Presentation Outline

- Overview
- Anatomy of the Human Brain
- Multiple Primary and Histology Coding Rules
- Collaborative Stage Data Collection System (CSv2)
- C.S. Site Specific Factors
- Treatment Options
Brain tumors are:

- **Primary brain tumors** - those that begin in the brain and tend to stay in the brain - occur in people of all ages, but they are statistically more frequent in children and older adults.

- **Metastatic brain tumors** – those that begin as a cancer elsewhere in the body and spread to the brain – are more common in adults than in children.

Source: American Brain Tumor Association Facts and Statistics http://abta.org

Brain tumors are:

- the second leading cause of cancer-related deaths in children (males and females) under age 20 (leukemia is the first)

- the second leading cause of cancer-related deaths in males ages 20-39

- the fifth leading cause of cancer-related deaths in females ages 20-39

Source: American Brain Tumor Association Facts and Statistics http://abta.org

Brain tumors are:

- Usually described as intracranial neoplasms with varying behaviors (benign, borderline, malignant)

- Are frequently grouped in discussions, statistics, training, treatment planning, and research to include pretty much any structure within the cranial (including hormone secreting ducts like the pineal and pituitary gland), the cranial nerves (optic nerve, olfactory nerve, acoustic nerve), the lining of the brain or meninges which also lines the rest of the central nervous system’s critically important feature capable of distributing chemically charged nerve impulses with incredible speed and accuracy, and a critical component of the function of the central nervous system, the spinal cord.
Brain tumors are classified as either intra- or extra-cranial and both produce clinical/symptomatic effects that are similar in terms of mass effect, hemorrhage, seizure activity, and edema.

<table>
<thead>
<tr>
<th>Intracranial Sites</th>
<th>Extracranial Sites</th>
</tr>
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<tbody>
<tr>
<td>Brain</td>
<td>Spinal cord</td>
</tr>
<tr>
<td>Cerebral meninges</td>
<td>Cauda equina</td>
</tr>
<tr>
<td>Cranial nerve and other intracranial parts of the CNS</td>
<td>Spinal meninges</td>
</tr>
<tr>
<td>Cerebellopharyngeal duct</td>
<td></td>
</tr>
<tr>
<td>Pituitary gland</td>
<td></td>
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</table>

ALL Brain Tumors are Reportable

- Public Law 107-260, the [Benign Brain Tumor Cancer Registries Amendment Act.](https://pdf-185KB) requires programs participating in the National Program for Cancer Registries (NPCR) to collect data on benign and borderline tumors of the central nervous system in addition to the previously required data on malignant tumors.
- In addition to NPCR, the National Cancer Institute’s (NCI) Surveillance, Epidemiology and End Results (SEER) program and the American College of Surgeons' (ACoS) Commission on Cancer began requiring that these tumors be reported, starting with cases diagnosed on January 1, 2004.
Brain and CNS Tumors – All Ages

- 2011 estimates in the United States
- 64,540 new cancer cases

This includes:

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Number</th>
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</thead>
<tbody>
<tr>
<td>Malignant brain tumors</td>
<td>24,070</td>
</tr>
<tr>
<td>Non-malignant brain tumors</td>
<td>40,470</td>
</tr>
</tbody>
</table>

Source: American Brain Tumor Association Facts and Statistics

Brain and CNS Tumors - Children

- Approximately 4,150 children younger than age 20 will be diagnosed with primary brain tumors in 2011
- 2,960 will be less than 15 years of age
- 1,190 will be between the ages of 15 and 19
- Gliomas represent a high percentage of childhood tumors
  - 55% of all tumors and 71% of malignant tumors in children age 0-14
  - 39% if all tumors and 74% of malignant tumors in children age 15-19

Source: American Brain Tumor Association Facts and Statistics
50% of childhood brain and CNS tumors are infratentorial, originating below the tentorium.

