UNDERSTANDING CANCER:
BRAIN TUMORS

Abstract

The field of brain tumor research, diagnosis, and treatment is rapidly evolving. Over 120 types of brain tumors have been identified to date, and that number continues to increase. As the information available about brain tumors grows, so does the ability to target screening and therapies to provide patients with optimal outcomes. It is critical that health clinicians understand the surgical and treatment options in order to educate patients and to develop a care plan that has a positive outcome while respecting the patient's needs and desires.

Statement of Learning Need

Health clinicians need to be able to differentiate between malignant and benign tumors and to understand the commonly used classification system identifying tumor types. Once the type of tumor and its prognosis are identified, the important responsibility of explaining treatment options to the patient will help to guide the patient and their family to make informed choices that is right for them.

Course Purpose

To provide health clinicians with knowledge of brain tumor types and surgical interventions in order to educate patients and their families,
as well as to better collaborate with all members of the health team on
the best course of care.

**Introduction**

The field of brain tumor research, diagnosis, and treatment is rapidly
evolving. Over 120 types of brain tumors have been identified to date,
and that number continues to increase. Physicians diagnose brain
tumors by conducting a neurologic exam and tests including an MRI,
CT scan, and biopsy. Treatment options include watchful waiting,
surgery, radiation therapy, chemotherapy, and targeted therapy.
Targeted therapy uses substances that attack cancer cells without
harming normal cells. Many people typically receive a combination of
treatments. As the information available about brain tumors grows, so
does the ability to target screening and therapies to provide patients
with optimal outcomes. It is critical that health clinicians understand
surgery and treatment options in order to communicate it to their
patients and develop a care plan that has a positive outcome while
respecting the patient's needs and desires.

**Anatomy Of The Brain**

This section will first review the normal anatomy of the brain before
continuing forward with a discussion of the common types of brain
tumors and treatment in children. The brain and spinal cord together
form the central nervous system (CNS). The CNS controls personality,
thoughts, memory, intelligence, speech and understanding, emotions,
senses, and basic body functions, as well as how individuals function in
their environment. Many factors influence how a child will experience
and report symptoms associated with a brain tumor, such as the age
and ability of the child to communicate symptoms. Clinicians may have to depend on the observation of parents or teachers to determine how the child diagnosed with a brain tumor may be affected.

**Brain Structure**

The brain is made up of three main components: the forebrain, midbrain, and hindbrain. The forebrain is comprised of the cerebrum, thalamus, and hypothalamus, which is part of a complex system of nerves and networks in the brain called the limbic system. The midbrain consists of the tectum and tegmentum. The cerebellum, pons and medulla are in the area of the brain known as the hindbrain.

**Cerebrum**

The largest area of the brain is the cerebrum, which consists of the left and right cerebral hemispheres. Generally speaking, the right cerebral hemisphere controls the left side of the body and the left cerebral hemisphere controls the right side of the body. Research has shown that the right cerebral hemisphere is responsible for such functions as innovation, intuition, and creativity. The left cerebral hemisphere is associated with analytic thought, logic, and language.\(^1\)
The cerebrum is comprised of four main lobes: frontal, parietal, temporal, and occipital. Each lobe controls a specific group of activities.²

- **Frontal** — Movement, intelligence, reasoning, behavior, memory, personality, planning, decision making, judgment, initiative, inhibition, mood.
- **Parietal** — Intelligence, reasoning, telling right from left, language, reading, and sensation.
- **Temporal** — Speech, behavior, memory, hearing, vision, smell, and emotions.
- **Occipital** — Vision.

**Cerebellum**

The cerebellum is the second largest area of the brain. It is made up of two hemispheres, or halves, as well as a middle section. The cerebellum is connected to the brain stem.

**Corpus Callosum**

The corpus callosum is made of nerve fibers, deep in the brain, that connect the two halves of the cerebral hemispheres.

**Brain Stem**

The brain stem is the bottom-most portion of the brain, connecting the cerebrum with the spinal cord. The midbrain, pons, medulla oblongata, and reticular formation are all part of the brain stem.
Midbrain

The midbrain is the short portion of the brain stem between the pons and the cerebral hemispheres. The top of the midbrain is called the tectum. The third and fourth cranial nerves originate in the midbrain.

Pons

The pons, a part of the brain stem, contains the origins of the fifth, sixth, seventh, and eighth cranial nerves.

Medulla Oblongata

The medulla oblongata, a part of the brain stem, connects the brain with the spinal cord. It contains the origins of the ninth, tenth, eleventh, and twelfth cranial nerves.

Reticular Formation

The reticular formation is the central core of the brain stem. It connects with all parts of the brain and brain stem.

Ventricles

The ventricles (passageways in the brain) are connected cavities; which are the lateral, third, and fourth ventricles. There are two lateral ventricles, one in each cerebral hemisphere. The third ventricle is beneath the corpus callosum and surrounded by the thalamus. The fourth ventricle is an expansion of the central canal of the medulla oblongata. These ventricles contain cerebrospinal fluid (CSF); and, the choroid plexus produces this clear, watery fluid. Cerebrospinal fluid
flows through the ventricles and the subarachnoid space as it bathes and cushions the brain and spinal cord.

Cranial Nerves

There are 12 pairs of cranial nerves. The cranial nerves are the 1) olfactory, 2) optic, 3) oculomotor, 4) trochlear, 5) trigeminal, 6) abducens, 7) facial, 8) vestibular cochlear, 9) glossopharyngeal, 10) vagus, 11) accessory, and 12) hypoglossal.

Optic Chiasm

The optic chiasm is the area under the hypothalamus where each of the two optic nerves crosses over to the opposite side, forming an X shape.

Pituitary Gland

The pituitary gland is attached to, and receives messages from, the hypothalamus. The pituitary gland is made up of two lobes — the anterior and the posterior. Several hormones are produced by the pituitary gland, including prolactin, corticotropin, and growth hormone.

Hypothalamus

The hypothalamus makes up part of the wall of the third ventricle and is the base of the optic chiasm.
Pineal Gland

The pineal gland lies below the corpus callosum. It produces the hormone melatonin. Melatonin is believed to control the biological rhythm of the body.

Spinal Cord

The spinal cord is made up of neurons and their extensions (i.e., nerve fibers). It begins in the medulla oblongata and continues through the hollow center of the vertebrae. The spinal cord is covered by meninges. Cerebrospinal fluid flows through the meninges.

Meninges

The meninges are three membranes that completely cover the brain and spinal cord. Cerebrospinal fluid flows in the space between two of the membranes. A tumor called meningioma can originate from the meninges.

Glial Tissue (Neuroglia)

Glia is the supportive tissue of the brain. The cells, which make up this tissue, are called glial cells. The most common glial cells are astrocytes and oligodendrocytes. Ependymal cells are another form of glia. The largest percentage of brain tumors originates from the glia.

Tentorium

The tentorium is a flap of meninges separating the cerebral hemispheres from the structures of the posterior fossa.
**Posterior Fossa/Infratentorium**

The tentorium separates the posterior fossa from the cerebral hemispheres. The area below the tentorium is called the infratentorium, or the posterior fossa. This area within the skull contains the cerebellum and the brain stem.

**Supratentorium**

The supratentorium is the area above the tentorium containing the cerebral hemispheres.

**Neuron Anatomy**

The human body is made up of trillions of cells. Cells of the central nervous system (CNS) are called neurons. Neurons are electrically excitable cells in the CNS that process and transmit information. They communicate with each other via chemical and electrical synapses, in a process known as synaptic transmission. Neurons are the core components of the brain, spinal cord, and peripheral nerves, and the human brain has approximately 100 billion of them.

Neurons are the oldest and longest cells in the body. Unlike many of the other types of cells in the body, an individual has many of the same neurons for his or her whole life. Neurons come in all shapes and sizes. Some of the smallest neurons have cell bodies that are just 4 microns wide. The largest ones have cell bodies that are 100 microns wide. Some of them, such as corticospinal neurons or primary afferent neurons, can be several feet long. 1-3
Brain Tumor Types

Brain tumors differ based on location, severity, size, shape, and prognosis. Some tumors are benign and others are malignant. The type of tumor will dictate the treatment and outcome.

Benign Tumors

Benign tumors are typically slow-growing and rarely spread to other areas of the body. They often have well-defined borders, so surgical removal can be an effective treatment. However, the location of a benign brain tumor can have a significant impact on treatment options and be as serious and life threatening as a malignant tumor. Benign brain tumors can be considered malignant if they are located in areas of the brain that control vital functions like breathing.\(^4\)

Malignant Tumors

Unlike benign tumors, the cell structure of a malignant brain tumor is significantly different than that of normal brain cells. Malignant tumors tend to grow faster and can be more invasive than benign tumors. Malignant tumors are life threatening. Sometimes malignant brain tumors are referred to as “brain cancer” though they do not share all of the characteristics of cancer. Most notably, cancer is characterized by the ability to spread from one organ to another. It is very rare for a primary brain tumor to spread beyond the brain or spine.\(^5\)
Primary Brain Tumors

Tumors that start in cells of the brain are called primary brain tumors. Primary brain tumors may spread to other parts of the brain or to the spine, but rarely to other organs.

Metastatic or Secondary Brain Tumors

Metastatic or secondary brain tumors begin in another part of the body and then spread to the brain. These tumors are more common than primary brain tumors and are named by the location in which they begin.

World Health Organization Classification System

The classification of brain tumors is based on the premise that each type of tumor results from the abnormal growth of a specific cell type. To the extent that the behavior of a tumor correlates with basic cell type, tumor classification dictates the choice of therapy and predicts prognosis. The new World Health Organization (WHO) system is particularly useful in this regard with only a few notable exceptions; for example, all or almost all gemistocytic astrocytomas are actually anaplastic and hence grade III or even grade IV rather than grade II as designated by the WHO system. The WHO classification also provides a parallel grading system for each type of tumor. In this grading system most named tumors are of a single defined grade. The new WHO classification provides the standard for communication between different centers in the U.S., and around the world. An outline of this classification is provided below.
Neuroepithelial Tumors of the CNS

Astrocytic tumors (glial tumors - categories I-V, below) may also be sub classified as invasive or non-invasive, although this is not formally part of the WHO system, the non-invasive tumor types are indicated below. Categories in italics are also not recognized by the new WHO classification system, but are in common use.

Astrocytoma (WHO grade II)

Variants: protoplasmic, gemistocytic, fibrillary, mixed

Anaplastic (malignant) astrocytoma (WHO grade III)

- Hemispheric
- Diencephalic
- Optic
- brain stem
- cerebellar

Glioblastoma multiforme (WHO grade IV)

Variants: giant cell glioblastoma, gliosarcoma

Pilocytic astrocytoma [non-invasive, WHO grade I]

- hemispheric
- diencephalic
- optic
- brain stem
- cerebellar

Subependymal giant cell astrocytoma [non-invasive, WHO grade I]

- Pleomorphic xanthoastrocytoma [non-invasive, WHO grade I]
Oligodendroglial tumors
- Oligodendroglioma (WHO grade II)
- Anaplastic (malignant) oligodendroglioma (WHO grade III)

Ependymal cell tumors
- Ependymoma (WHO grade II)
  variants: cellular, papillary, epithelial, clear cell, mixed
- Anaplastic ependymoma (WHO grade III)
- Myxopapillary ependymoma
- Subependymoma (WHO grade I)

Mixed gliomas
- Mixed oligoastrocytoma (WHO grade II)
- Anaplastic (malignant) oligoastrocytoma (WHO grade III)
- Others (i.e., ependymo-astrocytomas)

Neuroepithelial tumors of uncertain origin
- Polar spongioblastoma (WHO grade IV)
- Astroblastoma (WHO grade IV)
- Gliomatosis cerebri (WHO grade IV)

Tumors of the choroid plexus
- Choroid plexus papilloma
- Choroid plexus carcinoma (anaplastic choroid plexus papilloma)

Neuronal and mixed neuronal-glial tumors
- Gangliocytoma
- Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
• Ganglioglioma
• Anaplastic (malignant) ganglioglioma
• Desmoplastic infantile ganglioglioma
  \textit{desmoplastic infantile astrocytoma}
• Central neurocytoma
• Dysembryoplastic neuroepithelial tumor
• Olfactory neuroblastoma (esthesioneuroblastoma)
  \textit{variant: olfactory neuroepithelioma}

Pineal Parenchyma Tumors
• Pineocytoma
• Pineoblastoma
• Mixed pineocytoma/pineoblastoma

Tumors with neuroblastic or glioblastic elements (embryonal tumors)
• Medulloepithelioma
• Primitive neuroectodermal tumors with multipotent differentiation
• Medulloblastoma
  \textit{variants: medulomyoblastoma, melanocytic medulloblastoma,
  desmoplastic medulloblastoma}
  \textit{cerebral primitive neuroectodermal tumor}
• Neuroblastoma
  \textit{variant: ganglioneuroblastoma}
• Retinoblastoma
• Ependymoblastoma
Other CNS Neoplasms

1. Tumors of the Sellar Region
   - Pituitary adenoma
   - Pituitary carcinoma
   - Craniopharyngioma

2. Hematopoietic tumors
   - Primary malignant lymphomas
   - Plasmacytoma
   - Granulocytic sarcoma
   - Others

3. Germ Cell Tumors
   - Germinoma
   - Embryonal carcinoma
   - Yolk sac tumor (endodermal sinus tumor)
   - Choriocarcinoma
   - Teratoma
   - Mixed germ cell tumors

4. Tumors of the Meninges
   - Meningioma
     variants: meningothelial, fibrous (fibroblastic), transitional (mixed), psammomatous, angiomatous, microcystic, secretory, clear cell, chordoid, lymphoplasmacyte-rich, and metaplastic subtypes
   - Atypical meningioma
   - Anaplastic (malignant) meningioma

5. Non-menigothelial tumors of the meninges
   - Benign Mesenchymal
     - osteocartilaginous tumors
- lipoma
- fibrous histiocytoma
- others

• Malignant Mesenchymal
  - chondrosarcoma
  - hemangiopericytoma
  - rhabdomyosarcoma
  - meningeal sarcomatosis
  - others

• Primary Melanocytic Lesions
  - diffuse melanosis
  - melanocytoma
  - malignant melanoma
    variant meningeal melanomatosis

• Hemopoietic Neoplasms
  - malignant lymphoma
  - plasmactoma
  - granulocytic sarcoma

• Tumors of Uncertain Histogenesis
  - hemangioblastoma (capillary hemangioblastoma)

6. Tumors of Cranial and Spinal Nerves

• Schwannoma (neurinoma, neurilemoma)
  - cellular, plexiform, and melanotic subtypes

• Neurofibroma
  - circumscribed (solitary) neurofibroma
  - plexiform neurofibroma

• Malignant peripheral nerve sheath tumor (Malignant schwannoma)
- epithelioid
- divergent mesenchymal or epithelial differentiation
- melanotic

- Local Extensions from Regional Tumors
  - Paraganglioma (chemodectoma)
  - Chordoma
  - Chodroma
  - Chondrosarcoma
  - Carcinoma

- Metastatic tumors

- Unclassified Tumors

- Cysts and Tumor-like Lesions
  - Rathke cleft cyst
  - Epidermoid
  - Dermoid
  - Colloid cyst of the third ventricle
  - Enterogenous cyst
  - Neuroglial cyst
  - Granular cell tumor (choristoma, pituicytoma)
  - hypothalamic neuronal hamartoma
  - nasal glial herterotopia
  - plasma cell granuloma

The 2016 World Health Organization Classification of Tumors of the Central Nervous System is both a conceptual and practical advance over its 2007 predecessor. For the first time, the WHO classification of CNS tumors uses molecular parameters in addition to histology to define many tumor entities, thus formulating a concept for how CNS
tumor diagnoses should be structured in the molecular era. As such, in the 2016 CNS classifications, WHO presents major restructuring of the diffuse gliomas, medulloblastomas and other embryonal tumors, and incorporates new entities that are defined by both histology and molecular features, including glioblastoma, IDH-wildtype and glioblastoma, IDH-mutant, diffuse midline glioma, H3 K27M-mutant, RELA fusion-positive ependymoma, medulloblastoma, WNT-activated and medulloblastoma, SHH-activated, and embryonal tumor with multilayered rosettes, C19MC-altered.

