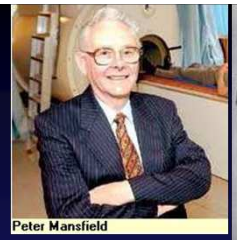
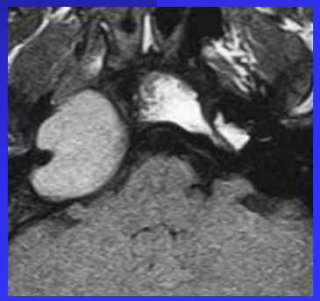
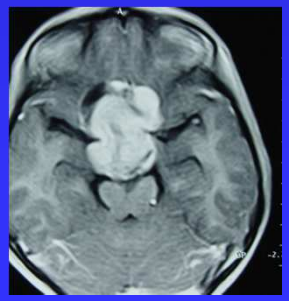
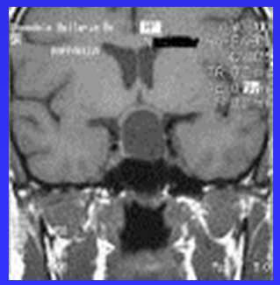
CNS Tumours

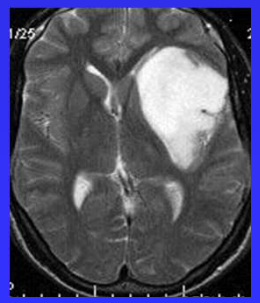


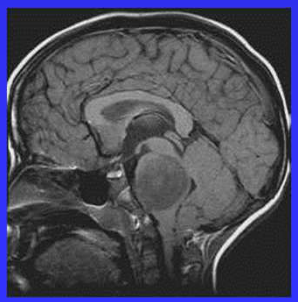
- Brain tumours are relatively rare but affects all AGES
- 482 patients/day worldwide, Leading cause of childhood cancer deaths
- 2nd leading cause of cancer death in males and 5th in females aged 20-39
- Varied clinical spectrum; no 2 tumours similar
- A lot of challenges in children and adults
- Fascination for brain for scientists, thinkers..



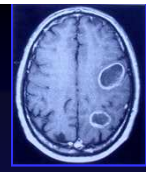








Management



Local control and survival quality of life

Management exemplifies a multidisciplinary approach

- Neurosurgeon
- Radiation Oncologist
- Medical and Paediatric Oncologist
- Neuro radiologist
- Neuropathologist
- Neurologist
- Physio and occupational therapist
- Speech therapist
- Neuropsychologist
- Rehabilitative services

Childhood brain tumours

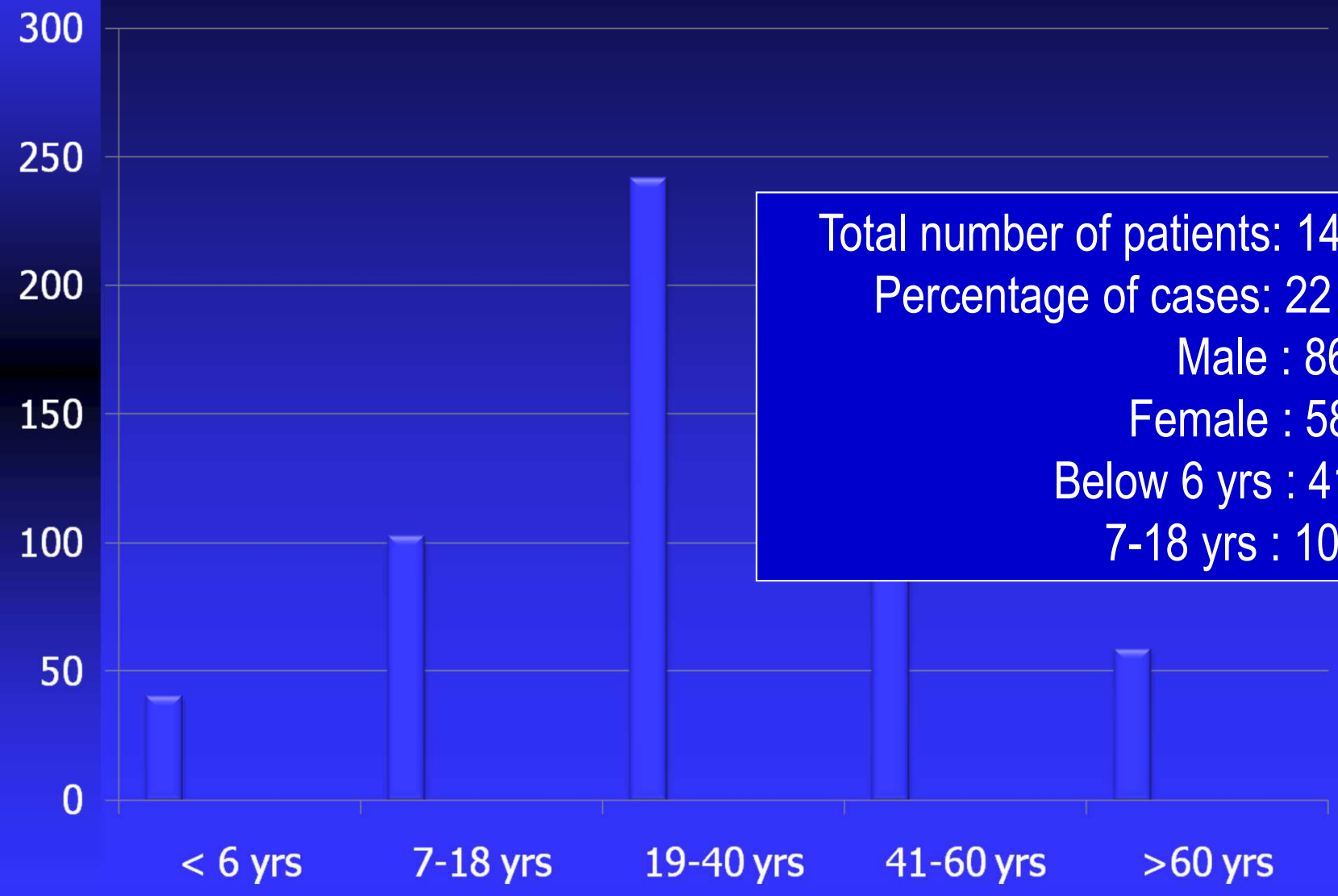
Second commonest cancer in children

High chance of cures (>70%)

Challenges in rehabilitation, social functioning and quality of life

Paediatric CNS tumours

Prospective TMH database (2006)



Total number of patients: 144
Percentage of cases: 22 %
Male : 86
Female : 58
Below 6 yrs : 41
7-18 yrs : 103

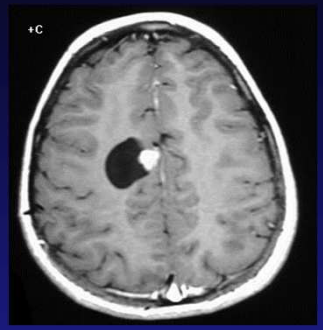
Comparison with published Western data

* SEER Cancer Registry and CBTRUS Cancer Registry

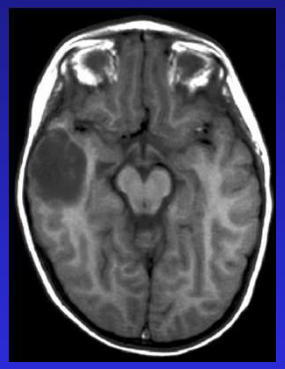
	Median age of presentation	
	TMH data	**Western data***
Medulloblastoma	10 yrs	9 yrs
Ependymoma	18.5 yrs	19 yrs
Brain stem glioma	11.5 yrs	11 yrs
Supratentorial PNET	15 yrs	9 yrs
Pineal tumour	18.5 yrs	18 yrs
Craniopharyngioma	*20 yrs*	*28 yrs*
Pilocytic Astrocytoma	*16 yrs*	*23 yrs*
Arteriovenous malformations	*21 yrs*	*33 yrs*

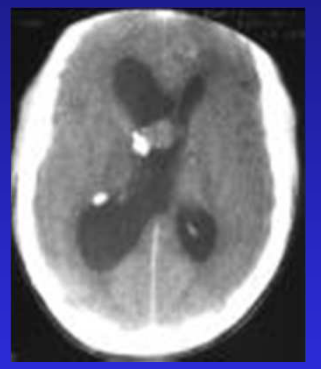
Jalali and Datta J NeuroOncol 2008; ;87(1):111-114