20%+ of childhood CNS tumors are located in the sellar or suprasellar region around the sella turcica (the bone that contains the pituitary gland).

Remainder of tumors occur in spinal cord, brain stem, cranial nerves, etc.
Pilocytic Astrocytoma

- Synonyms include:
  - Juvenile pilocytic astrocytoma
  - Cystic cerebellar astrocytoma
  - Juvenile pilomyxoid astrocytoma

- Characteristics:
  - Usually slow growing, well-circumscribed neoplasm
  - Associated with the formation of a single (or multiple) cyst(s)
  - Arise in cerebellum near brainstem
  - Other common sites include hypothalamic region and optic chiasm
  - May occur in cerebral hemispheres and spinal cord
  - Associated with neurofibromatosis Type 1 (NF1)
  - 10 year survival greater than 90% with total removal
  - Not associated with recurrence with total removal
  - WHO Grade I - benign

Pilocytic Astrocytoma

- HOWEVER, when the ICD-O-3 was published, the behavior code for pilocytic astrocytoma downgraded from /3 (malignant behavior) to 1 (borderline behavior) as it still appears in the ICD-O-3 reference sitting on your desktop.

- Registrars in the United States were in 2000 and continue to be instructed by our national standard setting agencies to assign the behavior code /3 to these tumors despite the WHO downgrade.

- Rationale: To ensure complete reporting and data consistency, registrars should continue to assign the malignant behavior code (3) to pilocytic astrocytoma. This is the standard for all U.S. registries in all programs.

- Confusing to researchers and public health studies since we reference ICD-O as our primary coding reference and ICD-O-3 has never published the U.S. change and does not assign a malignant behavior to this type of astrocytoma.

Causes and Risk Factors

No single risk factor accounting for the majority of brain tumors has been identified even though many environmental and genetic factors are being studied.
Causes and Risk Factors

ENVIRONMENTAL

- Many studies have examined a wide spectrum of environmental factors as a cause for brain tumors. Of the long list of factors studied, only exposure to ionizing radiation has consistently been shown to put one at increased risk for developing a brain tumor.

GENETIC

- There are a few rare genetic syndromes that involve brain tumors.
  - NF1 (NF1 gene)
  - NF2 (NF2 gene)
  - Turcots (APC gene)
  - Gorlin (PTCH gene)
  - Tubrous sclerosis (TSC1 and TSC2 genes)
  - Li-Fraumeni syndrome (TP53 gene)

Range of tumors and symptoms

- There are over 120 different types of brain/CNS tumors.

- CNS tumors are associated with a range of symptoms and complications such as edema, seizures, endocrinopathy, fatigue, psychiatric disorder, venous thromboembolism that can seriously impact quality of life.

- Symptoms depend very much on the size and location of the tumor. General symptoms include persistent headaches which tend to be worse with activity, at night or early in the morning, convulsions, vomiting, subtle changes in personality, memory, mental ability, drowsiness, lethargy.
Range of tumors and symptoms

- Symptoms are often location specific or provide clues
- Symptoms on the right side of the body may occur if the tumor is located on the left side of the brain and vice-versa.
  - The speech center in most people is on the left side of the brain. Symptoms of a tumor located here may include difficulty saying correct words while still capable of understanding what is being said.
  - If the tumor is located in the frontal lobe which controls intellectual function, thought process, behavior and memory, those activities may be affected.
- Similarity to closed head injury victims (motorcycle crash).

Midline Shift and Mass Effect

- The bony cranium protects the brain from outside impacts to the head. When swelling occurs in the brain, there isn’t much “give”.
- The swelling results in intracranial pressure and can cause a number of effects that begin to impact quality of life and comfort for the patient.
- The easiest way to describe midline shift is to bring to mind sitting in a movie theater. As soon as the person to one side of you puts his elbow onto the shared armrest between you, you tend to shift away.

