

Brain Tumors: an Introduction basic level

Overview

A tumor (also called a neoplasm or lesion) is abnormal tissue that grows by uncontrolled cell division. Normal cells grow in a controlled manner as new cells replace old or damaged ones. For reasons not fully understood, tumor cells reproduce uncontrollably.

Brain tumors are named after the cell type from which they grow. They may be primary (starting in the brain) or secondary (spreading to the brain from another area). Treatment options vary depending on the tumor type, size and location; whether the tumor has spread; and the age and medical health of the person. Treatment options may be curative or focus on relieving symptoms. Of the more than 120 types of brain tumors, many can be successfully treated. New therapies are improving the life span and quality of life for many people.

What is a brain tumor?

A **primary brain tumor** is an abnormal growth that starts in the brain and usually does not spread to other parts of the body. Primary brain tumors may be benign or malignant.

A **benign** brain tumor grows slowly, has distinct boundaries, and rarely spreads. Although its cells are not malignant, this tumor composed of benign cells and located in vital areas can be considered life-threatening.

A **malignant** brain tumor grows quickly, has irregular boundaries, and spreads to nearby brain areas. Although they are sometimes called brain cancer, malignant brain tumors do not fit the definition of cancer because they do not spread to organs outside the brain and spinal cord.

Metastatic (secondary) brain tumors begin as cancer elsewhere in the body and spread to the brain. They form when cancer cells are carried in the blood stream to the brain. The most common cancers that spread to the brain are lung and breast.

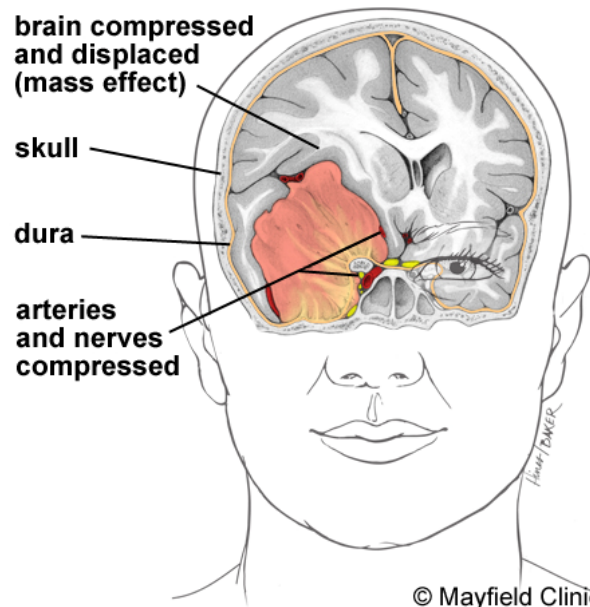


Figure 1. Brain tumors compress and displace normal brain tissue. Increasing size, pressure and swelling cause neurologic symptoms.

Whether a brain tumor is benign, malignant, or metastatic, all are potentially life-threatening. Enclosed within the bony skull, the brain cannot expand to make room for a growing mass. As a result, the tumor compresses and displaces normal brain tissue (Fig. 1). Some brain tumors cause a blockage of cerebrospinal fluid (CSF) that flows around and through the brain. This blockage increases intracranial pressure and can enlarge the ventricles (hydrocephalus). Some brain tumors cause swelling (edema). Size, pressure, and swelling all create "mass effect," which cause many of the symptoms.

Types of brain tumors

There are over 120 different types of brain tumors. Common brain tumors include:

Gliomas

- Astrocytoma
 - Pilocytic Astrocytoma (grade I)
 - Diffuse Astrocytoma (grade II)
 - Anaplastic Astrocytoma (grade III)
 - Glioblastoma Multiforme (grade IV)
- Oligodendroglioma (grade II)
 - Anaplastic Oligodendroglioma (grade III)
- Ependymoma (grade II)
 - Anaplastic Ependymoma (grade III)

- Craniopharyngioma
- Epidermoid
- Lymphoma
- Meningioma
- Schwannoma (neuroma)
- Pituitary adenoma
- Pinealoma (pineocytoma, pineoblastoma)
- Medulloblastoma

The World Health Organization (WHO) developed a classification and grading system to standardize communication, treatment planning, and predict outcomes for brain tumors. Tumors are classified by their cell type and grade by viewing the cells, usually taken during a biopsy, under a microscope.

