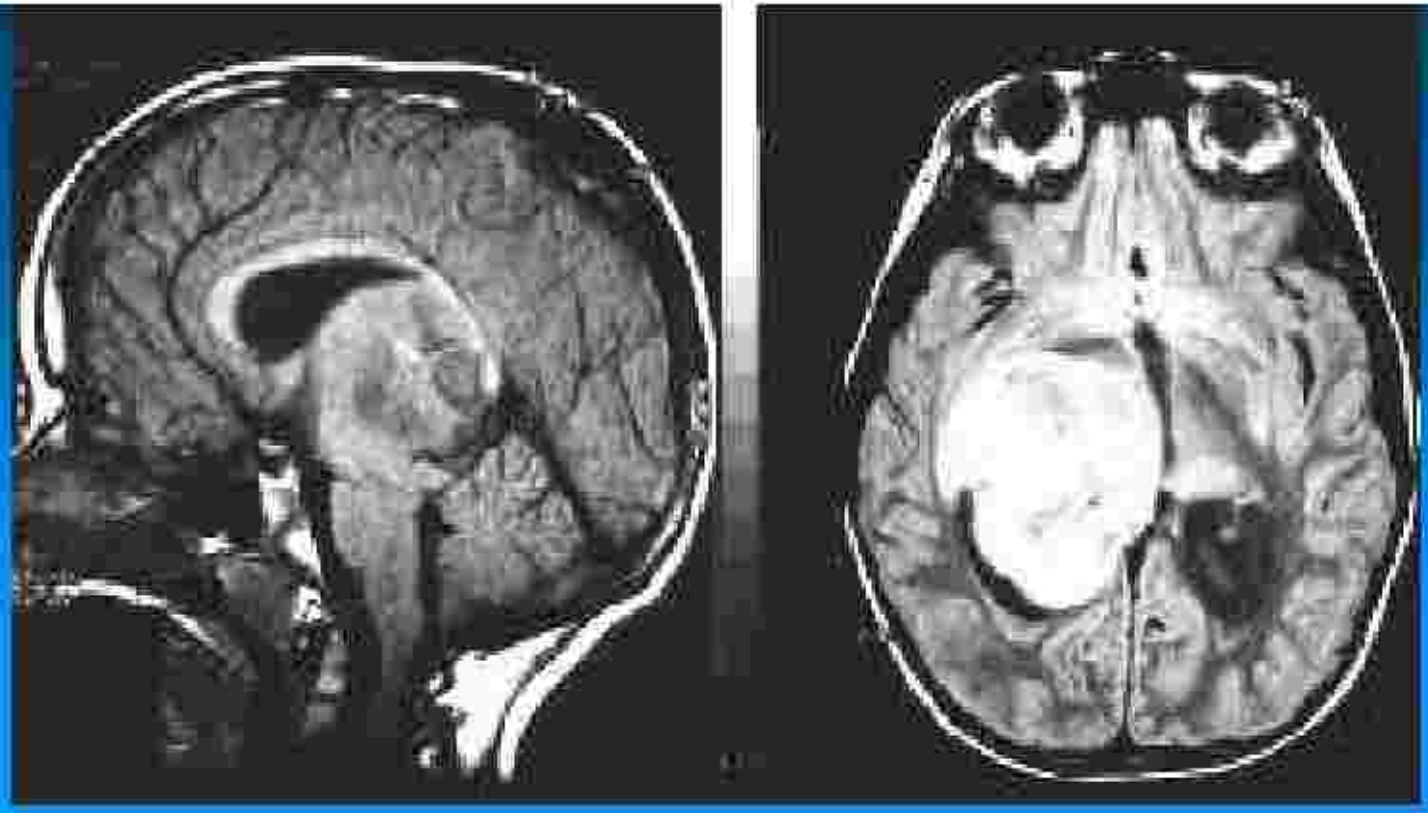
Cellular, with rosettes/pseudorosettes

Anaplastic: 10-30%

Spinal mets: 10-15%

Ependymoblastoma (PNET)

Spinal MRI/CSF for post fossa/anaplastic tumours



Surgery treatment of choice and the most important prognostic factor

Gross tumour resection (GTR) - 50-75% long term control

Subtotal resection (STR) - 0-30% GTR possible in only 50% cases, aggressive debulking/2nd look