- Midline is a central boundary separating the left and right hemispheres.
- Midline Shift – Tumor crosses the brain to shift across the center line
- Mass Effect is – Edema or swelling causes the brain to shift across center line
- Both create new symptoms at cross-over
  - Depends on the size and location of the tumor and level of spread
  - Edema caused by many things
  - Either cause pushes midline out of alignment
The Brain is Incapable of Feeling Pain

- Surgeons are able to cut living brains without fear of hurting their patients.
- However, symptoms from tumors and their effect within the cranial cavity on various functions of the brain is a different story, altogether.
- Much is dependent upon tumor location and infiltration.

Source: National Geographic, courtesy of Fred Hossler/Getty Images

Benign/Borderline/Malignant ???

<table>
<thead>
<tr>
<th>BENIGN TUMORS</th>
<th>MALIGNANT TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>slow growing</td>
<td>usually rapidly growing</td>
</tr>
<tr>
<td>distinct borders</td>
<td>invasive</td>
</tr>
<tr>
<td>rarely spread</td>
<td>life-threatening</td>
</tr>
</tbody>
</table>

Source: American Brain Tumor Association Facts and Statistics http://abta.org

Survival Trends

- SEER data from 1995-2007

  5-year relative survival

  - Males 34%
  - Females 38%

- Children age 0-19 have the highest 5-year relative survival rate 72%

- The survival rate diminishes as age increases, down to 5% for persons age 75 and older.
Tumor-Specific Statistics

Meningioma
- 10% of all primary brain tumors

Glioma
- 15% of all primary brain tumors

- Glioblastoma (10% of all gliomas)
- 17% of all primary brain tumors

- Astrocytoma
- 2% of all primary brain tumors

- Oligodendrogloma
- 2% of all primary brain tumors

- Ependymoma
- 1% of all primary brain tumors

Pituitary tumors
- 13% of all primary brain tumors

Nerve sheath tumors
- 9% of all primary brain tumors

- Meningiomas/embryonal or other tumors
- 3% of all primary brain tumors

- Lymphomas
- 2-3% of all primary brain tumors

- Embryonial, including Medulloblastoma
- 1.0% of all primary brain tumors

- Medulloblastoma/embryonal and other tumors
- 3% of all primary brain tumors

- Of primitive (pluripotential) nerve origin
- 1.0% of all primary brain tumors

- Of primitive (pluripotential) nerve origin
- 1.0% of all primary brain tumors

- Gliomas (CD-0-3, 0310-0
- 0391-0, 0395-0, 0394-0, 0394-0) account for
- 31% of all tumors and 10% malignant tumors
<table>
<thead>
<tr>
<th>WHO Classification Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumors of Neuroepithelial Tissue</strong></td>
</tr>
<tr>
<td><strong>Tumors of Cranial and Paraspinal Nerves</strong></td>
</tr>
<tr>
<td><strong>Tumors of Meninges</strong></td>
</tr>
<tr>
<td><strong>Lymphomas and Hematopoietic Malignancies</strong></td>
</tr>
<tr>
<td><strong>Germ Cell Tumors</strong></td>
</tr>
<tr>
<td><strong>Tumors of the Sellar Region</strong></td>
</tr>
<tr>
<td><strong>Metastatic Tumors</strong></td>
</tr>
</tbody>
</table>
WHO Grade

- Four categories of tumor
  - Grade I  slow growing, non-malignant, associated with long-term survival – benign tumors
  - Grade II relatively slow-growing, sometimes recur as higher grade tumors, can be malignant or non-malignant (borderline malignant)
  - Grade III malignant and often recur as higher grade tumors
  - Grade IV reproduce rapidly and are very aggressive malignant tumors
- WHO grade is not recorded as part of the histology
- WHO grade is used by the clinician to plan treatment and predict prognosis
ANATOMY OF THE HUMAN BRAIN

THE HUMAN BRAIN

- The brain is the largest intracranial organ.
- The brain is a 3-pound mass of jelly-like fats and tissues.
- It is the most complex of all known living structures.
- The skull or cranium is bone that covers the brain.
- Up to one trillion nerve cells working together coordinate the physical actions and mental processes (voluntary and involuntary) that set humans apart from all other species.