- **Cell type.** Refers to the cell of origin of the tumor. For example, nerve cells (neurons) and support cells (glial and schwann cells) give rise to tumors. About half of all primary brain tumors grow from glial cells (gliomas). There are many types of gliomas because there are different kinds of glial cells.
- **Grade.** Refers to the way tumor cells look under the microscope and is an indication of aggressiveness (e.g., low grade means least aggressive and high grade means most aggressive) (Table 1). Tumors often have a mix of cell grades and can change as they grow. Differentiated and anaplastic are terms used to describe how similar or abnormal the tumor cells appear compared to normal cells.

Table 1. Glioma Grading Scale.

Grade	Characteristics
I	Slow growing cells Almost normal appearance Least malignant Usually associated with long-term survival
II	Relatively slow growing cells Slightly abnormal appearance Can invade nearby tissue Sometimes recur as a higher grade
III	Actively reproducing abnormal cells Abnormal appearance Infiltrate normal tissue Tend to recur, often as a higher grade
IV	Rapidly reproducing abnormal cells Very abnormal appearance Area of dead cells (necrosis) in center Form new blood vessels to maintain growth

What causes brain tumors?

Medical science neither knows what causes brain tumors nor how to prevent primary tumors that start in the brain. People most at risk for brain tumors include those who have:

- cancer elsewhere in the body
- prolonged exposure to pesticides, industrial solvents, and other chemicals
- inherited diseases, such as neurofibromatosis

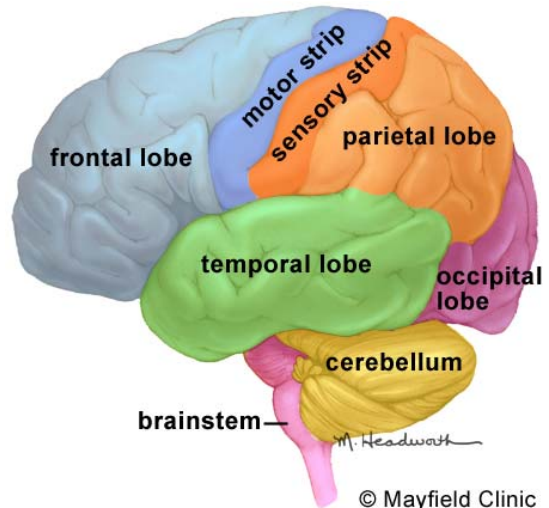


Figure 2. Brain tumor symptoms are related to the functional areas of the brain, giving doctors clues as to the tumor location.

- Frontal lobe** tumors may cause:
- Behavioral and emotional changes
 - Impaired judgment
 - Impaired sense of smell
 - Memory loss
 - Paralysis on one side of the body
 - Reduced mental abilities
 - Vision loss

- Parietal lobe** tumors may cause:
- Impaired speech
 - Inability to write
 - Lack of recognition
 - Spatial disorders

- Occipital lobe** tumors may cause:
- Vision loss in one or both eyes

- Temporal lobe** tumors may cause:
- Impaired speech
 - Memory difficulty

- Brainstem** tumors may cause:
- Behavioral and emotional changes
 - Difficulty speaking and swallowing
 - Drowsiness
 - Hearing loss
 - Muscle weakness on one side of the face (e.g., head tilt, crooked smile)
 - Muscle weakness on one side of the body
 - Uncoordinated gait
 - Drooping eyelid or double vision
 - Vomiting

- Pituitary gland** tumors may cause:
- Increased secretion of hormones (Cushing's Disease, acromegaly)
 - A stop in menstruation
 - Abnormal secretion of milk
 - Decreased libido

What are the symptoms?

Tumors can affect the brain by destroying normal tissue, compressing normal tissue, or increasing intracranial pressure. Symptoms vary depending on the tumor's type, size, and location in the brain (Fig. 2). General symptoms include:

- headaches that tend to worsen in the morning
- seizures
- stumbling, dizziness, difficulty walking
- speech problems (e.g., difficulty finding the right word)
- vision problems, abnormal eye movements
- weakness on one side of the body
- increased intracranial pressure, which causes drowsiness, headaches, nausea and vomiting, sluggish responses

Who is affected?

The American Brain Tumor Association estimates that about 40,900 people will be diagnosed with a primary brain tumor in the US this year (rate of 14 per 100,000 people). Metastatic (secondary) brain tumors are more common than primary brain tumors by at least 10 to 1, and they occur in 20% to 40% of cancer patients. The exact number of brain metastases is unknown, but it has been estimated that 98,000 to 170,000 new cases are diagnosed in the US each year. Unfortunately, each year about 12,690 people die of brain tumors in the US. Although brain tumors can occur at any age, they are most common in children 3 to 12 years old and in adults 40 to 70 years old.

