Overview of Brain Tumors

ICRO 2015
SRMS IMS, Bareilly

Prof Kamal Sahni
Overview of Brain Tumors

Incidence, prevalence & mortality

• Metastatic vs. Primary CNS tumors = 10:1
• World wide incidence of Primary CNS tumors = 3.4 (very high human development=5.1, high=4.7, medium=4.0, low=1.3).
• High mortality upto 75%.
• ↑ whites than in blacks.
• Dramatic improvement in children and young adult, mortality ↓ by 50% between 1975 to 2010.
• ↑ males except meningiomas and schwannomas (↑ blacks and low socioeconomic group).
Malignant & Non-malignant

Overview of Brain Tumors

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Non-Malignant</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14</td>
<td>1.56</td>
<td>3.70</td>
<td>5.26</td>
</tr>
<tr>
<td>0-19</td>
<td>2.03</td>
<td>3.39</td>
<td>5.42</td>
</tr>
<tr>
<td>20+</td>
<td>19.05</td>
<td>8.80</td>
<td>27.85</td>
</tr>
<tr>
<td>All Ages</td>
<td>14.17</td>
<td>7.25</td>
<td>21.42</td>
</tr>
</tbody>
</table>

a. Rates per 100,000 and age-adjusted to the 2000 United States standard population.

MALIGNANT 33.3%
NONMALIGNANT 66.6%
Etiologic Factors

- Environmental factors
  - Ionizing and non-ionizing radiation
  - Cellular telephones
  - Chemical exposures (formaldehyde, vinyl chloride, acrylonitrile, etc.)

- Viral Associations
  - EBV, HCMV, HIV

- Hereditary Syndromes
  - Cowden, Turcot, Lynch & Li-Fraumeni (Gliomas)
  - Gorlin (PNET), neurofibromatosis type I&II
    (meningiomas, optic nerve glioma, schwannoma)
  - VHL
    (haemangioblastoma)
SITE WISE DISTRIBUTION OF MALIGNANT TUMORS CBTRUS 2014

**AGE -- 0 TO 14 YRS**
- Frontal lobe: 23.2%
- Temporal: 17.0%
- Parietal: 17.0%
- Occipital: 2%
- Cerebellum: 18.7%
- Brainstem: 12.4%

**AGE -- 15 TO 19 YRS**
- Pituitary & cranioph: 28.8%
- Cerebellum: 8.8%
- Frontal: 12.4%

**SITE WISE DISTRIBUTION OF MALIGNANT TUMORS CBTRUS 2014**

- Pituitary & cranioph: 7.8%
- Cerebellum: 18.7%
- Brainstem: 12.4%
- Frontal lobe: 23.2%
- Temporal: 17.0%
- Parietal: 17.0%
- Occipital: 2%
WHO Classification of CNS Tumours, Lyon, 2007.

ASTROCYTIC TUMORS
GRADE I  Subependymal giant cell astrocytoma, Pilocytic astrocytoma,
         II  Pilomyxoid astrocytoma, Diffuse astrocytoma, pleomorphic xanthoastrocytoma
         III Anaplastic astrocytoma,
         IV Glioblastoma, Giant cell glioblastoma,, gliosarcoma

OLIGODENDROGLOMIA AND OLIGOASRTCTOMA
GRADE II  Oligodendroglioma, Oligoastrocytoma
         III Anaplastic Oligodendroglioma, Anaplastic Oligodastrocytoma

EPENDYMAL TUMORS
GRADE I  Subependymoma, Myxopapillary ependymoma
         II  Ependymoma
         III Anaplastic ependymoma

CHOROID PLEXUS TUMOR
GRADE I  Choroid plexus papilloma
         II Atypical choroid papilloma
         III Choroid plexus carcinoma
Overview of Brain Tumors

WHO Classification of CNS Tumours, Lyon, 2007.

Pineal tumors
GRADE I  Pineocytoma
II, III  Pineal parenchymal tumor of intermediate differentiation, Papillary tumor of the pineal region
IV  Pineoblastoma

Embryonal tumors
Grade IV  Medulloblastoma, PNET
Atypical teratoid/rhabdoid tumor

Tumors of the cranial and paraspinal nerves
GRADE I  Schwannoma, Neurofibroma
II-IV  Perineurioma
Malignant peripheral nerve sheath tumor (MPNST)
Overview of Brain Tumors

WHO Classification of CNS Tumours, Lyon, 2007.

