Brain and Spinal Cord Tumors

Hope Through Rese

National Institute of Neurological Disorders and Stroke
National Institutes of Health

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Introduction

A diagnosis of a brain or spinal cord tumor brings uncertainty and worry to you and your friends and family. It's easy to become overwhelmed by a new world of tests, technology, and treatments that you may know little or nothing about.

This guide will give you a better understanding of brain and spinal cord tumors, their treatment options, and the latest research to find safer, more effective ways to diagnose and treat them. You can take the best care of yourself by learning about your diagnosis and discussing it with your doctors.

What are brain and spinal cord tumors?

Brain and spinal cord tumors are found in the tissue inside the skull or the bony spinal column which make up the central nervous system (CNS).[1] A tumor is a mass of normal or abnormal cells that form a new growth or is present at birth (congenital). Tumors occur when genes that regulate cell growth become damaged or mutated, allowing cells to grow and divide out of control. Tumors can form anywhere in the body.

Depending on its type, a growing tumor can kill healthy cells or disrupt their function. It can move or press on sensitive tissue and block the flow of blood and other fluid, causing pain and inflammation. A tumor can also block the normal flow of electricity in the brain or nerve signaling to and from the brain. Some tumors cause no trouble at all.

[1] A Glossary of terms and their specific meanings is found at the end of this guide.

There are more than 120 types of brain and spinal cord tumors. Some are named by the type of cell in which they start (such as glioma) or location (such as meningioma, which form in the lining of the brain and spinal cord).

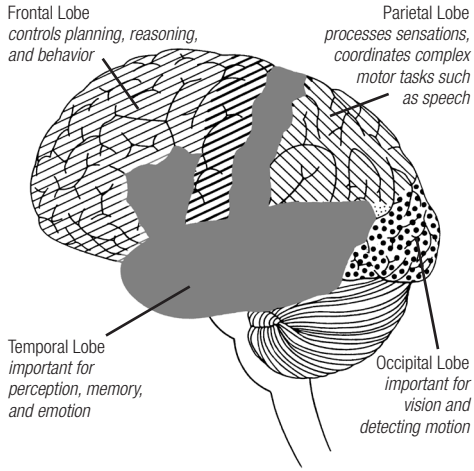
Overview of the brain and spinal cord

The following overview explains how the CNS works and what happens when a tumor is present.

The brain has three major parts:

- *brain stem*—This lowest part of the brain (above the neck) connects to the spinal cord and relays information between the brain and the body using bundles of long nerves. It controls basic life-sustaining functions, including blood pressure, heartbeat, breathing, consciousness, swallowing, and body temperature.
- *cerebrum*—This largest and outermost part of the brain processes information from our senses to tell the body how to respond. It controls functions including movement, touch, judgment, learning, speech, emotions, and thinking.
- *cerebellum*—Located at the lower rear of the brain, above the brain stem, the cerebellum controls balance, helps maintain equilibrium, and coordinates such complex muscle movements as walking and talking.

The brain's two halves, or hemispheres, use nerve cells (neurons) to speak with each other. Each side of the cerebrum controls movement and function on the other side of the body. In addition, each hemisphere has four sections, called *lobes*, which handle different neurological functions.



The brain's two hemispheres have four sections each, called lobes, which handle different functions. The frontal lobes manage voluntary movement and reasoning. The temporal lobes are linked to perception, memory, and understanding sounds and words. The parietal lobes let us receive and understand sounds and words. The occipital lobes receive and process light and visual images, and detect motion.

The *frontal lobes* manage voluntary movement, such as writing, and let us set and prioritize goals. A frontal lobe tumor can cause changes in personality, intellect, reasoning, and behavior; affect coordination and walking; and cause speech loss. The *temporal lobes* are linked to perception, memory, and understanding sounds and words. A tumor here might cause speech and hearing problems, blackouts, seizures, or sensations such as a feeling of fear. The *parietal lobes* let us simultaneously receive and understand sensations such as pressure and pain. A parietal lobe tumor might cause difficulty understanding or speaking words, problems with coordination, seizures, and numbness or weakness on one side of the body. The *occipital lobes* receive and process light and visual images, and detect motion. An occipital lobe tumor can affect the field of vision, usually on one side of the face, and how we understand written words.

Three layers of protective tissue (called the meninges) cover the brain—the thick dura mater (outer), the arachnoid (middle), and the pia mater (innermost to the brain).

Brain tumors in infants and adults tend to be located in the cerebrum; brain tumors in children ages one to 12 years are more commonly found in the cerebellum.

The spinal cord—an extension of the brain—lies protected inside the bony spinal column. It contains bundles of nerves that carry messages between the brain and other parts of the body, such as instructions from the brain to move an arm or information from the skin that signals pain.

A tumor that forms on or near the spinal cord can disrupt communication between the brain and the nerves or restrict the cord's supply of blood. Because the spinal column is narrow, a tumor here—unlike a brain tumor—can cause symptoms on both sides of the body at the same time.

Most spinal cord tumors form below the neck. Symptoms generally strike body areas at the same level or at a level below that of the tumor. For example, a tumor midway along the spinal cord (in the thoracic spine) can cause pain that spreads over the chest and gets worse when the individual coughs, sneezes, or lies down. A tumor that grows in the cervical spine can cause pain that seems to come from the neck or arms, and a tumor that grows in the lower, lumbar spine can trigger back or leg pain.

The three major groups of spinal cord tumor describe where they are found. Extradural tumors grow between the inner surface of the spinal canal and the tough dura mater. Tumors inside the dura (intradural tumors) are further divided into those outside the spinal cord (extramedullary tumors) and those inside the spinal cord (intramedullary tumors). Other descriptors for spinal cord tumors are intrinsic, meaning the tumor forms inside the spinal cord; and extrinsic, where the tumor forms outside of and presses on the cord as it grows.

CNS Tumor FAQs

What are benign and malignant tumors?

No matter where they are located in the body, tumors are classified as *benign* or *malignant*.

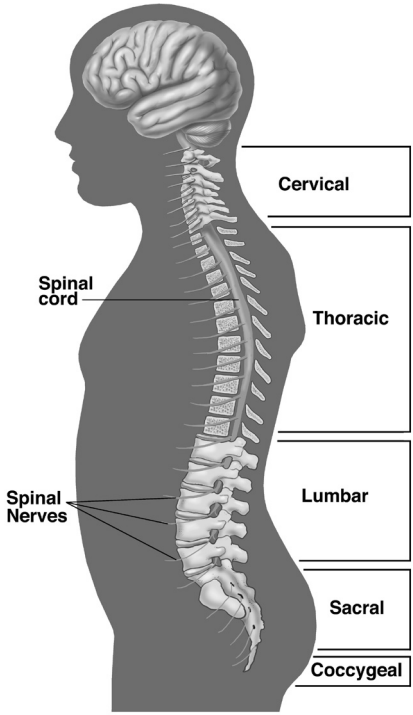
Benign tumors are slow growing, noncancerous cell masses that have a defined edge and do not spread to other parts of the body. Cells in the tumor are similar to normal cells. Often these tumors can be removed surgically and usually do not recur.

Malignant, or cancerous, tumors have cells that look different from normal cells. They can quickly invade surrounding tissue and often have edges that are hard to define, which makes it difficult to remove the entire tumor surgically.

What are primary and metastatic tumors?

Primary tumors of the CNS are growths that begin in the brain or spinal cord. They can be either malignant or benign and are identified by the types of cells they contain, their location, or both. Most primary CNS tumors occur in adults.

Metastatic, or secondary, tumors in the CNS are caused by cancer cells that break away from the primary tumor that first developed in a non-CNS part of the body. These tumors are named after the type of cancer that causes them. Metastastic tumors (also called metastases) in the CNS occur in about one-fourth of all cancers that develop in another part of the body, such as cancer of the lung, breast, or kidneys; or melanoma, a form of skin cancer. They are more common than primary tumors and occur more often in adults than in children.



The spinal cord lies protected inside the bony spinal column and contains bundles of nerves that carry messages between the brain and other parts of the body. A tumor can press on the spinal cord or nerve roots and cause symptoms that generally strike body areas at the same level or below that of the tumor. For example, a tumor in the cervical spine can cause pain in the neck or arms, and a tumor in the lower, lumbar spine can trigger back or leg pain.

Metastatic spine tumors usually form within the bony covering of the spinal column but may also invade the spinal canal from the chest or abdomen.

While cancers elsewhere in the body can easily cause tumors inside the brain and spinal cord, CNS tumors rarely spread outside the nervous system.

What causes CNS tumors?

Researchers really don't know why primary brain and spinal cord tumors develop. Possible causes under investigation include viruses, defective genes, exposure to certain chemicals and other hazardous materials, and immune system disorders. Although smoking, alcohol consumption, and certain dietary habits are associated with some types of cancers, they have not been linked to primary CNS tumors.

In a small number of individuals, CNS tumors may result from specific genetic diseases, such as neurofibromatosis and tuberous sclerosis, or exposure to radiation. Non-ionizing radiation (radio waves) from mobile phone use does not increase the risk of developing a brain tumor.[2]

Brain and spinal cord tumors are not contagious or, at this time, preventable.

Who is at risk?