Van Veelan JNS 2002

Schild IJROBP 1998

Radiotherapy

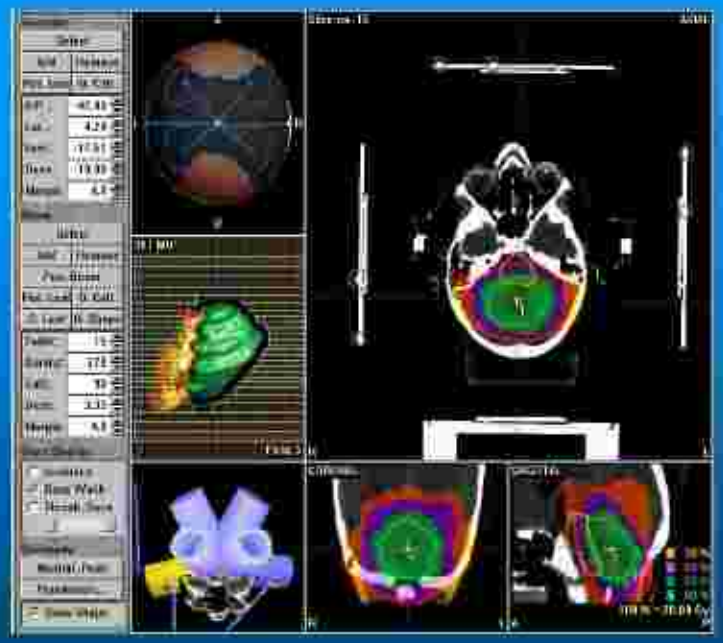
- No randomised trial of RT vs no RT, but large data about efficacy of RT
- CSI - in 1970's and 80's, but does not influence local control/survival
- Present recommendations- local RT (even in anaplastic)
- CSI – if spinal mets (CSF or MRI)
- Unresolved questions – a) RT in completely resected tumours
  b) can we avoid RT in very young children