Meningeal tumors:

GRADE I  Meningioma, Hemangioblastoma
GRADE II  Atypical meningioma, Hemangiopericytoma
GRADE III  Anaplastic/malignant meningioma, Anaplastic hemangiopericytoma

Tumors of the sellar region:

GRADE I  Craniopharyngioma,
   Granular cell tumor of the neurohypophysis
   Pituicytoma, Spindle cell onc cytoma of the adenohypophysis
Overview of Brain Tumors

Simplified Working Formulation

1) Neuroepithelial Tumors:
   - **Glial cell origin:** Asrocytoma, Oligodendrogliaoma, Ependymoma, choroid plexus
   - **Neuronal and mixed neuro–glial origin:** Gangliocytoma, Neurocytoma, Papillary glioneuronal tumor, Rosette-forming glioneural tumor of the fourth ventricle

2) Embryonal Tumors: Medulloblastoma, PNET

2) Tumors of specialized anatomic structures:
   - Pituitary adenoma, craniopharyngioma, pineocytoma, chordoma, haemangiopericytoma, germ cell tumors, choroid plexus tumors.

3) Tumors of meninges (meningoepithelial cells, mesenchymal)

4) Tumors of haematopoietic system: lymphoma, plasmacytoma.

5) Metastatic
Overview of Brain Tumors

Classification of Adult Brain Tumors

WHO grade I = low proliferative potential, a frequently discrete nature, and the possibility of cure following surgical resection alone.

WHO grade II = generally infiltrating and low in mitotic activity but recur more frequently than grade I malignant tumors after local therapy. Some tumor types tend to progress to higher grades of malignancy.

WHO grade III = anaplastic histology & infiltrative, usually treated with aggressive adjuvant therapy.

WHO grade IV = mitotically active, necrosis-prone, micro-vascular proliferation & generally associated with a rapid pre & post-operative progression & fatal outcomes, usually treated with aggressive adjuvant therapy.
Overview of Brain Tumors

Age vs. Malignant & Non-malignant CBTRUS 2014

Age-adjusted incidence rate per 100,000

- Vestibular Schwannoma
- All Other Astrocytoma
- Oligodendroglioma
- Oligoastrocytic Tumors
- Meningioma (non-malignant)
- Glioblastoma
- Tumors of the Pituitary

Age Groups:
- 20-44 years
- 45-54 years
- 55-64 years
- 65-74 years
- 75+ years
Overview of Brain Tumors

Age vs. Pediatric CNS Tumors CBTRUS 2014

The graph shows the age-adjusted incidence rate per 100,000 for different types of brain tumors across various age groups. The categories include:

- All Other Gliomas
- Tumors of the Pituitary
- Pilocytic Astrocytoma
- Primitive Neuroectodermal tumor
- Medulloblastoma

The incidence rates are plotted for age groups from 0-4 years to 15-19 years.
Meningiomas 36.1%

Gliomas 28% of all tumors and 80% of malignant tumors

Pituitary 15.1%

Nerve sheeth tumor 8%

Glioblastom 15.4%

Of all gliomas Glioblastom 54.7%
Adult Glioma Formation

Grade II
- IDH1 R132 mutation
- 1p/19q deletion
- CIC mutation
- FUBP mutation
- Oligodendrocyte or Progenitor

Grade III
- TERT promoter mutation
- CDKN2A loss
- PTEN loss
- Anaplastic Oligodendroglioma
- CDKN2A loss
- PTEN loss
- RB1 loss
- CDK4/6 amplification
- Additional hits to RTK/RAS/PI3K pathway

Grade IV
- Secondary Glioblastoma
- Primary Glioblastoma

- Anaplastic Astrocytoma
- Astrocytoma

- de novo pathway

- TP53 pathway dysregulation (TP53 loss/mutation, CDKN2A deletion, MDM1/2/4 amplification)
- RB pathway dysregulation (RB1 loss, CDKN2A deletion, CDK4/6 amplification)
- RTK/RAS/PI3K signalling dysregulation (EGFR amplification/mutation, PTEN loss/mutation, PI3K mutation, NF1 loss)
- TERT promoter mutation
### Overview of Brain Tumors