Source: CDC Data Collection of Primary CNS Tumors, NPCR Training Materials 2004

- The CNS includes both intracranial sites (inside the cranium) and extra-cranial sites (outside the cranium).
  - The pituitary gland, craniopharyngeal duct and pineal gland are found inside, alongside brain tissue.
  - Cranial nerves directly link to brain tissue.
  - The spinal cord is part of the CNS though not intracranial.

- Any tumor that originates in the brain, spinal cord, the cranial nerves, one of the glands/ducts within the cranium (pineal, pituitary, craniopharyngeal), or the lining of the cranium (meninges) is reportable regardless of behavior (benign, borderline, or malignant).

Source: CDC Data Collection of Primary CNS Tumors, NPCR Training Materials 2004
Ventricular System of the Brain

The Ventricular System of the Human Brain

Meninges and Brain Stem
Characteristics of Brain Tumors

- Start in the brain and grow steadily there.
- Very rarely spread to other organs through the bloodstream.
- Are named for the cells from which they arise, each having a certain function essential to normal physiological functioning of the brain. For example:
  - Gliomas arise from glial cells which support the CNS.
    - Astrocytomas arise from astrocytes
    - Ependymomas arise from ependymal cells which line the ventricles (fluid-filled spaces within the brain) or central canal of the spinal cord.
    - Oligodendrogliomas arise from oligodendrocyte cells which make up the fatty substance called myelin that covers nerves like electrical insulation.
    - Brain Stem Gliomas arise in the lowest part of the brain.
**Characteristics of Brain Tumors**

- **Histologic Type - Glioma**
  - Most common category of primary brain tumors. They begin in glial cells (supporting cells of the CNS).
  - Often spread into surrounding brain tissue along nerve fibers invading the spaces between nearby normal brain cells. Some invade the surrounding brain more than others.
  - Difficulty obtaining complete surgical removal. MRI scans show the largest part of the glioma, but cannot reliably show areas of the brain where tumor cells have invaded. Aggressive efforts to remove small numbers of tumor cells within the brain could cause loss of neurologic function.
  - When it is not possible to remove the entire glioma, post-op radiation therapy and chemotherapy may be advised.
  - Even with maximum safe resection followed by radiation and chemotherapy, gliomas can grow back.

**Glioma – 3 Main Histologic Types**

1. **Astrocytoma**: In adults most often arise in the cerebrum. In children they occur in the brain stem, cerebrum and cerebellum. Rarely in brain stem in adults. Felt to be most aggressive of brain tumors.
   - Grade I and II astrocytomas are low-grade astrocytomas.
   - Grade III astrocytoma is an "anaplastic astrocytoma".
   - Grade IV astrocytoma is a "glioblastoma multiforme".
2. **Oligoastroglioma**: Rare tumor that usually occurs in the cerebrum, grows slowly and usually does not spread into surrounding brain tissue like astrocytoma does. Most common in middle-aged adults.

3. **Ependymoma**: Most commonly arise in children and young adults. They are also seen with neurofibromatosis Type II. (which we will discuss a bit)

**Glioma – 3 Main Histologic Types**

**Glioma – Other Subtypes**

There are other subtypes of gliomas, each with their own specific characteristics and modes of growth.

- Brain Stem Glioma
- Juvenile Pilocytic Astrocytoma
- Pleomorphic Xanthoastrocytoma
- Subependymoma
- Ganglioglioma

**Glioma Tumor Markers**
Non-Glial Tumors

- **Medulloblastoma**: Usually arises in the cerebrum, is the most common brain tumor in children, and is sometimes called a “primitive neuroectodermal tumor” or PNET.