The 2016 edition has added newly recognized neoplasms, and has deleted some entities, variants and patterns that no longer have diagnostic and/or biological relevance. Other notable changes include the addition of brain invasion as a criterion for atypical meningioma and the introduction of a soft tissue-type grading system for the now combined entity of solitary fibrous tumor/hemangiopericytoma, which is a departure from the manner by which other CNS tumors are graded.6

**Grading System**

A number of grading systems are in common use for tumors of astrocytic lineage (*i.e.*, astrocytomas, anaplastic astrocytomas and glioblastomas). Grades are assigned solely based on the microscopic appearance of the tumor. The numerical grade assigned for a given tumor, however, can vary depending on which grading system is used. Thus, it is important to specify the grading system referred to when a grade is specified. The St. Anne/Mayo grade has proven to correlate better with survival than the previously common Kernohan grading
system. It can only be applied to invasive tumors of astrocytic lineage; however, is otherwise similar to the WHO grading system.

Grading helps clinicians understand how aggressive, or malignant, a tumor is, while staging identifies how the tumor has spread and if so, how far. There are four tumor grades — I, II, III, and IV. The higher the grade, the more malignant the tumor. Tumor grading helps the clinician, patient, and caregivers or family members to better understand the patient’s condition. It also helps the clinician plan treatment and predict outcome. Below are descriptions of the various tumor grades, based on the WHO grading system.7

**Grade I**

Grade I are the least malignant tumors and are usually associated with long-term survival. They grow slowly and have an almost normal appearance when viewed through a microscope. Surgery alone may be an effective treatment for this grade tumor. Pilocytic astrocytoma, craniopharyngioma, and many tumors of neurons — gangliocytoma and ganglioglioma, for instance — are examples of grade I tumors.

**Grade II**

Grade II tumors are slow growing and look slightly abnormal under a microscope. Some can spread into nearby normal tissue and recur, sometimes as a higher-grade tumor.
**Grade III**

Grade III tumors are, by definition, malignant although there is not always a big difference between grade II and grade III tumors. The cells of a grade III tumor are actively reproducing abnormal cells, which grow into nearby normal brain tissue. These tumors tend to recur, often as a grade IV.

**Grade IV**

Grade IV are the most malignant tumors. They reproduce rapidly, can have a bizarre appearance when viewed under the microscope, and easily grow into nearby normal brain tissue. These tumors form new blood vessels so they can maintain their rapid growth. They also have areas of dead cells in their centers. The glioblastoma multiforme is the most common example of a grade IV tumor. Tumors can contain more than one grade of cell. The highest, or most malignant, grade of cell determines the grade of the tumor, even if most of the tumor is made up of lower-grade cells.

**Staging**

Once cancer has been detected in a patient, the individual will go through the cancer staging process to determine how much cancer is in the body and where it is located. Staging is used to evaluate the severity of the cancer by assessing the magnitude of the primary cancer, as well as the extent to which it has spread. Cancer staging can be used to develop a prognosis and create a comprehensive treatment plan for the patient. Staging is important for several reasons, as highlighted below.
• Staging helps the clinician plan the appropriate treatment.
• Cancer staging can be used to estimate a person’s prognosis.
• Knowing the stage of cancer is important in identifying clinical trials that may be a suitable treatment option for a patient.
• Staging helps health care clinicians and researchers exchange information about patients; it also gives them a common terminology for evaluating the results of clinical trials and comparing the results of different trials.
• Staging helps clinicians understand the way the cancer has progressed.

By example, staging for central nervous system (CNS) tumors is usually performed based on CT scans or MRI images, or by looking at the cerebrospinal fluid. Scans taken after surgery are used to determine if any tumor is left behind.

Central nervous system tumors that are usually prone to spread and are studied with both scan images and laboratory tests. Patients with medulloblastoma, for example, will often have their cerebrospinal fluid examined for the presence of tumor cells. These patients also require spinal cord scans because of that tumor’s tendency to spread to the spinal cord.

**Types of Staging**

There are four different types of staging. These are briefly described below.\(^10\)
**Clinical Staging**

Clinical staging determines how much cancer there is based on the physical examination, imaging tests, and biopsies of affected areas.

**Pathologic Staging**

Pathologic staging can only be determined from individual patients who have had surgery to remove a tumor or explore the extent of the cancer. Pathologic staging combines the results of both the clinical staging (physical exam, imaging test) with surgical results.

**Post-Therapy or Post-Neoadjuvant Therapy Staging**

Post-therapy or post-neoadjuvant therapy staging determines how much cancer remains after a patient is first treated with systemic (chemotherapy or hormone) therapy and/or radiation therapy prior to their surgery or where no surgery is performed. This can be assessed by clinical staging guidelines and/or pathologic staging guidelines.

**Restaging**

Restaging is used to determine the extent of the disease if a cancer comes back after treatment. Restaging helps determine the best treatment options for cancer that has returned.

Staging systems for cancer have evolved over time. They continue to change as scientists learn more about cancer. Some staging systems cover many types of cancer; others focus on a particular type. The common elements considered in most staging systems are important for clinicians to know, such as:11
• Site of the primary tumor and the cell type
  (i.e., adenocarcinoma, squamous cell carcinoma)
• Tumor size and/or extent
• Regional lymph node involvement (the spread of cancer to
  nearby lymph nodes)
• Number of tumors (the primary tumor and the presence of
  metastatic tumors, or metastases)
• Tumor grade (how closely the cancer cells and tissue resemble
  normal cells and tissue)

The most widely used staging system is the TNM Staging System,
which is monitored and maintained by the American Joint Committee
on Cancer (AJCC) and the Union for International Cancer Control
(UICC). The TNM system uses letters to describe the different areas of
cancer development.\textsuperscript{12}

| T = Tumor | The T score is a rating of the extent of the primary tumor. The primary tumor is the first mass of cancer cells in the body. If not treated, the primary tumor can grow large. It can also grow through the layers of tissue in which it started. This is called tumor extension.

Once the tumor has grown through the outer edge of a structure, it can grow into other nearby structures. This is called invasion. T scores are based on the presence, size, and extension of the primary tumor. A TX score means that the primary tumor can’t be assessed. A T0 score means there is no primary tumor. It is possible to have cancer but not have a primary tumor.

A Tis score means there are abnormal or cancer cells, but there is no chance for the cells to spread to distant sites.

Scores of T1, T2, and so on are based on the primary tumor’s size, extension, or both. Higher values mean a greater extent of the cancer. |
### N = Nodes
The N category reflects the extent of cancer within nearby lymph nodes. Lymph nodes are small disease-fighting organs that filter lymph. Lymph is a clear fluid within tissue that gives cells water and food. It also collects waste from cells and has white blood cells that fight germs.

Lymph drains from tissue into lymph vessels that transport it to the lymph nodes. Cancer cells can invade lymph vessels and travel to lymph nodes. Once in lymph nodes, the cancer cells can multiply and form new tumors.

N scores are based on whether there’s cancer in nearby lymph nodes and the number or region of nodes with cancer. An NX score means that the lymph nodes can’t be assessed. An N0 score means that no cancer was found in the lymph nodes. N1, N2, and N3 scores are based on the number of nodes with cancer or which nodal groups have cancer. Higher values mean a greater extent of the cancer.

### M = Metastasis
The M category tells you if the cancer has spread to distant sites. Such sites include distant lymph nodes beyond nearby lymph nodes. Cancer cells can break off the primary tumor and spread to distant sites. This process is called metastasis.

Cancer cells can spread to distant sites through lymph or blood. M0 means there is no cancer in distant sites. M1 means there is cancer in distant sites.

### Stage Groups
Each type of cancer will be identified using its own staging group, which are developed based on the primary location of the cancer and the extent of growth. Each type of cancer is ranked using four or five distinct stage groups. The ranking system uses Roman numerals that begin with either Stage 0 or Stage I. All ranking systems end with Stage IV. “Cancers that can’t spread to distant sites are rated as stage 0. Stage I includes small primary tumors that haven’t spread to lymph nodes. Stage II and III are larger or more extensive primary tumors with or without cancer in nearby lymph nodes. Stage IV is cancer that
has spread to distant sites at diagnosis.”

Although there can be some variations in the number of T, N, and M, depending on the site of the tumor, the following is the most common numbering system assigned to staging groups:

- **T: Tumor**
  - Tx: primary tumor cannot be assessed
  - T0: no evidence of primary tumor
  - Tis: carcinoma in situ
  - T1: site/tumor specific, generally small
  - T2: site/tumor specific
  - T3: site/tumor specific, generally large
  - T4: site/tumor specific but usually refers to direct extension into adjacent organs/tissues.

- **N: Nodes**
  - Nx: nodes cannot be assessed
  - N0: no evidence of nodal involvement
  - N1: site/tumor specific
  - N2: site/tumor specific
  - N3: site/tumor specific

- **M: Metastases**
  - Mx: presence of metastases cannot be assessed
  - M0: no evidence of metastases
  - M1: distant metastases present
  - Other descriptors
The TNM system has been expanded to include other measures:

- **R**: resection status
- **V**: vascular invasion

Prefix: (additional prefixes can be appended to define the TNM stage):

- **c**: clinical assessment data
- **p**: pathological data
- **y**: clinical (yc) or pathological (yp) data following systemic or radiation therapy be it prior to surgery or as a primary treatment
- **r**: clinical or pathological staging at the time of retreatment for recurrence or disease progression
- **a**: autopsy data

Suffix

- **m**: multiple primary tumors, *i.e.*, T2(m) or T2(5)

In addition, TNMs can be combined into stages I, II, III, IV

- Primary Tumor (T)
  - TX: Primary tumor cannot be evaluated
  - T0: No evidence of primary tumor
  - Tis: Carcinoma in situ (CIS; abnormal cells are present but have not spread to neighboring tissue; although not cancer, CIS may become cancer and is sometimes called preinvasive cancer)
  - T1, T2, T3, T4: Size and/or extent of the primary tumor
• **Regional Lymph Nodes (N)**
  - NX: Regional lymph nodes cannot be evaluated
  - N0: No regional lymph node involvement
  - N1, N2, N3: Degree of regional lymph node involvement
    (number and location of lymph nodes)

• **Distant Metastasis (M)**
  - MX: Distant metastasis cannot be evaluated
  - M0: No distant metastasis
  - M1: Distant metastasis is present

The TNM combinations are used to create stages that rank the severity and scope of the cancer. Although the criteria may differ depending on the type of cancer, the following is an example of the standard staging combinations used for most forms of cancer.\(^{15}\)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>Stage I, Stage II, and Stage III</td>
<td>Higher numbers indicate more extensive disease: Larger tumor size and/or spread of the cancer beyond the organ in which it first developed to nearby lymph nodes and/or tissues or organs adjacent to the location of the primary tumor</td>
</tr>
<tr>
<td>Stage IV</td>
<td>The cancer has spread to distant tissues or organs</td>
</tr>
</tbody>
</table>
The TNM staging system is the most common staging system for cancer. However, in some instances of lymphoma, the Ann Arbor staging classification will be used. Another common method, which is supported by NCI’s Surveillance, Epidemiology, and End Results (SEER) Program, uses “summary staging” to group cancer into five main categories. They are defined as follows:

- **In situ**: Abnormal cells are present only in the layer of cells in which they developed
- **Localized**: Cancer is limited to the organ in which it began, without evidence of spread
- **Regional**: Cancer has spread beyond the primary site to nearby lymph nodes or tissues and organs
- **Distant**: Cancer has spread from the primary site to distant tissues or organs or to distant lymph nodes
- **Unknown**: There is not enough information to determine the stage

The types of tests used for staging depend on the type of cancer. Tests include the following methods:

- **Physical exams** are used to gather information about the cancer. The clinician examines the body by looking, feeling, and listening for anything unusual. The physical exam may show the location and size of the tumor(s) and the spread of the cancer to the lymph nodes and/or to other tissues and organs.
• Imaging studies produce pictures of areas inside the body. These studies are important tools in determining stage. Procedures such as X-rays, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and positron emission tomography (PET) scans can show the location of the cancer, the size of the tumor, and whether the cancer has spread.

• Laboratory tests are studies of blood, urine, other fluids, and tissues taken from the body. For example, tests for liver function and tumor markers (substances sometimes found in increased amounts if cancer is present) can provide information about the cancer.

• Pathology reports may include information about the size of the tumor, the growth of the tumor into other tissues and organs, the type of cancer cells, and the grade of the tumor. A biopsy may be performed to provide information for the pathology report. Cytology reports also describe findings from the examination of cells in body fluids.

• Surgical reports tell what is found during surgery. These reports describe the size and appearance of the tumor and often include observations about lymph nodes and nearby organs.

