NEUROSCIENCE PEARLS

Primary Brain Tumors

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Welcome to ***Neuroscience Pearls***: A publication from the **UW Medicine Neurosciences Institute**. Our goal is to provide useful information pertinent to your practice. Here we bring you key points related to **Primary Brain Tumors**.

***Richard G. Ellenbogen**, **MD, FACS,** Professor and Chairman, Department of Neurological Surgery, Director, UW Neurosciences Institute*
***Bruce R. Ransom, MD, PhD,** Professor and Chair, Department of Neurology, Adjunct Professor, Department of Physiology and Biophysics, Co-Director, UW Neurosciences Institute*
Contributing Authors:
***Manuel Ferreira, Jr., MD, PhD,** Associate Professor, Department of Neurological Surgery, Chief of Neurosurgery, University of Washington Medical Center*
***Jason K. Rockhill, MD, PhD,** Associate Professor, Radiation Oncology, University of Washington Medical Center, Clinical Director, Alvord Brain Tumor Center*

The newly opened **Alvord Brain Tumor Center (ABTC)** at UW Medicine provides comprehensive care for all patients with brain and spinal cord tumors. A key concept of the clinic is a multi-disciplinary evaluation with input from Neurological Surgery, Radiation Oncology, Neuro-Oncology, as well as other specialties when needed. This offers access to cutting edge neurosurgical techniques, access to the most complete set of radiation modalities in the country and adjuvant chemotherapy allowing for the safest and most effective treatment. The ABTC facilitates coordination of care across these platforms to be able to provide patients with the best treatment options utilizing all the resources available through UW Medicine.

PRIMARY AND METATASTATIC BRAIN TUMORS: Primary brain tumors arise from cells within the cranium. Metastatic brain tumors, on the other hand, come from tumors elsewhere in the body and travel to the brain via the blood stream. Microscopic analysis of a sample of the tumor, including evaluation with special stains and flourescent antibodies, helps predict such important characteristics as responsiveness to different treatments and long-term patient survival. The most common primary brain tumors are gliomas (e.g. astrocytomas and glioblastomas) and meningiomas as shown in **Figure 1**.

EPIDEMIOLOGY: There are 45,000 new cases of primary malignant and benign brain tumors diagnosed each year in the United States. Forty-five percent are gliomas and 30% are meningiomas, corresponding to the most common malignant and benign tumors respectively. Brain tumors are responsible for 13,000 deaths each year. The incidence of primary malignant tumors is 7 per 100,000. Gliomas are more frequent in men, and meningiomas ar twice as common in women. Overall, the median ages of onset of primary brain tumors is 57, and the median ages of onset of glioblastoma and meningioma are 64 and 63, respectively. The World Health Organization (WHO) classifications are used by pathologists to classify meningiomas into benign (WHO grade 1), atypical (WHO grade 2) and anaplastic/malignant (WHO grade 3). For gliomas, the WHO grading proceeds from grade 1 (benign) to malignant astrocytomas (grade 3) and glioblastoma (grade 4). Higher grade tumors recur more frequently after treatment and patients with such tumors have lower survival rates.

- **33.8%** **Meningioma**
- **12.7%** **Pituitary**
- **1.0%** **Embryonal Including Medulloblastoma**
- **0.7%** **Craniopharyngioma**
- **8.7%** **Nerve Sheath**
- **2.1%** **Oligodendroglioma**
- **2.4%** **Lymphoma**
- **1.9%** **Ependymoma**
- **12.7%** **All other**
- **6.8%** **Astrocytoma**
- **17.1%** **Glioblastoma**

Fig 1: Distribution of primary CNA tumors by histology (n=158,088). Adapted from the SBTRS statistical report Feb. 2010.

CLINICAL PRESENTATIONS: Tumor symptoms can include headaches, nausea, vomiting, sensory symptoms, weakness, difficulty with memory or speech, in-coordination, vision changes, hearing loss, hoarseness, dysphagia or coma.

WORK-UP: Neuroimaging with magnetic resonance imaging (MRI) or computed tomography (CT) has revolutionized diagnostic accuracy and tumor staging. Magnetic resonance angiography or venography aids in evaluating the precise relationship between vital blood vessels both near and within the tumor. Diffusion-Tensor imaging can aid in tractography, an important technique is visualizing neuronal pathways such as the cortical spinal tract. Further, MR spectroscopy (MRS) can aid in distinguishing a neoplasm from infection or demyelinating disease when the diagnosis proves difficult.

MULTI-MODALITY TREATMENT: Current therapy for brain tumors often incorporates a three-pronged approach: neurosurgical resection, radiation therapy and systemic chemotherapy.

***SURGERY*:** Neurosurgery for the brain tumor patient ranges from stereotactic biopsy for tissue diagnosis to a craniotomy (temporary removal of a portion of the skull for access to the tumor) for complete resection of the lesion. Intra-operative image guidance is used for localizing the lesion and confirming the location of normal critical neurovascular structures. Neurophysiological monitoring is used during surgery on the awake or anesthetized patient. By stimulating the brain, a neurosurgeon is able to locate and avoid damaging critical areas that mediate language or motor functions **(see Fig 2 and 3)**. Brainstem auditory evoked potentials (BAEPs) allow the monitoring of hearing during surgery. Additional cranial nerve monitoring assesses the functions of chewing, facial movement, swallowing, shoulder shrugging, turning the head and moving the tongue. These techniques greatly reduce the risk of inadvertent neurological injury during tumor resection.