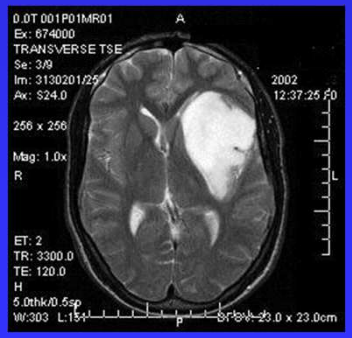
Low grade gliomas



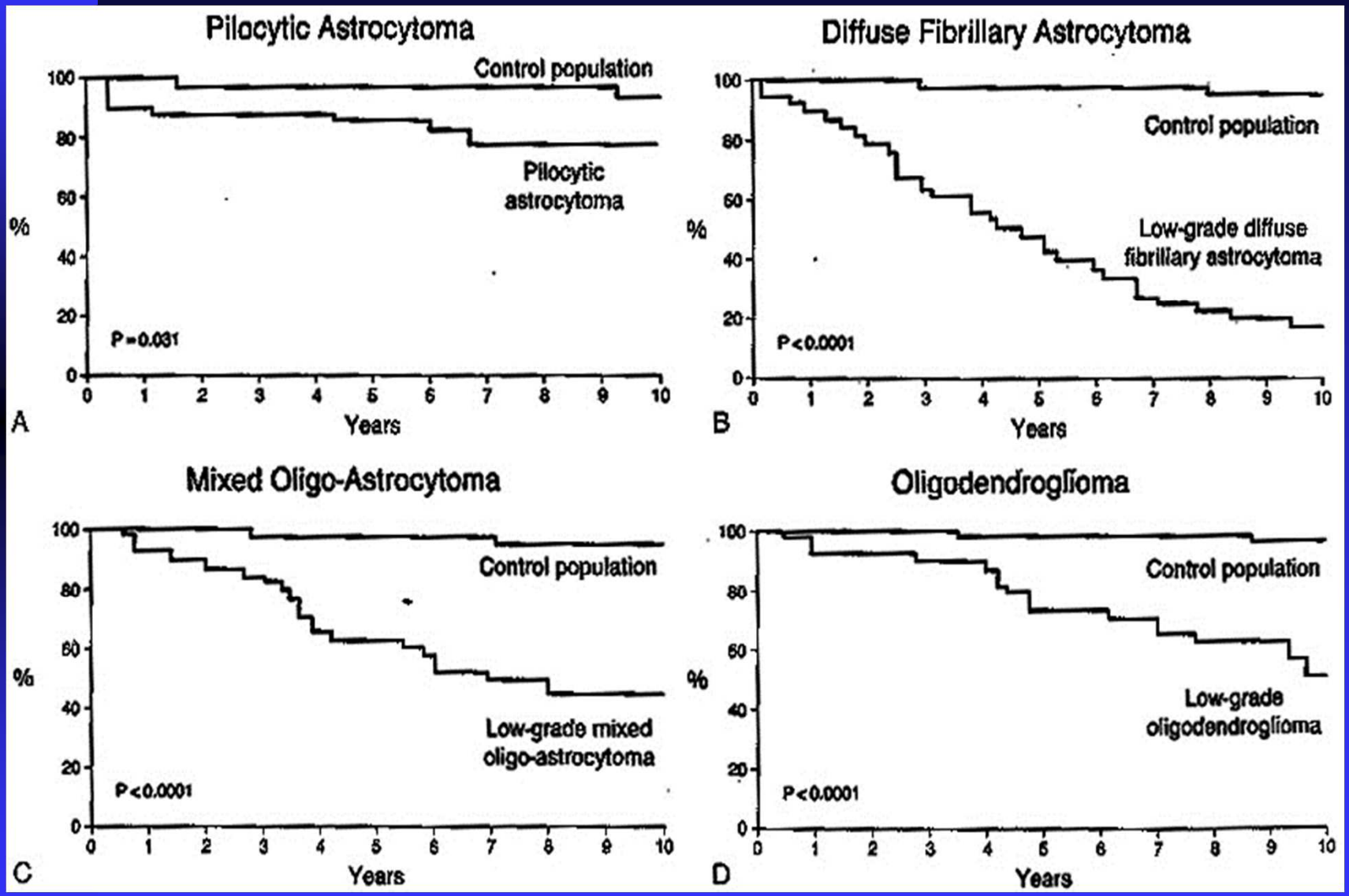
- Wide Range of tumours (three groups)
- Pilocytic asytocytomas (children)
- DNET, PXA, SEGA, gangliogliomas (young adults)
- astrocytoma, oligodendroglioma (WHO Grade II), Mixed oligoastrocytoma (adults)