How is a diagnosis made?

Physical exam

First, the doctor will obtain your personal and family medical history and perform a complete physical examination. In addition to checking your general health, the doctor performs a neurological exam to check mental status and memory, cranial nerve function (sight, hearing, smell, tongue and facial movement), muscle strength, coordination, reflexes, and response to pain. Additional tests may include:

- Audiometry, a hearing test performed by an audiologist, detects hearing loss due to tumors near the cochlear nerve (e.g., acoustic neuroma).
- An endocrine evaluation measures hormone levels in your blood or urine to detect abnormal levels caused by pituitary tumors (e.g., Cushing's Disease).
- A visual field acuity test is performed by a neuro-ophthalmologist to detect vision loss and missing areas in your field of view.
- A lumbar puncture (spinal tap) may be performed to examine cerebrospinal fluid for tumor cells, proteins, infection, and blood.

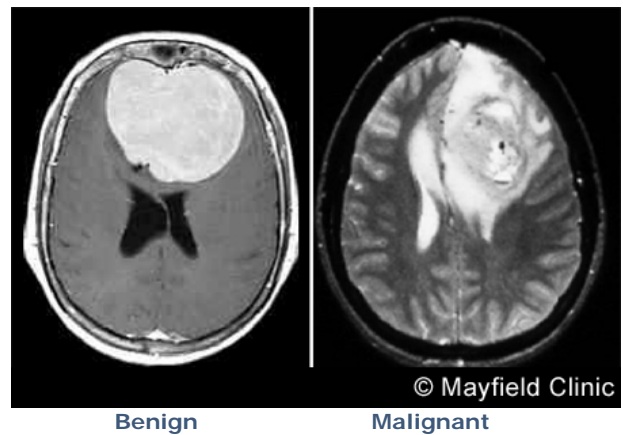


Figure 3. MRI scans of a benign and malignant brain tumor. Benign tumors have well defined edges and are more easily removed surgically. Malignant tumors have an irregular border that invades normal tissue with finger-like projections making surgical removal more difficult.

Imaging tests

- **Computed Tomography (CT) scan** is a safe, noninvasive test that uses an X-ray beam and a computer to make 2-dimensional images of the brain. Similar to an MRI, it views the brain in slices, layer-by-layer, taking a picture of each slice. A dye (contrast agent) may be injected into your bloodstream. CT is especially useful for viewing changes in bony structures.
- **Magnetic Resonance Imaging (MRI) scan** is a noninvasive test that uses a magnetic field and radiofrequency waves to give a detailed view of the soft tissues of the brain. It views the brain 3-dimensionally in slices that can be taken from the side or from the top as a cross-section. A dye (contrast agent) may be injected into your bloodstream. MRI is very useful to evaluate brain lesions and their effects on surrounding brain (Fig. 3).

Biopsy

In some cases, if a diagnosis cannot be made clearly from the scans, a biopsy may be performed to determine what type of tumor is present. Biopsy is a procedure to remove a small amount of tumor to be examined by a pathologist under a microscope. A biopsy can be taken as part of an open surgical procedure to remove the tumor or as a separate diagnostic procedure, known as a needle biopsy via a small hole drilled in the skull. A hollow needle is guided into the tumor and a tissue sample is removed. A stereotactic biopsy is like a needle biopsy but is performed with the use of a stereotactic head frame and a computer to precisely locate the tumor and direct the needle. This more complex procedure is used for deep tumors in critical locations.

Who treats brain tumors?

Because there are so many kinds of brain tumors and some are complex to treat, many doctors may be involved in your care. Your team may include a neurosurgeon, oncologist, radiation oncologist, radiologist, neurologist, and neuro-ophthalmologist.

What treatments are available?

Treatment options vary depending on the type, grade, size and location of the tumor; whether it has spread; and your age and general health. The goal of treatment may be curative or focus on relieving symptoms (palliative care). Treatments are often used in combination with one another. The goal is to remove all or as much of the tumor as possible through surgery to minimize the chance of recurrence. Radiation therapy and chemotherapy are used to treat tumors that cannot be removed by surgery alone. For example, surgery may remove the bulk of the tumor and a small amount of residual tumor near a critical structure can later be treated with radiation.

