What is the brain?

The brain is the organ in a person's skull that controls the functions of all of the other organs. Together, the brain and spine make up the central nervous system. The brain is responsible for the experience of the five senses (taste, touch, sight, hearing and smell). The brain is where thought, language, personality, creativity and memory are controlled. The brain controls movement, sensation, balance, and coordination. In order to do its job, the brain needs oxygen and nutrient energy that a person takes in regularly.

The brain is made up of of nerve cells (called neurons), which carry signals, and the cells that support these nerve cells (called glial cells). There are a number of different types of glial cells, all with different names and functions. The glial cells outnumber the neurons in the brain by a ratio of 10:1.

What is brain cancer?

Brain tumors occur when cells in the brain begin to grow out of control and start to displace or invade nearby tissues. Occasionally, brain tumors can spread throughout the body. Tumors that have the potential to spread to other sites of the brain or body are called malignant. When tumors start in the brain, they are called primary brain tumors. Any of the various normal cell types of the brain can change and become a primary tumor, and the particular cell type that makes up the tumor controls how the tumor is likely to behave. Secondary brain tumors, or brain metastases, are cancers that start elsewhere in the body and metastasize (spread) to the brain. These are not classified as primary brain tumors, but instead as brain metastases. Brain metastases are more common than primary brain tumors.

Brain tumors are classified by both the cell of the brain that makes them up, and how the tumor looks under a microscope. Primary brain tumors can arise from any of the cells in the brain. They can come from the neurons, the glial cells, the lining of the brain, or from specific structures in the brain. Glial cells support the neurons of the brain and tumors which arise from these cells are known as gliomas. The membrane that surrounds the brain can also develop tumors and these are known as meningiomas. There are other types of tumors, which involve other structures of the brain including ependymomas, among others.

About 80% of malignant primary brain tumors arise from the glial cells of the brain and are called gliomas. A majority of these tumors are the most aggressive type, called Glioblastoma Multiforme (or GBM). Astrocytic tumors are another type of glioma, which arise from star shaped cells called astrocytes.

Brain tumors are not really thought of as a single disease, but rather as a collection of several diseases that are characterized by cell type, clinical behavior, and type of therapy. One of the special characteristics of brain tumors is that sometimes benign tumors can be as challenging to treat as a malignant tumor, depending on their size and location within the brain. This is because the brain is locked into place by the skull and can't move out of the way if a tumor is growing near it. Even a benign tumor can cause pressure on the brain. This pressure can cause symptoms and be life-threatening.

What causes brain tumors and am I at risk?

According to the American Cancer Society there will be more than 79,000 new cases of primary brain tumors diagnosed this year with about one third (around 23,880) of those being malignant. The average age of diagnosis is 59 years old but they most commonly occur in children and older adults. Brain tumors occur more frequently in men than women.

Exposure to ionizing radiation, both therapeutic (treatment for a disease) and from atomic bomb exposure, has been linked to
the development of certain types of primary brain tumors, including meningiomas, gliomas, and sarcomas, particularly if the exposure took place in childhood. Higher radiation doses are generally felt to increase the risk of eventually developing a brain tumor, and radiation-induced brain tumors can take anywhere from 10-30 years to form.

With the recent popularity of cellular phones, many people have worried that their use may be a risk factor for developing brain tumors, but there has been no conclusive evidence that cell phones increase the risk of brain tumors. There has also been concern regarding exposure to powerful magnetic fields (high power lines) and some sugar substitutes (aspartame), however, there has not been any conclusive evidence linking these factors to increased risk of brain cancer.

Certain hereditary disorders can predispose someone to the development of certain brain tumors, but only about 5% of primary brain tumors have known hereditary factors. Genetic diseases like neurofibromatosis type 1, neurofibromatosis type 2, von Hippel-Lindau disease, and tuberous sclerosis are all associated with an increased risk of developing a primary brain tumor.

**How can I prevent brain tumors?**

Currently, there are no proven strategies to prevent the development of primary brain tumors.