**Common Tumor Types**

There are 120 different types of brain tumors, and they differ in location, severity, shape, size, and prognosis. The following table provides an overview of the most common types of tumors.\(^{5,17,18}\)
## Acoustic Neuroma

An acoustic neuroma, known as a vestibular schwannoma, is a benign (non-cancerous) growth that arises on the eighth cranial nerve leading from the brain to the inner ear. This nerve has two distinct parts, one part associated with transmitting sound and the other with sending balance information to the brain from the inner ear. The eighth nerve, along with the facial or seventh cranial nerve, lie adjacent to each other as they pass through a bony canal called the internal auditory canal. This canal is approximately 2 cm (0.8 inches) long and it is generally here that acoustic neuromas originate from the sheath surrounding the eighth nerve. The seventh or facial nerve provides motion to the muscles of facial expression.

Acoustic neuromas usually grow slowly over a period of years. They expand in size at their site of origin and when large can displace normal brain tissue. The brain is not invaded by the tumor, but the tumor pushes the brain as it enlarges. The slowly enlarging tumor protrudes from the internal auditory canal into an area behind the temporal bone called the cerebellopontine angle. The tumor now assumes a pear shape with the small end in the internal auditory canal. Larger tumors can press on another nerve in the area (the trigeminal nerve), which is the nerve of facial sensation.

Vital functions to sustain life can be threatened when large tumors cause severe pressure on the brainstem and cerebellum. Tumors are typically described as small (less than 1.5 cm), medium (1.5 cm to 2.5 cm) or large (more than 2.5 cm).

There is a growing body of evidence that sporadic defects in tumor suppressor genes may give rise to these tumors in some individuals. Other studies have hinted at exposure to loud noise on a consistent basis. One study has shown a relationship of acoustic neuromas to prior exposure to head and neck radiation, and a concomitant history of having had a parathyroid adenoma (tumor found in proximity to the thyroid gland controlling calcium metabolism). There are even controversies on hand-held cell phones.

It remains to be seen whether or not the radiofrequency radiation has anything to do with acoustic neuroma formation. To date, no environmental factor (such as cell phones and diet) has been scientifically proven to cause these tumors.
NF2, a genetic disorder, occurs with a frequency of 1 in 30,000 to 1 in 50,000 births. The hallmark of this disorder is bilateral acoustic neuromas (an acoustic neuroma on both sides). This creates the perplexing problem of the possibility of complete deafness if the tumors are left to grow unchecked. Preventing or treating the complete deafness that may befall individuals with NF2 requires complex decision-making.

The trend at most academic U.S. medical centers is to recommend treatment for the smallest tumor, which has the best chance of preserving hearing. If this goal is successful, then treatment can also be offered for the remaining tumor. If hearing is not preserved at the initial treatment, then usually the second tumor, in the only-hearing ear, is just observed. If it shows continued growth and becomes life threatening, or if the hearing is lost over time as the tumor grows, then treatment is undertaken. This strategy has the highest chance of preserving hearing for the longest time possible.

There are now several options to try to rehabilitate deafness in NF2 patients. Implanting the hearing part of the brainstem (Auditory Brainstem Implant) can help restore some sound perception to these patients. Also cochlear implants can be used if the cochlear nerve is preserved following surgery. Radiosurgery may be an option although stereotactic radiosurgery may not have the effect on the NF2 patient as in patients with unilateral sporadic tumors.

There are some centers using radiation therapy for NF2 with mixed results. The risk of malignant transformation after radiation is higher in this group. Recent studies have shown that these individuals may have more tumors that are resistant to radiation, due to the cell type. These cases should be handled in centers with very experienced skull base teams.

**Astrocytoma**

Astrocytomas are tumors that arise from astrocytes—star-shaped cells that make up the “glue-like” or supportive tissue of the brain. These tumors are “graded” on a scale from I to IV based on how normal or abnormal the cells look. There are low-grade astrocytomas and high-grade astrocytomas. Low-grade astrocytomas are usually localized and grow slowly. High-grade astrocytomas grow at a rapid pace and require a different course of treatment. Most astrocytoma tumors in children are low grade. In adults, the majority are high grade.
Below are descriptions of the various grades of these tumors:

- **Pilocytic Astrocytoma** (also called Juvenile Pilocytic Astrocytoma) — These grade I astrocytomas typically stay in the area where they started and do not spread. They are considered the “most benign” (noncancerous) of all the astrocytomas.

  Two other, less well-known grade I astrocytomas are cerebellar astrocytoma and desmoplastic infantile astrocytoma.

- **Diffuse Astrocytoma** (also called Low-Grade or Astrocytoma Grade II) Types: Fibrillary, Gemistocytic, Protoplasmic Astrocytoma — These grade II astrocytomas tend to invade surrounding tissue and grow at a relatively slow pace.

- **Anaplastic Astrocytoma** — An anaplastic astrocytoma is a grade III tumor. These rare tumors require more aggressive treatment than benign pilocytic astrocytoma.

- **Astrocytoma Grade IV** (also called Glioblastoma, previously named “Glioblastoma Multiforme,” “Grade IV Glioblastoma,” and “GBM”) — There are two types of astrocytoma grade IV — primary, or de novo, and secondary. Primary tumors are very aggressive and the most common form of astrocytoma grade IV.

  The secondary tumors are those that originate as a lower-grade tumor and evolve into a grade IV tumor.

- **Subependymal Giant Cell Astrocytoma** — Subependymal giant cell astrocytomas are ventricular tumors associated with tuberous sclerosis.

**Location**

Astrocytomas can appear in various parts of the brain and nervous system, including the cerebellum, the cerebrum, the central areas of the brain, the brainstem, and the spinal cord.
**Description**

- **Pilocytic Astrocytomas** generally form sacs of fluid (cysts), or may be enclosed within a cyst. Although they are usually slow growing, these tumors can become very large.

- **Diffuse Astrocytomas** tend to contain microcysts and mucous-like fluid. They are grouped by the appearance and behavior of the cells for which they are named.

- **Anaplastic Astrocytomas** tend to have tentacle-like projections that grow into surrounding tissue, making them difficult to completely remove during surgery.

- **Astrocytoma Grade IV** (glioblastoma) may contain cystic material, calcium deposits, blood vessels, and/or a mixed grade of cells.

**Symptoms**

Headaches, seizures, memory loss, and changes in behavior are the most common early symptoms of astrocytoma. Other symptoms may occur depending on the size and location of the tumor.

**Incidence**

Pilocytic astrocytomas are typically seen in children and young adults. The other types tend to occur in males more often than females, and most often in people age 45 and over.

**Cause**

Like many tumor types, the exact cause of astrocytoma is not known.

**Treatment**

Treatment options depend on the type, size, and location of the tumor, if and how far it has spread, previous treatment received, and the patient’s overall health. Treatment methods for the various types of astrocytomas are briefly explained below.

- **Pilocytic Astrocytoma**: These tumors are often removed by surgery alone. In adults and older children, radiation may follow surgery if the tumor cannot be completely removed. Or, the patient may be watched carefully for signs that the tumor has returned.
| **Chondrosarcoma** | Chondroma is a rare, benign tumor that tends to arise at the base of the skull, especially in the area near the pituitary gland. These tumors are generally very slow growing and may be present for a long time before causing any symptoms. The malignant (cancerous) form of chondroma is chondrosarcoma.

There are several different types of chondrosarcoma, including conventional, clear cell, mesenchymal, and dedifferentiated. Conventional chondrosarcoma are further subdivided into grade I, grade II, and grade III.

**Location**
Chondromas are usually attached to the dura mater, which is the outermost layer of the meninges (the covering of the brain). Chondrosarcomas are most commonly found in the sphenoid bone—the bony ridge running along the back of the eyes. They are also often found near the clivus, a bony area at the base of the skull.

**Description**
These tumors are made up of cartilage or cartilage-like cells. Chondromas can grow to a large size, and may occur as a single or as multiple tumors. |

• **Diffuse Astrocytoma:** If the tumor is accessible and can be completely removed, the only additional care required is follow-up scans. In adults and older children, radiation may be suggested in addition to surgery. Radiation may also be used to treat an unremovable low-grade astrocytoma. The role of chemotherapy in treating these tumors is being investigated.

• **Anaplastic Astrocytoma:** The first step in treatment of anaplastic astrocytoma is surgery. Radiation is then used to treat the remaining tumor. Chemotherapy may be recommended immediately after radiation or when and if the tumor recurs.

• **Astrocytoma Grade IV:** The first treatment step is surgery to remove as much tumor as possible. Surgery is almost always followed by radiation. Chemotherapy is often given at the same time as radiation and may be used to delay radiation in young children.
### Symptoms
Headaches and vision and hearing disturbances are among the most common symptoms of these tumors.

### Incidence
Chondroma and chondrosarcoma are very rare. Chondrosarcoma is more common in older adult males.

### Cause
Like many tumor types, the exact causes of chondroma and chondrosarcoma are not known.

### Treatment
Surgery might be the only treatment required for chondroma. Standard treatment for chondrosarcoma is surgical removal, which may be followed by radiation therapy.

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### CNS Lymphoma
Lymphoma is a cancer that arises from the cells of the lymphatic system. In the brain, this type of cancer is called Primary CNS Lymphoma (PCNSL).

#### Location
Lymphoma occurs most often in the cerebral hemisphere, but may also involve the cerebrospinal fluid, the eyes, or the spinal cord. In addition, some people may have evidence of lymphoma elsewhere in the body. It is not unusual for this tumor to be found in multiple areas of the cerebral hemisphere, as it can spread throughout the central nervous system.

#### Description
Lymphoma is a cancer that starts in the cells of the lymphatic system.

#### Symptoms
The most common symptoms of CNS lymphoma include personality and behavioral changes, confusion, symptoms associated with increased pressure within the brain (e.g., headache, nausea, vomiting, drowsiness), weakness on one side of the body, and seizures. Problems with eyesight may also occur.

#### Incidence
This disease affects people with healthy immune systems, as well as those whose immune systems are not functioning properly, for example organ transplant recipients, patients with autoimmune disease or people who are HIV positive.
The incidence of CNS lymphoma has been increasing over the past 20 years; it now represents between 2% and 3% of all primary brain tumors.

**Cause**
CNS lymphoma usually originates from B-lymphocytes and is classified as non-Hodgkin’s (meaning it is different from Hodgkin’s disease).

**Treatment**
Once a diagnosis is confirmed, steroids are used to control brain swelling; this may result in the immediate disappearance of the tumor on a later scan. Chemotherapy and radiation, or chemotherapy alone may then be used the primary treatment. Surgery is not usually an option because lymphomas tend to occur deep within the brain and the risk of surgical complications is too high.

**Craniopharyngioma**
A craniopharyngioma is a benign (noncancerous) tumor arising from small nests of cells near the pituitary stalk. Adamantinomatous (ordinary) craniopharyngioma occurs in children and tends to be less solid than papillary craniopharyngioma. Papillary craniopharyngioma occurs in adults and is a more solid tumor.

**Location**
Craniopharyngiomas occur in the sellar region of the brain, near the pituitary gland. They often involve the third ventricle, optic nerve, and pituitary gland.

**Description**
Craniopharyngiomas are localized tumors and become large before they are diagnosed. How malignant they are and how quickly they are likely to spread are unknown.

**Symptoms**
Increased pressure within the brain causes many of the symptoms associated with this tumor. Other symptoms result from pressure on the optic tract and pituitary gland. Obesity, delayed development, impaired vision, and a swollen optic nerve are common.

**Incidence**
Craniopharyngiomas represent 2-5% of all primary brain tumors, and 5-10% of all childhood brain tumors. This tumor tends to be found in two age groups—patients up to age 14 and patients over age 45. They are more common in African-American patients.
### Cause
Like many tumor types, the exact cause of craniopharyngioma is not known.

### Treatment
Surgery to remove the tumor is usually the first step in treatment. If hydrocephalus (excess water in the brain) is present, a shunt (drainage system) may be placed during surgery. The shunt will help remove excess cerebrospinal fluid from the brain and ease the pressure.

Radiation therapy may be suggested if all visible tumors cannot be removed. In children younger than 3, radiation may be delayed by the use of surgery or hormone therapies.

This tumor tends to be located close to the pituitary gland, which controls hormone balance in the body. To ensure the best outcome, an endocrinologist (a doctor trained to treat hormone imbalances) may work with the treatment team to develop a long-term care plan.

### Ependymoma
Ependymomas arise from the ependymal cells that line the ventricles of the brain and the center of the spinal cord.

These tumors are divided into four major types:

- **Subependymomas (grade I):** Typically slow-growing tumors.

- **Myxopapillary ependymomas (grade I):** Typically slow-growing tumors.

- **Ependymomas (grade II):** The most common of the ependymal tumors. This type can be further divided into the following subtypes, including cellular ependymomas, papillary ependymomas, clear cell ependymomas, and tancytic ependymomas.

- **Anaplastic ependymomas (grade III):** Typically faster-growing tumors.

### Location
The various types of ependymomas appear in different locations within the brain and spinal column. Subependymomas usually appear near a ventricle. Myxopapillary ependymomas tend to occur in the lower part of the spinal column. Ependymomas are usually located along, within, or next to the ventricular system.
Anaplastic ependymomas are most commonly found in the brain in adults and in the lower back part of the skull (posterior fossa) in children. They are rarely found in the spinal cord.

**Description**
Ependymomas are soft, grayish, or red tumors that may contain cysts or mineral calcifications.

**Symptoms**
Symptoms of an ependymoma are related to the location and size of the tumor. In babies, increased head size may be one of the first symptoms. Irritability, sleeplessness, and vomiting may develop as the tumor grows. In older children and adults, nausea, vomiting, and headache are the most common symptoms.

**Incidence**
Ependymomas are relatively rare tumors in adults, accounting for 2-3% of primary brain tumors. However, they are the sixth most common brain tumor in children. About 30% of pediatric ependymomas are diagnosed in children younger than 3 years of age.

**Cause**
Like many tumor types, the exact cause of ependymomas is not known.

**Treatment**
The first step of ependymoma treatment is to remove as much of the tumor as possible. Radiation is usually recommended for older children and adults following surgery, in some cases even if the tumor was completely removed.

The role of chemotherapy in treating newly diagnosed ependymomas is not clear. However, it may be used to treat tumors that have grown back after radiation therapy, or to delay radiation in infants and very young children.