Anyone can develop a primary CNS tumor, although the risk is very small. Having one or more of the known risk factors does not guarantee that someone will develop a tumor. Brain tumors occur more often in males than in females and are most common in middle-aged to older persons. They also tend to occur more often in children under age 9 than in other children, and some tumors tend to run in families. Most brain tumors in children are primary tumors.

Other risk factors for developing a primary CNS tumor include race (Caucasians are more likely to develop a CNS tumor than other races) and occupation. Workers in jobs that require repeated contact with ionizing radiation or certain chemicals, including those used to manufacture building supplies or plastics and textiles, have a greater chance of developing a brain tumor.

[2] Cellular Phone Use and Cancer Risk: Update of a Danish Nationwide Cohort. Schüz et. al., *Journal of the National Cancer Institute*, Vol. 98, No. 23, December 6, 2006, pp. 1703-1713.

How many people have these tumors?

More than 359,000 persons in the United States are estimated to be living with a diagnosis of primary brain or central nervous system tumor.[3] More than 195,000 Americans are diagnosed with a brain tumor each year.[4] Brain tumors are the most common form of solid tumor in children.

Spinal cord tumors are less common than brain tumors. Although they affect people of all ages, spinal cord tumors are most common in young and middle-aged adults. Nearly 3,200 central nervous system tumors are diagnosed each year in children under age 20.[5]

How are tumors graded?

The generally accepted scale for grading CNS tumors was approved by the World Health Organization in 1993. Grading is based on the tumor's cellular makeup and location. Tumors may also be classified as low-grade (slowly growing) or high-grade (rapidly growing). Some tumors change grades as they progress, usually to a higher grade, and can become a different type of tumor. The tumor is graded by a pathologist following a biopsy or during surgery.

[3] Central Brain Tumor Registry of the United States, 2005-2006
[4] American Brain Tumor Foundation
[5] Central Brain Tumor Registry of the United States, 2005-2006

How Tumors Are Graded	
Grade I tumors	Slow-growing tumors that generally do not spread to other parts of the brain. It is often possible to surgically remove an entire Grade I benign tumor, but this type of tumor may be monitored periodically, without further treatment.
Grade II tumors	Also grow slowly, sometimes into surrounding tissue, and can become a higher-grade tumor. Treatment varies according to tumor location and may require chemotherapy, radiation, or surgery followed by close observation.
Grade III tumors	Malignant tumors that can spread quickly into other CNS tissue. Tumor cells will look different than those in surrounding tissue. Aggressive treatment, often using a combination of chemotherapy, radiation, and/or surgery, is required.
Grade IV tumors	Malignant tumors that invade nearby tissue very quickly and are difficult to treat. The cancerous tissue will look very different from surrounding tissue. Aggressive treatment is required.

What are the possible symptoms?

Brain and spinal cord tumors cause many diverse symptoms, which can make detection tricky. Symptoms depend on tumor type, location, size, and rate of growth. Certain symptoms are quite specific because they result from damage to particular areas of the brain. Symptoms generally develop slowly and worsen as the tumor grows.

The most obvious sign of a brain tumor in infants is a rapidly widening head or bulging crown.

Common symptoms of a brain tumor in adults include headaches, seizures, problems with balance or coordination, loss of muscle control, hydrocephalus, and changes in personality or behavior.

Headaches are the most common symptom of a brain tumor. Headaches may progressively worsen, become more frequent or constant, and recur, often at irregular intervals. Headache pain may worsen when coughing, changing posture, or straining and may be severe upon waking.

Seizures can occur with symptoms that may include convulsions, loss of consciousness, or loss of bladder control. Seizures that first start in adulthood (in someone who has not been in an accident or who had an illness that causes seizures) are a key warning sign of brain tumors.

Nausea and vomiting may be more severe in the morning and may accompany headaches.

Vision or hearing problems can include blurred or double vision, partial or total loss of vision or hearing, ringing or buzzing sounds, and abnormal eye movements.

Personality, behavior, and cognitive changes can include psychotic episodes and problems with speech, language, thinking, and memory.

Motor problems can include weakness or paralysis, lack of coordination, or gradual loss of sensation or movement in an arm or leg. A sudden, marked change in handwriting may be a sign of a tumor.

Balance problems can include dizziness, trouble with walking, clumsiness, or loss of the normal control of equilibrium.

Hydrocephalus and increased intracranial pressure are caused when a tumor blocks the flow of the cerebrospinal fluid (CSF) that surrounds the

brain and spinal cord. Symptoms may include headaches, nausea, and vomiting.

Other symptoms may include endocrine disorders or abnormal hormonal regulation, difficulty swallowing, facial paralysis and sagging eyelids, fatigue, weakened sense of smell, or disrupted sleep and sleep pattern changes.

Common symptoms of a spinal cord tumor include pain, numbness or sensory changes, motor problems, and loss of muscle control.

Pain can feel as if it is coming from various parts of the body. Back pain may extend to the hips, legs, feet, and arms. This pain is often constant and may be severe. It is often progressive and can have a burning or aching quality.

Numbness or sensory changes can include decreased skin sensitivity to temperature and progressive numbness or a loss of sensation, particularly in the legs.

Motor problems and loss of muscle control can include muscle weakness, spasticity (in which the muscles stay stiffly contracted), and impaired bladder and/or bowel control. If left untreated, symptoms may worsen to include muscle wasting, decreased muscle strength, an abnormal walking rhythm known as ataxia, and paralysis.

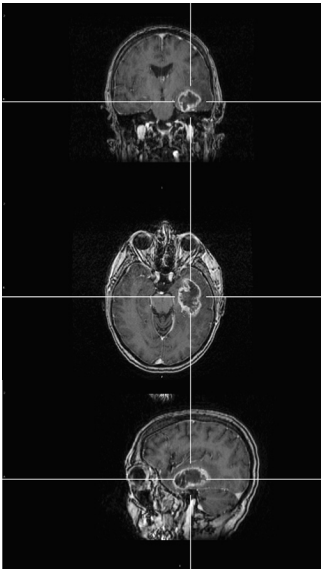
Symptoms may spread over various parts of the body when one or more tumors extend over several sections of the spinal cord.

How are CNS tumors diagnosed?

A doctor, usually a neurologist, oncologist, or neuro-oncologist, can confirm a diagnosis of a brain or spinal cord tumor based on a patient's symptoms, personal and family medical history, and results of a physical exam and specialized tests and techniques.

A neurological exam—the first test—assesses movement and sensory skills, hearing and speech, reflexes, vision, coordination and balance, mental status, and changes in mood or behavior, among other abilities. Some tests require a specialist to perform and analyze results.

Diagnostic imaging shows extremely detailed views of body structures, including tissues, organs, bones, and nerves. If there is a tumor, diagnostic imaging will confirm this diagnosis and help doctors determine the tumor's type, detect swelling and other associated conditions, and, over time, check the results of treatment.



Diagnostic imaging allows doctors to better determine the type of tumor, choose treatment options, and monitor treatment results. These MRI scans show a tumor (the dark area surrounded by a white ring) as seen from different angles and pinpoint its location in the left temporal lobe of the brain.

See the NINDS publication, "Neurological Diagnostic Tests and Procedures," for a more complete description of the following tests: *http://www.ninds.nih.gov/disorders/misc/diagnostic_tests.htm*.

Computed Tomography (CT) uses x-rays and a computer to produce fast, detailed cross-sectional images or "slices" of organs, bones, and tissues, including a tumor. It is also good for detecting the buildup of calcium, which causes tissue to harden and can develop into a tumor.

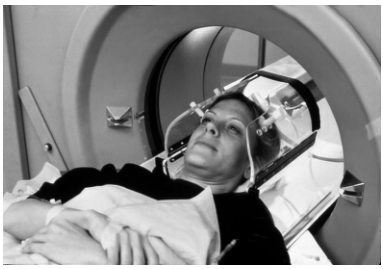
Magnetic Resonance Imaging (MRI) uses a computer, radio waves, and a strong magnetic field to produce two-dimensional slices or a detailed three-dimensional model of tissue being scanned. MRI takes longer to perform than does a CT but is more sensitive and gives better pictures of tumors located near bone.

Both CT and MRI scans for tumor are usually performed before and after administration of a "contrast agent" or dye has been given into a vein. Many tumors become much brighter on the scan taken after the contrast agent is given.

Functional MRI (fMRI) creates images of areas of the brain with specific functions such as movement and language. It can assess brain damage from head injury or degenerative disorders, identify and monitor other neurological disorders such as stroke, and show the distance between specific brain functions and tumors in particular areas of the brain.

Magnetic Resonance Spectroscopy (MRS) gives doctors a chemical snapshot of tissues being studied. It uses the MRI scanner's magnetic field and radio waves to measure and analyze the chemical make-up of the tissue sample.

Positron Emission Tomography (PET) provides computer-generated two- and three-dimensional scans of the brain's chemical activity and cellular function. PET traces and measures glucose (used by the brain for energy) that is attached to small amounts of radioactivity and injected into the bloodstream. Since malignant tissue uses more glucose than normal tissue, it usually shows up on the scan as brighter than surrounding tissue.