- **Meningioma**: Arises from the meninges which are the outside coverings of the brain between the skull and the brain itself. It usually presses on the brain, but does not invade it and often grows slowly.

Non-Glial Tumors

- **Schwannoma**: Arises from Schwann cells present in certain nerves, including those that control balance and hearing.

  - A common site is the vestibular nerve which carries signals from the inner ear to the brain stem.

  - Tumors in this location are called “acoustic neuromas” (a.k.a. vestibular schwannoma), and occur most often in adults.

Non-Glial Tumors

- **Craniopharyngioma**: Grows at the base of the brain, arises from the tissue connecting the brain and the pituitary gland and occurs in both adults and children.

- **Pituitary Adenoma**: Arises from the pituitary gland and may cause compression of the optic nerves causing vision problems. Some produce excessive amounts of hormones that can disrupt the body’s metabolism.
Observing Migration of Glioma Cells

Source: Case Western Reserve University School of Medicine, public release 8/25/11

Neurofibromatosis

- The neurofibromatoses (NF) are a group of genetic disorders which cause tumors to grow along nerves and can also affect the development of non-nervous tissues such as bones and skin.

- **Neurofibromatosis Type I (NF-I)**, also known as Peripheral NF and historically as von Recklinghausen Disease
  - Occurs in 1:4,000 births
  - Multiple cafe-au-lait spots (not reportable)
  - Many, many neurofibromas on or under the skin (not reportable)
  - Enlargement and deformation of bones and curvature of the spine
  - Tumors may develop in brain, on cranial nerves, or the spinal cord

NF Type I: First documented photo 1871

Source Credit: Dr. Stanley R. Burns
http://www.cbsnews.com/2300-204_162-50560195300.html?tag=sra;txt;ad
Other Manifestations of NF Type I

- Lisch nodules on the eye
  - Melanocytic hemartomas
- Café-au-lait spots on skin
  - Discolored birth marks

Medscape Source: Dermnet.com; Dermatologic Manifestations of NF Type I

Neurofibromatosis Type II

- Neurofibromatosis Type II (NFII), also known as Multiple Inherited Schwannomas, Meningiomas and Ependymomas (MISME) or Bilateral Acoustic Neurofibromatosis (BAN).

- Is a genetically inherited disease caused by mutations of the "Merlin" gene, which appears to influences the form and movement of cells

- Primary manifestation is a development of non-malignant brain tumors in the region of the cranial nerves, frequently bilaterally. The eighth cranial nerve is the auditory-vestibular nerve which transmits sensory information from the inner ear to the brain and is commonly affected.

Source: California Ear Institute

Acoustic Neuroma/Schwannoma

Source: http://thrivingwithneurofibromatosis.blogspot.com
Multiple Primary Rules

Histology Coding Rules

Different Rules for Benign and Malignant

Sequence Numbering for Brain Tumors

- **Malignant primary brain and CNS tumors** are assigned
  Sequence Codes in the range 00-35
  - Sequence Chronologically 00-35
  - Only count malignant tumors in the sequence
  - If only one malignant tumor occurs, it is coded 00
  - If subsequent (multiple) primary malignant and/or in situ neoplasms, the sequence number for the first tumor begins at 01, the sequence number for the second primary tumor is 02, and so forth.

- **Non-malignant primary brain and CNS tumors** are assigned
  Sequence Codes in the range 60-87
  - Sequence Chronologically 60-87
  - Only count benign/borderline or reportable by agreement neoplasms in the sequence
  - If only one non-malignant tumor occurs, it is coded 60.
  - If subsequent (multiple) non-malignant neoplasms are diagnosed, the first tumor should be sequenced as 61, the second 62 and so forth.
Benign and Borderline Tumor Rules

- When multiple tumors are present, registrars should identify and document specific characteristics for MPH Rules text.
- Date of Diagnosis (Timing is not used to determine number of abstracts or primary neoplasms to abstract)
- Method and Details of Diagnosis (some are never resected)
- Location of Tumor
- Laterality
- Histologic Type – refer to Chart 1
- Tumor Behavior
- Multiple Meningioma’s (meningiomatosis)
- Neurofibromatosis Characteristics (when applicable)