#### Common CNS Tumors and Corresponding Gene Alterations

<table>
<thead>
<tr>
<th>Common Adult Tumors</th>
<th>Frequent Gene and Chromosomal Alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade II astrocytoma</td>
<td>IDH1 R132, TP53, ATRX</td>
</tr>
<tr>
<td>Grade III anaplastic astrocytoma</td>
<td>IDH1, TP53-MDM2/4, CDKN2A, CDK4/6-RB, PTEN</td>
</tr>
<tr>
<td>Grade IV glioblastomas</td>
<td>TP53-MDM2/4, CDKN2A, CDK4/6-RB, EGFR, PTEN, NF1, RTK/RAS/PI3K pathway</td>
</tr>
<tr>
<td>Grade II oligodendrogioma</td>
<td>IDH1 R132, chromosome 1p-19q translocations, CIC, FUBP1</td>
</tr>
<tr>
<td>Grade III oligodendrogioma</td>
<td>IDH1, chromosome 1p-19q translocations, CIC, FUBP1, TERT promoter, CDKN2A, PTEN</td>
</tr>
<tr>
<td>Meningioma</td>
<td>NF2 (posterior &amp; lateral), TRAF7 (anterior), AKT1, KLF4 (central) Sonic hedgehog signalling,</td>
</tr>
</tbody>
</table>

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# Overview of Brain Tumors

## COMMON CNS TUMORS AND CORRESPONDING GENE ALTERATIONS

<table>
<thead>
<tr>
<th>Common Pediatric Tumors</th>
<th>Frequent Gene and Chromosomal Alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medulloblastoma</strong> :</td>
<td>MYCC, MYCN, <em>(Poor Prognosis)</em> chromosome 17p deletions, CTNNB1, DOX3X, SMARCA4, MLL2 <em>(Good prognosis : WNT group)</em>, TP53, SUFU, SMO, MLL2, PTCH, KDM6A <em>(Intermediate prognosis : SHH group)</em></td>
</tr>
<tr>
<td><strong>Ependymoma</strong></td>
<td>Lateral infratentorial: NF2/chromosome 22 loss, Medial infratentorial: chromosome 1q gain</td>
</tr>
<tr>
<td><strong>Pilocytic astrocytoma</strong></td>
<td>KIAA1549-BRAF fusion rearrangements</td>
</tr>
</tbody>
</table>

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### Medulloblastoma

- CDKN2A delet
- EPHB2 amplification

### Ependymoma

- 4th Vent Central canal
- Chr1q gain (medial)
- NF2/chr22 loss (lateral)
- NF2/chr22 loss
GLIOBLASTOMA
(Cd133+ stem cells, tumor cells, stroma, blood vessels, microglia, infiltrating lymphocytes ...)

CD133 positive cancer stem cell

Resistant to radiotherapy, chemotherapy

Cancer stem cells remain

Dividing cells are destroyed

TUMOR RELAPS

Resistant tumor cells spread

POTENTIAL THERAPIES TARGETED TO CANCER STEM CELLS

Neural stem cells engineered to deliver cytokine
Stem cell-based prodrug gene therapy
BMP4 non-cytotoxic modulation
Inhibitors of DNA repair checkpoints
# Overview of Brain Tumors