Observation

Sometimes the best treatment is observation. For example, benign, slow growing tumors that are small and have few symptoms may be observed with routine MRI scans every year until their growth or symptoms necessitate surgery. Observation may be the best option for older patients with other health conditions.

Medication

Medications are used to control some of the common side effects of brain tumors.

- Corticosteroid medications, such as dexamethasone (Decadron), are prescribed to reduce swelling and inflammation around the tumor. Because steroid medications can cause stomach ulcers and gastric reflux, famotidine (Pepcid) or pantoprazole (Protonix) are prescribed to reduce the amount of acid produced in the stomach.
- Furosemide (Lasix) or mannitol (Osmitrol) may be used to control edema and intracranial pressure.
- Anticonvulsant medications are used to prevent or control seizures. The most common ones include phenytoin (Dilantin), valproic acid (Depakote), carbamazepine (Tegretol), and levetiracetam (Keppra).

Surgery

Surgery is the treatment of choice for brain tumors that can be reached without causing significant injury to vital parts of the brain (eloquent tissue). Surgery can help to refine the diagnosis, remove as much of the tumor as possible, and release pressure within the skull caused by the tumor. A neurosurgeon performs a craniotomy to open the

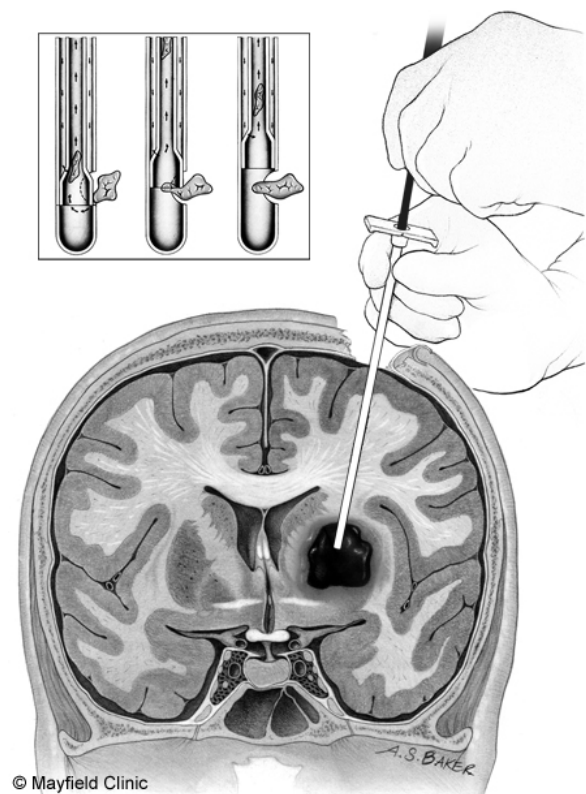


Figure 4. During a needle biopsy, a hollow cannula is inserted into the tumor. Small biting instruments remove bits of tumor for the pathologist to examine and determine the exact tumor cell type.

skull and remove the tumor. Sometimes only part of the tumor is removed if it is near critical areas of the brain. A partial removal can still relieve symptoms. Radiation or chemotherapy may be used on the remaining tumor cells.

Improvements in surgical techniques, particularly image-guided stereotaxy, intraoperative MRI/CT, and functional cortical mapping have improved the surgeon's ability to precisely locate the tumor, define the tumor's borders, avoid injury to vital brain areas, and confirm the amount of tumor removal while in the operating room.

Radiation

Radiation therapy uses controlled high-energy rays to treat brain tumors. Radiation works by damaging the DNA inside cells making them unable to divide and reproduce. The goal of radiation therapy is to maximize the dose to abnormal cells and minimize exposure to normal cells. The benefits of radiation are not immediate but occur over time. Aggressive tumors, whose cells divide rapidly, typically respond more quickly to radiation. There are two ways to deliver radiation, external and internal beams.

External beam radiation is delivered from outside the body by a machine that aims high-energy rays (x-rays, gamma rays) at the tumor.

- **Stereotactic radiosurgery (SRS)** delivers a high dose of radiation during a single session. Although it is called surgery, no incision is made.
- **Fractionated stereotactic radiotherapy (FSR)** delivers lower doses of radiation over many visits. Patients return daily over several weeks to receive the complete radiation dose.
- **Whole brain radiotherapy (WBRT)** delivers the radiation dose to the entire brain. It is often used to treat multiple brain tumors and metastases.

