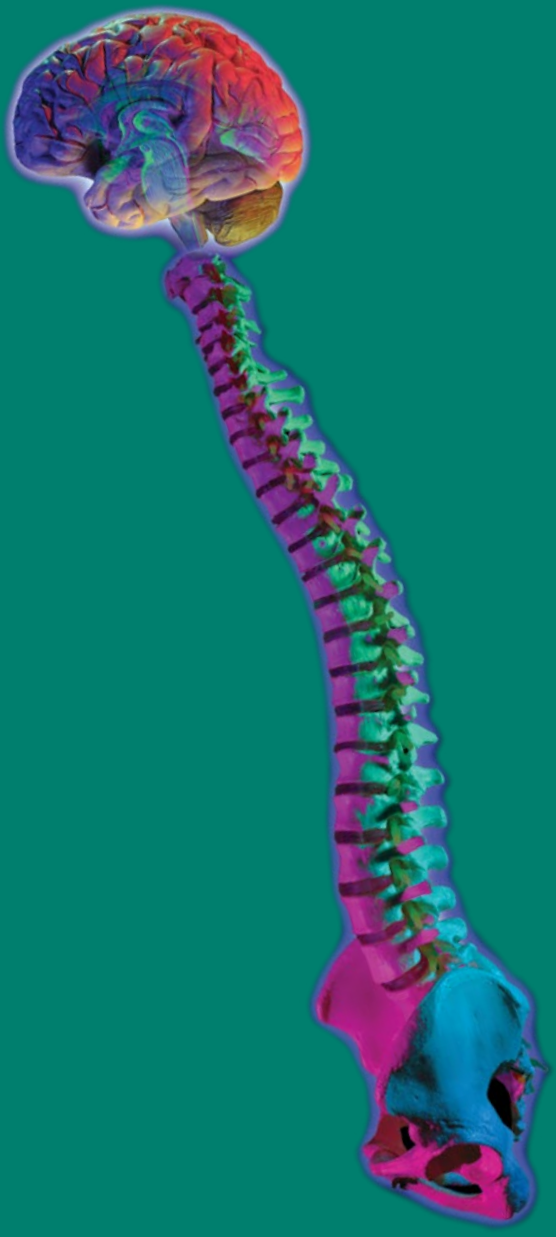
Brain and Spinal Cord Tumors



Hope Through Research

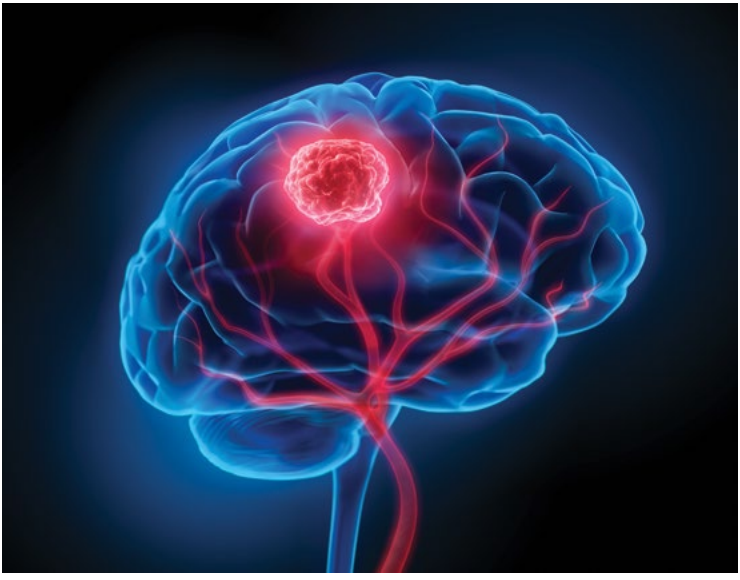
National Institute of Neurological Disorders
and Stroke
National Institutes of Health

Table of Contents

What are Brain and Spinal Cord Tumors?

A tumor is a mass of abnormal cells that either form into a new growth or the growth was there when you were born (congenital). Tumors occur when something goes wrong with genes that regulate cell growth, allowing cells to grow and divide out of control. Tumors can form anywhere in your body. Brain and spinal cord tumors form in the tissue inside your brain or spinal cord, which make up the central nervous system (CNS).

Depending on its type, a growing tumor may not cause any symptoms or can kill or displace healthy cells or disrupt their function. A tumor 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 activity in the brain or signaling to and from the brain. Some tumors don't cause any changes.



Brain and spinal cord tumors form in the tissue inside of the brain and spinal cord which make up the central nervous system.

Tumors can be noncancerous (**benign**) or cancerous (**malignant**).

- Benign tumors can grow slowly or fast, don't spread to other parts of the body, and often can be removed surgically.
- Malignant tumors can invade surrounding tissue. Some cancerous brain tumors can be removed entirely through surgery. Some malignant tumors have edges that are hard ot define, which makes it difficult for surgeons to remove the entire tumor.

Tumors can be primary or secondary.

- **Primary tumors** of the CNS are growths that begin in your brain or spinal cord. They can be either malignant or benign.
- Metastatic tumors, or **secondary tumors**, of the CNS are caused by cancer cells that break away from a primary tumor somewhere else in your body and spread to the CNS. They are more common than primary tumors of the CNS and occur more often in adults than in children.

There are more than 120 types of brain and spinal cord tumors. Some are named by the type of normal cell they most closely resemble or by location. Brain and spinal cord tumors are not contagious or, at this time, preventable.

See the Appendix at the end of this guide for a listing of some CNS tumors and tumor-related conditions.

Overview of the brain and spinal cord

The brain has three major parts:

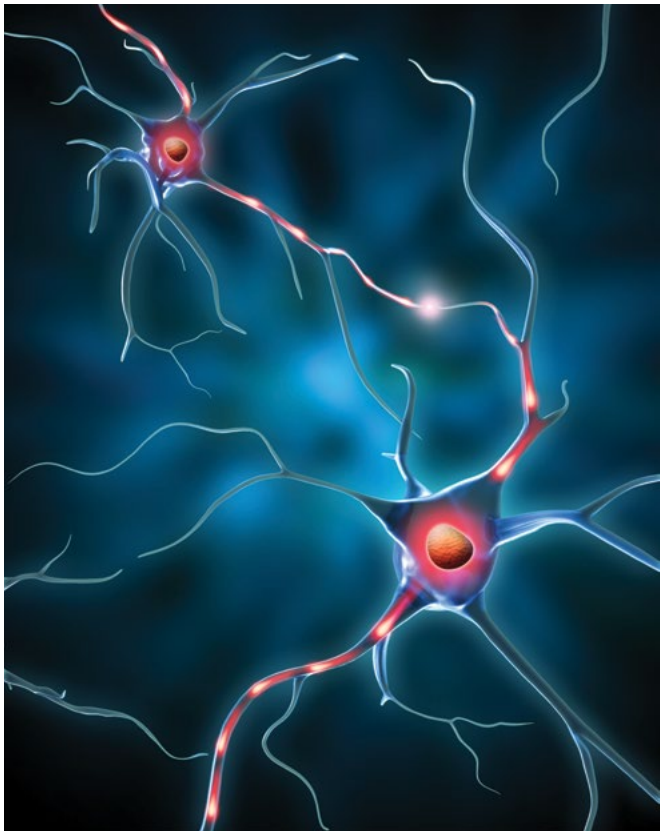
- *brain stem*—This lowest part of the brain (above the neck) connects to the spinal cord and relays information between the brain and the body using bundles of long nerves. It controls basic life-sustaining functions, including blood pressure, heartbeat, breathing, consciousness, swallowing, and body 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 complex muscle movements like walking and talking.

The brain's two halves, or hemispheres, use nerve cells (*neurons*) to speak with each other. Each hemisphere has four sections, called lobes, which handle different neurological functions.

- 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, and the way we understand written words.

For more information, see https://www.cancer.gov/types/brain/patient/adult-brain-treatment-pdq#_1.



The brain's hemispheres use nerve cells to speak with each other.

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 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.

Spinal cord tumors, regardless of location, often cause pain, numbness, weakness or lack of coordination in the arms and legs, usually on both sides of the body. They also often cause bladder or bowel problems.

Spinal cord tumors are described based on where on the cord the tumor is located and each vertebra (part of a series of bones that form the backbone) is numbered from top to bottom. The neck region is called cervical (C), the back region is called thoracic (T), and the lower back region is called lumbar (L) or sacral/cauda equina (S). Tumors are further described by whether the tumor begins in the cells inside the spinal cord (intramedullary) or outside the spinal cord (extramedullary). Extramedullary tumors grow in the membrane surrounding the spinal cord (intradural) or outside (extradural).

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

What causes CNS tumors?

Researchers really don't know why primary brain and spinal cord tumors develop. Possible causes include viruses, defective genes, exposure to certain chemicals and other hazardous materials, and immune system disorders. Sometimes CNS tumors may result from specific genetic diseases, such as neurofibromatosis and tuberous sclerosis, or exposure to radiation.

Who is at risk?

Anyone can develop a primary brain or spinal cord tumor, but the overall risk is very small. Brain tumors occur more often in males than in females and are most common in middle-aged to older persons. Although uncommon in children, brain tumors tend to occur more often in children under age 9, and some tumors tend to run in families. Most brain tumors in children are primary tumors.

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

How are tumors graded?

The grade of a tumor may be used to tell the difference between slow-growing and fast-growing types of the tumor. The World Health Organization (WHO) tumor grades are based on how abnormal the cancer cells look under the microscope and how quickly the tumor is likely to grow and spread. Some tumors change grade as they progress, usually to a higher grade. The tumor is graded by a pathologist following a biopsy or during surgery.

- **Grade I (low grade)** – The tumor cells look more like normal cells under a microscope and grow and spread more slowly than grade II, III and IV tumor cells. They rarely spread into nearby tissues. Grade I brain tumors may be cured if they are completely removed by surgery.

- **Grade II** – The tumor cells grow and spread more slowly than grade III and IV tumor cells. They may spread into nearby tissue and may recur (come back). Some tumors may become a higher-grade tumor.
- **Grade III** – The tumor cells tend to grow rapidly and can spread quickly into other CNS tissue. Tumor cells will look different than those in surrounding tissue.
- **Grade IV** – The tumor cells do not look like normal cells under a microscope and grow and spread very quickly. There may be areas of dead cells in the tumor. Grade IV tumors usually cannot be cured.

What are the possible symptoms?

Brain and spinal cord tumors cause many different 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 and spinal cord. Symptoms generally develop slowly and worsen as the tumor grows.

Brain tumor

In infants, the most obvious sign of a brain tumor is a rapidly widening head or bulging crown. Other more common symptoms of a pediatric brain tumor can include:

- Headaches that may become more frequent or severe
- Seizures
- Feelings of pressure inside the skull

A tumor can cause a variety of symptoms, including headaches and vision problems.

- Nausea and vomiting
- Sudden onset of vision problems

In older children and adults, a tumor can cause a variety of symptoms, including headaches, seizures, balance problems, and personality changes.

- Headaches are the most common symptom of a brain tumor. Headaches may get worse over time, become more frequent or constant, and recur, often at irregular intervals.
- Seizures. Seizures that start in adulthood with no underlying cause are a key warning sign of a brain tumor.
- Nausea and vomiting
- Vision or hearing problems
- Personality, behavior, and cognitive changes with psychotic episodes and problems with speech, language, thinking, and memory
- Motor problems, including weakness or paralysis, lack of coordination, or gradual loss of sensation or movement in an arm or leg
- Balance problems, including dizziness, trouble walking, clumsiness, or loss of equilibrium

- Hydrocephalus and increased intracranial pressure are caused when a tumor blocks the flow of the cerebrospinal fluid (CSF) that bathes the brain and spinal cord. This can cause 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 changes in sleep patterns.

Spinal cord tumors

Common symptoms of a spinal cord tumor include:

- Pain may occur in a specific area along the spine or can radiate from the spine to other parts of the body. The pain may be sharp or feel like burning or tingling feelings due to compression of nerves. The pain is often constant and progressive and may be severe. Back pain is a common early symptom of a spinal tumor.
- 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.
- Other symptoms, such as problems with bowel or bladder control or sexual dysfunction, can also occur but are less common.

How are CNS tumors diagnosed?

If you are suspected of having a brain or spinal cord tumor, your doctor (usually a neurologist, oncologist, or neuro-oncologist) will perform a neurologic exam and may order a variety of tests based on your symptoms, personal and family medical history, and results of the physical exam. Once a tumor is found on diagnostic imaging studies, surgery to obtain tissue for a biopsy or removal is often recommended.

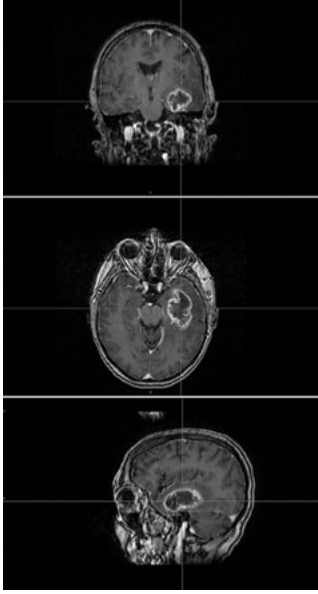
Diagnosing the type of brain or spinal cord tumor is often difficult. Some tumor types are rare and the molecular and genetic alterations of some tumors are not well understood. You may want to ask your primary care doctor or oncologist for a second opinion from a comprehensive cancer center or neuro-oncologist with experience treating your diagnosis or tumor type. Even a second opinion that confirms the original diagnosis can be reassuring and help you better prepare for your care and treatment.

A neurological exam

A neurological exam can be done in your doctor's office. It assesses your movement and sensory skills, hearing and speech, reflexes, vision, coordination and balance, mental status, and changes in mood or behavior. Some advanced tests are performed and analyzed by a specialist.

Diagnostic imaging

Diagnostic imaging produces extremely detailed views of structures inside the body, including tissues, organs, bones, and nerves. Such imaging can confirm the diagnosis and help doctors determine the tumor's type, treatment options, and later, whether the treatment is working.



Diagnostic imaging can confirm the diagnosis and help doctors determine the tumor's type and treatment options. 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:

- Computed Tomography (CT scan) is no longer the standard for evaluating for a brain tumor. However, CT scans can detect the buildup of calcium, which causes tissue to harden and develop into a tumor and can often detect hemorrhage (blood) or the development of hydrocephalus. CT scans can be done in a few minutes so are often used in emergency situations.
- Magnetic Resonance Imaging (MRI) is the gold standard for diagnosing brain and spinal tumors and is more sensitive than a CT scan. In addition to higher resolution and better anatomic detail, MRI can provide information about blood flow (perfusion), tumor cell density, and provide better pictures of tumors located near bone.

Usually a contrast agent (such as a dye) is injected into a vein before a CT or MRI. Many tumors become much easier to identify on the scan after the contrast is given.

- Functional MRI (fMRI) can help assess the distance between specific brain functions and tumors in particular areas of the brain. This is useful in planning surgery in areas of the brain that contain important function such as language.
- Magnetic Resonance Spectroscopy (MRS) can measure and analyze metabolic changes and the chemical make-up of a tissue sample.

- Positron Emission Tomography (PET) traces and measures the brain's use of glucose (sugar, used by the brain for energy) that is attached to small amounts of radioactivity and injected into your bloodstream. Because malignant tissue uses more glucose than normal tissue, it usually shows up on the scan as brighter than surrounding tissue.
- 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
- Angiography (or arteriogram) can distinguish certain types of tumors that have a characteristic pattern of blood vessels and blood flow. A dye is injected into a major blood vessel and a series of x-rays is taken as the dye flows to your brain. Often, MRI can be used to evaluate blood vessels, a procedure call MR angiography.

Laboratory and other tests

- Testing blood, urine, and other substances can provide clues about the tumor and monitor levels of therapeutic drugs.
- An electroencephalogram, or EEG, monitors brain activity through the skull (tumors can alter brain wave activity and cause seizures).
- A spinal tap (also called a lumbar puncture or CSF analysis) uses a special needle inserted into the spinal column to remove a small amount of the cerebrospinal fluid. The fluid is examined for abnormal cells or unusual levels of various molecules such as glucose and protein that suggest a brain or spinal cord tumor.

- Magnetoencephalography (MEG) studies brain function by measuring the magnetic field generated by nerve cells in the brain.

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 neuro-oncologist is a neurologist or oncologist who specializes in CNS tumors.
- An oncologist is a doctor who specializes in cancer.
- A neurologist is a doctor who specializes in CNS disorders.
- A neuroradiologist is a doctor who specializes in the CNS and is trained in reading diagnostic imaging results.

A neurosurgeon is a brain or spinal cord surgeon who may have completed specialized training in removal of central nervous system tumors.

- A pathologist is a clinical doctor who diagnoses diseases of tissues or cells using a variety of laboratory tests.
- A neurosurgeon is a brain or spinal cord surgeon. Specialized training in removal of central nervous system tumors may have been completed.
- A radiation oncologist is a doctor who specializes in using radiation to treat cancer.

For more information, see: https://www.cancer.gov/rare-brain-spine-tumor/tumors/about-cns-tumors#who-treats-central-nervous-system-cns-tumors.

Your health care team will recommend a treatment plan based on the tumor's location, type, size and aggressiveness, as well as medical history, age, and general health. Malignant tumors require some form of treatment, while some small benign tumors may need only monitoring. Treatment for a brain or spinal tumor can include surgery, radiation therapy, chemotherapy, targeted therapy, or a combination of treatments.

Initial treatment for a CNS tumor may involve a variety of drugs to treat or ease symptoms, including:

- anticonvulsants to treat or prevent seizures
- pain medications
- steroids or other anti-inflammatory drugs to reduce swelling and improve blood flow
- antidepressants to treat anxiety or depression that might occur following a tumor diagnosis
- anti-nausea drugs

Neurosurgery

Surgery is usually the first treatment to both obtain tissue for diagnosis and remove as much tumor as can be done safely. Surgery may be the only treatment you need if your tumor is considered benign or low grade. Based on the type and grade (low versus high), doctors often recommend follow-up treatment, including radiation and chemotherapy, or an experimental treatment. You will be referred to the specialists above to provide guidance on this treatment.

Surgery is usually the first step in treating an accessible tumor—one that can be removed without risk of neurological damage. Many low-grade tumors and secondary (metastatic) cancerous tumors can be removed entirely. Some tumors have a clearly defined shape and can be removed more easily. Your surgeon will try removing (called resecting or excising) all or as much tumor as possible. For malignant CNS tumors, this is best performed by a neurosurgeon.

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 and may not have well-defined edges. In these cases, a biopsy may be performed.

A **biopsy** is sometimes performed to diagnose and help doctors determine how to treat a tumor. Biopsies can sometimes be performed by inserting a needle through a small hole in the body and taking a small piece of the tumor tissue. A pathologist will examine the tissue for certain changes that signal cancer and determine its stage or grade.

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.

During **surgery**, some tools used in the operating room include a surgical microscope, the endoscope (a small 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. Other tools include:

- Intraoperative MRI uses a special type of MRI to provide real-time monitoring and evaluation of the surgery. Constantly updated images let doctors see how much of the tumor has been removed.
- Navigation equipment used in computer-guided, or stereotactic, neurosurgery gives doctors a precise, three-dimensional map of the spine or brain as the operation progresses. A computer uses pre-operative diagnostic images to reduce the risk of damage to surrounding tissue.
- Intraoperative nerve monitoring tests use real-time recordings of nerve cell activity to determine the role of specific nerves and to monitor brain activity as the surgery progresses. 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.

For more information, see: https://www.cancer.gov/about-cancer/treatment/types/surgery.

Radiation therapy

Radiation therapy usually involves repeated doses of high-energy beams such as x-rays or protons to kill cancer cells or keep them from multiplying. Radiation therapy can shrink the tumor mass. It can be used to treat surgically inaccessible tumors or tumor cells that may remain following surgery.

Radiation treatment can be delivered externally, using focused beams of energy or charged particles that are directed at the tumor, or from inside the body, 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 current radiation treatment is designed to minimize injury to normal tissue.

Treatment often begins soon after surgery and may continue for several weeks. Depending on the tumor type and location, a person may be able to receive a modified form of therapy to lessen damage to healthy cells and improve the overall treatment.

Radiation therapy can shrink a tumor mass and can be used to treat surgically inaccessible tumors or tumor cells that may remain following surgery.

Externally delivered radiation therapy poses no risk of radioactivity to the person 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.
- **Conventional external beam radiation** aims a uniform dose of high-energy radiation at the tumor and surrounding tissue. 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 location, sparing nearby organs and surrounding tissue.
- **Intensity modulated radiation therapy** (IMRT) is similar to 3D-CRT but varies in the intensity of the hundreds of radiation beams to deliver more precise doses to the tumor or its specific areas, 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.
- **Proton beam therapy** directs a beam of high-energy protons directly at the tumor site, without spread of the radiation beyond the target. The dosing is similar to standard radiation (also called photon radiation), but proton beam radiation is best for treating tumors near important structures such as the brain

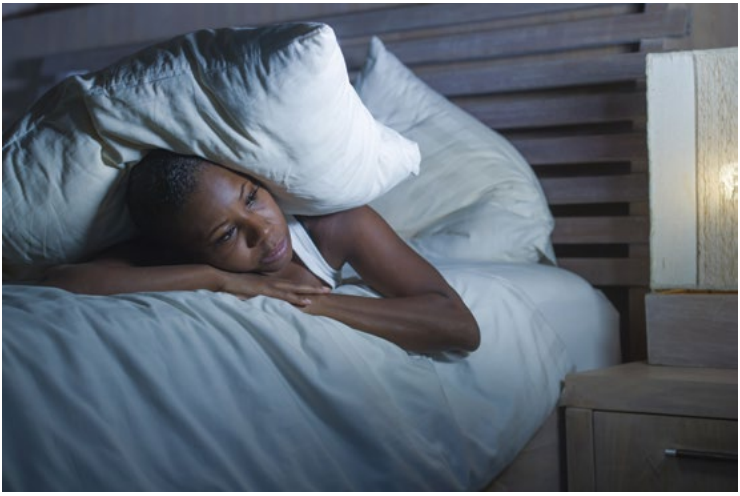
stem and spinal cord. Proton beam therapy can be used as a stand-alone treatment or in combination with chemotherapy or as follow-up to surgery.

Radiosurgery

Radiosurgery is usually a one-time treatment using multiple, sharply focused radiation beams aimed at the brain or spinal cord tumor from multiple angles. It does not cut into the person but, like other forms of radiation therapy, harms a tumor cell's ability to grow and divide. It is commonly used to treat surgically inaccessible tumors and may be used at the end of conventional radiation treatment. Two common 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.
- **Radiosurgery** can be given by a number of techniques, all designed to provide a precise dose of radiation to a small area. It has proven beneficial for tumors that do not spread into the surrounding brain, but radiosurgery is less beneficial for the common brain tumors that do spread into the brain.

Side effects of radiation: 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 treated area, headache, hearing loss, problems with sleep, and hair loss (although the hair usually grows back once the treatment has stopped). Radiation therapy in



Side effects of radiation therapy vary from person to person and may include headache, hearing loss, and problems with sleep.

young children, particularly those age three years or younger, can cause problems with learning, processing information, thinking, and growing.

There are late side effects of radiation that may occur months to years after treatment that include shrinkage (atrophy) of the brain or spinal cord region that was treated.

Chemotherapy

Chemotherapy uses powerful drugs to kill cancer cells or stop them from growing or spreading. These drugs are usually given orally, intravenously, or through a catheter or port and travel through the body to the cancerous cells. Your oncologist will recommend a treatment plan based on the type of cancer, drug(s) to be used, the frequency of administration, and the number of cycles needed. Chemotherapy is given in cycles to more effectively damage and kill cancer cells and give normal cells time to recover from any damage.

Individuals might receive chemotherapy to shrink the tumor before surgery called neo-adjuvant therapy (a first step treatment to shrink a tumor before the primary treatment). Radiation therapy can also be given as neo-adjuvant therapy. After surgery, or radiation treatment if radiation is the primary treatment, chemotherapy could be called adjuvant therapy (treatment in addition to the primary treatment). Metronomic therapy involves continuous low-dose chemotherapy to block mechanisms that stimulate the growth of new blood vessels needed to feed the tumor.

Not all tumors are vulnerable to the same anticancer drugs, so a person's treatment may include a combination of drugs. Common CNS chemotherapies include temozolomide, carmustine (also called BCNU), lomustine (also called CCNU), and bevacizumab. Individuals should be sure to discuss all options with their medical team.

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 side effects often improve or stop once the treatment has ended.

For more information about chemotherapy, see: https://www.cancer.gov/about-cancer/treatment/types/chemotherapy.

Targeted therapy

Targeted therapy is a cancer treatment that uses drugs to target specific genes and proteins that are involved in tumor cell growth. This helps slow uncontrolled growth and reduce the production of tumor cells. Targeted therapies include oncogenes, growth factors, and molecules aimed at blocking gene activity.

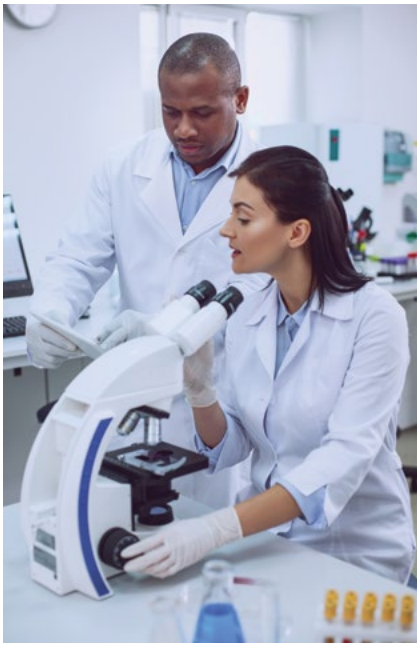
Alternative and complementary approaches

Alternative and complementary approaches may help tumor patients 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 in advance with a doctor. Common approaches include nutritional and herbal supplements, vitamins, special diets, and mental or physical techniques to reduce stress.

What research is being done?

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

Clinical studies are research studies that test or observe how well medical approaches work in people. Some clinical studies test new treatments such as a new drug or medical therapy. Treatment studies help researchers learn if a new treatment is effective or less harmful than standard treatments. Studies can be considered at any point, from the time of diagnosis through recurrence. For more information about clinical studies, see: https://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials.



Scientists are exploring a variety of approaches to treat CNS tumors.

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 federal agencies, 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, advanced imaging and artificial intelligence, biologic immuno-agents, surgery, and radiation. Information about these trials, and trials for other disorders, can be accessed at the federal government's database of clinical trials, http://clinicaltrials.gov.

Scientists at NIH and universities across the United States are exploring a variety of approaches to treat CNS tumors. These experimental approaches include boosting the immune system to better fight tumor cells, developing 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.

Biological therapy (also called **immunotherapy**) 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, but because 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, including:

- Proteins such as interleukin and interferon and other substances that slow tumor growth
- Antibodies (proteins that are normally produced by the body to ward off bacteria and viruses) that are linked to immunotoxin drugs that seek out tumor cells and deliver their toxin, with minimal damage to surrounding normal cells
- Gene therapy, which uses a virus that can pass through the brain's protective blood-brain barrier to deliver a suicide gene to the tumor cell
- Vaccine therapy, which strengthens the immune response by inserting an antigen (a substance that triggers an immune system reaction) that the body will attack. Some vaccines attempt to target multiple antigens which the tumor may express.

Targeted therapy uses molecularly targeted drugs that seek out the cellular changes that convert normal cells into cancer. Targeted therapies include:

- Compounds that block blood vessel growth and the flow of nutrients and oxygen to the tumor. These compounds may also hamper cell signaling and stop tumor cells from spreading elsewhere in the body.
- Developing diagnostic and therapeutic screening tools for oncogenes—transformed genes that are involved in cell growth and cause normal cells to divide uncontrollably and become malignant.

- Kinase inhibitors—proteins that block growth-signaling enzymes without harming normal cells—that may make CNS tumors more sensitive to chemotherapy.

Biomarkers are molecules or other substances in the blood or tissue that can be used to diagnose or monitor a disorder. 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. Identifying biomarkers may also lead to the development of new disease models and novel therapies for tumor treatment.

Radiation therapy research includes testing several new anticancer drugs, either independently or in combination with other drugs. Researchers are also investigating combined therapies including drugs, radiation, and radiosurgery to effectively treat CNS tumors. Research areas under investigation include radiosensitizers—drugs that make rapidly dividing tumor tissue more vulnerable to radiation.

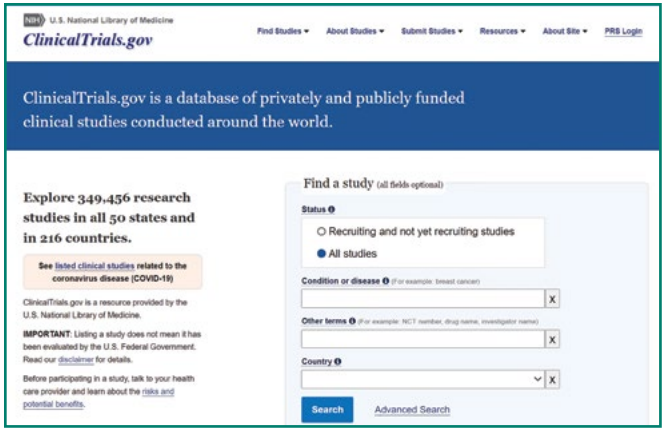
Chemotherapeutic drug research focuses on ways to better deliver drugs across the blood-brain barrier and into the site of the tumor. Since chemotherapeutic drugs work in different ways to stop tumor cells from dividing, several trials are testing whether giving more than one drug, and perhaps giving them in different ways (such as staggered delivery and low-dose, long-term treatment), may kill more tumor cells without causing damaging side effects than present therapy. Researchers are examining different levels of chemotherapeutic drugs to determine whether they are less toxic to normal tissue when combined with

other cancer treatments, and ways to make cancer cells more sensitive to chemotherapy. Research areas include:

- Drugs that change dividing cells into non-dividing cells and can halt tumor growth
- Certain chemotherapeutic drugs that may kill cancer cells without harmful side effects
- Convection enhanced delivery, which bypasses the blood-brain barrier by sending a continuous, uniform stream of toxic drugs into the tumor via catheters that are inserted into the brain during surgery.

Surgery studies are ongoing to better define the potential benefits of surgery, including better response to biologic therapy and chemotherapy, improved quality of life, and prolonged survival.

Clinical trials can help doctors and scientists discover whether new treatments are effective and safe for many people with spinal and brain tumors. Both healthy people and those with a disease participate



Clinical trials can help doctors and scientists discover whether new treatments are effective and safe for many people with spinal and brain tumors. Clinicaltrials.gov is a database of thousands of studies, some of which include results and papers on findings.

in clinical trials, which increases our understanding about diseases including brain and spinal tumors. To learn more about clinical trials for CNS tumors and how to participate in them, visit www.clinicaltrials.gov, a database of thousands of studies, some of which include results and papers on findings.

Appendix: Some 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. Some tumor types are more prevalent in children than in adults. Here is a listing of some common benign and malignant CNS tumors.

Glioma

Glioma tumors grow from several types of glial cells, which support the function of neurons. Gliomas usually occur in the brain's cerebral hemispheres but may also strike other areas. Gliomas are classified based on the type of normal glial cells they resemble.

- Astrocytoma. These tumors, which have star-shaped glial cells called astrocytes, can be low-grade or malignant. Astrocytomas tend to form in the cerebrum in adults and in most parts of the brain in children. The most common forms of astrocytoma are:
- Anaplastic astrocytoma, which grows rapidly and invades other tissue.
- Ependymoma, which develops from cells that line the cavities of the brain and spinal canal where the cerebrospinal fluid (CSF) is made and stored.

- Ganglioglioma, a very rare, slow-growing, benign tumor that forms from nerve cells and glial cells and can occur in the brain and the spine.
- Glioblastoma multiforme, a malignant, highly invasive tumor that spreads quickly and often recurs following initial treatment.
- Oligodendroglioma, a tumor that resembles glial cells within the cerebral hemispheres that help insulate the nerve fibers that transmit nerve impulses.
- Pilocytic astrocytoma, a slow-growing tumor that rarely spreads into surrounding tissue.

Mixed gliomas contain more than one type of glial cell and are usually found in the cerebrum. These tumors can spread to other sites in the brain.

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.
- 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.

Chordoma

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.

Choroid plexus papilloma

This rare, usually benign childhood tumor develops slowly and can increase the production and block the flow of CSF, causing symptoms that include headaches and increased intracranial pressure. A rarer cancerous form can spread via the cerebrospinal fluid.

Germ cell tumors

These very rare childhood tumors may start in cells that fail to leave the CNS during development. Germ cell tumors usually form in the center of the brain and can spread elsewhere in the brain and spinal cord. Different tumors are named after the type of germ cell.

Meningioma

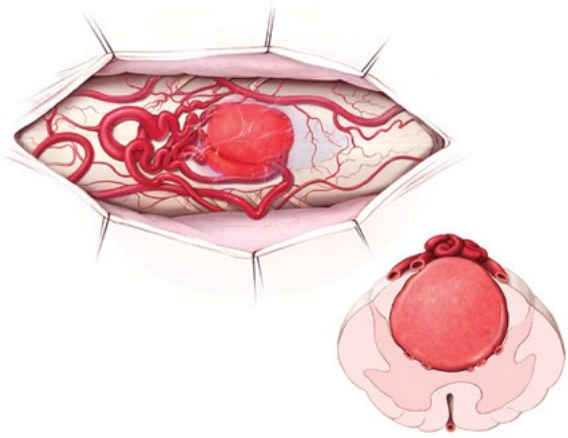
Meningiomas are benign tumors that develop from the thin membranes, or meninges, that cover the brain and spinal cord. Meningiomas usually grow slowly, generally do not invade surrounding normal tissue, and rarely spread to other parts of the CNS or body.

Pineal Tumors

These tumors form in the pineal gland, a small structure located between the cerebellum and the cerebrum. The three most common types of pineal region tumors are gliomas, germ cell tumors, and pineal cell tumors.

Pituitary Tumors (also called pituitary adenomas)

These small tumors form in the pituitary gland. Most pituitary tumors are benign and their incidence increases with age. Pituitary tumors are classified as either non-secreting or secreting (secreting tumors release unusually high levels of pituitary hormones, which can trigger neurological conditions and symptoms including Cushing's syndrome—a harmful overproduction of the hormone cortisol).



Credit: NIH Medical Arts

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. This illustration shows a cross section of the spinal cord and tumor.

Primitive Neuroectodermal Tumors (PNET)

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. The two most common PNETs are:

- Medulloblastomas, which usually form in the cerebellum and can spread throughout the brain and along the spine.
- Neuroblastomas, which generally appear above the adrenal glands but can be found in the brain and elsewhere in the body.

Vascular Tumors

These rare, noncancerous tumors arise from the blood vessels of the brain and spinal cord. The most common vascular tumor is the hemangioblastoma, a cyst-like mass of tangled blood vessels, which does not usually spread.

For information on some rare brain and spinal cord tumors, see: https://www.cancer.gov/rare-brain-spine-tumor/tumors.

Other Tumor-Related Conditions

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.

Hydrocephalus involves the build-up of cerebrospinal fluid in the brain. The excessive fluid can cause harmful pressure, headaches, and nausea.

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.

Neurofibromatosis refers to related genetic disorders that cause tumors to grow around nerves. Most tumors are benign but can become malignant over time. 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 nerves involved with hearing.

Pseudotumor cerebri, also called "false brain tumor," mimics brain tumor symptoms and may be caused by the abnormal buildup of cerebrospinal fluid.

Tuberous sclerosis is a genetic disorder that causes numerous neurological and physical symptoms, including benign tumors of eyes and CNS. It may be present at birth or develop over time. About half of people who have tuberous sclerosis develop benign astrocytomas.

von Hippel-Lindau disease is a rare, genetic multisystem disorder characterized by tumors that grow in certain parts of the body. Hemangioblastomas may develop in the brain and nervous system.

Where can I get more information?

For more information on neurological disorders or research programs funded by 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
http://www.ninds.nih.gov

National Cancer Institute (NCI)
National Institutes of Health, DHHS
6116 Executive Boulevard, Suite 3036A
Bethesda, MD 20892-8322
800-4-CANCER (422-6237); 800-332-8615
http://cancer.gov

Information also is available from the following organizations:

American Brain Tumor Association (ABTA)
phone 773-577-8750; 800-886-2282
http://www.abta.org

American Cancer Society
phone 800-227-2345
http://www.cancer.org

Brain Tumor Network
phone 904-395-5220; 844-286-6110
https://braintumornetwork.org/

Childhood Brain Tumor Foundation
phone 877-217-4166; 301-515-2900
http://www.childhoodbraintumor.org

Children's Brain Tumor Foundation
phone 212-448-9494
http://www.cbtf.org

National Brain Tumor Society
phone 617-924-9997
http://www.braintumor.org

Pediatric Brain Tumor Foundation
phone 828-665-6891; 800-253-6530
http://www.pbtfus.org

Nevus Outreach, Inc.
phone 918-331-0595
http://www.nevus.org

Hope for Hypothalamic Hamartomas (Hope for HH)
phone 918-331-0595
http://hopeforhh.org/

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