## GBM Sub-classification Schemes

<table>
<thead>
<tr>
<th>Primary (de Novo, ~90%)</th>
<th>Secondary (~10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Elderly (&gt;62)</td>
<td>• Younger (&lt;40)</td>
</tr>
<tr>
<td>• EGFR amplification</td>
<td>• TP53 alteration</td>
</tr>
<tr>
<td>• PTEN inactivation</td>
<td>• IDH1 mutation</td>
</tr>
<tr>
<td>• CDKN2A deletion</td>
<td>• Chromosome 19 loss</td>
</tr>
<tr>
<td>• Shorter survival</td>
<td>• Longer survival</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mesenchymal</th>
<th>Classical</th>
<th>Proneural</th>
<th>Neural</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 29%</td>
<td>• 27%</td>
<td>• 28%</td>
<td>• 16%</td>
</tr>
<tr>
<td>• 57.7 yrs</td>
<td>• 55.7 yrs</td>
<td>• 51.8 yrs</td>
<td>• 62.8 yrs</td>
</tr>
<tr>
<td>• NF1 (+)</td>
<td>• EGFR (+)</td>
<td>• TP53 (+)</td>
<td></td>
</tr>
<tr>
<td>• IDH1 (-)</td>
<td>• TP53 (-)</td>
<td>• IDH1 (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IDH 1/2 Mutation</td>
<td>1p/19q Co-deletion</td>
<td>MGMT promoter methylation</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Diffuse astro (GRII)</td>
<td>70%-80%</td>
<td>15%</td>
<td>40%-50%</td>
</tr>
<tr>
<td>Oligod/astro (GRII)</td>
<td>70%-80%</td>
<td>30%-60%</td>
<td>60%-80%</td>
</tr>
<tr>
<td>Astro(GR III)</td>
<td>50%-70%</td>
<td>15%</td>
<td>50%</td>
</tr>
<tr>
<td>Oligod/astro (GR III)</td>
<td>50%-80%</td>
<td>50%-80%</td>
<td>70%</td>
</tr>
<tr>
<td>GBM (GR IV)</td>
<td>5% - 10%</td>
<td>&lt;5%</td>
<td>35%</td>
</tr>
<tr>
<td>Diagnostic role</td>
<td>DD glioma vs. gliosis Typical for transformed LGG</td>
<td>Pathognomonic for oligodendroglioma</td>
<td>None</td>
</tr>
<tr>
<td>Prognostic role</td>
<td>Protracted natural history in IDH-mutated tumors</td>
<td>Protracted natural history in 1p/19q codeleted tumours</td>
<td>Prognostic for AG (+/- with IDH mutations) treated with RT / CT</td>
</tr>
<tr>
<td>Predictive role</td>
<td>Absence of mutation suggests predictive role for MGMT promoter methylation</td>
<td>Prolongation of survival with early chemotherapy in 1p/19-co-deleted OD</td>
<td>Predictive in GBM for benefit from alkaling CT Elderly GBM: MGMT-methyl = TMZ MGMT – unmethyl=RT</td>
</tr>
</tbody>
</table>
Overview of Brain Tumors

ANATOMIC LOCATION AND CLINICAL CONSIDERATIONS

- Increased intracranial pressure
- Seizures
- Physiological deficits specific to location
- Neurocognitive deficits
- Endocrinal dysfunction
Overview of Brain Tumors

Clinical presentation

**Frontal Lobe**
- Behavioral and emotional changes
- Impaired judgment
- Impaired sense of smell
- Memory loss
- Hemiplegia
- Cognitive dysfunction
- Vision loss
- Papilledema

**Parietal Lobe**
- Impaired speech
- Inability to write
- Lack of recognition
- Seizures
- Spatial disorders

**Brainstem**
- Behavioral and emotional changes
- Difficulty speaking and swallowing
- Drowsiness
- Headache
- Hearing loss
- Muscle weakness on one side of the face
- Hemiparesis
- Uncoordinated gait
- Vision loss, ptosis, strabismus
- Vomiting

**Occipital Lobe**
- Seizures: 20% in supratent. tumors, 70% in slow growing, May antidate the clinical diagnosis by months

**Temporal Lobe**
- Often asymptomatic
- Impaired speech
- Seizures
- Homonymous superior quadrantanopsia
- Auditory hallucinations
- Abnormal behavior
DIAGNOSTIC TESTS

• Magnetic Resonance Imaging: Most useful imaging studies are T1-weighted sagittal images, gadolinium (Gd)-enhanced and unenhanced T1 axial images, and T2-weighted axial images

• CT Scan

• Newer Imaging Modalities
  – Magnetic resonance spectroscopy,
  – Dynamic contrast-enhanced MRI,
  – Diffusion-perfusion MRI, and
  – Functional MRI
  – Quick brain MRI

• PET
Cerebrospinal Fluid Examination

Medulloblastoma, ependymoma, choroid plexus carcinoma, lymphoma, and some embryonal pineal and suprasellar region tumors have high likelihood of spreading to CSF.