Diagnostic imaging can help doctors confirm a tumor diagnosis, determine the tumor's type, detect swelling and other associated conditions, and, over time, check the results of treatment. One type of imaging, called positron emission tomography or PET (shown above), provides computer-generated two- and three-dimensional scans of the brain's chemical activity and cellular function.

Single Photon Emission Computed Tomography (SPECT) studies blood flow to tissue. Certain tumors grow new blood vessels to increase their supply of blood and nutrients. A radioactive isotope is injected intravenously and traced as it travels into the skull. A sophisticated computer processes and stacks the data into a detailed three-dimensional image of activity within the brain.

Angiography (or arteriogram) can distinguish certain types of tumors that have a characteristic pattern of blood vessels and blood flow. A dye that deflects x-rays is injected into a major blood vessel and a series of x-rays is taken as the dye flows to the brain. In many situations angiography has been replaced by non-invasive tests such as CT and MRI.

Testing blood, urine, and other substances can provide clues about the tumor and monitor levels of therapeutic drugs.

Additional tests may include an electroencephalogram, or EEG, which monitors brain activity through the skull (tumors can disrupt the normal flow of brain wave activity and cause seizures); CSF analysis, in which a small amount of the cerebrospinal fluid is removed by a special needle and examined for abnormal cells or unusual levels of various compounds that suggest a brain or

spinal cord tumor; and magnetoencephalography (MEG), which studies brain function by measuring the magnetic field generated by nerve cells in the brain. CSF fluid analysis should be performed with extreme caution on individuals with very large brain tumors.

Diagnosing the distinct type of brain tumor is often difficult. Individuals should consider asking their primary care physician or oncologist for a second opinion, particularly from a neuro-oncologist or neurosurgeon, as there may be new information available and some tumors can change grade or recur. Even a second opinion that confirms the original diagnosis can help people better prepare for their care and treatment.

How are brain and spinal cord tumors treated?

A specialized team of doctors advises and assists individuals throughout treatment and rehabilitation. These doctors may include:

- A neurologist is a specialist in nervous system disorders.
- A medical oncologist is a specialist in cancer.
- A neuro-oncologist is a neurologist who specializes in nervous system tumors.
- A neuroradiologist is a doctor trained in reading diagnostic imaging results who specializes in the CNS.
- A pathologist is a clinical physician who diagnoses diseases of tissues or cells using a variety of laboratory tests.

- A neurosurgeon is a brain or spinal cord surgeon.
- A radiation oncologist is a doctor who specializes in using radiation to treat individuals with cancer.

This team will recommend a treatment plan based on the tumor's location, type, size and aggressiveness, as well as on the individual's medical history, age, and general health.

Initial treatment for a CNS tumor may involve a variety of drugs, including anticonvulsants to treat seizures, pain medications, steroids or other anti-inflammatory drugs to reduce swelling and improve blood flow, antidepressants to treat anxiety or ease depression that might occur following a tumor diagnosis, and drugs to fight nausea caused by various treatments.

Malignant tumors require some form of treatment, while some small benign tumors may only need periodic monitoring. The three standard treatment options for malignant CNS tumors are neurosurgery, radiation therapy, and chemotherapy. Some individuals may receive a combination of treatments.

"Each tumor is unique, and the tumor type and grade may change over time. There are several different treatment options available, depending upon the type, size, and progression of the tumor."

Neurosurgery is usually the first step in treating an accessible tumor—one that can be removed without unacceptable risk of neurological damage. Surgery is aimed at removing all or as much tumor as possible (called resecting or excising) and can slow worsening of neurological function.

An inaccessible or inoperable tumor is one that cannot be removed surgically because of the risk of severe nervous system damage during the operation.

These tumors are frequently located deep within the brain or near vital structures such as the brain stem.

A biopsy is usually performed to help doctors determine how to treat a tumor. A brain biopsy involves surgically removing a small part of the skull to sample the tumor tissue. Biopsies can sometimes be performed by a needle inserted through a small hole. A small piece of tissue remains in the hollow needle when it is removed from the body. A pathologist will stain and examine the tissue for certain changes that signal the type of tumor and grade it to reflect the degree of malignancy.

If the sample is cancerous, the surgeon will remove as much of the tumor as possible. For some primary brain tumors it is not possible to surgically remove all malignant cells. Malignant brain tumors commonly recur from cells that have spread from the original tumor mass into the surrounding brain tissue. Many benign tumors and secondary metastatic tumors can be completely removed surgically.

In some cases, a surgeon may need to insert a shunt into the skull to drain any dangerous buildup of CSF caused by the tumor. A shunt is a flexible plastic tube that is used to divert the flow of CSF from the central nervous system to another part of the body where it can be absorbed as part of the normal circulatory process.

Fortunately, research has led to advances in neurosurgery that make it possible for doctors to completely remove many tumors that were previously thought to be inoperable. These new techniques and tools let neurosurgeons operate within the tight, vulnerable confines of the CNS. Some tools used in the operating room include a surgical microscope, the endoscope (a small

Neurosurgery is usually the first step in treating an accessible tumor. The goals of surgery are to remove all or as much tumor as possible and slow worsening of neurological function.

viewing tube attached to a video camera), and miniature precision instruments that allow surgery to be performed through a small incision in the brain or spine.

Intraoperative MRI uses a special type of MRI to provide a real-time evaluation of the surgery. Constantly updated images during surgery let doctors see how much tumor material has been removed. Intraoperative MRI can also help doctors choose the best surgical approaches and monitor any complications during surgery.

Navigation equipment used in computer-guided, or stereotactic, neurosurgery gives doctors a precise, three-dimensional map of an individual's spine or brain as the operation progresses. A computer uses pre-operative diagnostic images of the individual to reduce the risk of damage to surrounding tissue.

Intraoperative nerve monitoring tests such as evoked potentials use real-time recordings of nerve cell activity to determine the role of specific nerves and monitor brain activity as the surgery progresses. Small electrodes are used to stimulate a nerve and measure its electrical response (or evoked potential). Some surgeries may be done while the individual is awake under monitored anesthesia care, rather than under general anesthesia. This allows doctors to monitor the individual's speech and motor functions as a tumor is being removed.

A possible side effect of surgery is swelling around the site of the tumor, which can be treated with steroids. Bleeding into the tumor site or infection are other serious risks of brain surgery.

In the case of a metastatic tumor, doctors usually treat the original cancer. However, if there are only one or two metastases to the brain or if a metastatic tumor causes serious disability or pain, doctors may recommend surgery—even if the original cancer has not been controlled.

Surgery may be the beginning and end of your treatment if the biopsy shows a benign tumor. If the tumor is malignant, doctors often recommend additional treatment, including radiation and chemotherapy, or one of several experimental treatments.

Radiation therapy usually involves repeated doses of x-rays or other forms of radiation to kill cancer cells or keep them from multiplying. When successful, this therapy shrinks the tumor mass but does not actually remove it. Radiation therapy can be used to treat surgically inaccessible tumors or tumor cells that may remain following surgery.

Depending on tumor type and stage, radiation treatment might be delivered externally, using focused beams of energy or charged particles that are directed at the tumor, or internally, using a surgically implanted device. The stronger the radiation, the deeper it can penetrate to the target site. Healthy cells may also be damaged by radiation therapy but most are able to repair themselves, while the damaged tumor cells cannot.

A radiation oncologist will explain the therapy and how much radiation is needed. Treatment often begins a week after surgery and may continue for several weeks. Depending on tumor type and location, individuals may be able to receive a modified form of therapy to lessen damage to healthy cells and improve the overall treatment.

Externally-delivered radiation therapy poses no risk of radioactivity to the individual or family and friends. Types of external radiation therapy include:

- Whole brain radiation is generally used to shrink multiple cancerous tumors, rather than to target individual tumors. It may be given as the sole form of treatment or in advance of other forms of radiation therapy and microsurgery. Whole brain radiation is generally used for metastatic tumors and rarely for primary tumors.
- Conventional external beam radiation aims a uniform dose of high-energy radiation at the tumor and surrounding tissue from outside the body. It is used to treat large tumors or those that may have spread into surrounding tissue.

- Three-dimensional conformal radiotherapy (3D-CRT) uses diagnostic imaging to prepare an accurate, computer-generated three-dimensional image of the tumor and surrounding tissue. The computer then coordinates and sends multiple beams of radiation to the tumor's exact shape, sparing nearby organs and surrounding tissue.
- Intensity modulated radiation therapy (IMRT) is similar to 3D-CRT but varies the intensity of the hundreds of individual radiation beams to deliver more precise doses to the tumor or to specific areas within it. IMRT can provide a highly effective dose of radiation to the tumor, with less exposure to surrounding tissue.
- Hyperfractionation involves giving two or more smaller amounts of radiation a day instead of a larger, single dose. It can deliver more radiation to certain tumors and reduce damage to normal cells.

Radiosurgery is usually a one-time treatment involving a large amount of high intensity, sharply focused radiation that is aimed at the brain tumor. Stereotactic radiosurgery uses computer imaging to direct precisely focused radiation into the tumor from multiple angles. It does not actually cut into the person but, like other forms of radiation therapy, harms a tumor cell's ability to grow and divide. Stereotactic radiosurgery is commonly used to treat surgically inaccessible tumors. It may also be used at the end of conventional radiation treatment. Two common stereotactic radiosurgery procedures are:

- Linear-accelerated radiosurgery (LINAC) uses radar-like technology to prepare and fire a single beam of high-energy x-rays into

the tumor. Also called high linear-energy transfer radiation, LINAC forms the beam to match the tumor's shape, avoiding surrounding tissue. A special machine that rotates around the head then fires a uniform dose of radiation into the tumor.