Internal radiation (brachytherapy) is delivered from inside the body by surgically placing radioactive material (sealed in catheters, seeds, wafers, or balloons) directly into the tumor. After the patient undergoes a craniotomy to remove the tumor, the radioactive material is placed inside the tumor cavity. The radiation dose is delivered to the first few millimeters of tissue that surrounded the tumor cavity where malignant cells may still remain. Patients have no risk of radiation injury to other parts of their own body or to others around them because the radiation dose is precisely delivered and short lived.

Chemotherapy

Chemotherapy drugs work by interrupting cell division. However, it affects not only tumor cells but normal cells, thus causing side effects, especially in fast growing cells (e.g., hair, digestive, blood). Treatment is delivered in cycles with rest periods in between to allow the body to rebuild healthy cells. Chemotherapy drugs can be administered orally as a pill, intravenously (IV), or as a wafer placed surgically into the tumor. The drugs most commonly used to treat brain tumors are carmustine (BCNU), lomustine (CCNU), and temozolomide (Temodar). Chemotherapy is also used as a radio-sensitizing agent that increases tumor cell death during radiation therapy. Agents that often work in high-grade gliomas include procarbazine, platinum analogs (cisplatin, carboplatin), the nitrosureas (BCNU, CCNU), and alkylating agents (temozolomide, vincristine). BCNU has been proven effective when applied locally to the tumor bed after the tumor has been removed. By applying it directly to the diseased area of the brain, side effects are limited and the drug has a more beneficial effect. Chemotherapy is not routinely used for benign tumors.

Adjunct therapies

- Immunotherapy or biotherapy activates the immune system (T-cells and antibodies) to destroy cancer cells. Experimental research is exploring ways to prevent or treat cancer through vaccines.
- Gene therapy uses viruses or other vectors to introduce new genetic material into tumor cells. This experimental therapy can cause tumor cells to die or increase their susceptibility to other cancer therapies.
- Hyperbaric oxygen uses oxygen at higher than normal levels to promote wound healing and help fight infection. It may also improve the tumor's responsiveness to radiation and is being studied experimentally. Currently it is being used to help the body naturally remove dead tumor cells and treat radiation necrosis.

Clinical trials

Clinical trials are research studies in which new treatments—drugs, diagnostics, procedures, vaccines, and other therapies—are tested in people to assess their safety and efficacy. Research is always being conducted to improve the standard of medical care. Information about current clinical investigations, including their eligibility, protocol, and participating locations are found on the web. Clinical trials are sponsored by the National Institutes of Health (NIH), www.clinicaltrials.gov, as well as by private industry and pharmaceutical companies, www.centerwatch.com

Current Studies

Go to www.mayfieldclinic.com/ClinicalTrials.htm for information about clinical trials conducted by our doctors at local Cincinnati hospitals or call 1-800-325-7787 ext. 5260.

Self care

Your primary care doctor and oncologist should discuss any home care needs with you and your family. Supportive measures vary according to your symptoms. For example, canes or walkers can help those having trouble walking. A plan of care to address changes in mental status should be adapted to each patient's needs.

Driving privileges may be suspended while taking anticonvulsant medication. As each state has different rules about driving and seizures, discuss this issue with your doctor.

It may also be appropriate to discuss advance medical directives (e.g., living will, health care proxy, durable power of attorney) with your family to ensure your medical care and wishes are followed.

Rehabilitation

Because brain tumors develop in parts of the brain that control movement, speech, vision and thinking, rehabilitation may be a necessary part of recovery. Although the brain can sometimes heal itself after the trauma of treatment, it will take time and patience. A neuropsychologist can help patients evaluate changes caused by their brain tumor and develop a plan for rehabilitation. A neuropsychological evaluation assesses the patient's emotional state, daily behavior, cognitive (mental) abilities, and personality. Physical therapy, occupational therapy, and speech therapy may be helpful to improve or correct lost functions.

Recurrence

How well a tumor will respond to treatment, remain in remission, or recur after treatment depends on the specific tumor type and location. A recurrent tumor may be a tumor that still persists after treatment, one that grows back some time after treatment destroyed it, or a new tumor that grows in the same place as the original one.

When a brain tumor is in remission, the tumor cells have stopped growing or multiplying. Periods of remission vary. In general, benign tumors recur less often than malignant ones.