Biopsy (craniotomy / stereotactic)

IHC

Cytogenetics
Management of Brain Tumors

• Surgery
• Radiation Therapy
• Chemotherapy and targeted agents
Surgical Procedures

- Biopsy
- Total Resection
- Surgical Debulking
- CSF Diversion
- Re-resection
The process of radiation injury depends on

**Technical factors:** dose, volume, fraction size, specific target cell population,

- **Secondary mechanisms** of expression of injury such as vascular leak causing edema, vascular endothelial loss resulting in hypoxic injury,
- Reactive gliosis,
- ? Host factors.

Some structures (e.g., optic chiasm, hypothalamus, lacrimal gland, lenses, etc.) appear to be substantially more sensitive to radiation than others.
Radiotherapy Techniques

- Partial-brain irradiation, 3DCRT, IMRT, IGRT
- Whole-brain radiotherapy (WBRT),
- Cranio-spinal irradiation (CSI),
- Stereotactic radiosurgery (SRS),
- Fractionated stereotactic radiotherapy (FSRT),
- Brachytherapy, (less commonly)
- Proton beam therapy (3DPT, IMPT).
Overview of Brain Tumors

Importance of CT simulation

CT SIMULATION ADVANTAGE: Coverage of meninges in subfrontal region and sparing of lens in CSI.
CT SIMULATION

- Contouring of the cord and overlying meninges that extend laterally to the lateral aspect of the spinal ganglia results in a field width than one based on bony anatomy.

- The addition of shielding further reduces the volume of normal tissues included in the treated volume.
Axial images of an **Image Guided RT** for a whole posterior fossa (A) and a reduced-volume posterior fossa boost (B) for a patient with medulloblastoma. (C) DVH show significant sparing of organs at risk with the reduced-volume boost.
IMRT SPARES CRITICAL ORGANS Example Opticchiasm a & pituitary in this case
Overview of Brain Tumors

X-Rays vs. Proton
Clivus sarcoma. The maximum and mean relative doses to the brainstem are 71% and 42% with IMRT compared to 59% and 11% with protons, respectively (sharp dose gradient with protons).
• Mean body and brain doses are 1/3\textsuperscript{rd} with Protons than IMRT or SRT.
• The mean right cochlear dose is 807 cGy with IMRT, 388 cGy with SRT, and 7 cGy (RBE) with protons. The mean left cochlear dose is 792 cGy with IMRT, 887 cGy with SRT, and 5 cGy (RBE) with protons.
The total-body $V_{10}$ and total body integral dose are 37.2% and 0.223 Gy·m³ with 3DCRT compared with 28.7% and 0.185 Gy·m³ with proton therapy, respectively.
Surgery:
Except deep seated lesions such as pontine glioma
Complete resection not achievable frequently

Radiotherapy:
RT immediately or after progression
EORTC TRIAL 22845 – 7.4 vs .7.2 yrs OS. but PFS 5.3 vs. 3.4
Conclusion in doubt
No difference in survival of dose escalation
Surveillance
Overview of Brain Tumors

Risk factors for survival in Low Grade Gliomas

- Age (<40 vs. ≥ 40 years old)
- Tumor largest diameter (<6 cm vs. ≥ 6 cm)
- Tumor crossing midline (yes vs. no)
- HPE tumor type (oligodendroglioma or mixed vs. astrocytoma)
- Neurologic deficit present preoperatively (absent vs. present)

Survival
- Low risk (0-2) 7.8 (6.8 - 8.9) yrs.
- High risk (3-5) 3.7 (2.9 - 4.7) yrs.
An algorithm for the management of patients with low-grade astrocytoma

Children & Adults

Maximal surgical resection compatible with
A good neurological outcome

Second surgical resection (if feasible) at time of progressive disease

Radiotherapy (or chemotherapy for children < 10 years and children of all ages with NF-1) at time of progressive disease that is not resectable

Follow-up with routine imaging
High Grade Glioma Algorithm (NOA-04, EORTC, RTOG)