**What screening tests are available?**

Primary brain tumors are rare enough that they are not screened for with any specific tests. The best way to find a brain tumor early is to see your doctor regularly for a thorough physical examination and to report any new, worrisome symptoms promptly. People with genetic disorders that predispose them for the development of primary brain tumors will often get periodic imaging studies of their brains to look for any evidence of abnormalities.

**What are the signs of brain tumors?**

The very early stages of brain tumors may not cause any symptoms. As the tumor grows in size, it can produce a variety of symptoms, depending on its location and what areas of the brain it is putting pressure on, including:

- Headache.
- Nausea.
- Vomiting.
- Loss of appetite.
- Seizures.
- Memory loss.
- Weakness.
- Difficulty walking / balance problems.
- Visual changes.
- Problems with speech and language.
- Personality changes.
- Thought processing problems.

Many of these symptoms are non-specific, meaning they could be caused by many conditions; however, your doctor needs to see you if you have any of these problems. Because the brain controls so many different functions, the symptoms caused by brain tumors can be extremely variable. Headache is the most common symptom for patients with brain tumors, occurring in about 50% of cases.

**How are brain tumors diagnosed?**

When a patient presents with symptoms suggestive of a brain tumor, the provider will perform a thorough history and physical examination. After that, the key to making the diagnosis is radiology imaging.

Imaging can be performed with either a CT scan or MRI scan. A CT scan is a three dimensional x-ray, and patients will often be injected with a contrast agent to help visualize any abnormalities. CT scans are good tests because they are quick and easy to
obtain, and will often be used as the first step towards making a diagnosis. However, an MRI scan is a better test for evaluating abnormalities in the brain. MRI scans utilize powerful magnets to make a three-dimensional picture. An MRI picks up more detail than a CT scan, and is the study of choice to make the diagnosis of a brain tumor. MRI scans are usually obtained with the use of an injectable contrast agent as well.

There are some further imaging studies that may be used to determine if a mass in the brain is a tumor (as opposed to other causes, such as infection) and if it is a tumor, what type it is. There is a special type of MRI, known as MR spectroscopy or MRS, which allows your provider to learn more about the contents of the mass and helps them determine what the mass is.

A functional MRI is another special type of MRI that can help define areas of the brain, which activate when a person moves or speaks. This allows the provider to "map the brain" and helps the provider know which areas to avoid during surgery if the tumor is close to a portion of the brain, which is critical for movement or speech.

The primary management of most brain tumors is surgery. If imaging reveals that a mass suspicious for a brain tumor is in a surgically accessible spot, the patient is generally scheduled for surgery without any further diagnostic testing. After surgery, the specimen can be examined under the microscope by a pathologist, and a final diagnosis can be made.

However, sometimes, tumors are not in a safe location for surgery. In those cases, in order to make a diagnosis, patients will often need a biopsy. A biopsy is a procedure where a small piece of the tumor is obtained using a needle under image guidance. The biopsy is usually done as a stereotactic biopsy, where the head is immobilized with a frame that is attached to the skull with pins. A scan of the brain is then done with the frame in place. With the same immobilization device on, the person is taken to surgery and the surgeon can use the scan to guide them precisely to the tumor.

Occasionally, your healthcare provider may want to examine the fluid that surrounds the brain and spinal cord (cerebrospinal fluid or CSF for short) to see if there are any cancer cells that have spread to this liquid. This can be done with a procedure known as a lumbar puncture, or an LP for short. A needle is inserted between the vertebral bodies (bones of the spinal cord) and into the sack that holds the spinal cord. Some of the CSF is taken out and a pathologist can examine it and determine if there are cancer cells present.

**How are primary brain tumors staged?**

Primary brain tumors do not have a classic staging system the way most other cancers do. This is because the size of a brain tumor is less important than its location and the type of brain cell that makes it up. When a pathologist (a doctor who studies cells in the laboratory) looks at brain tumors under a microscope, he/she can get a sense of how aggressive the tumor is by the way the cells look, and based on this, assign the tumor a grade. The most common classification system is the World Health Organization (WHO) system, which classifies CNS tumors according to histology (cell appearance under the microscope) as well as tumor grade. The WHO numerical grade represents the overall biologic potential for malignancy (or aggressiveness) from I (benign) to IV (malignant).