Malignant Tumor Rules
Malignant Tumor Rules

- When multiple tumors are present registrars should identify and document specific characteristics for MPH Rules:
  - Date of Diagnosis (Timing is not used to determine number of abstracts or primary neoplasms to abstract)
  - Method and Details of Diagnosis (most attempt resection)
  - Location of Tumor (not spread or invasion - but bulk of tumor)
  - Histologic Type – refer to Chart 1 and/or Chart 2
  - Tumor Behavior
  - Variations or Combinations of One or More Glial Tumors Over Lifetime – astrocytoma, glioblastoma, ependymoma, or oligodendroglioma
  - Special rules for determining # abstracts
  - Special rules for determining whether or not is mixed glioma
  - Note: Recurrence, progression, or any reappearance of histologies on the same branch in Chart 1 or Chart 2 is always the same disease process.

Report /Sequence All Tumors Over Lifetime

REMINDER: Sequence numbers for malignant neoplasms and for benign, borderline, and other reportable-by-agreement cases are assigned over a lifetime.

- Therefore,

  IF A PATIENT WAS DIAGNOSED WITH A NON-MALIGNANT CNS Neoplasm BEFORE REPORTING WAS REQUIRED (January 1, 2004),

  THE NEW (SECOND) NEOPLASM SHOULD BE ASSIGNED SEQUENCE NUMBER 62 AND THE FIRST NEOPLASM (Seq 61) IS REPORTABLE AS A HISTORICAL CASE TO FCDS.

(An abstract/accession is not be required by CoC or SEER but is by FCDS)

- Any benign and/or borderline brain or CNS tumor(s) diagnosed before January 1, 2004 ARE REPORTABLE TO FCDS as historical cases when accompanied by another reportable primary.
Decisions regarding aggressiveness of surgery for primary brain lesions are complex and depend on the:
- Age and performance status of the patient
- Proximity to "eloquent" areas of the brain
- Feasibility of decreasing the mass effect with aggressive surgery
- Resectability of the tumor (including the number and location of lesions)
- In patients with recurrent disease, the time since the last surgery

Surgical options include:
- Stereotactic biopsy
- Open biopsy or debulking procedure
- Subtotal resection
- Maximal safe resection

Craniotomy
Any bony opening that is cut into the skull.
Craniotomy Procedure

A section of the skull, (called a bone flap) is removed to access the brain underneath.

Typically the bone flap is replaced.

If the flap is not replaced, the procedure is called a craniectomy.

Source: MedlinePlus/US National Library of Medicine, NIH

Surgeon has drawn the cutline circle around the tumor location

Source: The Alien - a set on Flickr www.flickr.com/photos/woodcreeper/set/598206

Surgeon has cut the scalp and pulled it back to expose the skull over the tumor

Source: The Alien - a set on Flickr www.flickr.com/photos/woodcreeper/set/598206
The skull is removed revealing the dura layer under which is the brain and tumor.

Source: The Alien - a set on Flickr www.flickr.com/photos/woodcreeper/set/598206

Here you see the circular cut through the dura layer with the brain and tumor exposed.

Source: The Alien - a set on Flickr www.flickr.com/photos/woodcreeper/set/598206

Meningioma Resected
Pre- and Post-Operative Imaging
Pre-op tumor is outlined in red
Post-operative MRI shows complete resection of the tumor

Source: Desert Spine and Neurosurgical Institute

Surgery Codes

APPENDIX B. Site-Specific Surgery Codes

BRAIN
Mononges C74.6-C74.9, Brain C71.6-C71.9
Spinal Cord, Cranial Nerves and Other Parts of Central Nervous System C72.0-C72.9
(Except for M72.77, 72.78, 72.84, 72.85, 72.86, 72.87, 72.88, 72.89, 72.90, 72.91, 72.92, and 72.93)

Do not code laminotomy for spinal cord primaries.