**Gliomas**
“Glioma” is a general term used to describe any tumor that arises from the supportive (“gluey”) tissue of the brain. This tissue, called “glia,” helps to keep the neurons in place and functioning well. There are three types of normal glial cells that can produce tumors. An astrocyte will produce astrocytomas (including glioblastomas), an oligodendrocyte will produce oligodendrogliomas, and ependymomas come from ependymal cells. Tumors that display a mixture of these different cells are called mixed gliomas.
Tumors such as “optic nerve glioma” and “brain stem glioma” are named for their locations, not the tissue type from which they originate.

**Location**
The location of the tumor depends on the type of cells from which it originates.

**Description**
Three types of normal glial cells can produce tumors—astrocytes, oligodendrocytes, and ependymal cells. Tumors that display a mixture of these cells are called mixed gliomas.

- **Astrocytoma**: See section on astrocytomas for more information about astrocytomas, including juvenile pilocytic astrocytoma, low-grade astrocytoma, anaplastic astrocytoma, or glioblastoma.

- **Ependymoma**: See section on ependymomas for more information about ependymoma.

- **Mixed Glioma (also called Oligoastrocytoma)**: These tumors usually contain a high proportion of more than one type of cell, most often astrocytes and oligodendrocytes. Occasionally, ependymal cells are also found. The behavior of a mixed glioma appears to depend on the grade of the tumor. It is less clear whether their behavior is based on that of the most abundant cell type.

- **Oligodendroglioma**: See section on oligodendrogliomas for more information about oligodendroglioma.

- **Optic Glioma**: These tumors may involve any part of the optic pathway, and they have the potential to spread along these pathways. Most of these tumors occur in children under the age of 10. Grade I pilocytic astrocytoma and grade II fibrillary astrocytoma are the most common tumors affecting these structures. Higher-grade tumors may also arise in this location. Twenty percent of children with neurofibromatosis (NF-1) will develop an optic glioma. These gliomas are typically grade I, pilocytic astrocytomas. Children with optic glioma are usually screened for NF-1 for this reason. Adults with NF-1 typically do not develop optic gliomas.
• **Gliomatosis Cerebri:** This is an uncommon brain tumor that features widespread glial tumor cells in the brain. This tumor is different from other gliomas because it is scattered and widespread, typically involving two or more lobes of the brain. It could be considered a "widespread low-grade glioma" because it does not have the malignant features seen in high-grade tumors.

The widespread nature of gliomatosis cerebri causes enlargement of any part of the brain it involves. This may include the cerebral hemispheres, or less often, the cerebellum or brain stem.

**Symptoms**
Symptoms vary based on tumor type:

- **Astrocytoma:** See section on astrocytomas for more information about astrocytoma symptoms.

- **Ependymoma:** See section on ependymomas for more information about ependymoma symptoms.

- **Mixed Glioma (also called Oligoastrocytoma):** The initial symptoms, including headache and nausea, usually are the result of increased pressure inside the brain. Vision problems, as well as changes in behavior and personality, are also fairly common in mixed glioma patients.

- **Oligodendroglioma:** See section on oligodendrogliomas to learn more about oligodendroglioma symptoms.

- **Optic Glioma:** These tumors may cause few or no symptoms. Their placement along the optic nerve, however, can cause vision loss (depending on the location of the tumor) or strabismus ("crossed eyes"). Hormonal disturbance might also occur, causing developmental delay(s), early puberty, and other symptoms.

- **Gliomatosis Cerebri:** Symptoms are often nonspecific and can include personality and behavioral changes, memory disturbance, increased intracranial pressure with headache and sometimes seizures.

**Incidence**
The incidence of this tumor varies by type.
Cause
Like many tumor types, the exact cause of glioma is not known.

Treatment
Treatment is based on tumor type:

- **Astrocytoma**: See section on astrocytomas for more information about treatment for astrocytoma.
- **Ependymoma**: See section on ependymomas for more information about treatment for ependymoma.
- **Mixed Glioma (also called Oligoastrocytoma)**: Treatment may include surgery followed by radiation therapy, particularly if the tumor is high-grade. Chemotherapy will also generally be used in high-grade tumors.
- **Oligodendroglioma**: See section on oligodendrogliomas to learn more about treatment for oligodendroglioma.
- **Optic Glioma**: Careful observation may be an option for patients with stable or slow-growing tumors. Surgery might be recommended for a growing tumor that involves only the optic nerve. Radiation might be used for a tumor of the chiasm or other pathways. Local radiation and chemotherapy with radiation therapy are used for recurrent tumors. Patients with primary and/or recurrent tumors may wish to take part in a clinical trial.
- **Gliomatosis Cerebri**: Treatment is less well defined because this tumor is so rare. Surgical removal is generally not attempted, because it is so widespread. Radiation and chemotherapy may be considered.

Medulloblastoma
Medulloblastoma is a fast-growing, high-grade tumor. The various types of medulloblastoma include:
- classic medulloblastoma
- desmoplastic nodular medulloblastoma
- large-cell or anaplastic medulloblastoma
- medulloblastoma with neuroblastic or neuronal differentiation
- medulloblastoma with glial differentiation
• medulloblastoma
• melanotic medulloblastoma

Each type of medulloblastoma is described in our Medulloblastoma publication, which can be downloaded at the bottom of the page.

**Location**
Medulloblastoma is always located in the cerebellum—the lower, rear portion of the brain. It is unusual for medulloblastomas to spread outside the brain and spinal cord.

**Description**
Medulloblastoma is a fast-growing, high-grade tumor. It is the most common of the embryonal tumors—tumors that arise from “embryonal” or “immature” cells at the earliest stage of their development.

**Symptoms**
The most common symptoms of medulloblastoma include behavioral changes, changes in appetite, symptoms of increased pressure on the brain (e.g., headache, nausea, vomiting, and drowsiness, as well as problems with coordination). Unusual eye movements may also occur.

**Incidence**
Medulloblastoma is relatively rare, accounting for less than 2% of all primary brain tumors and 18% of all pediatric brain tumors. More than 70% of all pediatric medulloblastomas are diagnosed in children under age 10. Very few occur in children up to age 1.

Medulloblastoma in adults is less common, but it does occur. About one-third of all medulloblastomas diagnosed in the United States are found in adults between the ages of 20-44. The incidence in adults sharply decreases in frequency after age 45, with very few older adults having this tumor. Medulloblastoma occurs more often in men than in women.

**Cause**
Like many tumor types, the exact cause of medulloblastoma is not known. However, scientists are making significant strides in understanding its biology. Changes have been identified in genes and chromosomes (the cell’s DNA blueprints) that may play a role in the development of this tumor. There are also a few rare, genetic health syndromes that are associated with increased risk for developing this tumor.
## Treatment
Treatment consists of surgical removal of as much tumor as possible, radiation, and then chemotherapy (in older children and adults).

New approaches to treatment are currently in development. These new therapies are offered in organized research studies called clinical trials.

## Prognosis
How well a patient responds to treatment is affected by the age they are at the time of diagnosis, the size and extent of the tumor, the amount of mass that can be removed safely, and the level of metastatic disease.

Overall, the Central Brain Tumor Registry of the United States reports about 57%-60% of adults (age 20+) with medulloblastoma are alive at five years following diagnosis, and 44% at 10 years.

It is important to realize these statistics do not reflect the differences in outcome between low risk and high-risk groups (since high risk groups may not do as well), differences in patient characteristics, nor differences in patient responses to treatment. And "10 year survival" means the patients were followed for only 10 years; we do not know how well they did beyond that length of time.

With current therapies, 70% - 80% of children with average-risk medulloblastoma can be expected to be alive and free of disease five years from diagnosis. Even in those children with high-risk disease, effective therapy is possible and results in long-term disease control in as high as 60% - 65% of patients. Outcome for infants is poorer, but for those infants with localized disease at the time of diagnosis, survival rates in the 30% - 50% range are being seen.

## Meningioma
Meningiomas are often benign tumors arising from the coverings of the brain and spinal cord. They represent about one-third of all primary brain tumors and occur most frequently in middle-aged women.

## Location
Although meningiomas are referred to as brain tumors, they do not grow from brain tissue. They arise from the meninges, which are three thin layers of tissue covering the brain and spinal cord. These tumors are most often found near the top and the outer curve of the brain. Tumors may also form at the base of the skull.
Description
Meningiomas usually grow inward, causing pressure on the brain or spinal cord. They also can grow outward toward the skull, causing it to thicken. Most meningiomas are noncancerous, slow-growing tumors. Some contain sacs of fluid (cysts), mineral deposits (calcifications), or tightly packed bunches of blood vessels.

Symptoms
Meningiomas usually grow slowly, and may reach a large size before interfering with the normal functions of the brain. The resulting symptoms depend on the location of the tumor within the brain. Headache and weakness in an arm or leg are the most common symptoms. However, seizures, personality changes, and/or visual problems may also occur.

Incidence
Meningiomas account for about 36.1% of all primary brain tumors, which are tumors that form in the brain or its coverings. They are most likely to be found in adults older than 60; the incidence appears to increase with age. Rarely are meningiomas found in children. They occur about twice as often in women as in men.

Cause
Researchers are studying meningiomas carefully to find out what causes them. Between 40% and 80% of meningiomas contain an abnormal chromosome 22. The cause of this abnormality is not known. We do know, however, that this chromosome is normally involved in suppressing tumor growth. Meningiomas also frequently have extra copies of the platelet-derived growth factor (PDGFR) and epidermal growth factor receptors (EGFR), which may contribute to the growth of these tumors.

Previous radiation to the head, a history of breast cancer, or neurofibromatosis type 2 may be risk factors for developing meningioma. Multiple meningiomas occur in 5% to 15% of patients, particularly those with neurofibromatosis type 2.

Some meningiomas have receptors that interact with hormones, including progesterone, androgen, and less commonly, estrogen. Although the exact role of hormones in the growth of meningiomas has not been determined, researchers have observed that meningiomas occasionally grow faster during pregnancy.
### Treatment
Surgery and radiation are the most common forms of treatment for meningioma. Surgery is the primary treatment for meningiomas, although some tumors may not be removed this way. Radiation therapy may be used to tumors that cannot be removed with surgery, tumors that are not completely removed in surgery, malignant/anaplastic tumors, or recurrent tumors.

Careful observation is sometimes the best course of action for patients with meningioma. Scans are performed at regular intervals during this time, and any new or unusual symptoms should be reported to the doctor right away.

<table>
<thead>
<tr>
<th>Metastatic Brain Tumors</th>
<th>A metastatic, or secondary, brain tumor is formed by cancer cells from a primary cancer elsewhere in the body that have spread to the brain.</th>
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</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>The locations of metastatic brain tumors varies.</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Cancers that frequently spread to the brain include lung cancer, breast cancer, melanoma (a malignant form of skin cancer), colon cancer, and kidney cancer.</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Symptoms depend on the size and location of the tumor.</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>People are surviving cancer longer than ever before. As a result, it is likely that the incidence of metastatic brain tumors will rise in the years to come.</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
<td>Metastatic brain tumors are caused by cancer that has spread from another part of the body.</td>
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<thead>
<tr>
<th>Oligondendroglioma</th>
<th>Oligodendrogliomas come from oligodendrocytes, one of the types of cells that make up the supportive, or glial, tissue of the brain. They can be low-grade (grade II) or high-grade (grade III, or anaplastic).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>These tumors can be found anywhere within the cerebral hemisphere of the brain, although the frontal and temporal lobes are the most common locations.</td>
</tr>
</tbody>
</table>
**Description**
Oligodendrogliomas are generally soft, grayish-pink tumors. They often contain mineral deposits (called calcifications), areas of hemorrhage, and/or cysts. Under the microscope, these tumor cells appear to have “short arms,” or a fried-egg shape.

Sometimes oligodendrogliomas are mixed with other cell types. These tumors may be graded using an “A to D” system, which is based on microscopic features of the individual tumor cells. The grade indicates how quickly the tumor cells reproduce and how aggressive the tumor is.

**Symptoms**
Because of their generally slow growth, oligodendrogliomas are often present for years before they are diagnosed. The most common symptoms are seizures, headaches, and personality changes. Other symptoms vary by location and size of the tumor.

Tumors of the frontal lobe may cause weakness on one side of the body, personality or behavior changes, and difficulty with short-term memory. Temporal lobe tumors are usually “silent,” causing few symptoms other than perhaps seizures or language problems.

**Incidence**
About 4% of primary brain tumors are oligodendrogliomas, representing about 10-15% of the gliomas. Only 6% of these tumors are found in infants and children. Most oligodendrogliomas occur in adults ages 50-60, and are found in men more often than women.

**Cause**
Like many tumor types, the exact cause of oligodendroglialoma is not known. However, scientists have identified chromosomal abnormalities, which may play a role in the development of these tumors.

**Treatment**
If the tumor is accessible, standard treatment for oligodendroglialoma is surgical removal of as much of the tumor tissue as possible. Biopsy is typically performed on tumors that are not accessible to confirm the diagnosis and determine the grade of tumor. Recurrent low-grade oligodendroglialomas can be treated with surgery, radiation therapy (if not given initially), and chemotherapy.
| Grade II Oligodendrogliomas: Close follow-up with regular MRI scans is recommended following the successful removal of low-grade oligodendrogliomas. If some of the tumor remains (also called “residual” tumor), radiation treatment is recommended following surgery. The best timing for radiation therapy (i.e., immediately or when the tumor appears to be growing again), is currently being studied in clinical trials.

| Grade III Oligodendrogliomas: Anaplastic oligodendroglioma is typically treated with a combination of radiation therapy and chemotherapy. Recurrent anaplastic oligodendroglioma may be treated with surgery and/or chemotherapy.

Low-grade oligodendrogliomas tend to be slow growing tumors. Anaplastic oligodendrogliomas are more aggressive tumors, which grow more quickly. Oligoastrocytoma growth generally depends on the percent of astrocytoma in the tumor, as astrocytomas tend to grow more rapidly than oligodendrogliomas. Scientists continue to study the impact of natural biologic differences amongst all of these tumors and the role of various treatment plans.

| Pituitary Tumors | The pituitary gland is involved in the production of several essential hormones. Tumors arising from the pituitary gland itself are called adenomas when they originate from glandular tissue, or carcinomas if they originate from the lining of the pituitary gland. Pituitary adenomas are benign, slow-growing masses that represent about 10% of primary brain tumors. Pituitary carcinoma is the rare malignant form of pituitary adenoma.