- Gamma knife® radiosurgery focuses more than 200 beams of gamma radiation into one intersecting beam that is fired into the tumor. It also uses computer imaging to prepare a model of the tumor. This single treatment takes between one and four hours and is often recommended for inaccessible or hard to treat tumors.

Both procedures may be given on an outpatient basis but an overnight stay in the hospital is often recommended.

Radiation therapy can be used to treat surgically inaccessible tumors or tumor cells that may remain following surgery. Repeated doses of radiation can kill cancer cells or keep them from multiplying, and can be delivered externally or internally.

Proton beam therapy directs a beam of high-energy radiation into the tumor, leaving surrounding healthy tissue and organs intact. It is best used to treat tumors that are solid and have not spread to other parts of the body. Proton beam therapy can be used as a stand-alone treatment or in combination with chemotherapy or as follow-up to surgery.

Internal tumor radiation therapy, also called brachytherapy or interstitial radiation therapy, involves placing a small amount of radioactive material into or near the tumor (or its cavity, if the tumor has been surgically removed). In most cases, the radiation is inserted at the time of surgery or using imaging and a catheter. The radiation may be left in place for several days and, if more than one treatment is needed, the doctor may leave the catheter in place for a longer period.

Individuals may need to be hospitalized for a few days following this procedure as the radiation may extend outside their body and could possibly harm others. The radiation becomes less active each day until it is safe for individuals who have been treated to be around others.

Side effects of radiation therapy vary from person to person and are usually temporary. They typically begin about two weeks after treatment starts and may include fatigue, nausea, vomiting, reddened or sore skin in the area receiving treatment, headache, hearing loss, problems with sleep, and hair loss (although the hair usually grows back once the treatment has stopped). Radiation therapy in young children, particularly those children age three or younger, can cause problems with learning, processing information, thinking, and growing. Radiation therapy is painless.

Chemotherapy uses powerful drugs to kill cancer cells or stop them from growing or dividing. These drugs are usually given by pill or injection and travel through the body to the brain, or can be inserted surgically using dissolvable wafers that have been soaked in a chemotherapeutic drug. These wafers slowly release a high concentrate of the drug to kill any remaining malignant cells.

Chemotherapy may also be given to kill cancer cells in the spinal column.

Chemotherapy is given in cycles to more effectively harm cancer cells and give normal cells time to recover from any damage. The oncologist will base the treatment on the type of cancer, drug(s) to be used, the frequency of administration, and the number of cycles needed.

Individuals might receive chemotherapy to shrink the tumor (called neo-adjuvant therapy), in combination with radiation therapy, or after radiation treatment (called adjuvant therapy) to destroy any remaining cancer cells. Metronomic therapy involves giving continuous low-dose chemotherapy to block mechanisms that stimulate the growth of new blood vessels needed to feed the tumor. Chemotherapy is also used to treat CNS lymphoma (caused by cancer cells which form in the lymph system and are present in the CNS) and inaccessible tumors or tumors that do not respond to radiation therapy.

Not all tumors are vulnerable to the same anti-cancer drugs, so a person's treatment may include a combination of drugs. Common CNS chemotherapeutics include temozolomide, carmustine (also called BCNU), lomustine, tamoxifen, carboplatin, methotrexate, procarbazine, and vincristine.

Side effects of chemotherapy may include hair loss, nausea, digestive problems, reduced bone marrow production, and fatigue. The treatment can also harm normal cells that are growing or dividing at the same time, but these cells usually recover and problems stop once the treatment has ended.

Alternative and complementary approaches may help individuals better cope with their diagnosis and treatment. Some of these therapies, however, may be harmful if used during or after cancer treatment and should be discussed with a doctor beforehand. Common approaches include nutritional and herbal supplements, vitamins, special diet, and mental or physical techniques to reduce stress.

What are the different CNS tumors and tumor-related conditions?

There are many types of brain and spinal cord tumors. These tumors are named by their location in the body, cell of origin, rate of growth, and malignancy, if any. Some tumor types are more prevalent in children than in adults. Here is a listing of some common benign and malignant CNS tumors.

Glioma tumors grow from several types of glial cells. Glial cells support the function of neurons. Gliomas usually occur in the brain's cerebral hemispheres but may also strike other areas, especially the optic nerve, the brain stem and, particularly among children, the cerebellum. Gliomas are classified based on their type of glial cells.

Astrocytomas include nearly half of all CNS tumors. They develop from star-shaped glial cells called astrocytes and can be benign or malignant. Astrocytomas tend to form in the cerebrum in adults and in most parts of the brain in children.

These tumors occur most often in middle-aged men. The most common forms of astrocytoma are:

- *Anaplastic astrocytoma*. Also called mid-grade astrocytomas, these tumors grow rapidly and invade other tissue. Treatment includes surgery followed by radiation and, sometimes, chemotherapy.
- *Pilocytic astrocytoma*. These slow-growing tumors occur most often in children and young adults and rarely spread into surrounding tissue. They usually have well-defined borders and may be removed entirely by surgery.
- *Glioblastoma multiforme*. These malignant, highly invasive tumors spread quickly and often recur following initial treatment. Also called grade IV astrocytoma, these tumors are often found in adults between the ages of 45 and 70 years. Doctors usually treat glioblastomas with surgery followed by radiation therapy and chemotherapy.

Ependymomas usually affect children and develop from cells that line the cavities of the brain and spinal canal where the CSF is made and stored. These tumors can also spread along the spinal canal. Most ependymomas are benign. Treatment usually includes surgery followed by radiation therapy. Chemotherapy is sometimes used, especially for recurrent tumors.

Gangliogliomas are very rare, slow-growing, benign tumors that form from nerve cells and glial cells. They can occur in the brain and the spine. Gangliogliomas can often be removed entirely by surgery. Radiation therapy may be needed if the entire tumor cannot be resected.

Oligodendrogliomas, which develop from glial cells within the cerebral hemispheres that help insulate the nerve fibers that transmit nerve impulses, represent about 5 percent of all gliomas. Oligodendrogliomas occur most often in men ages 40-70 but can be found in children. Treatment usually involves surgery followed by radiation therapy and chemotherapy for hard to reach tumors.

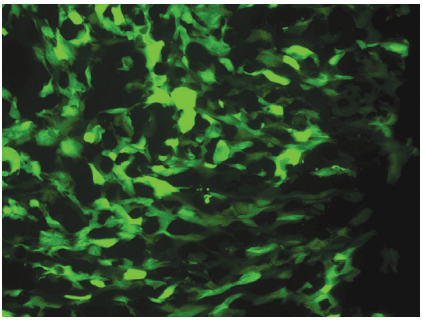
"There are more than 120 types of brain and spinal cord tumors. Some are named by their location, the type of cell in which they start, or rate of growth."

Mixed gliomas contain more than one type of glial cell and are usually found in the cerebrum. They occur more frequently in adult men than women and can occur in children. These tumors can spread to other sites in the brain. Treatment focuses on the most malignant cell type found within the tumor.

Other gliomas are named after the part of the body they affect. Among them are:

Brain stem gliomas are found at the lowest part of the brain, which controls many vital body functions. They are most common in children and middle-aged adults. Surgery is not usually used to treat brain stem gliomas because of their vulnerable location. Radiation therapy sometimes helps to reduce symptoms and improve survival by slowing tumor growth.

Optic gliomas are found on or near the nerves that travel between the eye and brain vision centers and are particularly common in individuals who have neurofibromatosis. These tumors usually occur in children and adolescents. Treatment includes surgery or radiation.



Brain and spinal cord tumors are named by their location in the body, cell of origin, rate of growth, and malignancy. Gliomas grow from several types of glial cells and usually occur in the brain's hemispheres but may also strike other areas, such as the optic nerve, the brain stem, and the cerebellum. This photograph shows glioma cells in green.

Other childhood and adult CNS tumors include:

Chordomas are rare congenital tumors which develop from remnants of the flexible spine-like structure that forms and dissolves early in fetal development (and is later replaced by the bones of the spine). Chordomas often occur near the top or the bottom of the spine, outside the dura mater, and can invade the spinal canal and skull cavity. Most often seen in persons in their 50s or 60s, chordomas are usually treated by a combination of surgery and radiation.

Choroid plexus papillomas are rare, usually benign childhood tumors that develop slowly and can increase the production and block the flow of CSF, causing symptoms that include headaches and increased intracranial pressure. Treatment usually involves surgery to remove all or as much of the tumor as possible. A rarer cancerous form that can spread via the cerebrospinal fluid is typically treated with surgery, chemotherapy, and radiation therapy.

Craniopharyngiomas, like chordomas, develop from cells left over from early fetal development. They often grow at the base of the brain, near the brain's pituitary gland (which releases chemicals important for the body's growth and metabolism), and may also affect the optic nerve and surrounding tissue. Craniopharyngiomas usually affect young children and adolescents. Treatment includes surgery and, in some people, radiation therapy.