Codes:
00 None; no surgery of primary site; autopsy ONLY
10 Tumor resection, NORE

No specimen sent to pathology from surgical event 10.

Do not report stereotactic radiosurgery (SRS), Gamma knife, Cyber knife, or Linac radiosurgery as surgical tumor destruction. All of these modalities are recorded in the radiation treatment fields.

Surgery Codes

20 Local excision of tumor, lesion or mass; excisional biopsy
21 Subtotal resection of tumor, lesion or mass in brain
22 Total resection of tumor or lesion or mass in brain
30 Radical, total, gross resection of tumor, lesion or mass in brain
40 Partial resection of lobe of brain, when the surgery cannot be coded as 20-30
55 Gross total resection of lobe of brain (lobectomy)

Codes 20 - 55 are not applicable for spinal cord or spinal nerve primary sites.

Specimen sent to pathology from surgical events 20-55.
Radiation Therapies

- Primary XRT for brain tumors includes tumor volume/margins
- Tumor volume is defined by pre- and post-operative imaging
- Standard fractionated external beam radiation is most common
- Hypofractionation (daily dose given in smaller increments with 4 or 6 hours between treatments) is an emerging option
- Whole brain XRT and stereotactic radiosurgery for brain mets

Source: NCCN

Tumor Volume

- The larger the brain tumor, the more desirable "fractionation" (e.g. multiple smaller treatments, rather than one big one)
- Tumor size can determine schedule for fractionation and dose/tx
- Why: The "shell" of normal tissue outside the tumor volume will receive some part of the dose. For larger tumors, this "shell" volume increases rapidly as a function of tumor diameter
- Why: Fractionation spares this "shell" of normal tissue much more effectively than the single "shot" techniques

Source: Johns Hopkins Medicine

Stereotactic Radiosurgery (SRS)

- Despite name, SRS is an XRT treatment, not a surgical procedure
- Acoustic neuroma, pituitary tumors, spinal cord tumors and brain metastasis are candidates for this technique
- Special equipment focuses up to 200 beams of radiation on tumor
- Although each beam has very little effect on the brain tissue it passes through, a strong dose of radiation is delivered to the site where all the beams meet.
- Results in minimal damage to healthy tissues surrounding target.

Source: Mayo Clinic
Chemotherapy

- Chemotherapy is not an effective initial treatment for low-grade brain tumors. Why? Because most standard chemo agents have a hard time passing into the brain because of how the brain protects itself (the blood-brain barrier)
- Not all types of brain tumors respond to chemotherapy
- In general, chemotherapy for brain tumors is usually administered following surgery or radiation therapy
- Participation in clinical trials should be encouraged

Blood Brain Barrier

- Composed of special cells that make up brain’s blood vessels
- Selectively prevents substances from entering the blood and brain, only allowing essential molecules such as amino acids, oxygen, glucose and water through
- Adenosine, a molecule produced by the body, seems to modulate the entry of large molecules into the brain
- When adenosine receptors are activated on cells that comprise the blood-brain barrier, a gateway into the barrier can be established
Approved Chemotherapy Agents

- Carmustine (BCNU) – IV or dissolvable wafers placed surgically
- Temozolomide (Temodar) – oral
- Lomustine (CCNU) – oral
- Carboplatin
- Cisplatin
- Etoposide
- Irinotecan
- Vincristine
- Procarbazine (Matulane) – oral
- Methotrexate - oral, by injection or intrathecally