**Detailed Grading System from the World Health Organization is as follows:**

**Grade I**

- Slow growing.
- Almost normal appearance under a microscope.

**Grade II**

- Relatively slow growing cells.
- Slightly abnormal appearance.
- Can invade normal tissue.
- Can recur as a higher-grade tumor.

**Grade III**

- Actively reproducing abnormal cells.
- Abnormal appearance under a microscope.
Invasions of adjacent normal tissue.

Tumor tends to recur as a higher grade.

Grade IV

- Abnormal cells which reproduce rapidly.
- Very abnormal appearance under microscope.
- Form new blood vessels to maintain growth.
- Areas of necrotic tumor in middle of the tumor.

Gliomas classified are according to their WHO grading:

- Low grade astrocytomas include pilocytic astrocytomas (grade I) and diffuse astrocytomas (grade II).
- A grade III astrocytoma is called anaplastic astrocytoma.
- A grade IV astrocytoma is a glioblastoma, also called glioblastoma multiforme or GBM.

Other brain tumors include:

- Ependymomas arise from glial cells that line the open spaces in the brain and the spinal cord. They are most commonly found in children and young adults. Includes grade I and II ependymomas and grade III anaplastic ependymoma.
- Oligodendrogliomas arise from cells that make the fatty substance that covers and protects nerves. Under the microscope, the cells have a “fried egg” appearance. They are most common in middle-aged adults. These include oligodendroglioma (grade II) and anaplastic oligodendroglioma (grade III).
- Medulloblastomas (primitive neuroectodermal tumor) often arise in the cerebellum. It is the most common brain tumor in children and is grade IV.
- Meningiomas arise in the meninges, which are the tissues that cover the brain. They are typically benign and slow-growing, though there are also rare grade II and III malignant meningeal tumors.
- Pituitary tumors and craniopharyngiomas form in the center of the brain and can occur in children and adults.

How are brain tumors treated?

There are a number of different treatments for brain tumors. Some brain tumors are treated with a combination of different types of therapies. The exact location and type of brain tumor will dictate which treatments are recommended.

Surgery

Whenever possible, surgical resection is used in the treatment of many brain tumors. It is rare that a primary brain tumor can be cured without a surgical resection. However, the location of the brain tumor will dictate whether or not surgery is an option, and to what extent surgery can be performed safely. Some tumors are located in places in the brain that are just too dangerous to operate on, and surgery cannot be used. The risks to the patient from surgery depend on the location and size of the tumor. Talk to your neurosurgeon about the specific risks of your planned surgery.

Chemotherapy

Chemotherapy is the use of anti-cancer drugs that go throughout the entire body. These drugs may be given through a vein or as pills by mouth. One of the special challenges in treating brain tumors with chemotherapy is that there is a natural barrier between the brain and the blood, which blocks many medications from entering the brain. Only certain chemotherapy medications can cross this blood-brain barrier to treat disease in the nervous system. For certain high grade tumors, particularly glioblastoma multiforme, the most commonly used chemotherapy istemozolomide, an alkylating chemotherapy. It has been shown to be effective when used in combination with radiation therapy after surgery. Additional temozolomide is given after completing radiation therapy, usually for an additional 6 months.

Other chemotherapy medications used for brain tumors include carmustine (BCNU), carboplatin, CCNU and bevacizumab. Your cancer care team can explain why they recommend one particular regimen over another in your case. In addition, other chemotherapy medications may be used in clinical trials.

Radiation
Radiation therapy uses high energy rays (similar to x-rays) to kill cancer cells. Radiation for brain tumors comes from an external source (called external beam radiation therapy), and it requires patients to come 5 days a week, for approximately 6 weeks to a radiation therapy treatment center. The treatment takes just a few minutes, and it is painless. External beam radiation therapy is often employed for brain tumors, either as a primary treatment for unresectable tumors or after surgical resection. Typically, the technique of external beam radiation is via Intensity Modulated Radiation Therapy (IMRT). When treating brain tumors close to critical structures within the brain that are more sensitive to radiation damage, such as the nerves of the eyes or the brainstem, IMRT can be used to limit the dose of radiation received by these important structures. IMRT is not beneficial in every case and your provider can discuss this treatment option with you further.