**Location**
Most pituitary adenomas grow in the front two-thirds of the pituitary gland. These tumors are classified as "secreting" and "non-secreting." A “secreting tumor” produces excessive amounts of hormones. Most pituitary tumors fall into this category; they are further classified by the type(s) of hormone they produce.

**Description**
Pituitary adenomas are benign, slow-growing tumors. Pituitary carcinoma is the rare malignant form of pituitary adenoma. It is diagnosed only when there is proven spread (metastases) inside or outside the nervous system.
**Symptoms**
Symptoms are caused when the growing tumor pushes on surrounding structures. This pressure can result in headache, visual impairment, and behavioral changes.

Tumors can also either produce excessive amounts of hormone or limit how much hormone is produced. The hormones most commonly affected include: growth hormone (regulates body height and structure), prolactin (controls lactation, or milk production), sex hormones (control the menstrual cycle and other sexual functions), thyroid gland hormones (control the thyroid gland), adrenal gland hormones, and vasopressin (a hormone involved in water and electrolyte balance).

Symptoms of pituitary adenoma and pituitary carcinoma are identical.

**Incidence**
Pituitary tumors account for 9% to 12% of all primary brain tumors. They can occur at any age, but they are more common in older people. Women are more affected than men, particularly during the childbearing years.

**Cause**
Like many tumor types, the exact cause of pituitary tumors is not known.

**Treatment**
Because the pituitary gland impacts so many of the body’s functions, a multi-disciplinary approach to tumor treatment is needed to ensure the best possible outcome.

Treatment of pituitary adenoma or carcinoma usually includes surgery to remove it. In some cases, however drug therapy may be used to reduce the size of the tumor without surgery. Radiation can be used to treat a persistent and/or recurring tumor that does not respond to medication, as long as the tumor is secreting hormone.

For tumors that do not secrete hormone, radiation may be used following partial removal, or if the tumor was invasive. Replacement hormone therapy is often prescribed following surgery and/or radiation.

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**PNET**
PNET (primitive neuroectodermal tumor) is a name used for tumors, which appear identical under the microscope to medulloblastoma, but occur primarily in the cerebrum.
<table>
<thead>
<tr>
<th><strong>Schwannoma</strong></th>
<th>Schwannoma is a benign tumor of the nerve of hearing (the 8th cranial nerve, also known as the acoustic or vestibulocochlear nerve).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Schwannomas are usually located in the angle between the cerebellum and the pons, in the back of the skull (the posterior fossa).</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Schwannomas are usually very slow growing.</td>
</tr>
</tbody>
</table>
Symptoms
Common symptoms of Schwannoma are one-sided hearing loss and buzzing or ringing in the ear. Dizziness may also occur, although it is less common. If the tumor affects the facial nerve (the 7th cranial nerve, which is located next to the 8th cranial nerve), facial paralysis may occur. Other symptoms include difficulty in swallowing, impaired eye movement, taste disturbances, and unsteadiness.

Incidence
Schwannomas account for about 8% of all primary brain tumors. They typically occur in middle-aged adults, and females are twice as likely as males to have this tumor.

Cause
Like many tumor types, the exact cause of Schwannoma is not known. However, it is believed to occur when there is a defect in a gene that normally prevents tumors from forming.

Treatment
Total removal using microsurgical techniques is often possible. Stereotactic radiosurgery may be used as an alternative to surgery in some patients.

Diagnostic Imaging And Cancer Assessment
In many cases, patients will require diagnostic imaging to assist with assessment and diagnosis. The specific procedure used will depend on the location of the nodes being assessed, as well as the primary location of the cancer. In some instances, patients will require more than one type of imaging to accurately assess the scope of the cancer.
Computed Tomography (CT) Scan

Computed tomography (CT scan) is a diagnostic imaging procedure that produces horizontal, or axial, images of the body. These images are often called “slices.” The CT scan uses a combination of X-Ray imaging and computer technology to obtain the images in a noninvasive format.²⁰ A CT scan is an important diagnostic tool as it is able to provide detailed images of different parts of the body. It is especially useful in obtaining images of the bones, muscles, fat and organs.²¹

Computed tomography scans are used more frequently than standard X-Rays because the images are more detailed. Standard X-Rays use a single beam of energy that is aimed at the specific body part being analyzed. The image is captured on a plate, which is placed behind the body, once the beam of light passes through the various body parts (skin, bone, muscle, and tissue).

An X-Ray is limited in its ability to provide detailed imaging, as the X-Ray cannot capture images of internal organs and other structures of the body. Therefore, a CT scan is often the primary assessment used. A CT scan uses a moving X-Ray beam to capture the images. The beam circles around the body, thereby capturing a number of different views of the same body part. The information is transmitted to a computer, which then interprets the data and creates a two dimensional form. The form is displayed on a monitor, which is then reviewed by the radiologist.²² CT scans are conducted in two ways, as explained below.²³
• Contrast

Patients ingest a substance orally, or receive an injection intravenously. The contrast solution enables the radiologist to view the specific body part or region more clearly.

• Non-Contrast

The CT scan is conducted without the use of any solution.

**Magnetic Resonance Imaging**

Magnetic Resonance Imaging (MRI) is a radiologic scan that produces images of various body structures using a combination of magnetism, radio waves and computer technology. The MRI is conducted using a large circular magnet that surrounds a scanner tube. Images are obtained by placing the patient on a movable surface and inserting the patient into the magnetic tube. Once the patient is in the tube, a strong magnetic field is created. This magnetic field aligns the protons of the hydrogen atoms. Once the hydrogen atoms are aligned, they are exposed to a beam of radio waves. The radio waves impact the protons within the body, causing them to spin, thereby producing a faint signal, which is easily detected by the MRI receiver. The information obtained by the scanner is sent to a computer, where it is processed to produce an image.

An MRI utilizes high-resolution technology, which allows it to produce highly detailed images that will show changes in many of the structures in the body. In some instances, additional agents will be used to enhance the accuracy of the images. It is most common to use
contrast agents such as gadolinium.\textsuperscript{21} Due to the MRI’s high level of sensitivity, it is able to detect many abnormalities that are undetectable using other methods.

While an MRI and CT scan both use the slicing technique for obtaining images, the process is different for each. The MRI uses a magnetic field while the CT scan uses X-Rays.\textsuperscript{26} As a result, the MRI provides more detailed images than a CT scan and is able to detect damage that is as small as 1 – 2 mm. A CT scan cannot detect damage this small.\textsuperscript{24} MRI is used to assess cancer in the CNS as it provides detailed images of areas that other diagnostic imaging technology cannot obtain.

**Positron Emission Tomography**

Positron Emission Tomography (PET) is a type of nuclear medicine imaging that uses a small amount of radioactive substance, or radiotracer, to diagnose and determine the severity of cancer in the CNS.\textsuperscript{27} A PET scan measures important body functions, such as blood flow, oxygen use, and glucose metabolism, to help clinicians evaluate how well organs and tissues are functioning. With this procedure, the radioactive substance is injected in the patient’s vein. After approximately two hours, the patient will be scanned to identify the presence of cancer. The radioactive emissions from the radiotracer will accumulate in the area being examined, and will be able to be detected by an imaging device that can produce images and provide molecular information.\textsuperscript{23}
In many instances, PET scanning will be combined with CT scans or MRIs to create superimposed images that provide special views of the suspected cancer site. These image fusions, or co-registrations, allow for exam correlation and more accurate diagnoses. Combining PET and CT scans has proven to be especially useful in revealing the presence and severity of cancer. This combined procedure enables physicians to detect cancer, evaluate the extent of the disease, select the most appropriate treatment, determine if therapy is working, and detect the presence of recurring tumors.²⁸

The following is a description of the PET/CT scan procedure.²⁹

Before a PET/CT scan, the patient receives an intravenous injection of radioactive glucose. Many cancer cells are highly metabolic and rapidly synthesize the radioactive glucose. Information regarding the location of abnormal levels of radioactive glucose obtained from the whole-body PET/CT scan helps physicians effectively pinpoint the source of cancer and detect whether cancer is isolated to one specific area or has spread to other organs.

From this information physicians can plan an effective treatment strategy. Treatment options include surgery, radiation therapy, systemic therapy, or a combination therapy where one or more of these options are combined.

During the course of treatment, the information from the PET/CT scan allows physicians to monitor the effectiveness of cancer therapies and provides physicians with the opportunity to change the treatment strategy if it is not working, avoiding the cost and discomfort of ineffective therapeutic procedures.

After completing the treatment regimen, a follow-up whole-body PET/CT scan can provide information to assess if the treatment was successful and if areas that were previously abnormally metabolically active have responded. Often, scar
tissue at the site of surgical resection or radiation treatment may appear as an abnormality on the CT scan. The PET portion of the PET/CT scan can detect residual disease within the scar tissue and indicate if the treatment was successful or if the tumor has returned.

PET/CT scans provide information to help physicians perform the following:  
• Locate the site of the cancer  
• Determine the size of the tumor  
• Differentiate benign from malignant growths  
• Discover if the cancer has spread  
• Select treatments that are likely to be appropriate  
• Monitor the success of therapy  
• Detect any recurrent tumors

Benefits

• Nuclear medicine examinations provide unique information — including details on both function and anatomic structure of the body that is often unattainable using other imaging procedures.  
• For many diseases, nuclear medicine scans yield the most useful information needed to make a diagnosis or to determine appropriate treatment, if any.  
• Nuclear medicine is less expensive and may yield more precise information than exploratory surgery.  
• By identifying changes in the body at the cellular level, PET imaging may detect the early onset of disease before it is evident on other imaging tests such as CT or MRI.
The benefits of a combined PET/CT scanner include:\textsuperscript{23}

- Greater detail with a higher level of accuracy; because both scans are performed at one time without the patient having to change positions, there is less room for error.
- Greater convenience for the patient who undergoes two exams (CT & PET) at one sitting, rather than at two different times.

\textit{Risks}\textsuperscript{29}

- Because the doses of radiotracer administered are small, diagnostic nuclear medicine procedures result in relatively low radiation exposure to the patient, acceptable for diagnostic exams. Thus, the radiation risk is very low compared with the potential benefits.
- Nuclear medicine diagnostic procedures have been used for more than five decades, and there are no known long-term adverse effects from such low-dose exposure.
- The risks of the treatment are always weighed against the potential benefits for nuclear medicine therapeutic procedures. You will be informed of all significant risks prior to the treatment and have an opportunity to ask questions.
- Allergic reactions to radiopharmaceuticals may occur but are extremely rare and are usually mild. Nevertheless, you should inform the nuclear medicine personnel of any allergies you may have or other problems that may have occurred during a previous nuclear medicine exam.
- Injection of the radiotracer may cause slight pain and redness, which should rapidly resolve.
• Women should always inform their physician or radiology technologist if there is any possibility that they are pregnant or if they are breastfeeding.

*Limitations of Positron Emission Tomography – Computed Tomography (PET/CT)*

• Nuclear medicine procedures can be time consuming. It can take several hours to days for the radiotracer to accumulate in the body part of interest and imaging may take up to several hours to perform, though in some cases, newer equipment is available that can substantially shorten the procedure time.

• The resolution of structures of the body with nuclear medicine may not be as high as with other imaging techniques, such as CT or MRI. However, nuclear medicine scans are more sensitive than other techniques for a variety of indications, and the functional information gained from nuclear medicine exams is often unobtainable by other imaging techniques.

• Test results of diabetic patients or patients who have eaten within a few hours prior to the examination can be adversely affected because of altered blood sugar or blood insulin levels.

• Because the radioactive substance decays quickly and is effective for only a short period of time, it is important for the patient to be on time for the appointment and to receive the radioactive material at the scheduled time. Thus, late arrival for an appointment may require rescheduling the procedure for another day.
• A person who is very obese may not fit into the opening of a conventional PET/CT unit.

**Brain Tumor Surgery**

Surgery usually is the first step in treating most benign and many malignant tumors. Although a second opinion is not always necessary, many patients seek one before proceeding with surgery.

Surgery is the initial treatment for most benign and many malignant tumors. It is often the preferred treatment when a tumor can be removed without any unnecessary risk of neurological damage. Surgery may be recommended to do the following.\(^{31,32}\)

• Provide a tumor sample to establish an accurate diagnosis.
• Remove as much tumor as possible, either to relieve symptoms caused by the tumor itself or to reduce the amount of tumor to be treated with radiation or chemotherapy.
• Enable direct access for chemotherapy, radiation implants, or genetic treatment of malignant tumors.
• Relieve seizures (due to a brain tumor) that are hard to control.

The most common types of surgery for brain tumors are listed below. It is important to note that all of these procedures are performed on patients who are either asleep or heavily sedated. In addition, the brain does not “feel” pain, and all of the surrounding tissues (i.e., the scalp) are numbed prior to surgery.
• **Biopsy:** The surgical removal of a sample of tumor tissue.

• **Craniotomy:** The surgical removal of a portion of the skull. Doing so allows the neurosurgeon to find the tumor and remove as much of it as possible. The piece of skull that was removed is replaced following surgery.

• **Craniectomy:** Very similar to a craniotomy. The main difference is that, in this procedure, the portion of the skull that was removed to allow access to the brain is not replaced.

• **Debulking:** The surgical reduction of the size of the tumor.

• **Partial Removal:** The surgical removal of only part of the tumor (due to risk of neurological damage).

• **Complete Removal:** The surgical removal of the entire tumor. The surgeon often can tell if regrowth is likely based on the type of tumor.

• **Shunt:** The insertion of a drainage system designed to move excess fluid from the brain to another part of the body.

• **Ommaya Reservoir:** The insertion of a small container under the scalp, which is attached to a tube. This container can be used to:
  - Deliver chemotherapy treatment to the brain and the surrounding cerebrospinal fluid (CSF).
  - Remove CSF to detect the presence of normal cells.
  - Remove cystic fluid without the need for surgery.

• **Skull Base Surgery:** Refers both to the location of a tumor as well as a specialized technique used to remove a tumor in that area.

• **Transsphenoidal Surgery:** An approach often used to operate on pituitary adenomas and craniopharyngiomas.
• **Laser Interstitial Thermal Therapy (LITT):** Laser Interstitial Thermal Therapy (LITT) is a minimally invasive means of ablating (cooking) tissue with heat. Evidence to date supports that LITT is an effective and safe technique of ablating not only deep and poorly accessible tumors by conventional surgical techniques, but also can be considered as a minimally invasive option for new or recurrent primary and metastatic tumors nearly anywhere in the brain, as well as metastasis that have failed stereotactic radiosurgery either due to tumor progression or development of focal radiation necrosis. LITT is usually performed under a general anesthetic through small (typically 1/4 inch) twist drill holes through the skull using real-time magnetic resonance thermal monitoring with software that can predict ablative as well as safe zones for critical structures. One system allows remote control of probe depth and rotation with the option of a side-firing laser probe, in addition to the common spherical or diffuse pattern of laser energy distribution.