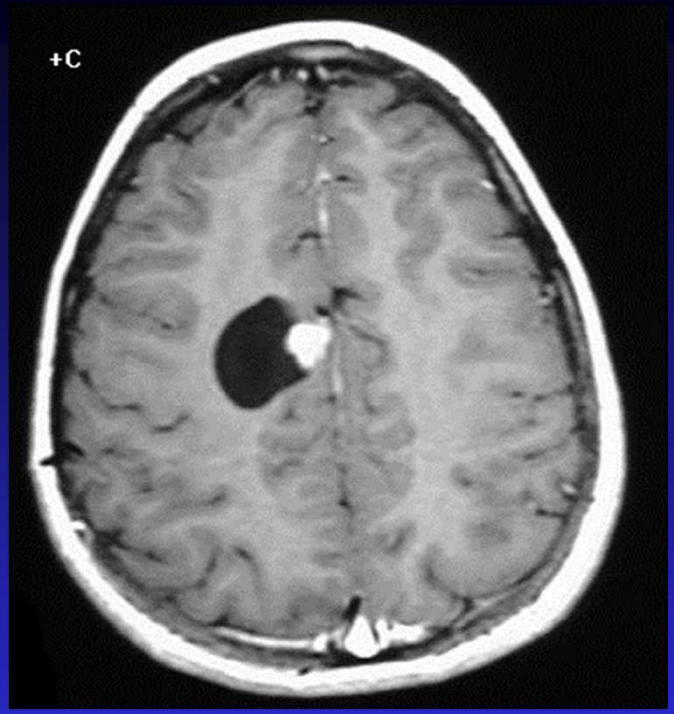


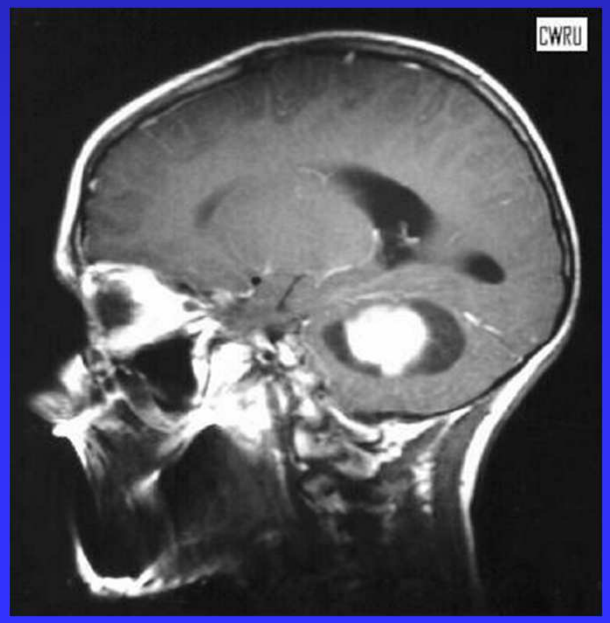


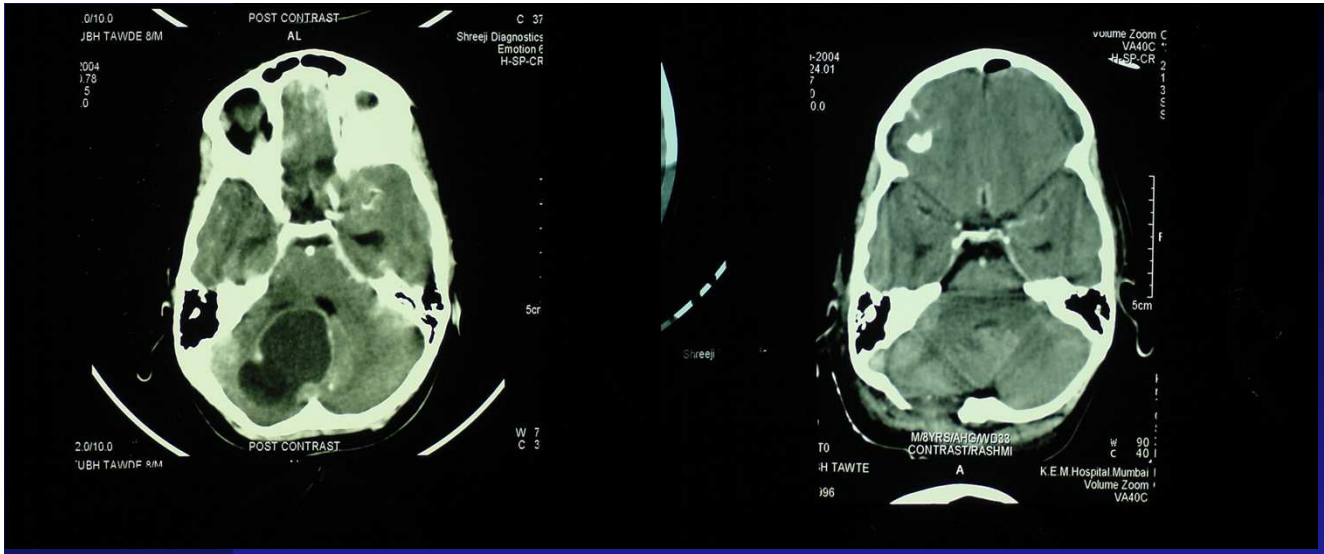


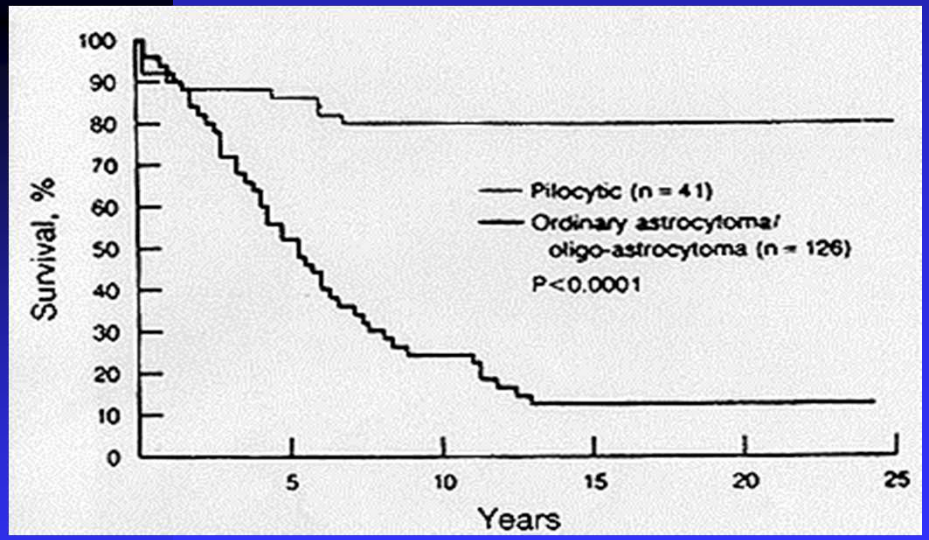
Long term survival




+C


CWRU



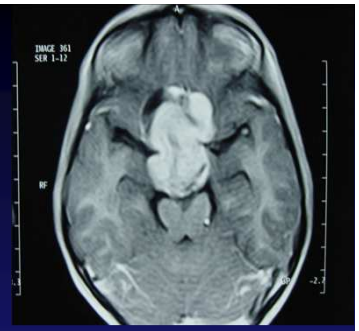


Benign/low-grade with indolent behaviour

Surgery treatment of choice

completely excised/small residual - observe excellent cure rates

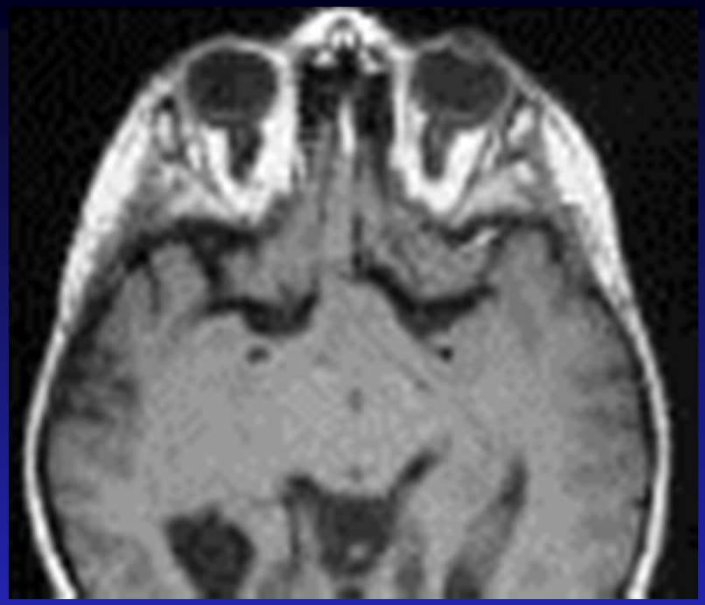
Optic – Hypothalamic Gliomas

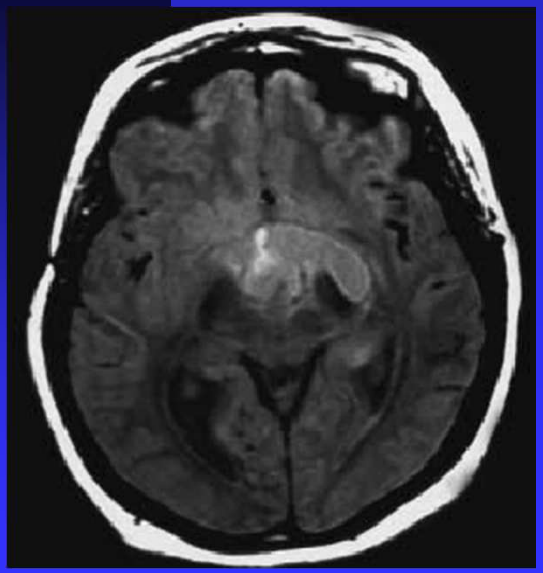


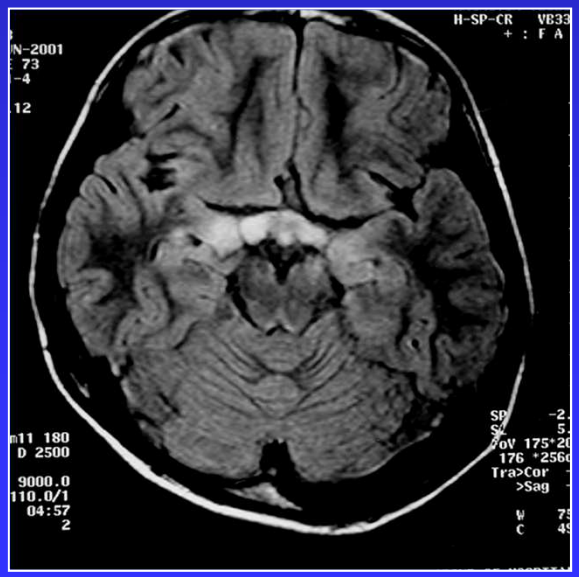
Common tumours; JPA; cure more than 90%

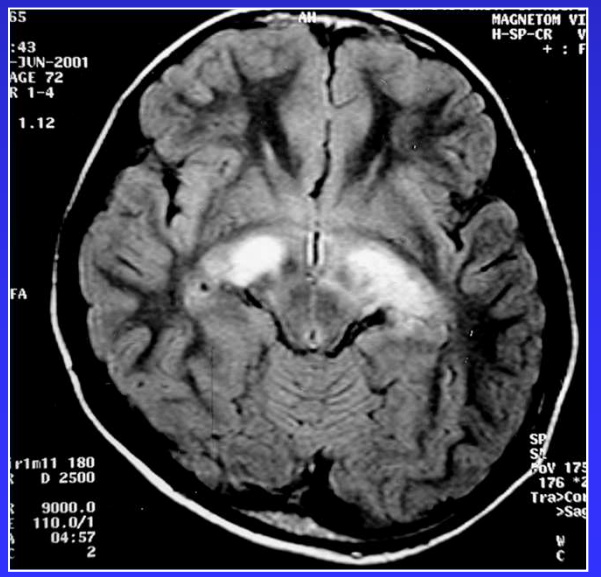
- frequently only a biopsy
- RT (45-54Gy/30 fraction) for older children/ progressive disease results in excellent long term outcome
- All efforts to contour all tumour and treat with conformal RT


IMAGE 361
SER 1-12
RF






H-SP-CR


MAGNETOM
H-SP-CR

Chemotherapy for Pilocytic astrocytoma

- Chemotherapy (baby brain protocol, Carboplatin + VCR) for very young children to avoid/defer RT

Packer JCO 1993;11:850-7

- Objective response rate (CR+PR): 42%
- 5Yr PFS: 34%; OS: 89%
- **5Yr RT free survival rate: 61%** (French prospective study)

- RT –large residual, and/or progressive tumours

3D 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 (92%)
- 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

JCO 2009

ELSEVIER

Radiotherapy and Oncology 74 (2005) 37–44

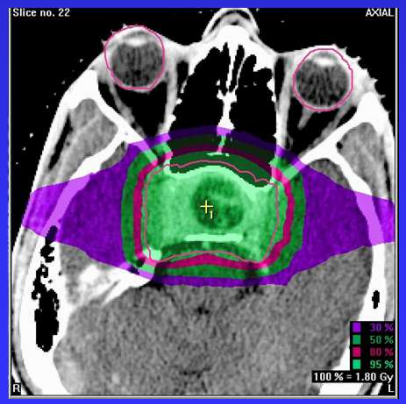
RADIOTHERAPY & ONCOLOGY
JOURNAL OF THE EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY

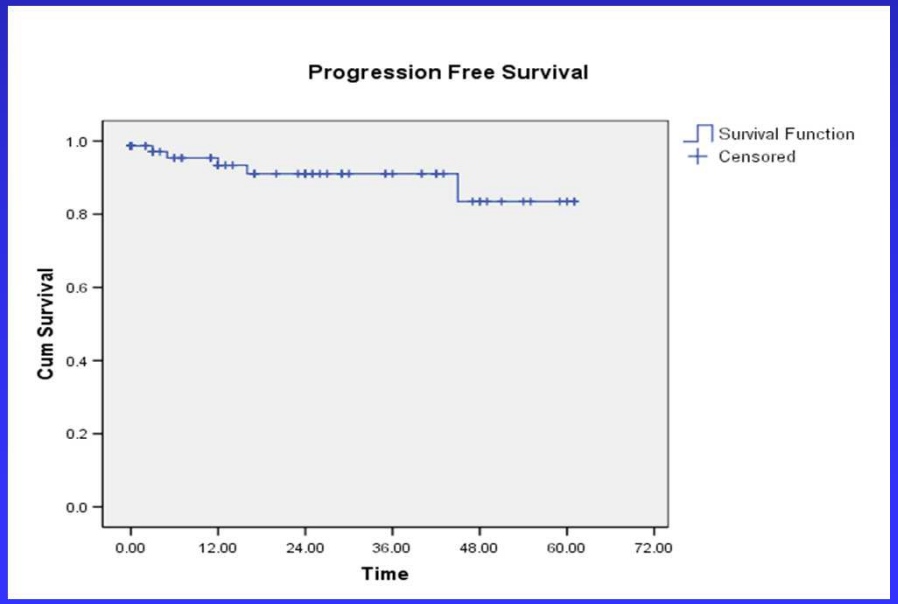
www.elsevier.com/locate/radonline

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

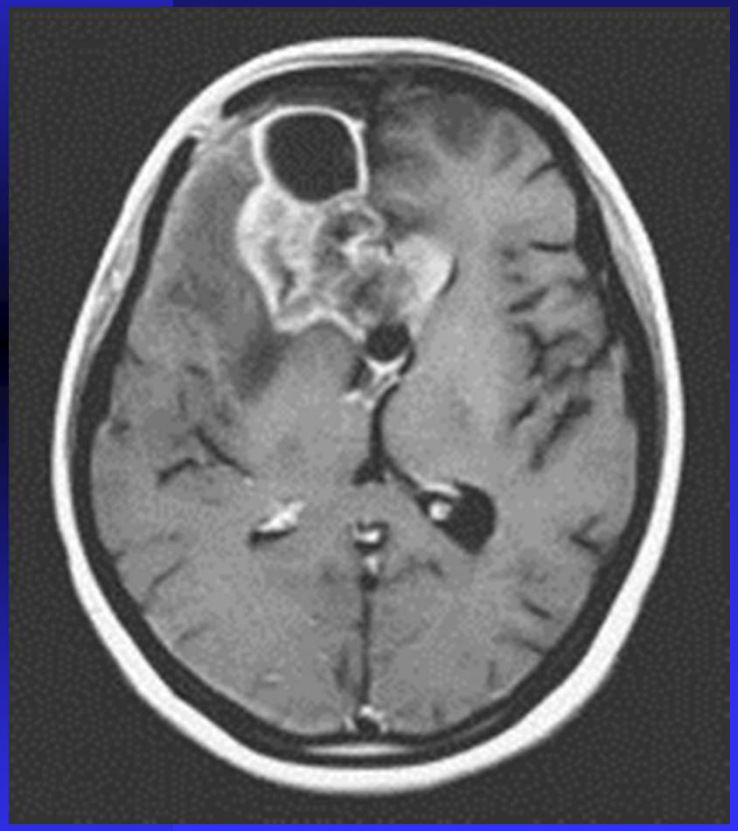
Rakesh Jalali[a,*], Ashwini Budrukkar[a], Rajiv Sarin[a], Dayananda S. Sharma[b]

[a]*Department of Radiation Oncology, 113 Tata Memorial Hospital, Parel, Mumbai, India*
[b]*Department of Medical Physics, Tata Memorial Hospital, Parel, Mumbai, India*