Since it is impossible to predict whether or when a particular tumor may recur, lifelong monitoring with MRI or CT scans is essential for people treated for a brain tumor, even a benign lesion. Follow-up scans may be performed every 3 to 6 months or annually, depending on the type of tumor you had.

Sources & links

If you have more questions, please contact the Mayfield Clinic at 800-325-7787 or 513-221-1100. Additional information is available on the web.

Support

Support groups provide an opportunity for patients and their families to share experiences, receive support, and learn about advances in treatments and medications. Local support groups in the Cincinnati area include:

- Wellness Community of Greater Cincinnati, 513-791-4060
- Wellness Community of Northern Kentucky, 859-331-5568
- Pediatric Brain Tumor Support Group at Cincinnati Children's Hospital, 513-636-6369

Links

- American Brain Tumor Association (www.abta.org) 1.800.886.2282
- National Brain Tumor Association (www.brainumor.org) 1.800.934.CURE
- National Cancer Institute (www.cancer.gov)
- www.oncologychannel.com/braincancer
- www.medicinenet.com/Brain_Tumor

Glossary

anaplastic: when cells divide rapidly and bear little or no resemblance to normal cells in appearance or function.

astrocytoma: a tumor arising in the supportive cells (astrocytes) of the brain or spinal cord; most often in the cerebrum.

benign: does not invade nearby tissues or spread; noncancerous.

biopsy: a sample of tissue cells for examination under a microscope to determine the existence or cause of a disease.

brachytherapy: a type of radiation therapy where capsules containing radioactive substances are surgically implanted into the tumor to deliver radiation; also called internal radiotherapy.

cancer: generic term for more than 100 different diseases caused by uncontrolled, abnormal growth of cells. Cancer cells can invade and destroy normal tissue, and can travel through the bloodstream and lymphatic system to reach other parts of the body.

chemotherapy: treatment with toxic chemicals (e.g., anticancer drugs).

chondrosarcoma: a rare, malignant bone tumor arising from primitive notochord cells and composed of cartilage.

chordoma: a rare, bone tumor arising from primitive notochord cells; usually occurs at the base of the spine (sacrum) or at the skull base (clivus).

craniopharyngioma: a benign tumor arising from cells located near the pituitary stalk.

differentiation: refers to how developed cancer cells are in a tumor. Well-differentiated tumor cells resemble normal cells and tend to grow and spread at a slower rate than undifferentiated, which lack the structure and function of normal cells and grow uncontrollably.

edema: tissue swelling caused by the accumulation of fluid.

ependymoma: a tumor arising from the ependyma cells lining the ventricles of the brain and central canal of the spinal cord.

epidermoid: a benign, congenital tumor arising from ectodermal cells; also called pearly tumor.

glioma: any tumor arising from glial tissue of the brain, which provides energy, nutrients, and other support for nerve cells in the brain.

hydrocephalus: an abnormal build-up of cerebrospinal fluid usually caused by a blockage of the ventricular system of the brain; also called "water on the brain."

immunotherapy: treatment designed to improve or restore the immune system's ability to fight infection and disease.

intracranial pressure (ICP): pressure within the skull. Normal ICP is 20 mm HG.

lesion: a general term that refers to any change in tissue, such as tumor, blood, malformation, infection, or scar tissue.

lymphoma: a rare tumor arising from lymph cells; may metastasize to the brain from lymphoma tumor elsewhere in the body.

malignant: having the properties of invasive growth and ability to spread to other areas.

mass effect: damage to the brain due to the bulk of a tumor, the blockage of fluid, and/or excess accumulation of fluid within the skull.

medulloblastoma: a tumor arising from primitive nerve cells; most often in the cerebellum.

meningioma: a tumor arising from the meninges, the membrane that surrounds the brain and spinal cord.

metastasis: the spreading of malignant cells.

metastatic: cancerous tumor that has spread from its original source through the blood or lymph systems.

oligodendroglioma: a tumor arising from the support cells (oligodendroglia) that produce myelin, the fatty covering around nerve cells.

pituitary adenoma: a tumor arising from cells in the pituitary gland; tumor may be hormone-secreting (prolactin, adrenocorticotrophic, growth hormone) or not.

radiation: high-energy rays or particle streams used to treat disease.

schwannoma (also called neuroma): a tumor arising from Schwann cells that produce myelin.

stereotactic: a precise method for locating deep brain structures by the use of 3-dimensional coordinates.

tumor: an abnormal growth of tissue resulting from uncontrolled multiplication of cells and serving no physiological function; can be benign or malignant.

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