**Types Of Brain Surgery**

This section will provide a comprehensive overview of each of the types of surgeries mentioned above.

**Brain Biopsy**

A brain biopsy is used to diagnose illness. In the procedure, a tumor or a piece of tissue is removed from the brain for examination under a microscope. Types of brain biopsies include:
• needle biopsy
• stereotactic biopsy
• incisional biopsy
• excisional biopsy

Tissue-based pathological diagnosis is the criterion standard in the diagnosis of brain tumors

**Needle Biopsy**

With a needle biopsy, a needle is used to remove a sample of cells from the tumor for examination under a microscope. If cancer is detected, the node may need to be removed.\(^33\)

There are two types of needle biopsy:\(^34\)

• Fine-needle Aspiration Biopsy - This procedure uses a thin needle to remove cells. A fine needle aspiration is the simplest, least invasive test and uses the smallest needle to simply remove cells from the abnormality. This is not always adequate to obtain a diagnosis, depending on the area to be biopsied.

• Core Biopsy - This procedure uses a wide needle to collect cells. A core needle biopsy removes not only cells, but also a small amount of the surrounding tissue. This provides additional information to assist in the identification of the lesion.

**Stereotactic Biopsy**

In situations in which surgical resection is not necessarily indicated but diagnosis of a brain lesion is needed to determine optimal treatment, a
Stereotactic brain biopsy offers a relatively safe and reliable method of obtaining diagnostic tissue. Frameless stereotaxy was derived from older neurosurgical procedures involving attaching a frame to the patient’s head with pins inserted into the skull. After application of the frame, CT or MRI imaging was performed for a highly accurate view of the patient’s anatomy. More recently, frameless stereotaxy, also known as computer interactive surgery or image-guided surgery, has emerged as a valuable alternative to this prior approach for obtaining a brain biopsy. It provides the surgeon with extensive visual information to optimize localization of the patient’s anatomy and assist in surgical planning.

Brain biopsy should be considered when a tissue diagnosis from a suspicious brain lesion is needed to guide treatment and less-invasive methods of diagnosis are exhausted or inappropriate. Generally, brain biopsy is performed in 2 different scenarios. First, and most commonly, it is performed to confirm a suspected brain tumor. A typical situation occurs when diagnostic imaging demonstrates the classic appearance of a primary brain tumor and resection is not felt appropriate, as when the treating team suspects a high-grade glial tumor on the basis of imaging characteristics and does not feel that an aggressive resection is achievable. Tissue diagnosis can confirm the suspected pathology and guide further non-operative treatments.35

The second and fortunately less-common scenario occur when a wide-ranging differential diagnosis has been cast, and a diagnosis remains elusive despite less invasive work-up.
Practically speaking, absolute contraindications to brain biopsy are limited to those lesions felt to be too small to accurately and safely target and to those patients who are coagulopathic or otherwise unable to safely tolerate intravenous sedation or general anesthesia. In patients whose mental status would not permit stereotactic frame placement while under local anesthetic, a general anesthetic could be considered.\(^{36}\)

In any patient considered for stereotactic brain biopsy, weighing the relative merits of biopsy, namely the ability to obtain a tissue diagnosis, against the potential risks is important. In making this decision, all less-invasive opportunities to obtain a diagnosis should be considered. These could potentially include imaging adjuncts such as MR spectroscopy, sampling of spinal fluid by lumbar puncture, or identification of alternative systemic lesions to biopsy, such as an accessible lung lesion in the setting of multiple intracranial metastases.

Exercising caution is important when considering biopsy of lesions that are suspicious for vascular malformations or with highly vascular tumors such as metastatic melanoma. With intraventricular tumors, an endoscopic biopsy can be entertained in favor of a stereotactic biopsy.

There are two types of stereotactic biopsy, which are outlined below.\(^{36-41}\)

<table>
<thead>
<tr>
<th>Framed Stereotactic Brain Biopsy</th>
<th>Frame Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The patient should have adequate intravenous sedation but remain alert enough to participate and maintain an upright-seated posture, which greatly facilitates frame placement. If sedation is performed without monitored anesthesia care, then pulse oximetry and oxygen delivered by nasal cannula should be used.</td>
</tr>
</tbody>
</table>
The authors do not routinely perform any head shave for frame placement, although this is preferred by some surgeons. An approximate entry point should be anticipated to avoid placement of a pin-site or frame post too close to the desired incision.

The frame should be assembled without pins in place, and placed on the patient’s head in the approximate position. The posts can be rotated into a position that optimizes fixation by avoiding excessively medial or lateral location. The pins should be located at or below the greatest circumference of the calvaria. This aids with fixation and places the localizing carbon fiber rods appropriately. Ensuring that the frame is not positioned too close to the bridge of the nose is also important.

The anticipated pin sites can then be wiped with an alcohol or Betadine wipe and injected with local anesthetic. The pins are then placed in the frame posts, with attention to use the appropriate length pins. With the CRW frame, generally the shorter pair of pins are placed in the posterior posts, while the longer pair of pins are placed in the anterior posts. Antibiotic ointment is applied to the pins, and the pins are advanced through the posts to each be flush with the skin surface.

The authors generally prefer to secure one anterior pin and a contralateral posterior pin first, which then allows the frame to be balanced relative to the horizon as desired. Once in satisfactory position, the remaining 2 pins are advanced until each is rigidly secured. As the pins are advanced, giving more local anesthetic as needed may be necessary. Ensuring that the posts exert no pressure on the scalp is important while advancing the pins. Placing 1 or 2 radio-opaque fiducial markers on the scalp near the planned incision can be useful. This can help tailor the incision, and, before the sterile stereotactic frame is attached to the base, it can help with approximating the skin incision and a smaller area of hair can be shaved if desired.

Trajectory Planning

With the frame satisfactorily placed, the patient can then be taken for a localizing CT scan or MRI. Generally, a contrast-enhanced head CT scan is sufficient for identifying a target. With high-grade intrinsic brain tumors, the area of thickest enhancement is conventionally targeted.

A target can also be selected such that slightly deeper or shallower samples could be obtained along the same trajectory. With low-grade gliomas, a T2-weighted MRI may allow for better targeting. The localizing CT scan is fused with the preoperative MRI, which provides adequate accuracy. Advanced planning of an MRI-based trajectory with subsequent fusion to a localizing CT scan reduces overall operative time.
The entry point should be planned to avoid entry into a dural blood vessel, cortical blood vessel, or sulcus. Depending on whether or not future attempts are resection are anticipated, the entry point could be planned to be incorporated into the craniotomy incision. The trajectory should then be reviewed to ensure that the biopsy cannula will avoid unnecessarily traversing pial or ependymal surfaces. Generally, the shortest distance that takes these structures into consideration and avoids eloquent cortex is preferred.

Separate specimens can be obtained from a single trajectory by altering the depth of the biopsy cannula and also by rotating the aperture of the side-cutting biopsy cannula. Although even further sampling heterogeneity may be afforded by planning multiple trajectories, this is reported to increase the risk of postoperative deficits in deeper lesions.

**Biopsy**

Once a trajectory is planned, the stereotactic coordinates should be confirmed and transferred from the planning station into the operating room. Once the patient arrives in the operating room, he or she can be positioned on the operating table and intravenous sedation resumed. The stereotactic frame should be assembled by a skilled operating room nurse or the surgeon. The stereotactic coordinates should be registered onto the frame and verified.

With the planned scalp entry site, a small area of hair can be shaved if desired. The patient can be prepped with caution to avoid the eyes. A custom drape, the Apuzzo Stereotactic Drape (Integra LifeSciences, Plainsboro, NJ) can be useful when using the CRW frame because it has 3 perforations in the drape that exist where the sterile stereotactic ring attaches to the nonsterile patient frame. Once the ring is placed, the trajectory should be verified, and any minor adjustments to the scalp incision can be made.

Local anesthetic is injected into the scalp for patient comfort and hemostasis.

The 2 methods of trephination are twist-drill or bur hole.

Twist-drill offers the advantage of a small punctate skin incision that can be made with a #11 or #15 scalpel and need measure no larger than a standard 2.7-mm diameter twist-drill. This allows for less scalp bleeding, quicker closure, improved cosmesis, and can also facilitate incorporation into a craniotomy if staged tumor resection is anticipated.
In contrast, a bur hole can be made with a high-speed cranial perforator or fluted matchstick bur. The theoretical advantage of making a bur hole is that any dural or cortical blood vessels can be directly cauterized with bipolar cautery. A bur hole requires a larger linear or curvilinear incision. If a twist-drill is made, the drill bit should be guided through the guide tube and reducer in the exact planned trajectory of the biopsy needle. If a bur hole is made, the ring of the stereotactic arc can be temporarily rotated out of the way to improve access.

Once the bur hole is made, the biopsy needle should be advanced down the guide tube to confirm that no bony edges deflect its trajectory. Once the dura is sharply opened, this should again be confirmed. The biopsy needle should be measured to the appropriate depth. The standard distance to the target should be borne in mind depending on the exact configuration of reducers and guide tubes. The authors use a disposable Nashold Biopsy Needle (Integra Radionics, Burlington, MA) and measure the distance from the mid position of the side-cutting port to the depth stop. The biopsy needle has a Luer lock attachment in which a saline-filled syringe can be attached in order to apply slight negative pressure.

The system is flushed with saline, and the side-cutting port is closed. When the hub of the inner cannula of the needle is rotated 180°, the side-cutting port is opened. The port should be flushed and closed and then gradually advanced to the planned depth, with attention to notice any change in resistance as the needle is advanced, which can be an indication that tumor is entered. Once at the planned depth, the side-cutting port is opened by rotating the inner hub 180°, and slight negative pressure is applied by withdrawing on the saline-filled syringe to pull tissue into the needle. The side-cutting port is then closed and the needle withdrawn.

The specimen can be retrieved in a similar manner, by opening the port and flushing saline through to eject the specimen. Additional specimens can be obtained by rotating the aperture in different directions, or alternatively by varying the depth slightly. The authors generally avoid taking more than 4 specimens. Once specimens are obtained, they can be sent to pathology, where frozen sections are obtained at the discretion of the surgeon.

The scalp can be closed with a single figure-of-8 absorbable suture in the case of twist drill. With a bur hole, the scalp is closed in layers with buried suture in the galea and a running suture or staples in the skin. The frame is removed, and any bleeding encountered from the pin sites can generally be controlled with tamponade or antibiotic ointment.
The stereotactic accuracy of frameless stereotactic brain biopsy has been reported to be comparable to that of frame-based systems. Frameless biopsy occurs without a stereotactic frame but typically is performed with the patient in pin-fixation. Generally, pin-fixation is better tolerated under general anesthesia, which is more common for frameless procedures. Because a stereotactic frame is not used, a coregistration process must be performed. Several methods for this include fiducial markers, anatomic landmarks, and surface matching.

Fiducial marks can be placed on the patient’s scalp prior to acquisition of CT scan or MR imaging. When placing fiducial markers on the scalp, shaving a patch of hair so the adhesive backing can adhere to the scalp may be necessary. The authors outline the fiducial with a marker in the event that it is removed. A minimum of 4 fiducial marks are typically necessary to accurately register the patient to an image set. The fiducial markers should be placed a sufficient distance from each other so that they can be easily distinguishable from one another. Effort should also be made to avoid placing them in a single plane. Confirming that the appropriately compatible fiducials are used depending on whether CT scan or MRI is performed is also important.

After the CT scan or MRI is obtained and the target is planned, the patient is brought to the operating room and placed under anesthetic. Generally, pin-fixation is performed such that a rigid reference probe can be attached to the frame. An optical imaging system is used to register the patient, and a reference probe to the preoperative images using one of the registration methods mentioned above is used to match image space with physical space. If surface matching registration is used with a laser, avoiding significant distortion of the scalp when performing pin-fixation is important. Among the 3 registration methods, no significant advantage exists regarding one method over another in regards to accuracy.

Once the patient is registered to the preoperative image with the planned target, the patient is prepped and draped. A sterile reference star is applied within the sterile field. Although a free-hand method can be performed through registering the biopsy needle within the navigation system, a guide tube may provide a more accurate method for smaller lesions. A guide-tube can be registered to the navigation system and then oriented in the desired trajectory and held rigidly in place with a retractor system. Once this is satisfactorily done, a small incision is made in the same manner as described above. A twist-drill is passed through the guide tube when it is replaced in the desired trajectory. Once the biopsy needle is measured to the appropriate depth, specimens can be obtained in the same manner as described above for frame-based biopsy.
Incisional and Excisional Biopsy

If a patient requires a follow up for a detected abnormality, he or she may undergo an incisional or excisional biopsy. Both of these procedures are performed in an outpatient setting using local anesthesia. The following provides a description of each type of biopsy:\textsuperscript{42,43}

- **Incisional Biopsy** - An incisional biopsy takes out even more surrounding tissue than a needle biopsy. It removes some of the abnormality, but not all. The doctor will slice into the lesion and remove only a portion of it. If the lesion is found to be cancerous, further surgery may be needed to remove the whole abnormality.

- **Excisional Biopsy** - An excisional biopsy generally removes the entire area in question.

Both procedures, while different in scope of extraction, are performed the same way.\textsuperscript{34} The following is a description of how these tests are performed:

- Incisional or excisional biopsies are generally done to follow up on an abnormality detected on a scan or physical exam. These are typically performed as an outpatient procedure, using local anesthesia (a numbing medicine). Occasional, depending on the location of the biopsy, a medicine may also be given to relax the patient.
- A small cut in the skin will be made to access to the area. If the area cannot be felt, X-ray or ultrasound can be used to locate the area.
• The procedure typically takes an hour. If a sedating medicine is given, the patient will need to recover for an hour or two. The patient will also require transportation home, as he or she will not be unable to drive.

• The sample is then sent for review to the pathologist. After the pathologist has established a diagnosis, a report will be generated for review by the patient’s physician.

• Similar to any biopsy, the most common risk associated with the procedure is bleeding. A hematoma, or a pocket of blood, can form and collect at the site of the biopsy. This can be uncomfortable but should resolve over the following week. If there is severe pain following the procedure, the patient should be seen immediately.