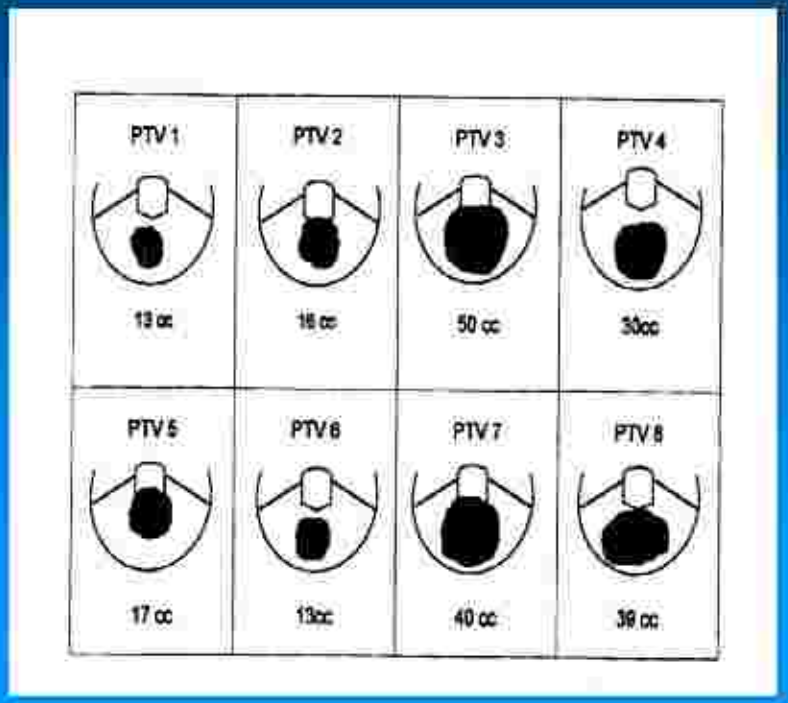
Merchant IJROBP 2002;53:51-7

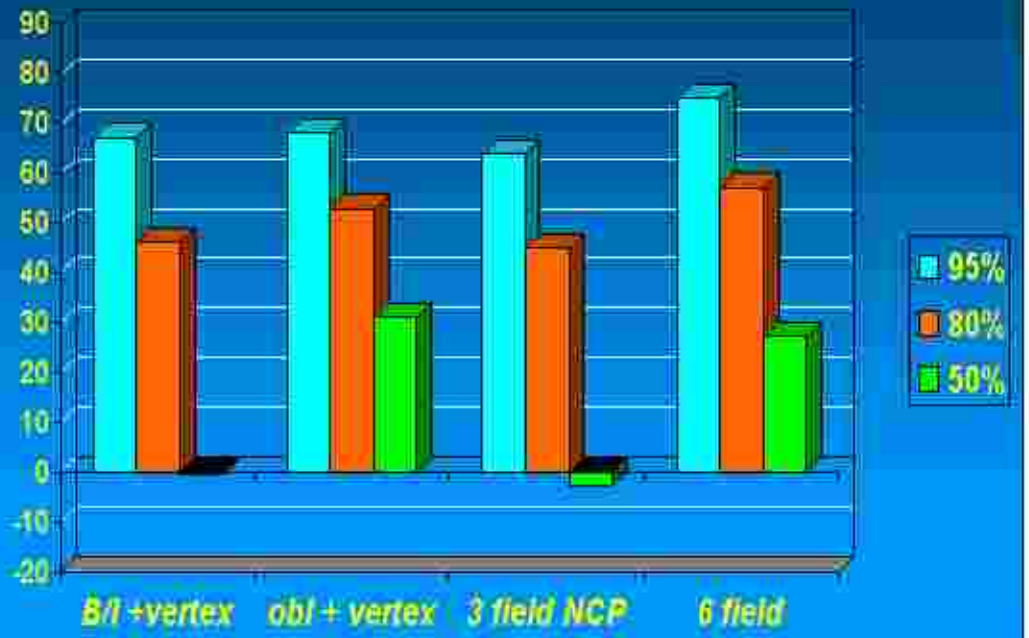
Vanuytsel IJROBP 1992;23:313-9

Radiotherapy

- Traditionally post fossa irradiation, cover inferiorly upto C3-C4
- Local RT= GTV + margin (2 cms)
- Conformal (3D CRT, Stereotactic RT with lesser margins)







Stereotactic conformal RT attractive option

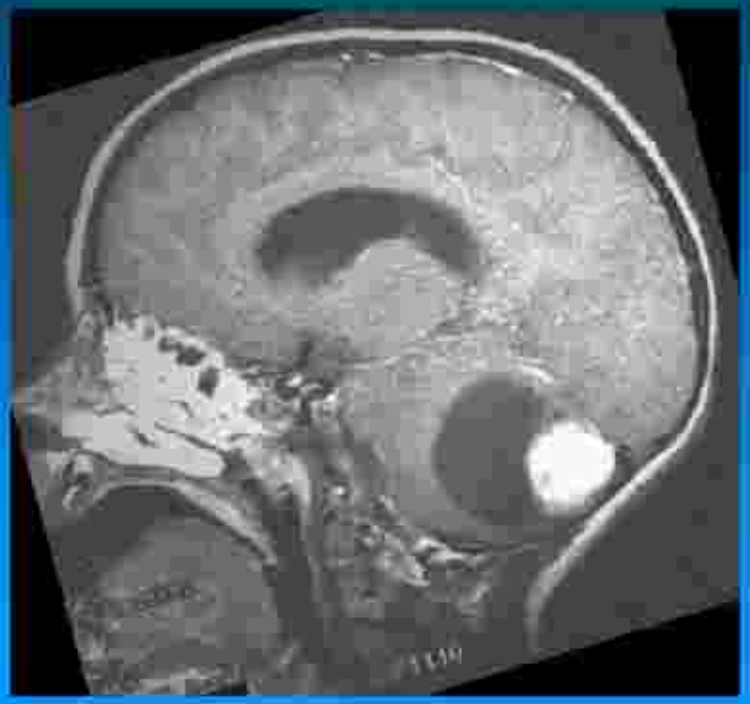
minimise treatment related toxicity; dose escalation

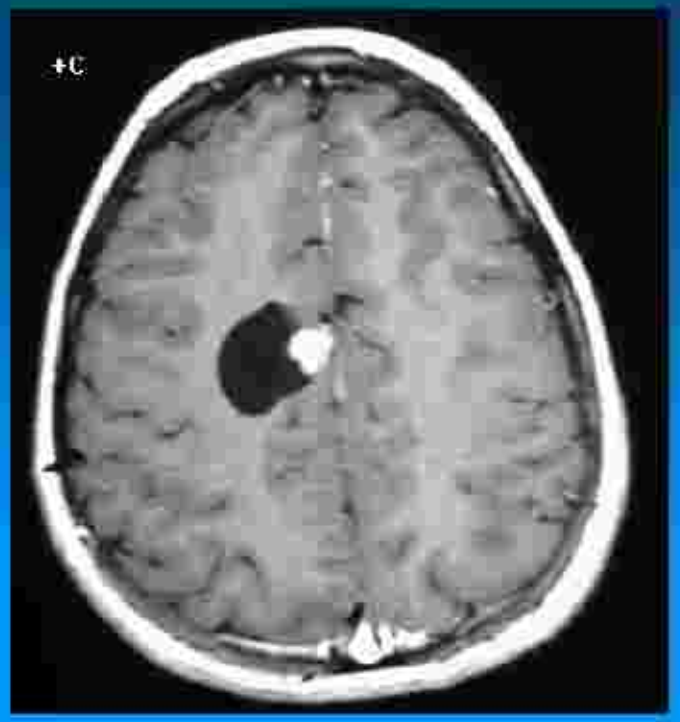
6 field noncoplanar technique the most optimal

Murthy Radioth.& Oncol 2003;67:191-8

Chemotherapy

- Role unknown
- Randomised trial of RT Vs RT + adj V, CCNU & P – no benefit (MPO 1996;27:8-14)
- CCG trial – V, CCNU, P Vs 8-in-1 chemo: no difference (JNS 1999;88:695-03)
- Could consider for children < 5 years with 40% not requiring RT for 2 years (JCO 2001)
- Role needs to be crystallised

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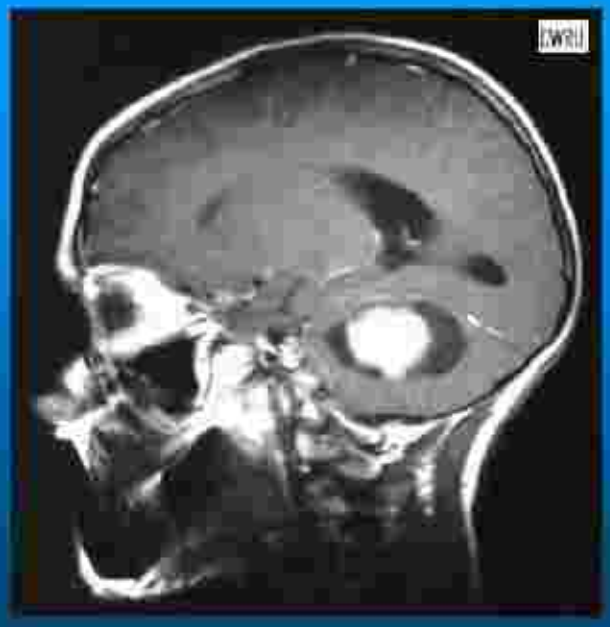