**Maximal Resection or Biopsy**
- Rapid onset 1° GBM
- Prior lower grade glioma / symptoms > 6 mo 2° GBM

**Molecular markers**
- MGMT
- IDH

**Treatments options**
- Alternate / investigational protocols
  - TMZ/RT ➔ T MZ

**Prognosis**
- Un-methyl
- methyl
- IDH mutation ➔ Prognosis ➔

**IDH mutation**
- No codeletion
- codeletion

**Anaplastic astrocytoma**
- 1p19q (IDH)

**Anap. Oligo-dendroglioma**

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High Grade Glioma Algorithm (NOA-04, EORTC, RTOG)
Overview of Brain Tumors

Radiotherapy vs. Radio-chemotherapy in GBM - NEJM 2005
## Overview of Brain Tumors

### Summary of Features of CNS Tumors in Adults

<table>
<thead>
<tr>
<th>Type : Location :</th>
<th>Clinical F</th>
<th>Survival</th>
<th>RT</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>A</em> Supratent</em>*</td>
<td>slow growing</td>
<td>5 yr MS</td>
<td>Yes</td>
<td>At recc.</td>
</tr>
<tr>
<td><strong>AA Supratent</strong></td>
<td>Rapid growing</td>
<td>2.5 yr MS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><em><em>GBM</em> Supratent</em>*</td>
<td>↑ Malignant</td>
<td>1 yr MS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><em><em>OG</em> Supratent</em>*</td>
<td>↑ Seizures</td>
<td>5 yr MS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>MN</strong></td>
<td>Women ↑</td>
<td>Long term</td>
<td>Yes</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>LYMP</strong></td>
<td>↑ CSF/ occular periventricular Diss.</td>
<td>3-5 Yr MS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

A*=Astrocytoma (adult>child), AA=Anaplastic astrocytoma, GBM=Glioblastoma (elderly), OG*=Oligodendroglioma (any age), MN=Meningioma, LYMP=Lymphoma, Diss=Dissamination
# Overview of Brain Tumors

## Summary of Features of CNS Tumors in Childhood & Young Adults

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>Clinical F:</th>
<th>Survival</th>
<th>RT</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSG*</td>
<td>Pons</td>
<td>Fatal</td>
<td>1 Yr MS</td>
<td>Yes</td>
<td>Seldom</td>
</tr>
<tr>
<td>PA*</td>
<td>Cerebellum</td>
<td>Cure with TR</td>
<td>80% 10 yr</td>
<td>in res</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hypothalamus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPDM*</td>
<td>4th ventricle, Cure with TR</td>
<td>70% 5 yr</td>
<td>Yes</td>
<td>Seldom</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cauda equina</td>
<td>can diss. in CSF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDBM</td>
<td>Cerebellum</td>
<td>likely to diss. in CSF</td>
<td>70% - 80%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>GERM*</td>
<td>Pineal &amp; suprasellar</td>
<td>Sensitive to CT &amp; RT</td>
<td>80% 5Yr</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>NGERM</td>
<td>“ “</td>
<td>Marker+</td>
<td>25% 5Yr</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

BSG=brain stem glioma, PA*=Pilocytic astrocytoma (child>adult), EPDM*=Ependymoma (child, adult), MDBM=medulloblastoma (child>adult), GERM=Germinoma, NGERM=Nongerm cell tumor (2nd & 3rd decade)
Ependymal Tumors

- Grade I and II ependymal tumors
  - Standard treatment options:
    - Surgery only if totally resectable.
    - Surgery $\rightarrow$ RT if residual

Anaplastic ependymomas
  - Standard treatment options:
    - Surgery plus radiation therapy.

- Children younger than 3 yrs Chemotherapy
Medulloblastomas

• Standard treatment options:
  – Surgery plus craniospinal radiation therapy for good-risk patients.

• Treatment options under clinical evaluation:
  – Surgery plus craniospinal radiation therapy and various chemotherapy regimens are being evaluated for poor-risk patients.

• Medulloblastoma occurs primarily in children, but it also occurs with some frequency in adults
Meningeal Tumors

• Standard treatment Options For Grade I:
  1. Active surveillance with deferred treatment, especially for incidentally discovered asymptomatic tumors.
  2. Surgery.
  3. SRS for tumors less than 3 cm.
  5. FRS for patients with unresectable tumors.

Standard treatment Options For Grade II - III:
  1. Surgery → RT