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

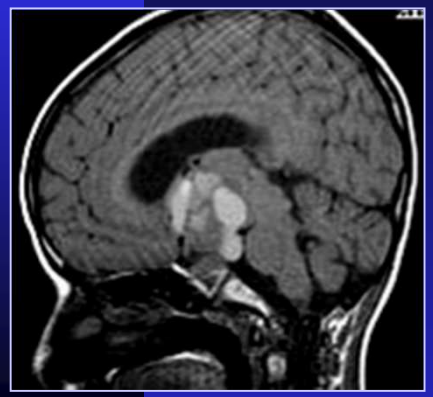
Paediatric glioblastomas: A histopathological and molecular genetic study

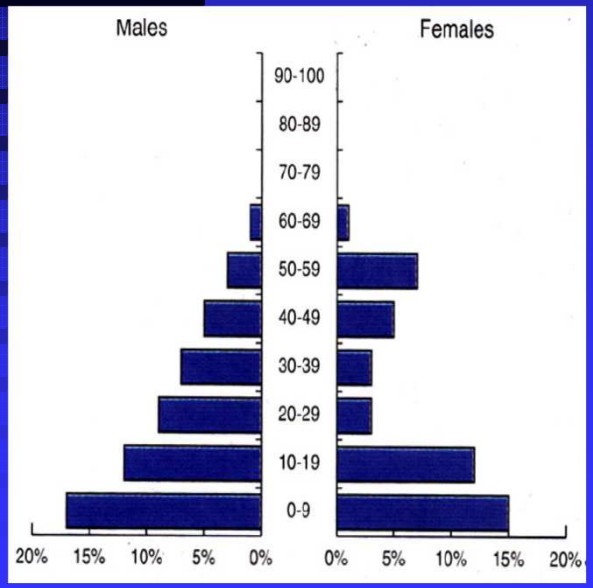
V Suri, P Das, A Jain, MC Sharma, S Borkar, A Suri, D Gupta and Chitra Sarkar
Departments of Pathology and Neurosurgery, AIIIMS, New Delhi, India

- 30 patients
- p53 in 63%
- EGFR protein overexpression in 23%
- EGFR gene amplificaion only in 5%
- PTEN deletion in 5%
- Different than in adults

NeuroOncology 2009; 11 (3): 274-80

Craniopharyngiomas





Age & Sex distribution

- 2-5% of all primary intracranial tumours
- Common age of presentation <20 yrs
- 5-15% of primary tumours in children

Two histopathological types:

1) Aadamantinomatous type
2) Papillary type - in adults

May be unpredictable in behaviour

- Challenging management, Controversial
- Emotive subject

Review of 144 published data; Adamson & Yasargil 2008

Recurrence rate after only partial excision

Author	yr	n	Recurrence	FU (years)
Carbezudo	1981	14	12	5-30
Carmel	1982	14	10	6.1
Djordjevic	1879	15	8	-
Hoff	1972	18	16	10
Hoffman	1977	15	8	2-16
Lichter	1977	9	7	1-20
McMurrary	1977	9	7	1-14
Shapiro	1979	9	7	7.8
Stahnke	1984	12	6	6.9
Sweet	1976	5	4	1-21
Thomsett	1980	11	10	8.2
Total		**131**	**93 (71%)**	

Issues with Surgery

- Morbidity & Mortality:
  - Hypothalamic morbidity -as high as 50%
  - Operative mortality - 2.5 to 10%
  - Late mortality - 11 to 28%
- Post-operative neuro-endocrine dysfunction - 97%
- More in *ultra* – radical surgery and repeated surgeries
- Radiotherapy as an option
- Primarily for local control

Conservative surgery + RT

- Recurrence rates :16 -25%
- Favourable long-term morbidity or mortality
- Avoids repeat surgery (Hypothalamic injury)

Treatment Group	Recurrence Rate
Partial excision alone	60%
Partial excision + RT	10-33%

No randomized study comparing the two groups

Dose and Volumes

- Dose schedule: 50-54 Gy @ 1.8-2 Gy/fr

Targets

GTV: Both cystic & solid components of any residual/recurrent disease; Entire surgical bed, disease left at the stalk

CTV = GTV + 0-5 mm margin

PTV depending of technique

- For 3D-CRT / IMRT (mask) - 5 mm margin
- For SCRT - 2mm margin
- Image guided / frameless - 2 mm

SCRT: Heidelberg experience (n=40)

- Median dose: 52.2Gy @ 1.8Gy/#
- Median FU : 98 months
- Median PFS at 5 & 10 yrs 97% & 89%
- OS at 5 & 10 yrs : 100%
- No pts had visual deterioration after RT

SCRT provides acceptable local control & toxicity

Coombs et al Cancer 2007

Challenges in long-term survivors

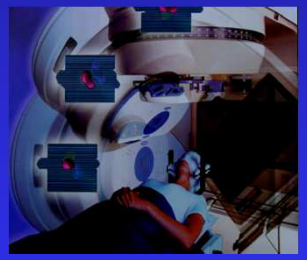
Approx 70% of the children with any type of brain tumour are **CURED**

cognitive dysfunction	38%
motor deficit	25%
visual impairment	20%
hormonal dysfunction	20%
psychological-emotional problems	14%

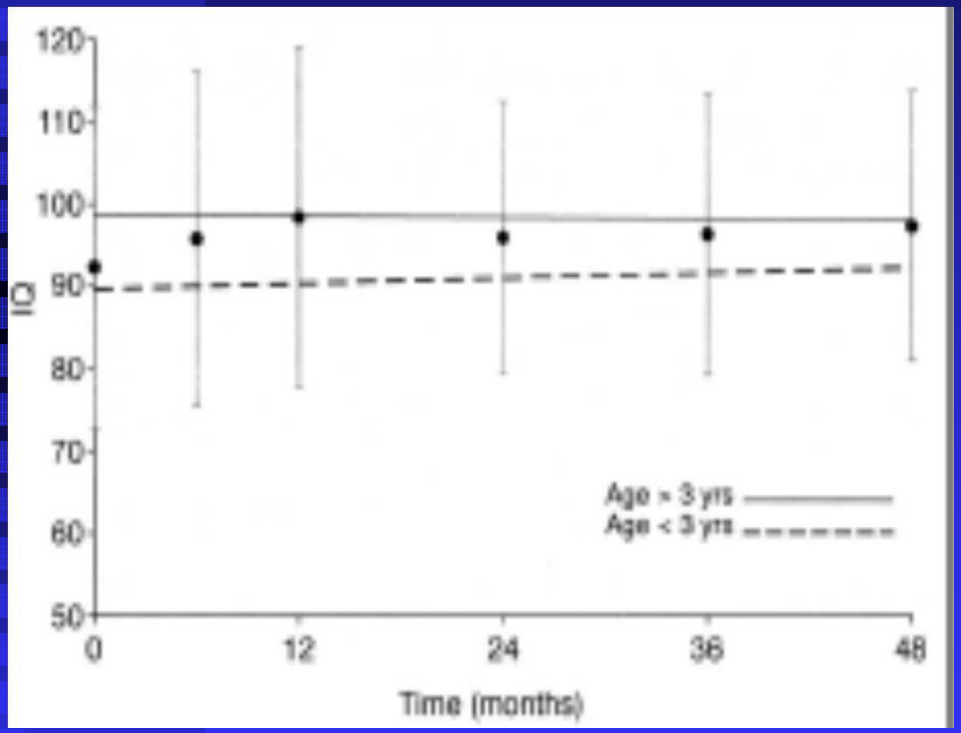
second malignancies
cereberovascular events

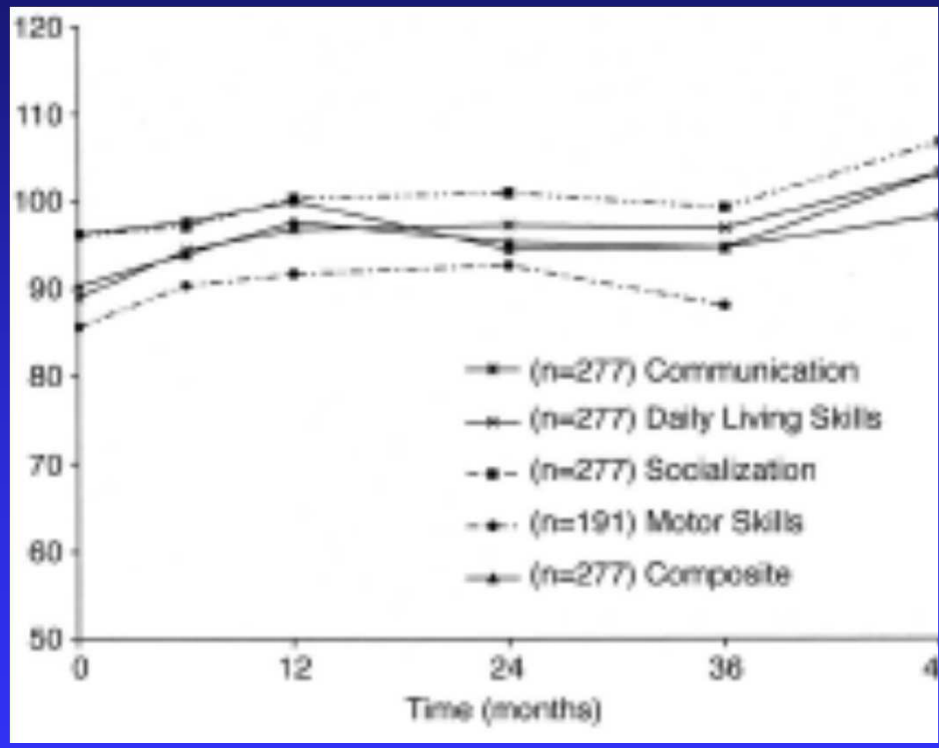
Modern RT to minimise toxicity

- Conformal RT
- SRS SRT/SCRT
- IMRS/IMRT
- Cyberknife
- Tomotherapy
- Proton beam