Dysembryoplastic Neuroepithelial Tumors (DNET) are benign, slow-growing tumors that are typically found in the top half of the brain. DNETs are seen most often in persons under age 20 but they can affect all ages. They are often diagnosed after a period of uncontrolled seizures, which can be treated surgically.

Germ cell tumors may start in cells that fail to leave the CNS during development. These very rare childhood tumors usually form in the center of the brain, near the pineal gland, and can spread elsewhere in the brain and spinal cord. Different tumors are named after the type of germ cell and include teratomas (most common in newborns and infants), embryonic carcinomas, and germinomas. Depending on the tumor type, treatment involves radiation, chemotherapy, or a combination of therapies.

Meningiomas are tumors that develop from the thin membranes, or meninges, that cover the brain and spinal cord. These benign tumors account for about 20 percent of all brain tumors and about 25 percent of all primary spinal cord tumors. They affect people of all ages, but are most common among those in their 40s. Meningiomas usually grow slowly, generally do not invade surrounding normal tissue, and rarely spread to other parts of the CNS or body. Surgery is the preferred treatment for accessible meningiomas.

Pineal Tumors account for about one percent of brain tumors. These tumors form in the pineal gland, a small structure located between the cerebellum and the cerebrum. When possible, physicians will begin treatment with surgery or perform a biopsy to confirm the tumor type. They may also recommend radiation or chemotherapy,

or both, for malignant pineal tumors. The three most common types of pineal region tumors are gliomas, germ cell tumors, and pineal cell tumors.

Pituitary Tumors (also called pituitary adenomas) are small tumors that form in the pituitary gland. This small gland releases hormones that influence the body's growth, metabolism, and maturation. Most pituitary tumors are benign and their incidence increases with age. Pituitary tumors account for about 10 percent of all primary brain tumors. Doctors classify pituitary tumors into two groups—secreting and nonsecreting. Secreting tumors release unusually high levels of pituitary hormones, which can trigger neurological conditions and symptoms including hyperthyroidism and Cushing's syndrome (the harmful over-production of the hormone cortisol). Treatment options include tumor resection, radiation therapy, and drug therapy.

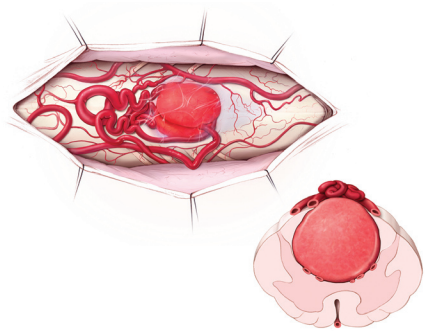
Primitive Neuroectodermal Tumors (PNETs) usually affect children and young adults. These malignant tumors may spring from primitive or immature cells left over from early development of the nervous system. PNETS can spread throughout the brain and spinal cord in a scattered, patchy pattern and, in rare cases, cause cancer outside the CNS. Doctors try to remove as much tumor as possible with surgery and follow up with radiation. Chemotherapy is used when the tumor affects the spinal canal or causes spinal cord compression.

- *Medulloblastomas*, the most common PNET, represent more than 25 percent of all childhood brain tumors. They usually form in the cerebellum and can spread throughout the brain and along the spine. Most often these tumors are found in children under age 10.

- *Neuroblastomas* account for up to 10 percent of childhood tumors. They generally appear above the adrenal glands but can be found in the brain and elsewhere in the body. Boys are slightly more at risk of developing these tumors than are girls.

Schwannomas are benign tumors that arise from the cells that form a protective sheath around the body's nerve fibers. They are usually benign and are surgically removed when possible. One of the more common forms of schwannoma affects the eighth cranial nerve, which contains nerve cells important for balance and hearing. Also known as vestibular schwannomas or acoustic neuromas, these tumors may grow on one or both sides of the brain.

Vascular Tumors arise from the blood vessels of the brain and spinal cord. The most common of these rare, noncancerous tumors is the *hemangioblastoma*, which is linked in a small number of people to a genetic disorder called von Hippel-Lindau disease. Hemangioblastomas do not usually spread, and doctors typically treat them with surgery.



Spinal cord tumors can disrupt communication between the brain and the nerves or restrict the cord's blood supply. Because the spinal column is narrow, a tumor here (illustrated above) can cause symptoms on both sides of the body at the same time. The illustration below shows a cross section of the spinal cord and tumor.

Tumor-related conditions

CNS lymphoma occurs when cancerous cells which form in the lymph system (a part of the body's immune system) are present in the CNS. Primary CNS lymphoma begins in the brain; it affects a small number

of otherwise healthy people and a larger fraction of those who have an impaired immune system, whether from organ transplants, infection with the AIDS virus, or other causes. Secondary brain lymphoma occurs when tumor cells from a lymphoma located outside the brain metastasize to the CNS. Doctors usually treat the disorder with chemotherapy or radiation. When the linings of the spinal canal are affected, chemotherapeutic drugs are either injected into the CSF either through a lumbar puncture needle or special equipment placed under the scalp that is connected to a tube that enters the normal CSF spaces (ventricles) within the brain.

Arachnoid cysts are benign, fluid-filled masses that form within a thin membrane lining (tumors are solid tissue masses). Cysts in the CNS can cause tumor-like symptoms, including headache and seizures. Some cysts occur more often in the spinal cord than in the brain, and certain cysts are seen most frequently in children. Depending on their size and location, cysts may be monitored periodically for any change or treated surgically.

Hydrocephalus involves the buildup of cerebrospinal fluid in the brain. The excessive fluid can cause harmful pressure, headaches, and nausea. Treatment includes surgical insertion of a shunt that drains excess fluid to another area of the body, where it is absorbed as part of the circulatory process, or surgical treatment without a shunt to restore CSF circulation.

Meningeal carcinomatosis is caused by cancer cells that metastasize to the CNS and spread around the brain and spinal cord via the cerebrospinal fluid.

These cells can form colonies or small tumors in many places, including the roots of nerves, the surface of the brain, the cerebrum, the brain stem, and the spinal cord. Treatments include radiation, which can sometimes slow growth of the cells, and chemotherapy.

Neurofibromatosis refers to related genetic disorders that cause tumors to grow around nerves. Most tumors are benign but can become malignant over time. The more common form of this disorder, neurofibromatosis type 1, usually causes tumors in nerves outside the CNS and affects the skin and bones. Neurofibromatosis type 2 causes multiple CNS tumors that typically affect the nerve involved with hearing. Treatment may include surgery and radiation therapy.

Pseudotumor cerebri, also called "false brain tumor," mimics brain tumor symptoms and may be caused by the abnormal buildup of cerebrospinal fluid. It is diagnosed by ruling out all other possible causes for symptoms and confirming that the cerebrospinal fluid pressure is increased. Pseudotumor cerebri is most common in women ages 20 to 50 years and can cause progressive visual loss in some individuals if left alone. Treatment may include drugs to relieve pressure and shunting to drain the fluid to another area of the body.

Tuberous sclerosis is a genetic disorder that causes such numerous neurological and physical symptoms as seizures and benign tumors of the eyes and CNS. It may be present at birth or develop over time. About half of people who have tuberous sclerosis develop benign astrocytomas. Treatment may include drug therapy and regular monitoring by a doctor.

von Hippel-Lindau disease is a rare genetic multi-system disorder characterized by tumors that grow in certain parts of the body. Slow-growing benign tumors called hemangioblastomas (cyst-like masses of tangled blood vessels) may develop in the brain and nervous system. Treatment usually involves surgical resection of the tumor.

What is the prognosis?

Each person is different. Prognosis depends greatly on prompt diagnosis and treatment, the individual's age and general health, whether the tumor is malignant or benign, tumor size and location, tumor grade, and response to therapy. An individual whose entire tumor has been removed successfully may recover completely. Generally, prognosis is poorer in very young children and in older individuals. Rehabilitation and counseling can help individuals and family members better cope with the disorder and improve quality of life.

Continued monitoring and long-term follow-up is advised as many tumors resist treatment and tend to recur.

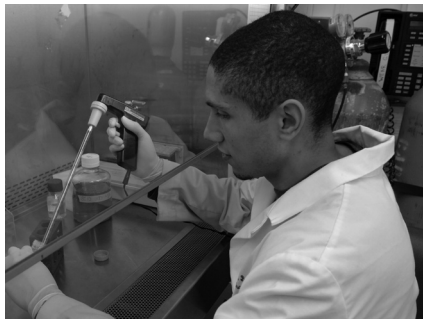
Normal tissue and nerves that may have been damaged or traumatized by the tumor or its treatment will need time to heal. Some post-treatment symptoms will disappear over time. Physical therapy can help people regain motor skills, muscle strength, and balance. Some individuals may need to relearn how to swallow or speak if the brain's cognitive areas have been affected. Occupational therapy can teach people new ways to perform tasks. Supportive care can help people manage any pain and other symptoms.

What research is being done?

Scientists continue to investigate ways to better understand, diagnose, and treat CNS tumors. Several of today's treatment regimens were experimental therapies only a decade ago. Current clinical studies of genetic risk factors, environmental causes, and molecular mechanisms of cancers may translate into tomorrow's treatment of, or perhaps cure for, these tumors.