\textit{Craniotomy}

A craniotomy is the most commonly performed surgery for brain tumor removal. It also may be done to remove a blood clot (hematoma), to control hemorrhage from a weak, leaking blood vessel (cerebral aneurysm), to repair arteriovenous malformations (abnormal connections of blood vessels), to drain a brain abscess, to relieve pressure inside the skull, to perform a biopsy, or to inspect the brain.\textsuperscript{44}

Craniotomies are named according to their size and complexity. Small dime-sized craniotomies are called burr holes or keyhole craniotomies. Sometimes stereotactic frames, image-guided computer systems, or endoscopes are used to precisely direct instruments through these small holes. Burr holes or keyhole craniotomies\textsuperscript{45} are used for minimally invasive procedures to:
• insert a shunt into the ventricles to drain cerebrospinal fluid (hydrocephalus)
• insert a deep brain stimulator to treat Parkinson Disease
• insert an intracranial pressure (ICP) monitor
• remove a small sample of abnormal tissue (needle biopsy)
• drain a blood clot (stereotactic hematoma aspiration)
• insert an endoscope to remove small tumors and clip aneurysms

Large or complex craniotomies are often called skull base surgery. These craniotomies involve the removal of a portion of the skull that supports the bottom of the brain where delicate cranial nerves, arteries, and veins exit the skull. Reconstruction of the skull base is often necessary and may require the additional expertise of head-and-neck, otologic, or plastic surgeons. Surgeons often use sophisticated computers to plan these craniotomies and locate the lesion. Skull base craniotomies\(^4\)\(^6\) can be used to:
- remove or treat large brain tumors, aneurysms, or AVMs
- treat the brain following a skull fracture or injury (\textit{i.e.}, gunshot wound)
- remove tumors that invade the bony skull

There are two methods commonly utilized by surgeons to open the skull. Either an incision is made at the nape of the neck around the bone at the back (occipital bone) or a curving incision is made in front of the ear that arches above the eye. The incision penetrates as far as the thin membrane covering the skull bone. During skin incision the surgeon must seal off many small blood vessels because the scalp has a rich blood supply.
The scalp tissue is then folded back to expose the bone. Using a high-speed drill, the surgeon drills a pattern of holes through the cranium (skull) and uses a fine wire saw to connect the holes until a segment of bone (bone flap) can be removed. This gives the surgeon access to the inside of the skull and allows him to proceed with surgery inside the brain. After removal of the internal brain lesion or other procedure is completed, the bone is replaced and secured into position with soft wire. Membranes, muscle, and skin are sutured into position. If the lesion is an aneurysm, the affected artery is sealed at the leak. If there is a tumor, as much of it as possible is resected (removed). For arteriovenous malformations, the abnormality is clipped and the repair redirects the blood flow to normal vessels.\textsuperscript{45,47,48}

Since the lesion is in the brain, the surgeon uses imaging studies to definitively identify it. Neuroimaging is usually accomplished by the following:

- CT (computed tomography) - uses x-rays and injection of an intravenous dye to visualize the lesion
- MRI (magnetic resonance imaging) - uses magnetic fields and radio waves to visualize a lesion
- arteriogram (an x-ray of blood vessels) - injected with a dye to visualize a tumor or cerebral aneurysm

Before surgery the patient may be given medication to ease anxiety and to decrease the risk of seizures, swelling, and infection after surgery. Blood thinners (warfarin, heparin, aspirin) and nonsteroidal anti-inflammatory drugs (ibuprofen, aspirin, naprosyn) have been correlated with an increase in blood clot formation after surgery. These
medications must be discontinued at least seven days before the surgery to reverse any blood thinning effects. Additionally, the surgeon will order routine or special laboratory tests as needed. The patient should not eat or drink after midnight the day of surgery. The patient's scalp is shaved in the operating room just before the surgery begins.47,49,50

Craniotomy is a major surgical procedure performed under general anesthesia. Immediately after surgery, the patient's pupil reactions are tested, mental status is assessed after anesthesia, and movement of the limbs (arms/legs) is evaluated. Shortly after surgery, breathing exercises are started to clear the lungs. Typically, after surgery patients are given medications to control pain, swelling, and seizures. Codeine may be prescribed to relieve headache. Special leg stockings are used to prevent blood clot formation after surgery. Patients can usually get out of bed in about a day after surgery and usually are hospitalized for five to 14 days after surgery. The bandages on the skull are be removed and replaced regularly. The surgeon removes the sutures to the scalp, but the soft wires used to reattach the portion of the skull that was removed are permanent and require no further attention.

Patients should keep the scalp dry until the sutures are removed. If required (depending on area of brain involved), occupational therapists and physical therapist assess the patient's status postoperatively and help the patient improve strength, daily living skills and capabilities, and speech. Full recovery may take up to two months, since it is
common for patients to feel fatigued for up to eight weeks after surgery.\textsuperscript{46,51-53}

The surgeon will discuss potential risks associated with the procedure. Neurosurgical procedures may result in bleeding, blood clots, retention of fluid causing swelling (edema), or the unintended injury to normal nerve tissues. Some patients may develop infections. Damage to normal brain tissue may cause damage to an area and subsequent loss of brain function. Loss of function in specific areas can cause memory impairment. Some other examples of potential damage that may result from this procedure include deafness, double vision, numbness, paralysis, blindness, or loss of the sense of smell.

Normal results depend on the cause for surgery and the patient's overall health status and age. If the operation was successful and uncomplicated recovery is quick, since there is a rich blood supply to the area. Recovery could take up to eight weeks, but patients are usually fully functioning in less time.\textsuperscript{48,54}

\textit{Cranietomy}

A craniectomy is a version of a craniotomy. However, craniectomy differs from craniotomy in that the bone is not replaced thus leaving a resultant cranial defect. Craniectomy may be used in non-emergent circumstances to augment the opening of a craniotomy or as a primary means of exposure. The latter is particularly true when exposing the suboccipital area—behind and below the ear. Reconstruction of the skull-cranioplasty may then be performed with titanium mesh or other artificial products. Craniectomy is also used in urgent or emergent
conditions where there is substantial brain swelling from bleeding, stroke, or infection and the patient's scalp is closed without reimplantation of the bone. After swelling subsides, the bone or other form fitting artificial material is implanted in a procedure called a cranioplasty.\textsuperscript{55-57}

\textit{Debulking}

Debulking is the surgical removal of as much of a malignant tumor as possible, so as to enhance the effectiveness of radiation or chemotherapy. It is used only in specific malignancies, as generally partial removal of a tumor is not considered a worthwhile intervention. Ovarian carcinoma and some types of brain tumor are debulked prior to commencing radio- or chemotherapy. It may also be used in the case of slow growth tumors to shift tumor cells from phase of cell cycle to replicative pool. It is usually a long and often complicated procedure taking several hours or more to perform, depending on internal involvement and location. Debulking is also known as cytoreduction surgery; "cytoreduction" refers to reducing the number of cancer cells.\textsuperscript{58-59}

\textit{Partial Removal}

Even for tumors that cannot be completely removed, partial removal has a role. There is increasing evidence that the more tumor is removed at surgery, the better the chances that other therapies, including radiation therapy and chemotherapy, will be effective. Neurosurgeons in general will recommend as complete a surgical
resection as possible, so long as tumor can be removed safely — *i.e.*, without leaving the patient with an unacceptable neurological deficit.

Tumors that are in deep parts of the brain or which involve critical structures, such as those that allow the patient to speak and understand, however, may not be even partially resectable. Furthermore, tumor debulking is a major surgical procedure, and like any other major operation, has certain risks, which become significant if the patient’s general medical condition is severely compromised (such as congestive heart failure, kidney failure, severe lung disease, etc.). In these cases, the surgeon may recommend instead a stereotactic biopsy. In this procedure, the surgeon uses a pencil-thin biopsy probe to remove a small amount of tissue, under computer guidance. This allows the surgeon to remove a small amount of tissue for pathological evaluation, under minimally invasive conditions that in general places the body under far less stress.

There are two general risks of stereotactic biopsy. First, because it removes only a small amount of tissue, it is possible to miss the tumor entirely or remove a fragment of tissue that is not representative of the overall tumor. Second, it is possible to produce local bleeding from the procedure; however, both of these problems can generally be dealt with effectively.\(^{60,61}\)

*Complete Removal*

Tumors that can often be removed entirely include some meningiomas, grade I astrocytomas, and ependymomas. However, complete removal does not mean that there is no chance that the
tumor will return, because these tumors can come back even if all visible signs of them are removed by the surgeon. For this reason, it is important that the patient follow up regularly with the neurosurgeon so any tumor recurrence can be detected early.\textsuperscript{31}

\textit{Shunt}

When there is excess fluid in the brain, or the fluid pathways are blocked due to a tumor or swelling, there may be a build-up of pressure inside the skull. A drainage system called a shunt can be used to remove the fluid. A shunt is a narrow, flexible tube used to move fluid from the brain to another part of the body. One end of the shunt is placed into one of four cavities, or ventricles, in the brain where cerebrospinal fluid (CSF) circulates. A small valve attached to tubing is placed under the scalp. The tubing is then threaded under the skin, down the neck, and into the abdominal cavity.

Sometimes the shunt empties near the right atrium of the heart rather than the abdomen. In either location, the fluid drains out of the shunt and is absorbed by the body. The shunt filter catches small pieces of tissue and stray tumor cells that might be in the CSF as it drains away from the brain. Small incisions in the neck, chest and/or abdominal area are made to attach the tubing securely. The shunt has a valve that permits the CSF to only flow away from the brain, and controls the rate of flow.\textsuperscript{62}

A shunt can be either temporary or permanent. Sometimes a tube is placed into one of the four cavities or ventricles in the brain and connected to a collecting bag outside of the body. This procedure is
called a ventriculostomy and is a temporary way of draining the cerebrospinal fluid.\textsuperscript{63}

After the shunt is in place, most patients, especially children, experience dramatic improvement within days or weeks. In others, symptoms of intracranial pressure, such as headaches, might remain for a period of several weeks. It is fairly common that a shunt might need maintenance. Reasons for this include blockage of the catheter, an infection, a disconnection, or in the case of a child, the catheter may need to be lengthened due to the child’s growth. When these situations occur, a surgical procedure known as shunt revision may be done to correct the problem.\textsuperscript{64}

Shunts may not be used if the pressure in the brain is too high. Abruptly changing the pressure may cause the brain to shift upward or downward toward the spine. In this situation, the doctor will use other methods to reduce the pressure before a shunt is inserted.\textsuperscript{65}

\textit{Ommaya Reservoir}

The Ommaya Reservoir is a device through which fluids can be put into, or removed, from around the brain. There are two parts to the Ommaya; a small plastic dome-like container or port that is put under the scalp and a small tube (or catheter) coming off from the dome. The end of the tube is directed into a open space in the brain called a ventricle. The cells in the ventricles produce Cerebral Spinal Fluid (CSF). The CSF flows around the brain and the spinal cord to provide a protective cushion and nutrients.\textsuperscript{66}
The Ommaya Reservoir is used to take out a sample of the fluid or give chemotherapy directly into the fluid surrounding the brain and spinal cord. This method of giving chemotherapy is called intrathecal chemotherapy. Intrathecal chemotherapy is administered so the drug(s) can get directly into the area around the brain and spinal cord where cancer cells may be. There is a network of blood vessels surrounding the brain that act as a screen (blood-brain barrier). This blood-brain barrier does not allow most chemotherapy to get from the bloodstream to the brain and spinal cord. Intrathecal chemotherapy is used to by-pass this barrier, allowing chemotherapy to reach cancer cells.\textsuperscript{67}

A surgeon will perform this surgical procedure in the hospital under general anesthesia. The patient’s head will be shaved in the area that the reservoir is to be placed. The Ommaya Reservoir is placed under the skin on the head and then the tube or catheter is positioned through the skull into a ventricle in the brain.\textsuperscript{68}

There are a few important things that the patient must watch for immediately after the Ommaya is placed:

- Keep the area dry until the stitches (or staples) are removed.
- Watch for signs of infection such as redness, tenderness or drainage at the incision site, fever greater than 100.5, headache with or without vomiting, or neck stiffness.
- After the Ommaya Reservoir is put in the patient will have a small bump on his or her head. Once the surgical incision from the Ommaya Reservoir is healed, no special care is needed for the site. The patient can participate in normal activities.
Intrathecal chemotherapy can be given in the hospital or the clinic. The skin over the Ommaya is cleaned and a small needle is inserted into the reservoir. A fluid sample is taken or chemotherapy is given, and the needle is removed. The needle stick site is covered with a band aid. Side effects of this procedure may include: headache, nausea/vomiting, stiff neck, pressure or pain from needle insertion. If there is difficulty to withdraw fluid from the reservoir, the patient may need to have an MRI to check placement. The MRI will show if the Ommaya is in the right place or if it needs to be moved by the surgeon.\textsuperscript{66,69,70} 

**Skull Base Surgery**

The skull is composed of bones and cartilage that form the face and the cranium, which surrounds the brain. The bones can be felt at the bottom of the cranium on top of the skull. The five bones that form the bottom, or base, of the cranium also form the eye socket, roof of the nasal cavity, some of the sinuses, and the bones that surround the inner ear. The skull base is a crowded and complicated area with different openings that the spinal cord, many blood vessels, and nerves all pass through.

Skull base surgery may be done to remove both benign and cancerous growths, and abnormalities on the underside of the brain, the skull base, or the top few vertebrae of the spinal column.

Because this is such a difficult area to see and reach, skull base surgery may be done by a minimally invasive endoscopic procedure in which instruments are inserted through the natural openings in the
skull — the nose or mouth — or by making a small hole just above the eyebrow. This type of surgery requires a team of specialists that may include ENT (ear, nose, and throat) surgeons, neurosurgeons, and radiologists.\textsuperscript{71,72}

Before endoscopic skull base surgery was developed, the only way to remove growths in this area of the body was by making an opening in the skull. Under some circumstances, this type of surgery may be necessary.\textsuperscript{73}

Skull base surgery can be done in two main ways.\textsuperscript{74-76} Although the preferred method is endoscopic, open surgery is also an option, depending on the type of growth that needs to be removed and its location:

• \textit{Endoscopic or minimally-invasive skull base surgery}

  Endoscopic surgery usually does not require a large incision. An ENT surgeon may make a small opening inside the nose to allow a neurosurgeon to remove a growth through a thin-lighted tube called an endoscope. An MRI is a type of picture taken of the skull base using magnets and a computer and may be done by a radiology specialist while the surgical specialists are operating to help them make sure all of the growth has been removed.