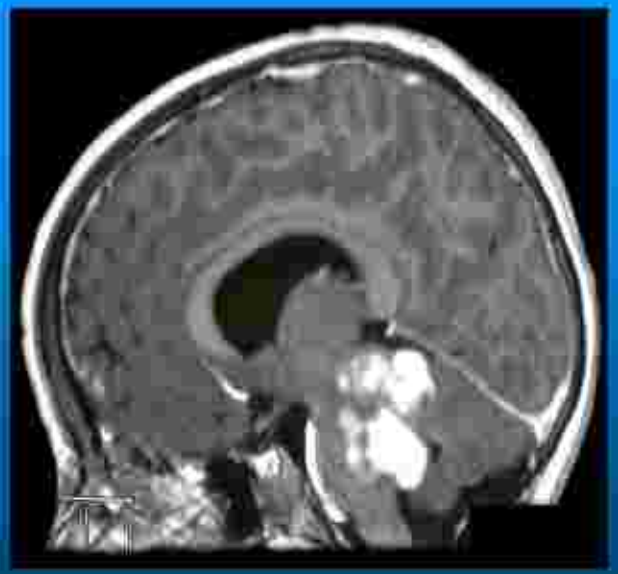

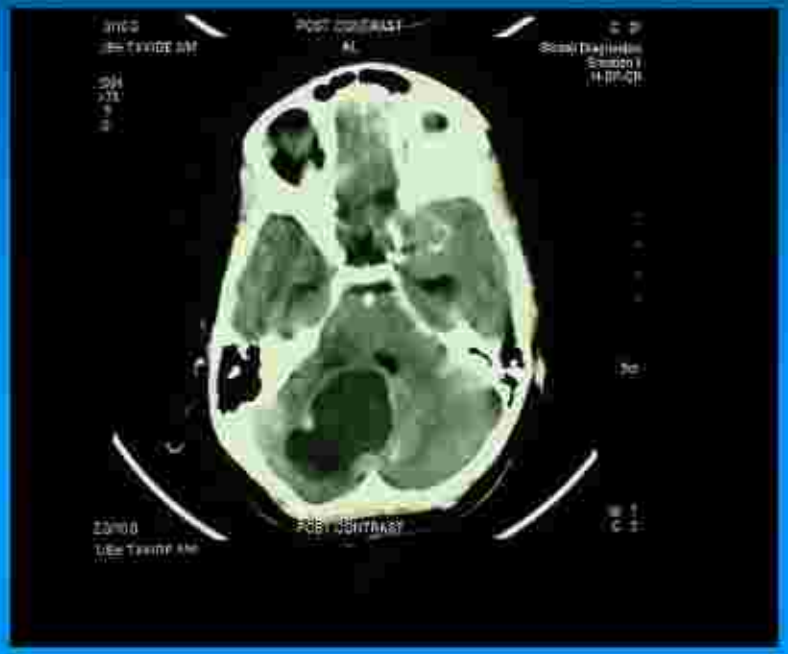

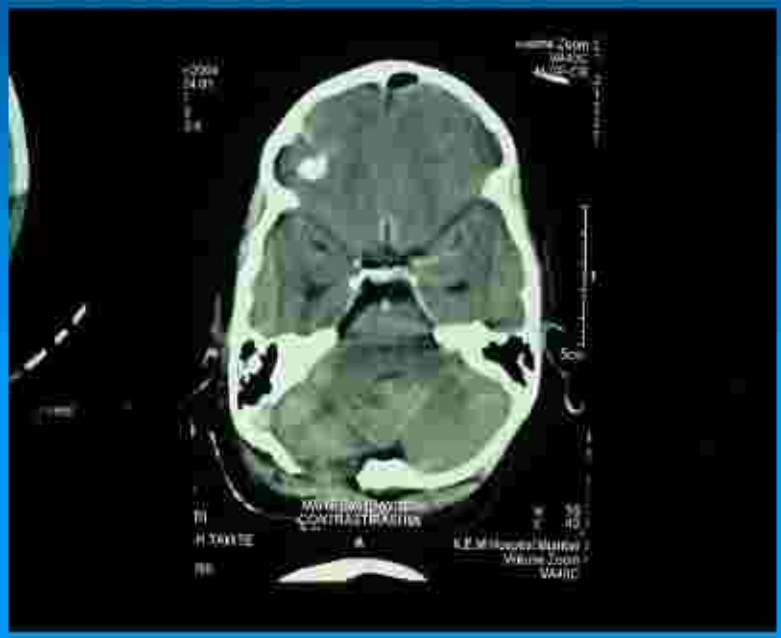

Benign/low-grade with indolent behaviour
Surgery treatment of choice
completely excised/small residual - observe
excellent cure rates

Fernandez Neurosurg 2003;53:544

Pilocytic astrocytoma

- Chemotherapy (baby brain protocol, Carboplatin + VCR) for very young children to avoid/defer RT
- RT – only for large residual, near brain stem or progressive
- Local RT (preferably with conformal RT to 50-54 Gy/30 #)

Packer JCO 1993;11:850-7

Conformal therapy
phase II data

- 102 children (64 EP, 38 LGA)
- PTV= GTV + 1.0 cm CTV + 0.5 cms
- Localised fields with conformal RT to 54 – 59 Gy
- median follow up of 17 months (3 - 43)
- 92 patients controlled
- 6 pts with EP failed (5 local, 1 disseminated)
- 4 pts with LGA failed (3 within CTV)
- Encouraging prelim results with narrow margins

Merchant IJROBP 2002;52:325-32

ELSEVIER

Radiotherapy and Oncology 74 (2005) 37–44

RADIOTHERAPY & ONCOLOGY

www.elsevier.com/locate/radonline

High precision conformal radiotherapy employing conservative margins in childhood benign and low-grade brain tumours

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[b]*Department of Medical Physics, Tata Memorial Hospital, Parel, Mumbai, India*