No IQ decline with conformal RT even in patients less than 3 years of age

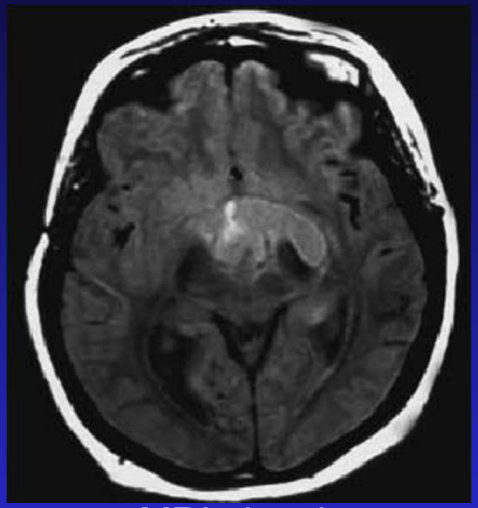




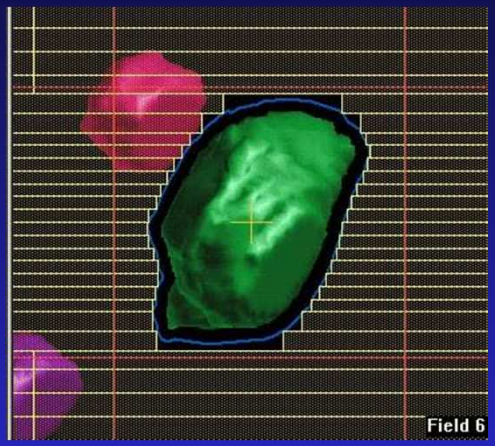
Merchant JCO 2004;22:3156-62

Stereotactic Conformal Radiotherapy (SCRT)

Accurate immobilisation



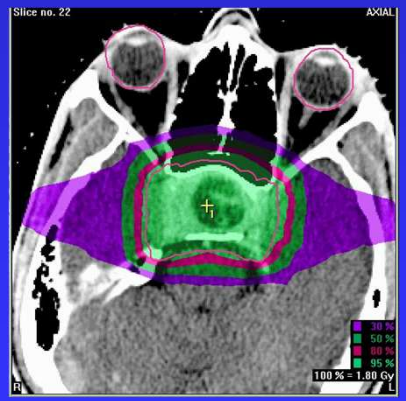
MRI planning



Tight conformation

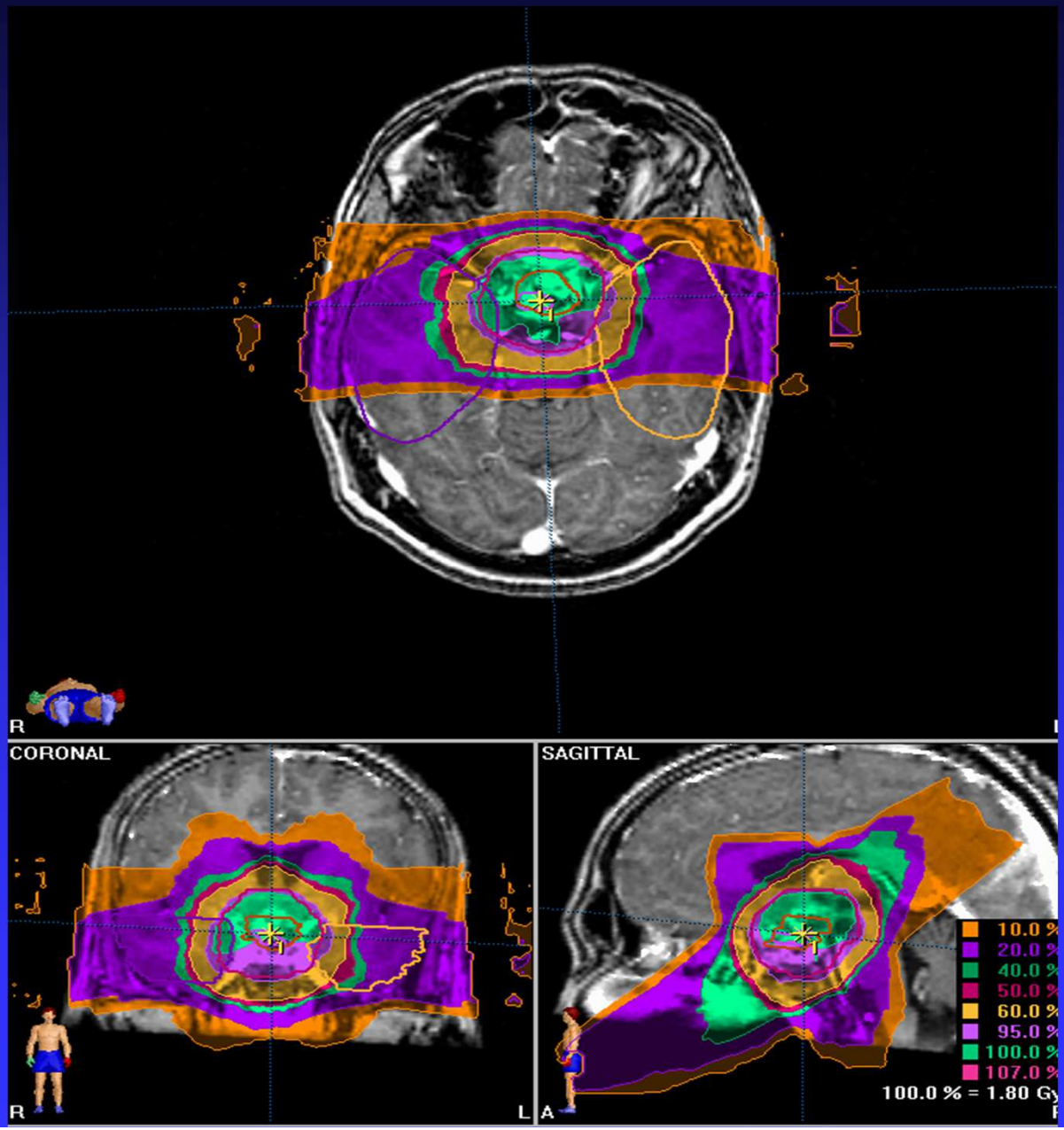
High Quality Assurance

Precise treatment delivery

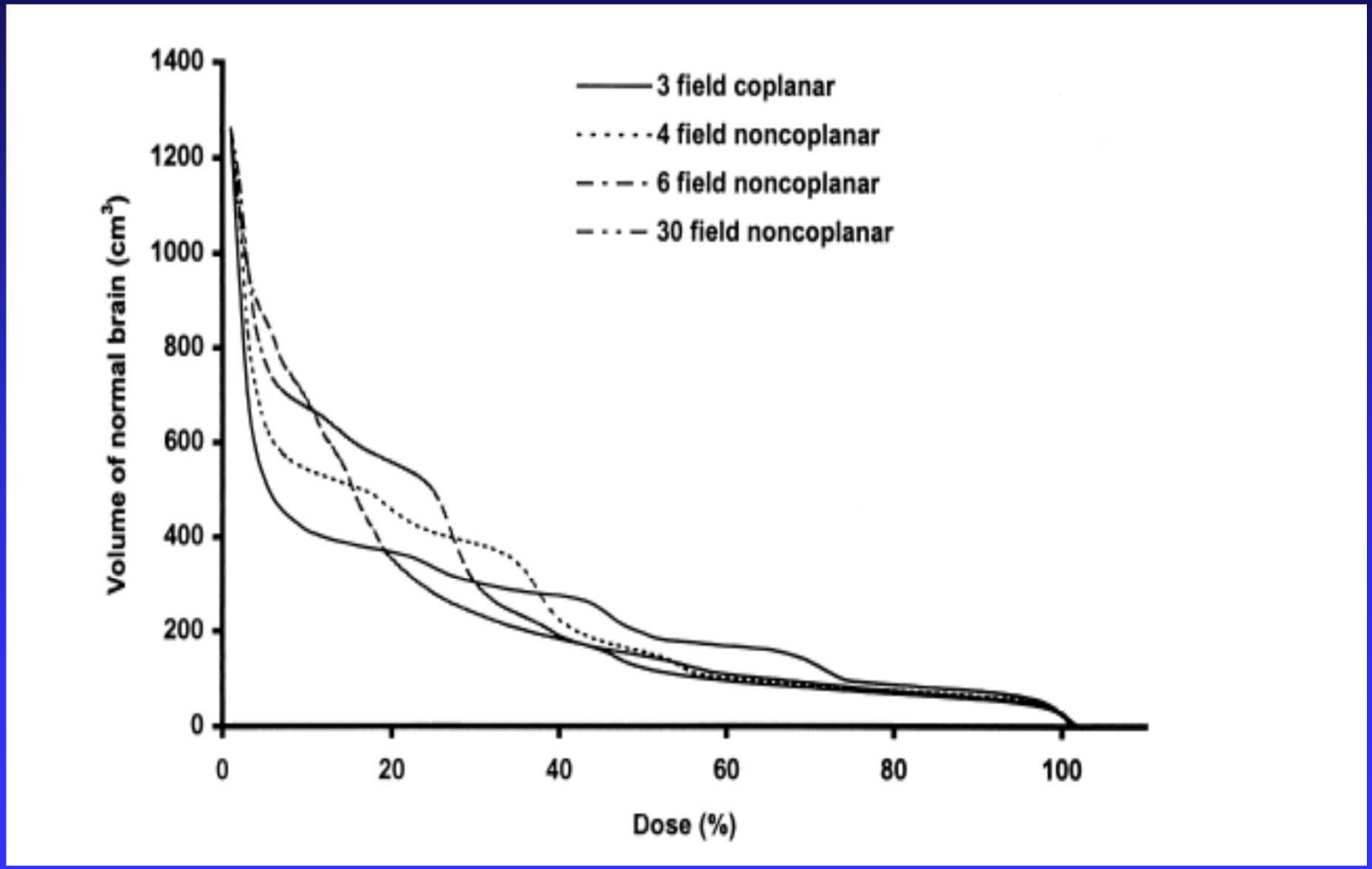


Dose distribution

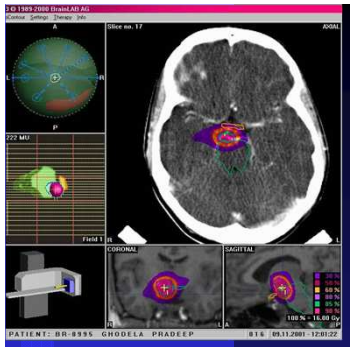
Dose distributions



Plenty of planning/dosimetric studies



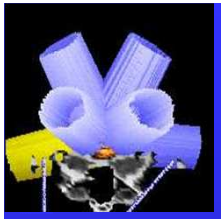
Perks, Jalali et al IJROBP 1999



Efficacy of High-precision techniques SRT

'Must have appropriate endpoints'

- Most of the toxicity data (esp cognitive) is for whole brain RT in medulloblastoma, acute leukaemias, brain metastasis where high precision RT rarely used
- Partial brain RT – little data, mostly retrospective and cross sectional
- Most data for SRT etc is dosimetric or phase II with little mention about late morbidity
- Need for prospective longitudinal CLINICAL data
- Ideally, randomised to generate level 1 evidence



Detailed evaluations

Neuro-cognitive Assessment

Neuropsychological function

Physical activity functions

Quality of life

Overall Survival, PFS & DFS

Neurological, endocrine, radiological and opthalomological assessments

Children (5-16 years):

Verbal Quotient:
General comprehension
Arithmetic
Simulation
Vocabulary
Digital span

Performance Quotient:
Picture completion
Picture arrangement
Block design
Object assembly
Coding
Maze

Full Scale IQ

Blind:

Vithoba Paknikar IQ tests for the blind

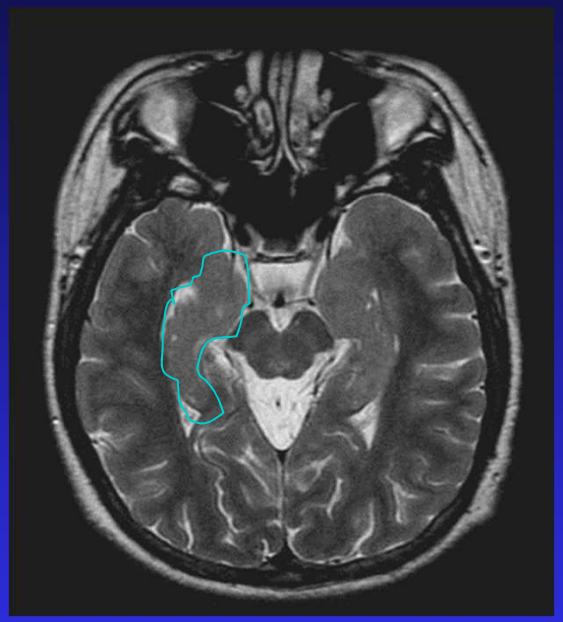
Adults (17-25 years):

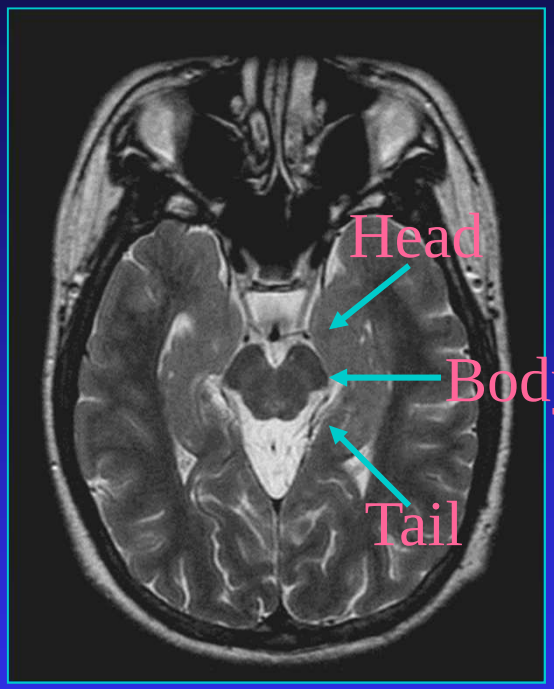
Performance Quotient:
Picture completion
Picture arrangement
Block design
Object assembly
Coding
Maze

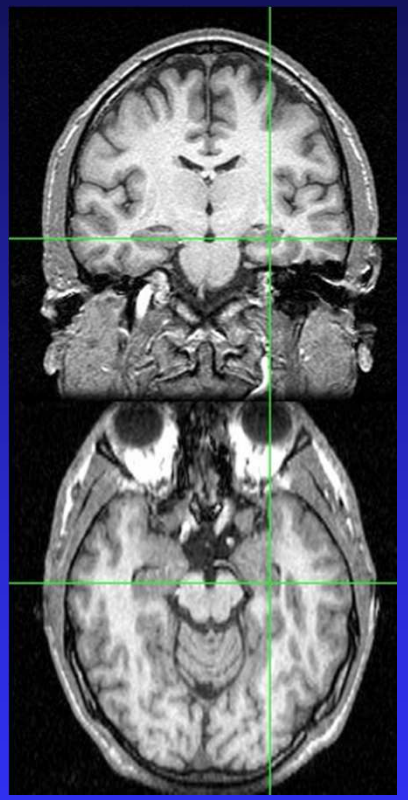
Global IQ

Memory Quotient:
Personal/Current Information
Orientation
Mental Control
Visual reproduction
Associate learning

Neurocognition







- Pathophysiology very complex
- Mesial temporal lobes, uncus, **hippocampus** etc
- RT induced vascular changes

Significantly poor IQ even before starting RT

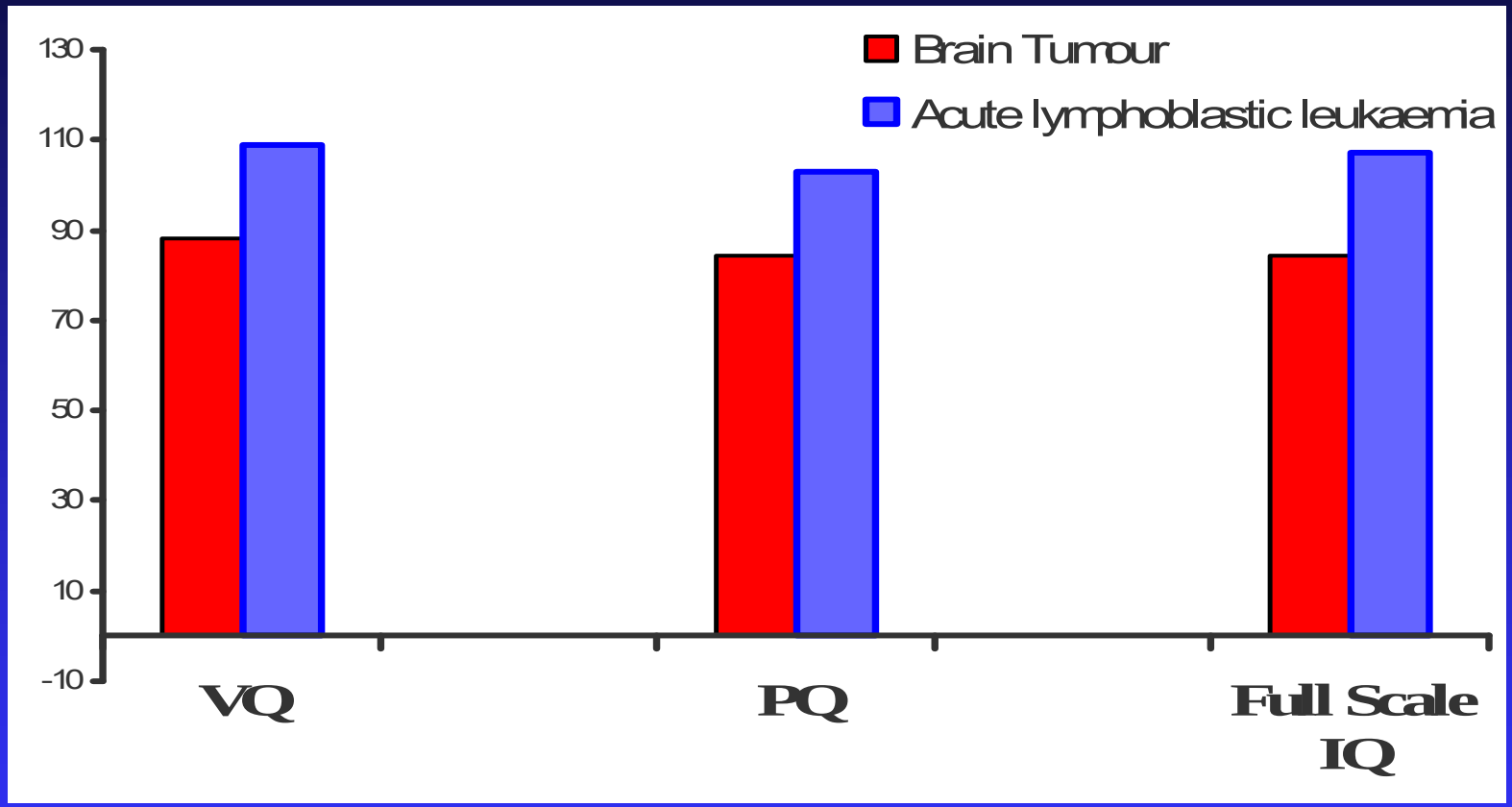
Common myth, power of prospective evaluations

60.4% patients had values below normal

	Full Scale IQ	No of Patients (%)
Defective	<69	9 (17%)
Borderline	70-79	10 (19%)
Dull Normal	80-89	13 (23.5%)
Average	90-109	18 (34%)
Bright Normal	110-119	3 (5.7%)
Superior	120-129	0 (0%)
Very Superior	>130	0 (0%)

Jalali Int J Radiat Oncol Biol Phys 2006;66:S14-19

Comparison with non CNS tumours



VQ : <0.001

PQ : <0.001

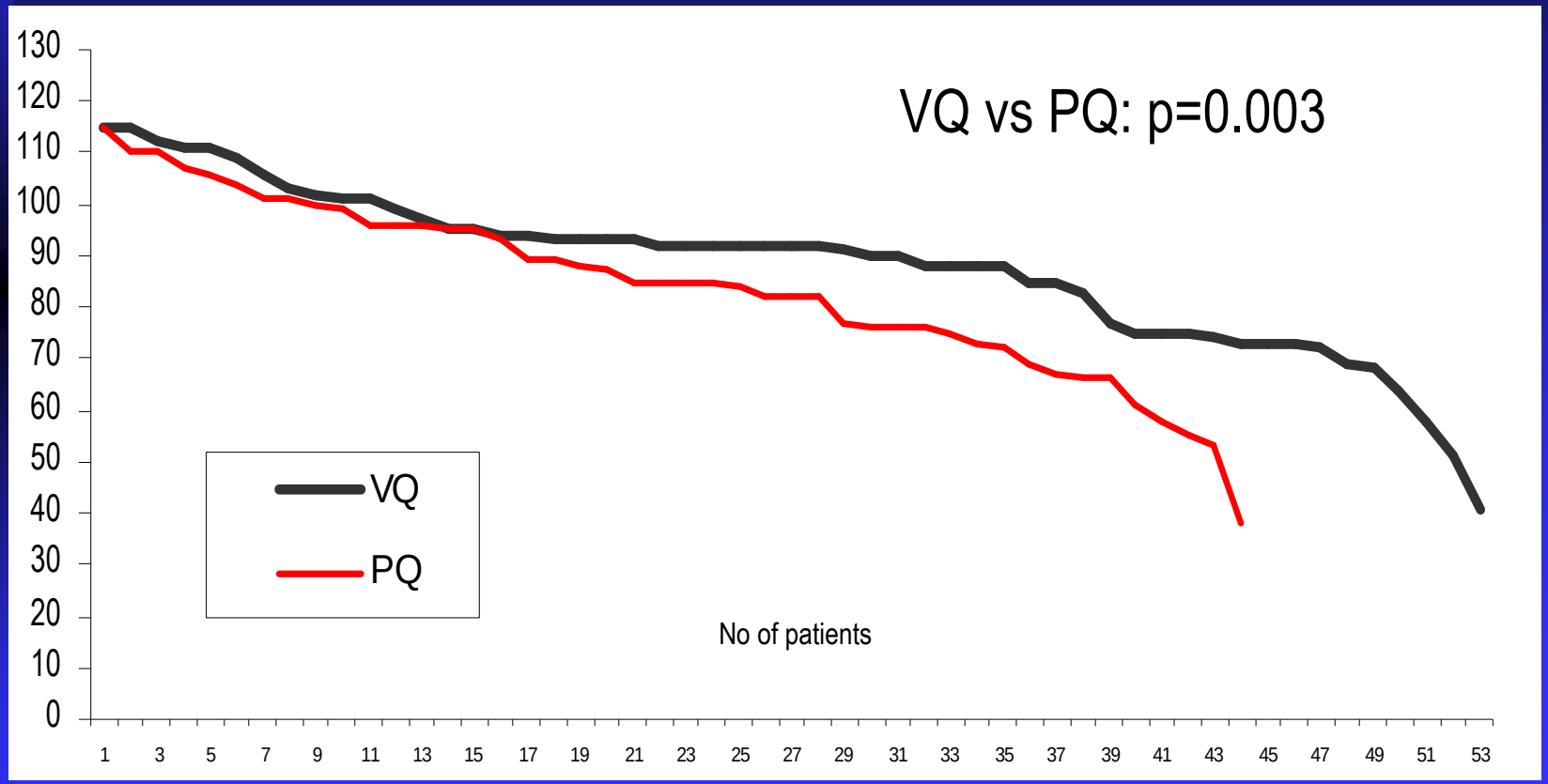
Full Scale IQ< 0.001

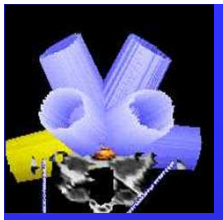
Present cohort
N= 53
Median age: 10 yrs

ALL:
N= 15
Median age 9 yrs

Jalali, et al NeuroOncology 2007

Verbal vs Performance Scores at baseline Before SCRT





Clinical proof of efficacy of modern RT

No drop in Intelligence quotient (IQ)

	IQ patterns after SCRT					
	Baseline	6 mo	2 yr	3 yr	4 yr	5 yr
Verbal/ Memory IQ	83	88	80	86	84	84
Performance IQ	84	89	88	94	103	110
Global/Full-scale IQ	**80**	**84**	**82**	**88**	**89**	**95**

Normal value: 90-109

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–6, 2
Copyright © 2009 Elsevier
Printed in the USA. All rights reser
0360-3016/09/$–see front ma

doi:10.1016/j.ijrobp.2009.06.025

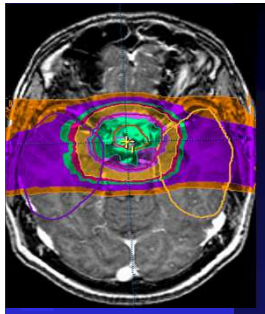
CLINICAL INVESTIGATION

FACTORS INFLUENCING NEUROCOGNITIVE OUTCOMES IN YOUNG PATIENTS WITH BENIGN AND LOW-GRADE BRAIN TUMORS TREATED WITH STEREOTACTIC CONFORMAL RADIOTHERAPY

RAKESH JALALI, M.D.,* INDRANIL MALLICK, M.D.,* DEBNARAYAN DUTTA, M.D.,* SAVITA GOSWAMI, M.SC.,† TEJPAL GUPTA, M.D.,* ANUSHEEL MUNSHI, M.D.,* DEEPAK DESHPANDE, PH.D.,‡ AND RAJIV SARIN, F.R.C.R.*

Departments of *Radiation Oncology, †Clinical Psychology, and ‡Medical Physics, Tata Memorial Centre, Mumbai, India

Purpose: To present the effect of radiotherapy doses to different volumes of normal structures on neurocognitive outcomes in young patients with benign and low-grade brain tumors treated prospectively with stereotactic con-



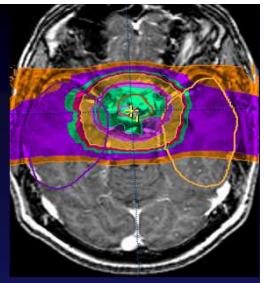
Logistic regression using age and left temporal lobe doses

Prescription dose: 54 Gy/30#/6 weeks

	Odds ratio	*P-value*
Age <15 yrs	13.58	0.041
> 80% dose (43.2 Gy) to >13% volume	7.57	0.048
> 50% dose (27 Gy) to 24% volume	-	0.06

Which area of the brain important?

Possible ? dose constraint



Left temporal lobe

- >13% volume receiving > 80% dose (43 Gy)
- >24% volume receiving > 50% dose (27 Gy)

Right temporal lobe

- No significant correlation between dose and drop in IQ

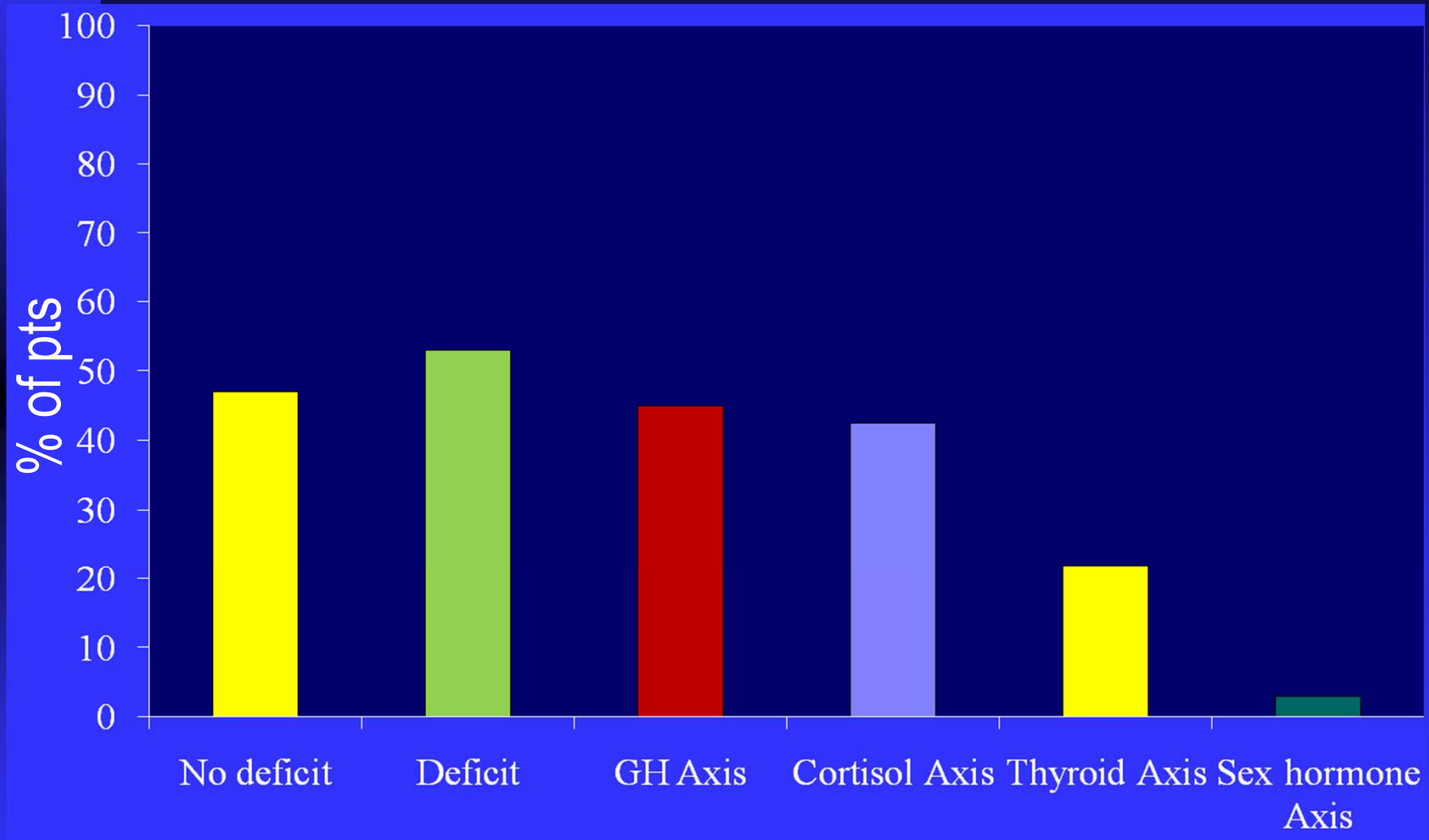
Normal brain

- No correlation

? Hippocampus

Hypopituitarism in childhood brain tumours

Pre-RT function=63



50% patient had hormone deficiency in any axis before RT

Dutta JCO 2008

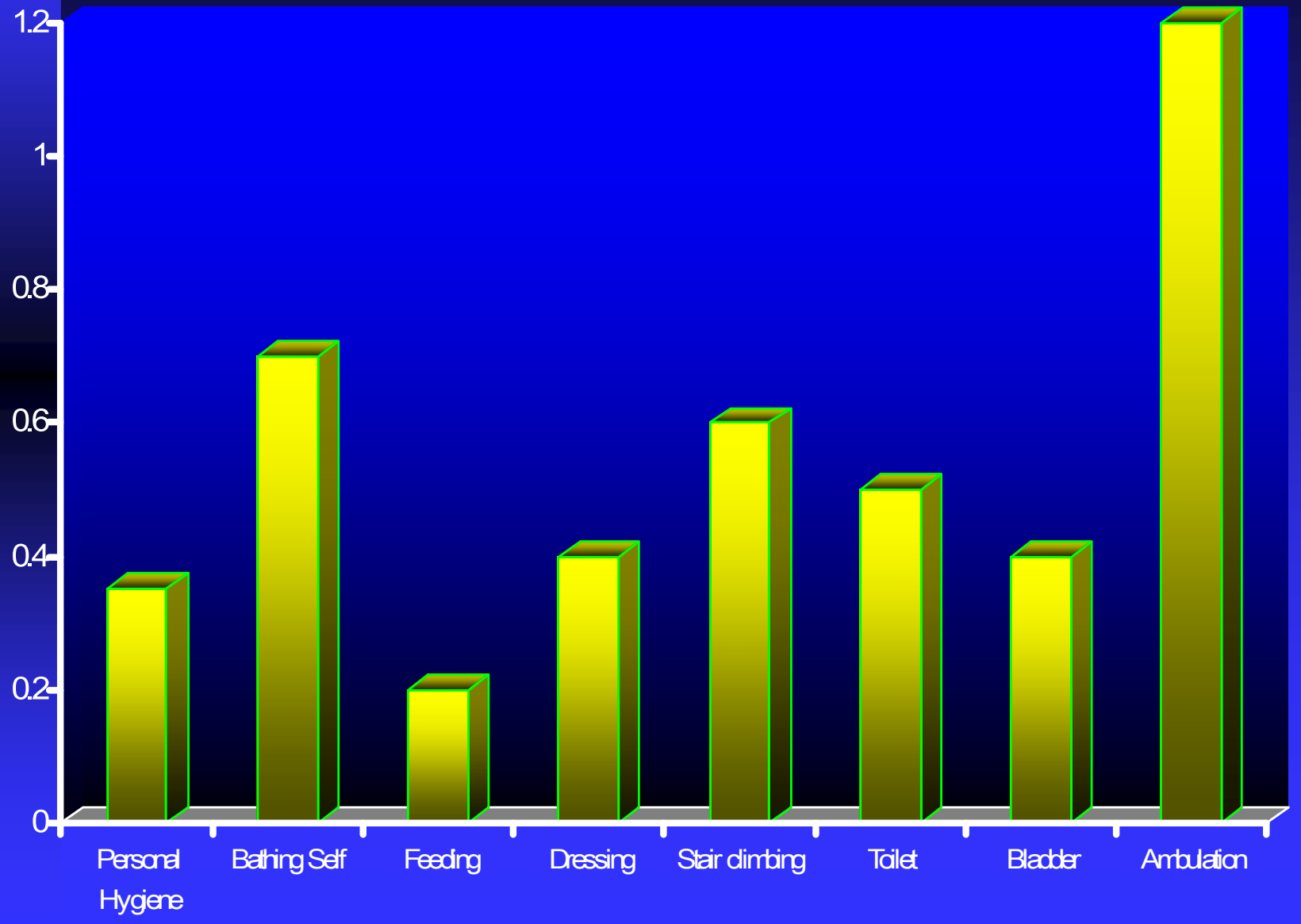
Replacement therapy at follow up

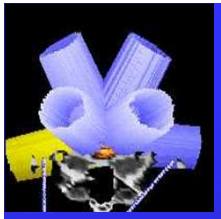
	No deficit	Additional Hormone axis deficit			
		Baseline	6 mo	2 yr	3 yr
GH Axis	24 (38%)	29 (45%)	9 (14%)	0	1 (1.5%)
Cortisol Axis	30 (47.5%)	27 (42.8%)	3 (5%)	2 (3%)	1 (1.5%)
Thyroid Axis	44 (79%)	14 (22%)	2 (3%)	2 (3%)	1 (1.5%)
Sex Hormone Axis	59 (94%)	2 (3%)	1 (1.5%)	1	0
Prolactin Axis	61 (97%)	1 (1.5%)	0	1 (1.5%)	0

At 2 and 3 years following Conformal RT, 17 – 24 % developed additional hormonal impairment

Activities of Daily Living after rehab

Jalali, et al J NeuroOncol 2008; 90(3):321-8





Acknowledgements

- Clinical Psychologist
- Radiation Oncology
- NeuroOncology
- Medical Physics
- Neurosurgery

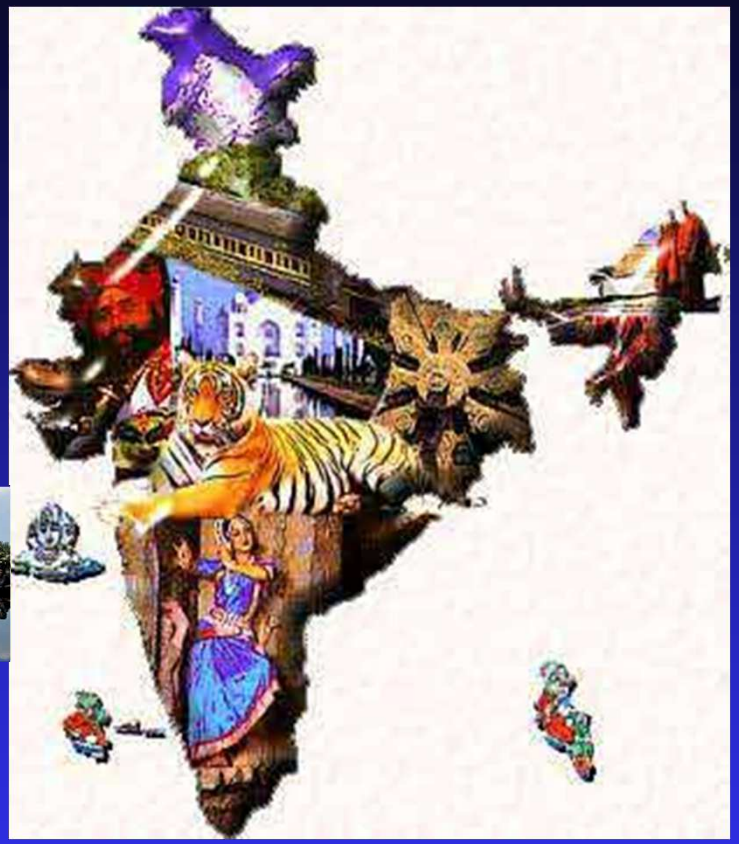
- Brain Tumour Foundation
- Terry Fox Foundation

http://tmc.gov.in

www.braintumourindia.com

INDIA

Interesting paradox



- Some of the poorest and some of the richest live here
- Majority still cannot afford
- Rehabilitative and support poor
- Social responsibility, ethical dilemmas

Brain Tumour Foundation of India

We shall overcome

Patients

If you have brain tumour or have a loved one suffering from it, you'll find a lot of information here.

Doctors

This is the doctor's meeting place. If you're a doctor looking for information on brain tumour, please enter here.

BRAIN TUMOUR FOUNDATION

www.braintumourindia.com

BTF

The Brain Tumour Foundation of India is a non-profit organisation committed to minimise the physical, emotional and financial suffering associated with the diagnosis, treatment and rehabilitation of patients with brain and spine tumours, and their families

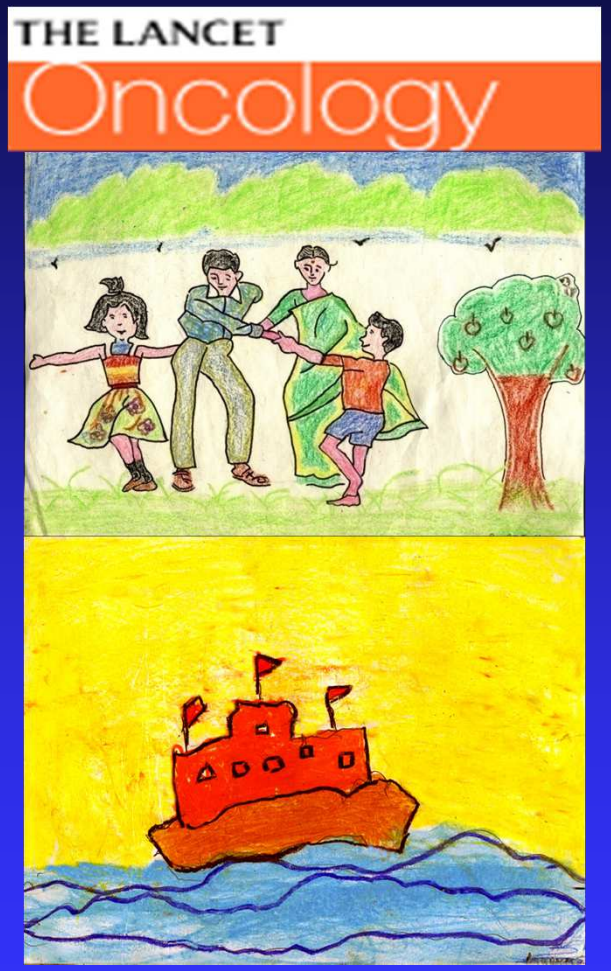
Support Team

At BTF, we can always do with some help. If you have anything to offer these victims of brain tumour, check this link out.

Brain Tumour Foundation of India

74, Ground Floor, Main Building, Tata Memorial Hospital, Parel, Mumbai - 400 012, INDIA
Tel: 91-22-2417 7153 / 2417 7159 . Fax: 022-2417 7159 / 2414 6937
Pager: dial 9602 and ask for 135135 or 122122
Email: btf@braintumourindia.com

BTF Annual Art Festivals



(Aug and Oct Issues 2008)

FRONT COVER

Care and rehabilitation

(physical, psychological, financial and social)