• \textit{Traditional or open skull base surgery}

  This type of surgery may require incisions in the facial area and in the skull. Parts of bone may need to be removed so that the
growth can be reached and removed. An operating room microscope is often used for this type of surgery.

Traditionally, neurosurgeons treated conditions that arose within the skull, and otolaryngologists (ear, nose, and throat doctors or head and neck surgeons) treated conditions that arose in the head outside the skull. In other words, the skull base divided these two worlds, and tumors and other diseases that affected the skull base or deep facial tissues were difficult to reach. With the collaboration between surgical specialties — otolaryngologists-head and neck surgeons and neurosurgeons working together as skull base surgeons — these deep areas can now be safely approached.77,78

Over the last decade, new surgical techniques have been pioneered that allows the majority of skull base surgeries to be performed through the nasal passages using an endoscope: the Endoscopic Endonasal Approach (EEA). An endoscope is a lighted instrument that provides visualization within a cavity. All three stages of surgery (approach, resection or tumor removal, and reconstruction) are performed through the nasal passages without the need for scalp or facial incisions. While these types of surgeries are described as minimally invasive, they often allow the surgeons to perform more complete surgeries.71,72

The concept of modern skull base surgery comes from doing a less invasive procedure that can result in a more effective outcome for the patient. While EEA can be the solution for most tumors at the skull base, it is not the answer for all of them. The modern skull base
surgeon needs to be versatile in order to offer the best approach for each situation.\textsuperscript{79}

The Endoscopic Endonasal Approach is a minimally invasive surgical approach to the skull base that was refined and is performed at UPMC by a multidisciplinary surgical team to remove skull base brain tumors and lesions through the nose. EEA is performed using a narrow telescope called an endoscope. A small area at the base of the skull is removed to allow direct access to the tumor, without manipulating the brain. The concept of "inside out surgery" — starting directly at the tumor and working outward — eliminates the need to move critical structures to reach the tumor.\textsuperscript{71}

There are many ways to approach the skull base. In the past, the favored technique was to approach the skull base from above (transcranial approach) and from below (transfacial approach), commonly at the same time. The transcranial approach consists of a scalp incision followed by a craniotomy (removing part of the skull). The brain is then lifted up to reach the skull base. The bones of the facial skeleton may be removed temporarily to increase the exposure.\textsuperscript{77,80}

The transfacial approach consists of incisions on the face or inside the mouth that provide access to the sinus cavities and skull base from below. Working both above and below the skull base, the surgeons then remove tumors. Surgery results in a defect of the skull base and dura (thick lining over the brain) that needs to be repaired to prevent leakage of spinal fluid and infection (meningitis).\textsuperscript{81}
For the majority of skull base pathologies, the Endoscopic Endonasal Approach (EEA) is generally enough for treatment. However, there are situations in which a traditional approach is still required. Often endonasal and open approaches are combined for specific lesions. This is the concept of 360° surgery around the skull base.

If a specific tumor can be totally removed using a single approach, such as endonasal surgery, then that approach will be used. However, if part of the tumor is located on the other side of important structures, such as blood vessels and nerves, it is preferred to remove the residual portion using a different corridor, which can be a focused traditional approach. There are also situations in which only a focused traditional approach is necessary.

For a routine surgery, the nasal passage is filled with compressible packing or a balloon catheter. This remains in place for up to one week, depending on the extent of the surgery. This is easily removed prior to discharge or in the office if already discharged. Plastic splints are also placed in the nasal passage, and these are removed several weeks after surgery. Once nasal packing is removed, patients are instructed to spray the nasal cavity with saline solution several times a day.

Patients are seen every few weeks initially for endoscopic examination of the nasal cavity and removal of nasal crusts. By three to four months, healing is usually complete and crusting diminishes. Additional follow up depends on the diagnosis, need for additional therapy, and symptoms.
Patients are instructed to avoid activities that increase pressure of spinal fluid inside the head (bending, lifting, straining, nose-blowing) for a month after surgery in order to minimize the risk of a spinal fluid leak. A spinal fluid leak is characterized by the drainage of clear fluid from the nose. If a spinal fluid leak is confirmed, this can be repaired using endoscopic surgical techniques in most cases. Most patients will notice a decrease in smell and taste for several months following surgery due to decreased airflow through the nose. This will often recover as healing occurs.\textsuperscript{71,74}

If a patient has a pituitary tumor or another tumor in which there is no plan to open the lining of the brain (dura), then the chance of having a postoperative leak and requiring follow-up surgery is very low (less than 2\%). On the other hand, if the patient has a tumor that requires the surgeons to open the lining of the brain through the nose, as for meningiomas and craniopharyngiomas, the risk is a little higher. With the development of the nasoseptal flap (vascularized tissue from the patient's own nose that is transplanted from the septum to the skull base), the chance of having a spinal fluid leak after surgery is just 5.4\%.\textsuperscript{80}

\textit{Transsphenoidal Surgery}

Transsphenoidal Surgery is a surgery performed through the nose and sphenoid sinus to remove pituitary tumors. Transsphenoidal surgery can be performed with an endoscope, microscope, or both. It is often a team effort between neurosurgeons and ear, nose, and throat (ENT) surgeons.
A traditional microscopic technique uses a skin incision under the lip and removal of a large portion of the nasal septum so that the surgeon can directly see the area. A minimally invasive technique, called endoscopic endonasal surgery, uses a small incision at the back of the nasal cavity and causes little disruption of the nasal tissues. The ENT surgeon works through the nostrils with a tiny camera and light called an endoscope. In both techniques, bony openings are made in the nasal septum, sphenoid sinus, and sella to reach the pituitary. Once the pituitary is exposed, the neurosurgeon removes the tumor.  

A patient may be a candidate for transsphenoidal surgery if he or she has a:

- Pituitary adenoma: a tumor that grows from the pituitary gland; may be hormone-secreting or not.
- Craniopharyngioma: a benign tumor that grows from cells near the pituitary stalk; may invade the third ventricle.
- Rathke’s cleft cyst: a benign cyst, or fluid-filled sac, between the anterior and posterior lobes of the pituitary gland.
- Meningioma: a tumor that grows from the meninges (dura), the membrane that surrounds the brain and spinal cord.
- Chordoma: a malignant bone tumor that grows from embryonic notochord remnants located at the base of the skull.

If the patient has a prolactinoma or a small (<10mm) non-secretory tumor, surgery may not be required. These types of tumors respond well to medication or may be observed with periodic MRIs to watch for tumor growth. Some tumors extend beyond the limits of the transsphenoidal approach. For these tumors, a more extensive
operation that uses a craniotomy combined with skull base approaches may be needed.\textsuperscript{83}

A neurosurgeon performs transsphenoidal surgery often with a team that includes an ENT surgeon who has the specialized training in endoscopic sinus surgery. A team approach allows comprehensive care of both brain- and sinus-related issues before, during, and after surgery.

The following is a list of the steps involved in the procedure.\textsuperscript{82,84} There are six steps in the procedure. The operation generally takes 2 to 3 hours.

Step 1: Prepare the patient
The patient will lie on his or her back on the operative table. An intravenous (IV) line will be placed in the patient’s arm and general anesthesia will be given. The nasal cavity is prepped with antibiotic and antiseptic solution. An image-guidance system may be placed on the patient’s head. This device is like a global positioning system (GPS) and helps the surgeon navigate through the nose using a 3D “map” created from the patient’s CT or MRI scans.

Step 2: Make an incision
In a minimally invasive endoscopic procedure, the ENT surgeon inserts the endoscope in one nostril and advances it to the back of the nasal cavity. An endoscope is a thin, tube-like instrument with a light and a camera. Video from the camera is viewed on a monitor. The surgeon passes long instruments through the nostril while watching the
monitor. A small portion of the nasal septum dividing the left and right nostril is removed. Using bone-biting instruments, the front wall of the sphenoid sinus is opened.

Step 3: Open the sella
At the back wall of the sphenoid sinus is the bone overlying the pituitary gland, called the sella. The thin bone of the sella is removed to expose the tough lining of the skull called the dura. The dura is opened to expose the tumor and pituitary gland.

Step 4: Remove the tumor
Through a small hole in the sella, the tumor is removed by the neurosurgeon in pieces with special instruments called curettes.

The center of the tumor is cored out, allowing the tumor margins to fall inward so the surgeon can reach it. After all visible tumor is removed, the surgeon advances the endoscope into the sella to look and inspect for hidden tumor. Some tumors grow sideways into the cavernous sinus, a collection of veins. It may be difficult to completely remove this portion of the tumor without causing injury to the nerves and vessels. Any tumor left behind may be treated later with radiation.

At some hospitals, surgery can be performed in a special OR room equipped with an intraoperative MRI scanner. The patient can undergo an MRI during surgery. This gives the surgeon real-time images of the patient’s brain to know exactly how much tumor has been removed before ending the procedure. This technology enables more complete tumor removal and may reduce the need for a second operation.
Step 5: Obtain fat graft (optional)
After tumor is removed, the surgeon prepares to close the sella opening. If needed, a small (2cm) skin incision is made in the abdomen to obtain a small piece of fat. The fat graft is used to fill the empty space left by the tumor removal. The abdominal incision is closed with sutures.

Step 6: Close the sella opening
The hole in the sella floor is replaced with bone graft from the septum. Synthetic graft material is sometimes used when there is no suitable piece of septum or the patient has had previous surgery. Biologic glue is applied over the graft in the sphenoid sinus. This glue allows healing and prevents leaking of cerebrospinal fluid (CSF) from the brain into the sinus and nasal cavity. Soft, flexible splints are placed in the nose along the septum to control bleeding and prevent swelling. The splints also prevent adhesions from forming that may lead to chronic nasal congestion.

Post-Operative
If the tumor is hormone secreting (prolactinoma, Cushing’s, or acromegaly), the endocrinologist will follow the hormone levels after surgery to determine whether the patient is cured. Patients with Cushing’s disease usually have small tumors (microadenomas) and are surgically cured about 90% of the time. Patients with acromegaly often have larger, more invasive tumors. The success rate is about 60% with growth-hormone secreting macroadenomas.
Some pituitary tumors remain surgically incurable due to invasion of the cavernous sinuses and other important structures. Radiosurgery can be used to treat unresectable tumor remnants with very good long-term control rates. If there is residual tumor after surgery for acromegaly, Cushing’s disease, or prolactinomas, medical treatments are available to control the excess hormone secretion.\textsuperscript{77,79,83}

\textit{Side Effects and Risks}

General complications of any surgery include bleeding, infection, blood clots, and reactions to anesthesia.\textsuperscript{82,84} Specific complications related to pituitary surgery include:

- Vision loss: the optic chiasm can be damaged during surgery. If vision problems were present before surgery, decompression may not restore normal visual function. The nerve may have been permanently damaged by the tumor.
- Damage to normal pituitary gland: can occur 5 to 10\% of the time for macroadenomas. Hormone replacement may be required after surgery, such as cortisol, thyroid hormone, growth hormone, estrogen, or testosterone.
- Diabetes insipidus (DI): caused by damage to the posterior lobe of the pituitary gland. DI leads to frequent urination and excessive thirst, because the kidneys inadequately concentrate the urine. This effect is usually temporary, lasting 1 to 3 days. DI can be controlled with medication called desmopressin acetate (DDAVP) in nasal spray or pill form. Permanent DI is rare and controlled with medication.
- Cerebrospinal fluid (CSF) leak: the fluid surrounding the brain can escape through a hole in the dura lining the skull. In 1\% of
transsphenoidal cases, a clear watery discharge from the nose, postnasal drip, or excessive swallowing occurs; may require surgery to patch the leak.

- **Meningitis:** an infection of the meninges often caused by CSF leak.
- **Sinus congestion:** small adhesions can stick together and form scars that block airflow through the nose.
- **Nasal deformity:** caused by bone removal or adhesions; may be corrected by surgery.
- **Nasal bleeding:** continued bleeding from the nose after surgery occurs in less than 1% of patients. May require surgery to correct.
- **Stroke:** the carotid arteries and cavernous sinuses located on either side of the pituitary may be damaged during surgery causing an interruption of blood supply to the brain.

**Laser Interstitial Thermal Therapy**

Laser Interstitial Thermal Therapy (LITT) uses a laser to heat brain tumor tissue while monitoring the destruction of the tissue with an MRI that can measure the temperature of the tissues in real time. The laser probe is directed into the tumor through one or more small holes using stereotactic techniques. The availability of LITT is relatively new and may provide the benefit of surgical removal for some tumors that are difficult or impossible to access with conventional craniotomy. LITT is an emerging treatment modality in glioma therapy.

The technology is most effectively applied in the treatment of deep-seated lesions that are difficult to access surgically without injury to
eloquent neurological structures. The catheter is implanted using advanced computer imaging techniques. The laser is guided through the catheter with real-time MRI, allowing neurosurgeons to limit thermal energy delivery only to the tumor. Most patients can go home the day after treatment and can quickly return to normal activities. Laser interstitial thermal therapy is minimally invasive. It typically requires only a 2-millimeter incision in the scalp, and takes only a few minutes to perform. LITT can also help patients who do not respond to stereotactic radiosurgery or have radiation necrosis (tissue death caused by radiation treatment).

Summary

Brain tumors are primarily identified as malignant or benign. Some are primary brain tumors while others are metastatic. Brain and spinal cord tumors develop differently in individuals. They form in different areas, develop from different cell types, and may have different treatment options. The types of brain tumors and the surgical treatment have been discussed. Other treatments of chemotherapy and radiation were not covered in this course however are important treatment options, which the learner is recommended to pursue. Whether the individual with a diagnosis of brain cancer chooses to undergo surgery or other medical options, the tumor type and staging of the tumor will need to be included in the diagnosis and prognosis when the clinician explains options in the treatment plan.

The most widely used staging system is the TNM Staging System, which is monitored and maintained by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control
(UICC). Once cancer has been detected in a patient, the individual will go through the cancer staging process to determine how much cancer is in the body and where it is located. Staging is used to evaluate the severity of the cancer by assessing the magnitude of the primary cancer, as well as the extent to which it has spread. Cancer staging can be used to develop a prognosis and create a comprehensive treatment plan for the patient. Surgery is the initial treatment for most benign and many malignant tumors. It is often the preferred treatment when a tumor can be removed without any unnecessary risk of neurological damage.
References

The References below include published works and in-text citations of published works that are intended as helpful material for your further reading.

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