Proton therapy is a type of radiation therapy that works a bit differently than IMRT or standard radiation. The main difference is in the physical properties of the proton beam itself, which allow it to enter the body at a fairly low dose of radiation and increase in the last 3mm of the beam to the dose required for treatment. In addition, the beam then stops, resulting in virtually no radiation to the tissue beyond the target- or no "exit dose" as it is called. This ability to spare healthy tissue is the main difference between x-rays and protons. Research has shown that the biologic effect, or the damage to exposed tissues, is essentially the same for both therapies. This means the therapies will destroy tumor cells in the same manner, but protons should result in less toxicity to surrounding healthy tissues. Proton therapy can be used to treat some types of brain tumors.

Radiation therapy can also be given to a very focused area of the brain using a technique called stereotactic radiosurgery. Stereotactic radiosurgery requires a patient to have a head frame attached, so that a precise map can be made of the patient's head. Radiation is then focused from a variety of different angles to deliver a large radiation dose to the tumor or tumor bed. This can be performed using the same machine that delivers external beam radiation or by a special machine called a gamma knife.

Your radiation oncologist can answer questions about the utility, process, and side effects of any of the above-mentioned types of radiation and can recommend the best type of radiation therapy in your particular case.

Other Treatments
Steroids, like prednisone or dexamethasone, may be a part of your brain tumor treatment. Steroids are anti-inflammatory medications that are used to decrease swelling in the brain that may develop from the tumor itself or its treatment. Some common side effects of steroids are infection, stomach ulcers or bleeding, weight gain, difficulty sleeping, and mood changes.

Another category of treatments used for brain tumors (especially high-grade and recurrent glioma) is the so-called "implants." They are used after surgical resection. Implants are typically small "seeds" or "wafers" which contain either chemotherapy or radiation. Implants are designed to bypass the blood-brain-barrier, by delivering treatment directly to the site of the tumor. Chemotherapy wafer implants (called Gliadel®) are small gel wafers containing the chemotherapy agent carmustine (BCNU). During surgery, a neurosurgeon places up to 8 wafers in the area where the tumor was (the so-called "tumor cavity"). Over the subsequent few days, the wafers release chemotherapy directly into the site of the tumor. The wafers dissolve completely in 2-3 weeks. Same question, is this used after surgery?

Brachytherapy is "internal" radiotherapy, meaning that the radiation source is inside the body, very close to the tumor. In the case of gliomas, brachytherapy can come in several forms, most commonly iodine-125 (125I) seeds and GliaSite®. GliaSite® is a radiation delivery system used for gliomas. During brain surgery, a neurosurgeon places a small balloon into the tumor cavity. A few weeks after the balloon is implanted, it is filled with liquid radiation, which delivers radiation to the surrounding tumor for a period of 3-6 days. After that time, the balloon and liquid are removed from the brain. Iodine-125 seeds are similar to GliaSite®; they too are placed by a neurosurgeon into the tumor cavity during brain surgery. The seeds also deliver radiation to the surrounding tumor, but, unlike GliaSite®, the iodine-125 seeds do not need to be removed.

Active Surveillance
In some cases, treatment may be withheld if the tumor is found early on and if it is slow growing. A patient will be closely monitored and a treatment plan will be decided when the tumor starts to grow or cause symptoms.

Clinical Trials
There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to
determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

**Follow-Up Care and Survivorship**

Once a patient has been treated for a brain tumor, he or she needs to be closely followed for a recurrence. At first, the patient will have follow-up visits fairly often. The longer he or she is free of disease, the less often he or she will have to go for checkups with examinations. The provider will decide when to obtain follow-up MRI scans.

Fear of recurrence, financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by brain tumor survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 15 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

**Resources for More Information**

**National Brain Tumor Society**

Aim to improve understanding of all brain tumors and transform research into new and effective treatments, as quickly as possible. