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

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

Local control and survival quality of life
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*

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>TMH data</th>
<th>Western data*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastoma</td>
<td>10 yrs</td>
<td>9 yrs</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>18.5 yrs</td>
<td>19 yrs</td>
</tr>
<tr>
<td>Brain stem glioma</td>
<td>11.5 yrs</td>
<td>11 yrs</td>
</tr>
<tr>
<td>Supratentorial PNET</td>
<td>15 yrs</td>
<td>9 yrs</td>
</tr>
<tr>
<td>Pineal tumour</td>
<td>18.5 yrs</td>
<td>18 yrs</td>
</tr>
<tr>
<td><strong>Craniopharyngioma</strong></td>
<td>20 yrs</td>
<td>28 yrs</td>
</tr>
<tr>
<td><strong>Pilocytic Astrocytoma</strong></td>
<td>16 yrs</td>
<td>23 yrs</td>
</tr>
<tr>
<td>Arteriovenous malformations</td>
<td>21 yrs</td>
<td>33 yrs</td>
</tr>
</tbody>
</table>

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

- **Pilocytic Astrocytoma**
  - Control population
  - Pilocytic astrocytoma
  - $P = 0.031$

- **Diffuse Fibrillary Astrocytoma**
  - Control population
  - Low-grade diffuse fibrillary astrocytoma
  - $P < 0.0001$

- **Mixed Oligo-Astrocytoma**
  - Control population
  - Low-grade mixed oligo-astrocytoma
  - $P < 0.0001$

- **Oligodendroglioma**
  - Control population
  - Low-grade oligodendroglioma
  - $P < 0.0001$
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
Chemotherapy for Pilocytic astrocytoma

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

  - 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

Packer JCO 1993;11:850-7
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
High precision conformal radiotherapy employing conservative margins in childhood benign and low-grade brain tumours

Rakesh Jalali\textsuperscript{a,\,*}, Ashwini Budrukkar\textsuperscript{a}, Rajiv Sarin\textsuperscript{a}, Dayananda S. Sharma\textsuperscript{b}

\textsuperscript{a}Department of Radiation Oncology, 113 Tata Memorial Hospital, Parel, Mumbai, India
\textsuperscript{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, AIIMS, New Delhi, India

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

NeuroOncology 2009; 11 (3): 274-80
Craniopharyngiomas

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

Two histopathological types:
1) Adamantinomatous type
2) Papillary type - in adults
May be unpredictable in behaviour

- Challenging management, Controversial
- Emotive subject

Age & Sex distribution

Review of 144 published data; Adamson & Yasargil 2008
## Recurrence rate after only partial excision

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

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Recurrence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial excision alone</td>
<td>60%</td>
</tr>
<tr>
<td>Partial excision + RT</td>
<td>10-33%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Health Issue</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>cognitive dysfunction</td>
<td>38%</td>
</tr>
<tr>
<td>motor deficit</td>
<td>25%</td>
</tr>
<tr>
<td>visual impairment</td>
<td>20%</td>
</tr>
<tr>
<td>hormonal dysfunction</td>
<td>20%</td>
</tr>
<tr>
<td>psychological-emotional problems</td>
<td>14%</td>
</tr>
<tr>
<td>second malignancies</td>
<td></td>
</tr>
<tr>
<td>cereberovascular events</td>
<td></td>
</tr>
</tbody>
</table>
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 ophthalmological assessments**

**Children (5-16 years):**
- **Verbal Quotient:** General comprehension, Arithmetic, Simulation, Vocabulary, Digital span
- **Performance Quotient:** Picture completion, Picture arrangement, Object assembly, Coding, Maze

**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

**Blind:**
Vithoba Paknikar IQ tests for the blind
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

<table>
<thead>
<tr>
<th></th>
<th>Full Scale IQ</th>
<th>No of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defective</td>
<td>&lt;69</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>Borderline</td>
<td>70-79</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Dull Normal</td>
<td>80-89</td>
<td>13 (23.5%)</td>
</tr>
<tr>
<td>Average</td>
<td>90-109</td>
<td>18 (34%)</td>
</tr>
<tr>
<td>Bright Normal</td>
<td>110-119</td>
<td>3 (5.7%)</td>
</tr>
<tr>
<td>Superior</td>
<td>120-129</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Very Superior</td>
<td>&gt;130</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

jalali int J Radiat Oncol Biol Phys 2006;66:S14-19
Comparison with non CNS tumours

### Results

- **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

VQ vs PQ: p=0.003

VQ
PQ

No of patients

Jalali SNO 2007
### IQ patterns after SCRT

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 mo</th>
<th>2 yr</th>
<th>3 yr</th>
<th>4 yr</th>
<th>5 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Verbal/ Memory IQ</strong></td>
<td>83</td>
<td>88</td>
<td>80</td>
<td>86</td>
<td>84</td>
<td>84</td>
</tr>
<tr>
<td><strong>Performance IQ</strong></td>
<td>84</td>
<td>89</td>
<td>88</td>
<td>94</td>
<td>103</td>
<td>110</td>
</tr>
<tr>
<td><strong>Global/Full-scale IQ</strong></td>
<td><strong>80</strong></td>
<td><strong>84</strong></td>
<td><strong>82</strong></td>
<td><strong>88</strong></td>
<td><strong>89</strong></td>
<td><strong>95</strong></td>
</tr>
</tbody>
</table>

*Normal value: 90-109*

Clinical proof of efficacy of modern RT

*No drop in Intelligence quotient (IQ)*
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

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;15 yrs</td>
<td>13.58</td>
<td>0.041</td>
</tr>
<tr>
<td>&gt; 80% dose (43.2 Gy) to &gt;13% volume</td>
<td>7.57</td>
<td>0.048</td>
</tr>
<tr>
<td>&gt; 50% dose (27 Gy) to 24% volume</td>
<td>-</td>
<td>0.06</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th></th>
<th>No deficit</th>
<th>Additional Hormone axis deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 mo</td>
</tr>
<tr>
<td>GH Axis</td>
<td>24 (38%)</td>
<td>29 (45%)</td>
</tr>
<tr>
<td>Cortisol Axis</td>
<td>30 (47.5%)</td>
<td>27 (42.8%)</td>
</tr>
<tr>
<td>Thyroid Axis</td>
<td>44 (79%)</td>
<td>14 (22%)</td>
</tr>
<tr>
<td>Sex Hormone Axis</td>
<td>59 (94%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Prolactin Axis</td>
<td>61 (97%)</td>
<td>1 (1.5%)</td>
</tr>
</tbody>
</table>

At 2 and 3 years following Conformal RT, 17 – 24 % developed additional hormonal impairment
Activities of Daily Living after rehab

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
Patients

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

Doors

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

Brain Tumour Foundation of India

We shall overcome

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)