Much of this work is supported by the National Institutes of Health (NIH), through the collaborative efforts of its National Institute of Neurological Disorders and Stroke (NINDS) and National Cancer Institute (NCI), as well as other agencies within the Federal government, nonprofit groups, pharmaceutical companies, and private institutions. Some of this research is conducted through the collaborative neuroscience and cancer research community at the NIH or through research grants to academic centers throughout the United States.

The jointly sponsored NCI-NINDS Neuro-Oncology Branch coordinates research to develop and test the effectiveness and safety of novel therapies for people with CNS tumors. These experimental treatment options may include new drugs, combination therapy, gene therapy, biologic immuno-agents, surgery, and radiation.



Scientists are developing and testing the effectiveness and safety of novel therapies for people with CNS tumors. These experimental treatment options may include new drugs, combination therapy, gene therapy, biologic immuno-agents, surgery, and radiation. Much of this work is supported by the National Institutes of Health (NIH).

Information about these trials, and trials involving other disorders, can be accessed at the Federal government's database of clinical trials, *http://clinicaltrials.gov*.

Part of this research involves creating a comprehensive public database of clinical, molecular, and genetic information on brain tumors to help researchers and clinicians identify and evaluate molecular targets in brain cancer. The joint NCI-NINDS Repository for Molecular Brain Neoplasia Data (REMBRANDT) will hold genetic and molecular analyses of samples from participants in NCI-sponsored clinical trials in what is slated to become the largest clinical/genetic corollary study ever conducted on brain tumors. It will also store a wide array of molecular and genetic data regarding all types of brain tumors. Understanding the biology behind these tumors will provide clues to new therapeutic approaches.

Researchers are also developing mouse models that mimic human CNS cancers, which may speed discovery of potential treatments in humans.

Beyond these efforts to develop needed resources, scientists at the NIH and at universities across the US are exploring a variety of approaches to treat developing CNS tumors. These experimental approaches include boosting the immune system to better fight tumor cells, therapies that target the tumor cell while sparing normal cells, making improvements in radiation therapy, disabling the tumor using genes attached to viruses, and defining biomarkers that may predict the response of a CNS tumor to a particular treatment.

"Scientists continue to investigate new ways to better understand, diagnose, and treat central nervous system tumors. Several of today's treatments were experimental therapies only a decade ago."

Biological therapy involves enhancing the body's overall immune response to recognize and fight cancer cells. The immune system is designed to attack foreign substances in the body; since cancer cells aren't foreign, they usually do not generate much of an immune response. Researchers are using different methods to provoke a strong immune response to tumor cells. Such proteins as interleukin and interferon (both of which are part of a group of immune system "messengers" called cytokines) and other substances can stimulate and restore the body's natural response against proteins on the surface of cancer cells and thus slow tumor growth. Other therapy uses viruses, T cells (a major component of immune system function), and other substances to increase immune response and target the tumor cells. Scientists are also experimenting with genetically altered T cells from the person's own body, which are cultured with an antigen and injected directly into the brain following surgery. Biological therapies to fight CNS tumors include vaccines, gene therapy, antibody therapy, and tumor growth factors.

Antibodies are proteins that are normally produced by the body to ward off bacteria and viruses. Monoclonal antibodies are multiple copies of a single antibody that act as a homing device to fit one—and only one—type of antigen (a protein on the surface of the tumor cell that stimulates the immune system response). Scientists at the NINDS and elsewhere are linking these antibodies

to immunotoxins that seek out tumor cells with a matching antigen, bind to these tumor cells, and deliver their toxin, with minimal damage to surrounding normal cells. Additional approaches include attaching a radioactive substance to the antibodies, which act as targeting agents to deliver radiation to the tumor cell.

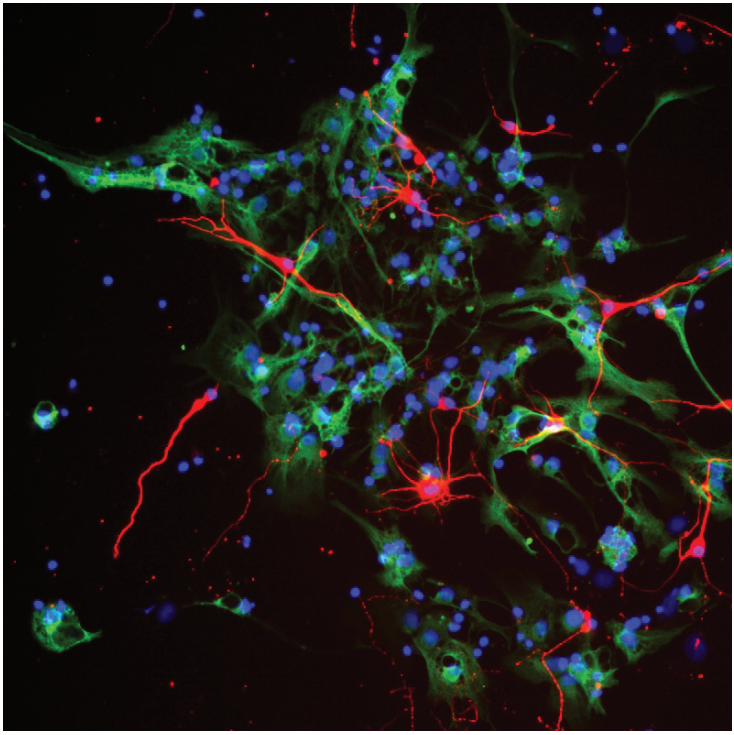
Gene therapy (also called gene transfer) aims to deliver a suicide gene to the tumor cell or to boost the immune system. A gene whose activity can be influenced to kill the cell is integrated into a virus that can cross the blood-brain barrier (an elaborate network of fine blood vessels and cells that filters the blood reaching the CNS) and travel to the tumor. Delivery methods under investigation include viruses and stem cells. Gene therapy may become an important add-on therapy for individuals who do not respond well to other treatments.

Scientists are testing the effectiveness of vaccine therapy for a variety of CNS tumors. Vaccine therapy strengthens the immune response by inserting an antigen that the body will attack. Some vaccines target a specific antigen, while others, using the whole tumor cell to make the vaccine, hope to target multiple antigens which the tumor may express. Research has shown the vaccine can be genetically engineered with tumor antigens and injected into the body to induce an immune response, which increases the attack on antigens expressed on the surface of the tumor cell. Experimental CNS tumor vaccines include those designed to stimulate an immune response to a particular protein or antigen, and dendritic cell vaccines (in which blood cells are taken from the body, processed in a laboratory and given

back to the body to break up the tumor cell outer protein into smaller pieces, which increases targeting by immune cells).

Findings from NIH-sponsored research on adult CNS tumor development and treatment suggest the immune system and, potentially, infection with the cytomegalovirus may play a critical role in certain tumor-type risk and prognosis. Repeated stimulation of the immune system to counter this herpes virus may serve as a tumor promotion factor. Scientists hope to identify immune factors and develop targeted immunotherapies for this disease.

Targeted therapy offers great promise for treating cancerous cells without destroying other cells. Targeted therapy uses different molecules to reduce tumor gene activity and suppress uncontrolled growth by killing or reducing the production of tumor cells. Of particular interest to scientists is the development of tailored therapeutics—involving a combination of targeted agents—to treat tumors based on their genetic makeup. Specifically, molecularly targeted drugs seek out the molecular and cellular changes that convert normal cells into cancer. Many targeted cancer therapies are being tested in animals for use alone or in combination with other cancer treatments, such as chemotherapy. Researchers also hope to discover tumor-specific cellular or molecular pathways that can be used to increase drug delivery and to find ways to identify people who may benefit from combined therapy. Targeted therapies include growth factors, anti-angiogenetics, antisense technology, and small molecules aimed at blocking gene activity.



Scientists are using a new genetically engineered mouse strain to study the role of the neurofibromatosis type 1 (NF1) gene in brain development. NF1 is a genetic disorder that causes brain and nerve tumors as well as learning disabilities. Brain neurons lacking NF1 gene expression (in red) are shorter than normal. The green color shows a protein and the blue is a counterstain.

Growth factors often govern normal cell growth. Growth factors are released from either the cell or the surrounding tissue. Cancer cells can either secrete these growth factors or respond to them, enabling them to divide out of control. A number of tumor growth factors have been identified, including those that trigger nerve tissue growth and stimulate blood vessels to grow (a process called angiogenesis). Researchers continue to identify and develop agents that can block these factors.

Oncogenes are transformed genes that are involved in cell growth and cause normal cells to divide uncontrolled and become malignant, either through mutation or over-production. Researchers have identified specific events that lead to this mutation and are developing diagnostic and therapeutic screening tools.

Anti-angiogenetics—compounds that block blood vessel growth and the flow of nutrients and oxygen to the tumor—are proving to be a promising therapy for brain tumors. These compounds also may hamper cell signaling and stop tumor cells from spreading elsewhere in the body. Clinical trials have shown that anti-angiogenetics can improve the outcome for glioblastoma multiforme tumors that recur following initial treatment with radiation and chemotherapy. More than a dozen such compounds have been identified, including bevacizumab, interferon, and endostatin. Researchers are studying the combination of anti-angiogenics and radiation or chemotherapy in treating newly diagnosed brain tumors. Other research is testing angiogenic inhibitors that have had positive results in adults on children with primary CNS tumors and in individuals with tumors that have not responded well to other tumor treatment.

Certain enzymes that are involved in cell division or the copying of genetic information may be overproduced in cancer cells, causing gene mutations and uncontrolled cell growth. Several different types of kinase inhibitors—proteins that block growth-signaling enzymes without harming normal cells—have been identified and approved for cancer treatment. Scientists are testing protein-level kinase inhibitors to see of they make CNS tumors more

sensitive to chemotherapy. Clinical trials for brain tumors are studying the safety and effectiveness of kinase inhibitors in children with CNS tumors and in other individuals with recurring or hard to treat tumors.

Antisense oligonucleotide technology uses short fragments of nucleic acid molecules to block gene expression in specific cells and prevent tumor growth. Unlike gene therapy, antisense oligonucleotide technology does not replace or substitute genetic material but inhibits the expression of select targets. This technology (also known as RNA interference, siRNA, or shRNA) may help scientists to identify additional genes involved in tumor formation and improve drug delivery with fewer side effects.

Also of particular interest are microRNAs (or miRNAs)—naturally occurring molecules that regulate gene activity and are involved in the formation and development of tumor stem cells. Scientists are using miRNAs to switch off tumor stem cell activity. Researchers are studying miRNAs as a possible diagnostic and therapeutic strategy for brain tumors and other forms of cancer.

Biomarkers are molecules or others substances in the blood or tissue that can be used to diagnose or monitor a particular disorder, among other functions. As cells become cancerous, they can release unique proteins and other molecules into the body which scientists use to speed diagnosis and treatment. Some CNS tumor biomarkers have been found, such as the epithelial growth factor receptor (EGRF) gene. Researchers continue to

search for additional clinical biomarkers of CNS tumors, to better assess risk from environmental toxins and other possible causes, and monitor and predict the outcome of CNS tumor treatment. NINDS-funded research has recently shown that mutation analysis of EGFR can be used to predict which tumors are most likely to respond to a specific class of cancer-fighting drugs. Identifying biomarkers may also lead to the development of new models of disease and novel therapies for tumor treatment.

Radiation therapy research includes testing several new anticancer drugs, either independently or in combination with other drugs, to improve treatment delivery and effectiveness. Researchers are also testing different drugs in combination with other therapies and are investigating combined therapies such as radiation and radiosurgery to effectively treat CNS tumors. Research areas being explored include tomotherapy, boron neutron capture therapy, liquid radiation therapy, and the use of radiosensitizers.

Radiosensitizers are drugs that make rapidly dividing tumor tissue more vulnerable to radiation. Early studies using radiosensitizers produced mixed results. While some trials suggested these drugs may improve survival in certain individuals, other trials showed little benefit. Scientists are now testing an experimental drug that increases the amount of oxygen that is released from the blood into the tissues, making cancer cells more responsive to radiation and chemotherapy. Studies show the lack of oxygen in a tumor can make radiation therapy less effective.

Tomotherapy combines CT scanning and intensity modulated radiation therapy to deliver small beams of high-dose radiation to the tumor while greatly reducing radiation exposure to surrounding tissue. Studies are examining the effectiveness of radiation delivery through tomotherapy and to see if long-term side effects of radiation therapy can be reduced.

Boron Neutron Capture Therapy (BNCT) is an experimental treatment that uses fission to kill tumor cells. An amino acid or other drug that carries boron is injected into the body, where it collects more readily in tumor cells than in regular tissue. A beam of low-energy neutrons is directed at the tumor from outside the body, causing the boron atoms to split (called neutron capture) and send high amounts of energy into the cancerous cells. Radiation damage to surrounding cells is extremely small. BNCT is being tested as a post-surgery treatment for people with certain head and neck tumors. If successful, BNCT could someday be used to treat children with brain tumors.

Many new approaches to treating CNS tumors appear promising and new clinical trial designs are being developed to more quickly evaluate novel agents. Past research has led to improved tumor treatments and techniques for many individuals with CNS tumors. In the years ahead, we can look forward to new, more effective forms of therapy.

Liquid radiation therapy is an experimental treatment that uses a balloon catheter to deliver internal radiation therapy to the cavity that remains following tumor surgery. A radioactive liquid is injected into the catheter and molds the balloon to the exact edges of the cavity. The

liquid stays in the balloon for several days until it and the catheter are removed.

Chemotherapeutic drug research focuses on ways to better deliver the drugs across the blood-brain barrier and into the site of the tumor. Since chemotherapeutic drugs work in different ways to stop tumor cells from dividing, several trials are testing whether giving more than one drug, and perhaps giving them in different ways (such as staggered delivery and low-dose, long-term treatment), may kill more tumor cells without causing or lessening damaging side effects than present therapy. Researchers are examining different levels of chemotherapeutic drugs to determine if they are less toxic to normal tissue when combined with other cancer treatments. Other studies are investigating gene therapy as a way to make cancer cells more sensitive to chemotherapy. Research areas include differentiating drugs, osmotic blood-brain barrier disruption, and convection enhanced delivery.

Differentiating drugs change dividing cells into nondividing cells and can halt tumor growth. An early study using retinoids (made from vitamin A) as an independent treatment for certain tumors showed no significant effect. Scientists are trying retinoids in combination with other chemotherapeutic drugs or treatments to slow the growth of malignant glioma.

Researchers are testing different drugs and molecules to see if they can modulate the normal activity of the blood-brain barrier and better target tumor cells and associated blood vessels.

Osmotic blood-brain barrier disruption uses certain drugs to open blood vessels throughout the brain. Scientists are currently studying whether certain chemotherapeutic drugs, when given with osmotic blood-brain barrier disruption, might be an effective way to kill cancer cells without harmful side effects.

Convection enhanced delivery sends a continuous, uniform stream of toxic drugs into the tumor via catheters that are inserted during surgery. This drug delivery system, which bypasses the blood-brain barrier, is being evaluated in children with recurring brain cancer and in individuals whose tumor location prevents its total surgical removal.

Also under investigation are ways to help the body respond to improved drug delivery or other cancer treatments. Bone marrow and stem cell transplants may replace blood-forming cells that are killed by chemotherapy, radiation treatment, or a combination of therapies. These transplants, which are given after radiation or chemotherapy, help the bone marrow recover and produce healthy blood cells. Researchers are studying the effectiveness of these transplants in protecting blood cells in children with certain types of CNS tumors and in other individuals with recurrent or hard to treat CNS cancer, who receive higher than normal doses of chemotherapy.

Although many new approaches to treatment appear promising, it is important to remember that all potential therapies must stand the tests

of well-designed, carefully controlled clinical trials and long-term follow-up of participants before any conclusions can be drawn about their safety or effectiveness. New trial designs are also being developed to more quickly evaluate novel agents and may involve pre-selection of participants based on the molecular abnormality in their tumor.

Past research has led to improved tumor treatments and techniques for many individuals with CNS tumors. Current research promises to generate further improvements. In the years ahead, physicians and individuals who have a CNS tumor can look forward to new, more effective, less toxic forms of therapy developed through a better molecular understanding of the unique traits of CNS tumors.

Where can I get more information?

For more information about brain and spinal cord tumors, other neurological disorders, or the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
(800) 352-9424
www.ninds.nih.gov

Also contact the National Cancer Institute for information about brain and spinal cord tumors and other cancers:

National Cancer Institute
National Institutes of Health, DHHS
6116 Executive Boulevard
Suite 3036A, MSC 8322
Bethesda, MD 20892-8322
(800) 4-CANCER (422-6237) or (800) 332-8615 (TTY)
www.cancer.gov

Private voluntary organizations that provide information on research, treatment, diagnosis, and other services regarding CNS tumors and tumor-related conditions include:

Accelerate Brain Cancer Cures, Inc. (ABC2)
1717 Rhode Island Avenue, NW
Suite 700
Washington, DC 20036
(202) 419-3140
www.abc2.org

American Brain Tumor Association
2720 River Road
Suite 146
Des Plaines, IL 60018
(847) 827-9910
(800) 886-2282
www.abta.org

American Cancer Society
National Home Office
1599 Clifton Road, NE
Atlanta, GA 30329-4251
(800) ACS-2345 or TTY (866) 228-4327
www.cancer.org

Brain Tumor Society
124 Watertown Street
Suite 311
Watertown, MA 02472-2500
(617) 924-9997
(800) 770-8287
www.tbts.org

Childhood Brain Tumor Foundation
20312 Watkins Meadow Drive
Germantown, MD 20876
(301) 515-2900
(877) 217-4166
www.childhoodbraintumor.org

Children's Brain Tumor Foundation
274 Madison Avenue
Suite 1004
New York City, NY 10016
(212) 448-9494
(866) 228-4673
www.cbtf.org

Cushing's Support and Research Foundation
65 East India Row
Suite 22B
Boston, MA 02110-3389
(617) 723-3674
http://csrf.net

International RadioSurgery Association
3002 North Second Street
Harrisburg, PA 17110
(717) 260-9808
www.irsa.org

Katie's Kids for the Cure/National Fund for Pediatric Brain Tumor Research
3741 Walnut Street
Box 612
Philadelphia, PA 19104
(610) 831-9026
(877) 587-5437
www.katieskids.org

Musella Foundation for Brain Tumor Research and Information
1100 Peninsula Boulevard
Hewlett, NY 11557
(516) 295-4740
(888) 295-4740
www.virtualtrials.com

National Brain Tumor Foundation
22 Battery Street
Suite 612
San Francisco, CA 94111-5520
(415) 834-9970
(800) 934-2873
www.braintumor.org

North American Brain Tumor Coalition
www.nabraintumor.org

Pediatric Brain Tumor Foundation
302 Ridgefield Court
Asheville, NC 28806
(828) 665-6891
(800) 253-6530
www.pbtfus.org

Pituitary Network Association
P.O. Box 1958
Thousand Oaks, CA 91358
(805) 499-9973
www.pituitary.org

The Preuss Foundation, Inc.
2232 Avenida de la Playa
Suite 220
La Jolla, CA 92037
(858) 454-0200

Glossary

accessible tumor—a tumor that can be reached and removed using surgical tools without unreasonable risk of severe damage.

angiogenesis—blood vessel formation. Certain tumors promote blood vessel formation in surrounding tissue.

angiography—an imaging technique that provides an X-ray picture of blood vessels.

anti-angiogenetics—compounds that block blood vessel growth and the flow of nutrients and oxygen to a tumor.

antigen—a protein on the surface of a cell that stimulates the immune system.

antineoplaston—a naturally occurring substance isolated from normal human blood and urine that is being tested as a type of treatment for some tumors.

antisense oligonucleotide technology—also known as RNA interference. Uses short fragments of nucleic acid molecules to block gene expression in specific cells and prevent tumor growth.

apoptosis—cell death triggered by molecular steps in the cell.

astrocytoma—a tumor found mostly in the brain that is made up of star-shaped nerve support cells called astrocytes.

benign—nonmalignant or noncancerous. Often used to describe tumor cells that are similar to other normal cells, grow relatively slowly, and are confined to one location.

biopsy—a diagnostic test in which a sample of a patient's cells or tissue is removed and examined for disease.

blood-brain barrier—a complex, natural, protective network of fine blood vessels and cells that filters blood and prevents most drugs and molecules from traveling through the blood stream and into the brain.

boron nuclear capture technology—a form of radiation therapy which uses boron to kill the tumor cells without harming normal cells.

brain stem—the lowest part of the brain, connected to the spinal cord. It controls basic life functions, including breathing, heart beat, and blood pressure.

brain stem glioma—a tumor found in the lowest part of the brain that begins in glial cells, which support other brain function.

central nervous system (CNS)—the brain and spinal cord.

cerebrospinal fluid (CSF)—the clear liquid that bathes the brain and spinal cord.

cerebellum—located at the lower rear of the head, above the brain stem, it controls balance, helps maintain equilibrium, and coordinates complex muscle movements like walking and talking.

cerebrum—the tissue that forms the bulk of the brain and is divided into broad regions, called lobes, that control different functions.

chemotherapy—treatment with drugs designed to kill cancer cells.

choroid plexus papilloma—a rare, usually benign, tumor that develops in an area of the brain that produces cerebrospinal fluid.

chordoma—a rare congenital tumor formed by remnants of the fetal structure that is replaced by the spine.

computed tomography (CT)—an imaging technique that uses X-rays and computer analysis to create a picture of body tissues and structures.

congenital tumor—an abnormal growth present at birth.

convection enhanced delivery—a drug delivery system in which a continuous stream of toxic drugs is sent to the tumor via catheters that are inserted following surgery.

craniopharyngioma—a tumor that develops from cells left over from early fetal development.

cyst—a noncancerous fluid-filled mass that forms within a thin membrane.

cytokines—messenger proteins that can strengthen or suppress immune system activity.

differentiating drugs—drugs that change cancer cells so they divide less often.

dura mater—a tough, fibrous, two-layered membrane covering the brain and spinal cord. The dura mater is located inside the spinal bones and skull and is the outermost layer of the meninges.

electroencephalogram (EEG)—a written recording of the brain's electrical activity.

ependymoma—a tumor that begins in cells that line the spinal cord and the cavities of the brain where cerebrospinal fluid is made and stored.

frontal lobe—a part of the brain that directs voluntary muscle movement and goal setting.

ganglioglioma—a very rare, nonaggressive, benign brain or spinal tumor that forms from nerve cells and glial cells.

gene therapy—treatment that inserts a new gene into the tumor cell, which causes tumor cell suicide.

germ cell tumor—a rare childhood tumor that may start in cells that fail to leave the central nervous system during development.

glial cell—a type of cell that supports and surrounds nerve cells.

glioblastoma—an often fast-growing tumor formed from star-shaped glial cells called astrocytes.

glioma—a tumor that begins in glial cells, which support other brain function.

grading—a scale used to assess a tumor's cellular makeup (abnormality of cancer cells as compared to normal cells) and location. Doctors use tumor grading and other factors to develop a patient's treatment plan.

growth factors—substances that regulate normal cell growth and division.

hydrocephalus—abnormal accumulation of cerebrospinal fluid within the brain.

immunotherapy—treatment that boosts the ability of the body's immune system to fight cancer and illnesses.

inaccessible or inoperable tumor—a tumor that cannot be reached surgically without unreasonable risk of severe damage to nearby tissue.

kinase inhibitors—proteins that block growth-signaling enzymes.

liquid radiation therapy—an experimental way to deliver liquid radiation to the cavity that remains following tumor surgery.

lobes—sections of each half of the brain that are involved in directing different neurological functions.

lumbar puncture (LP)—a diagnostic procedure in which a sample of cerebrospinal fluid is removed from the spinal cord using a needle (also called a spinal tap).

magnetic resonance imaging (MRI)—an imaging technique which uses radio waves, a magnetic field, and sophisticated computer analysis to create a picture of body tissues and structures.

malignant—harmful, cancerous. Often used to describe tumor cells that are very different from normal cells, grow relatively quickly, and can easily spread to other locations.

medulloblastoma—a malignant tumor most often seen in children and young adults that usually begins in the lower part of the brain and can spread throughout the brain and along the spine.

meninges—three layers of membranes that cover the brain and spinal cord. These tissue layers, from closest to the skull to the brain, are: dura mater, arachnoid, and pia mater.

meningioma—a tumor found in the meninges, the membranes that cover and protect the brain and spinal cord.

metastatic—means "to spread." Metastatic tumors are caused by cancerous cells that have spread from other parts of the body.

monoclonal antibodies—laboratory-produced immune molecules that target and bind to a specific protein on cancer cells.

neoplasm—a new, abnormal growth in the body.

neuroblastoma—a mostly childhood tumor that appears in nerve tissue above the adrenal glands and can spread to other parts of the body.

neurofibromatosis—a genetic disorder of the nervous system that causes tumors to grow around nerves.

neurosurgery—surgery on the spine, brain, or other parts of the nervous system.

occipital lobe—the brain part that receives and processes visual images and how we understand written words.

oligodendroglioma—a type of brain tumor that develops from cells that produce myelin, the fatty covering over nerves.

oncogene—a gene normally involved in cell growth that can, when altered, promote the uncontrolled growth of cancer.

osmotic blood-brain barrier disruption—experimental treatment that uses different drugs to open blood vessels in the hopes of delivering more chemotherapeutic drugs across the blood-brain barrier and to the brain tumor.

parietal lobe—a part of the brain that processes sensations.

pathologist—a physician specially trained in diagnosing diseases by examining blood, tissues, and other body materials.

pituitary tumor—a small, usually benign tumor that forms in the pituitary gland, which releases hormones that influence the body's growth and metabolism.

positron emission tomography (PET)—an imaging technique that provides a visual measure of metabolism, or activity, within body tissues.

primary—a term used to describe a growth that begins in the organ in which it is originally formed and has not spread from elsewhere in the body.

radiation therapy—the use of high-energy radiation to kill cancer cells.

radiosensitizer—a drug that makes tumor cells more sensitive to radiation therapy.

reflexes—automatic movements that the body makes in response to a given stimulus.

resection—surgery to remove the tumor or dead tissue.

schwannoma—a benign tumor that forms in the fatty sheath that covers nerve fibers.

shunt—a flexible plastic tube that is used to divert the flow of cerebrospinal fluid from the central nervous system to another part of the body where it can be absorbed as part of the normal circulatory process.

solid tumor—a localized growth of tissue (vs. a fluid-filled sac).

spasticity—abnormal, involuntary stiffness or contraction of the body's muscles.

stereotactic radiosurgery—high-dose radiation therapy that is directed into the tumor while sparing normal tissue; it does not involve actual surgery.

temporal lobe—the part of the brain that is involved with memory and understanding sounds and words.

tomotherapy—an experimental form of radiation therapy that uses computer imaging to deliver small beams of high-dose radiation to the tumor from 360 degrees.

tuberous sclerosis—a rare genetic disease that causes benign tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin.

tumor—an abnormal mass of tissue that can be cancerous or noncancerous.

vaccine therapy—a type of treatment that uses different substances to strengthen the normal immune system response to tumors and infectious materials.

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