- 26 children (benign and low-grade brain tumours)
- Localised fields with conformal RT to 54 Gy
- median follow up of 25 months (12 - 47)
- 25 patients controlled; Cognition **maintained**

Baseline score of Full Scale IQ for patients treated with SCRT (n=20)

Class	IQ Limits	Number of Patients
Defective	69 & below	4 (20%)
Borderline	70-79	5 (25%)
Dull-normal	80-89	5 (25%)
Average	90-109	5 (25%)
Bright-normal	110-119	0 (0%)
Superior	120-129	1 (5%)
Very Superior	130 & above	0 (0%)

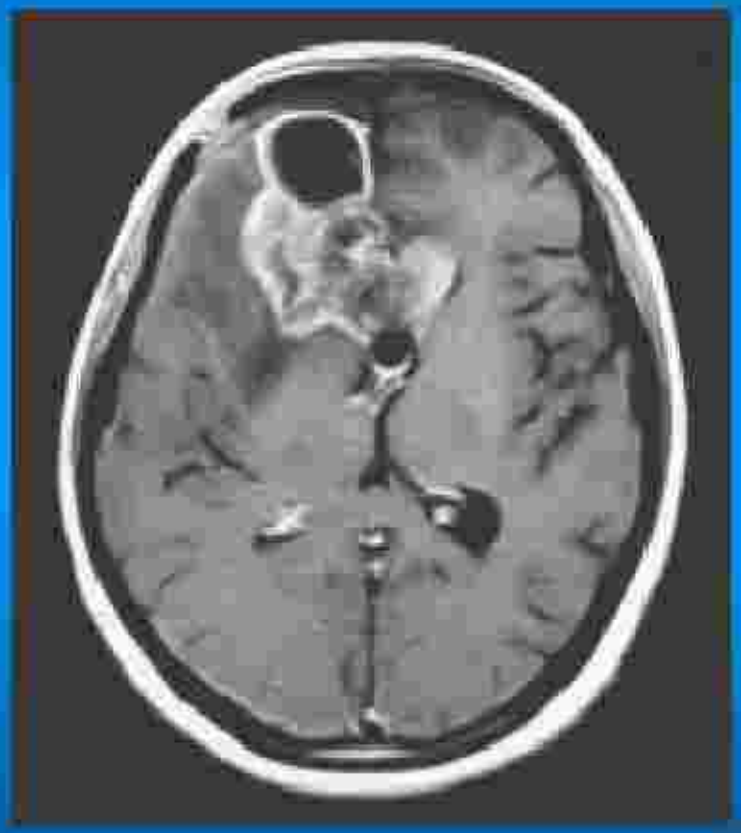
14/20 patients have below avg IQ

Neuropsychological profile in children treated with SCRT

Significance	Baseline before SCRT	6 months after SCRT	24 months after SCRT	Statistical (baseline Vs 24 months)
Verbal IQ	84 (41-99)	85 (66-110)	88 (74-117)	NS[¶]
No. of patients 14	13	7		
Performance IQ	87 (61-111)	89 (61-106)	96 (82-117)	NS
No. of patients 12	12	7		
Full Scale IQ	82 (33-105)	86 (66-108)	89 (81-118)	NS
No. of patients 14	14	8		
STAIC*				
C1	48 (27-78)	32 (4-64)	30 (20-38)	p=0.005
No. of patients	12	11	6	
C2	40 (15-72)	25 (4-57)	26 (24-30)	NS
No. of patients	12	11	6	
LOTCA[§]	85 (42-114)	85 (54-114)	100 (63-118)	NS
No. of patients	11	10	7	
Vithoba Paknikar Performance Test	89 (90-104)	92 (80-104)	83 (77-88)	NS
No. of patients	2	2	2	

Jalali IJROBP 2006 (In press)

High-grade hemispheric gliomas



Relatively rare

Somewhat better outcome than adults but long-term cure still rare

Overexp of p53 strong prognostic factor (NEJM 2002)

Surgery, conv RT std of care as in adults

Role of chemo not fully evolved

High-grade hemispheric gliomas

- Randomised trial of RT + adj pCV Vs RT alone (n=58): 5yr DFS of 46% Vs 18% (CCG 943)
- Results never duplicated (38 % slides reviewed were not high-grade, Boyett 1998)
- Intensive/pre irradiation chemo: no major impact
- Currently several regimens being tested (TMZ, thalidomide, carboplatin, topetecan, etc)

Sposto J NeuroOncol 1989