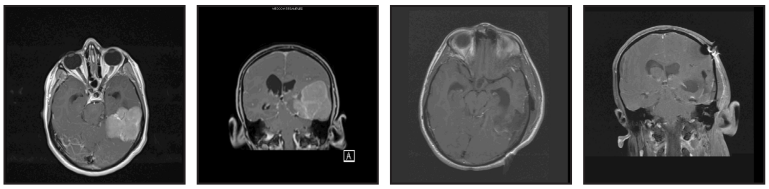

FIGURE 2: Giant left petrous meningioma (WHO grade 2, atypical meningioma) of the supra and infratentorial compartments was completely resected with neurophysiologial monitoring using BAEPs and facial nerve monitoring.

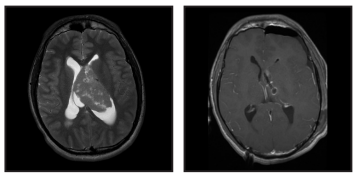

FIGURE 3: Exophytic left thalamic glioblastoma that underwent a superior parietal lobule approach using motor mapping and continuous somatosensory evoked potentials (SSEPs) with strip electrodes.

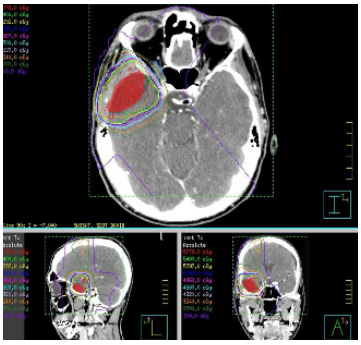

FIGURE 4: Example of an Intensity Modulated Radiation Therapy (IMRT) plan for a recurrent meningioma. The sharp dose gradient allowed for delivery of adequate dose to the resection cavity while minimizing the dose to the right optic nerve. Patient was aligned daily with cone-beam CT to allow for exact delivery.

***RADIATION*:**

Photon Therapy: Most brain tumor patients will require photon or "x-ray" therapy. This is generally given with daily treatments over a course of 5-6 weeks. Treatment can now be delivered with daily cone-beam CT to assure accurate patient alignment. This is important as the delivery of the more standard photon therapy is possible with highly conformal fields with fairly rapid dose drop off at the edge of the target volume. With sharper dose gradients, it is critical that patients are aligned in the correct position during treatment **(Fig 4)**.

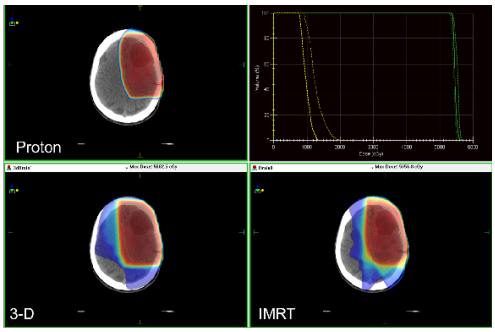

FIGURE 5: Comparison of IMRT (photon), 3-D Conformal, and Proton Therapy – The lack of blue in the proton plan shows that there is no exit dose into the contralateral right frontal lobe. This can be documented by looking at dose-volume histograms. The proton plan has no dose in the right hippocampus whereas the 3-D plan (solid yellow) has more than the IMRT (dashed yellow) (upper right of figure).

Proton Therapy: ABTC physicians treat patients with proton therapy at the Seattle Cancer Care Alliance Proton Therapy Center located at Northwest Hospital. The patients' care is coordinated through the ABTC to provide seamless integration across sites. Protons have the unique physical property of not having an exit dose, which avoids unwanted radiation to uninvolved brain. This can potentially reduce the risk of long-term complications of radiation therapy including neurocognitive effects **(Fig 5).**

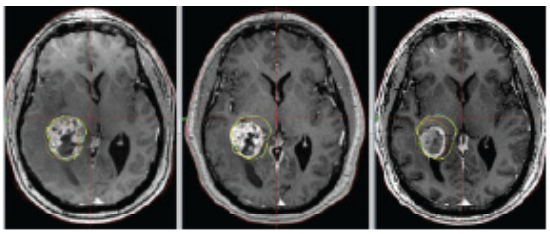

FIGURE 6: Example of Renal Cell Carcinoma metastasis treated with hypofractionated stereotactic radiotherapy. The first two panels represent treatment done two days apart. The patient was then rescanned (showing tumor regression) and given two more treatments two days apart. The third panel shows tumor response at one month with a yellow line noting treatment area had the original plan been followed throughout.

Stereotactic Radiosurgery and Hypofractionated Stereotactic Radiotherapy: Certain brain tumors benefit from treatment with Stereotactic Radiosurgery. The ABTC physicians use the Gamma Knife™ platform for precise delivery of ablative doses of radiation. Most patients can be treated in one day. However when a Hypofractionated Stereotactic Radiotherapy approach is advantageous, the Gamma Knife™ and Extend™ system delivers treatments over 3-5 sessions **(Fig 6).**

The **ABTC** allows for coordination of care across these platforms to be able to provide patients with the best treatment. In the ABTC clinic, all patients have the opportunity to discuss their personalized treatment options with all specialists, without leaving their seat.