NCCN Treatment Guidelines

Infiltrative Low-Grade Glioma

- Best management strategy has yet to be defined
- Small tumor samples can provide a lower histologic grade
- Rationale: Needle biopsies are often performed when lesions are in deep or critical regions of the brain, but can be misleading because gliomas often have varying degrees of cellularity, mitosis, or necrosis from one region to another
- General recommendation is to first attempt as complete an excision of tumor as possible (based on postsurgical MRI verification) without compromising function
- No consensus exists regarding proper timing of postoperative external beam radiation
- Chemotherapy is not a traditional upfront treatment modality
Infiltrative Low-Grade Glioma
* When possible, maximal safe resection

* If gross total resection is achieved, some patients may be observed without adjuvant therapy. However, close follow-up is essential as over half of patients will eventually progress

* These tumors behave aggressively in patients over 40 years old
  * Adjuvant radiation or chemotherapy is recommended

* If stereotactic biopsy, open biopsy, or other subtotal excision was done, immediate fractionated external beam RT or chemotherapy should be given

Anaplastic Glioma and Glioblastoma
* Whenever possible, major tumor removal should be performed

* If glioblastoma is confirmed, options include radiation, chemotherapy, best supportive care, chemoradiation only if carmustine wafer was implanted

* If high-grade glioma is confirmed, BCNU wafer is an option
  * In patients with good Karnofsky score (70 or above) options include fractionated external beam radiation therapy, chemotherapy or chemoradiation in the context of a clinical trial
  * In patients with poor Karnofsky score (below 70) management may include radiation, chemotherapy or best supportive care

Intracranial Ependymoma
* Whenever possible, maximal safe resection should be attempted

* Adjuvant treatment depends on the extent of surgical resection, histology and staging by cranial spinal MRI and CSF cytology

* CSF dissemination occurs in up to 15% of intracranial ependymomas

* If MRI spine/CSF reveal disease, craniospinal radiation is mandatory

* If gross total resection with negative spinal MRI and CSF, adjuvant regional fractionated EBRT or observation may be considered
Medulloblastoma and PNET (supratentorial)

- MRI is the gold standard to assess PNET
- Maximal safe resection is recommended when possible
- Average Risk Patients: craniospinal radiation alone or concurrent chemoradiation followed by chemotherapy are both options
- High Risk Patients: patients with large cell or anaplastic medulloblastoma, supratentorial PNET, disease dissemination, unresectable tumors, or residual tumors over 1.5 cm post-surgery are high risk and should undergo radiation followed by chemotherapy

Primary CNS Lymphoma

- Treatment to be initiated as immediately following diagnosis
- Treatment options depend on patient overall health and age
- For healthier patients a high-dose methotrexate regimen
- RT after systemic treatment depends on the responsiveness of the disease to the chemotherapy
- However, one or both may increase neurotoxicity, especially in patients older than 60 years of age

Primary Spinal Cord Tumors

- MRI is the gold standard for diagnosis of spinal cord lesions
- Asymptomatic patients may be observed or resected
- Symptomatic patients should undergo some form of surgery
- Maximal safe resection should be attempted
- Post-operative adjuvant radiation is not recommended
- However, if symptoms persist after incomplete resection or biopsy, radiation should be administered
**Meningioma**

- Meningiomas are typically diagnosed by CT or MRI imaging
- Biopsy may be considered for confirmation
- Options stratified by presence/absence of symptoms and tumor size
- Most asymptomatic patients with small tumors (<30mm) may just be observed. If neurological impairment is imminent, surgery (if accessible) or radiotherapy (EBRT OR SRS) is feasible
- Asymptomatic tumors >30mm can be either resected or observed

**Meningioma**

- Symptomatic disease requires active treatment by surgery if possible
- Non-surgical candidates should undergo radiation
- All patients with surgically resected grade III meningiomas (even after gross total resection) should receive adjuvant radiation for local control regardless of tumor size and symptom status

**Additional Resources**

- NCCN Evidence Based Treatment Guidelines, nccn.org, 2011
- Collaborative Stage Data Collection System, AJCC, 2010
- Multiple Primary and Histology Coding Rules, SEER 2007
QUESTIONS ???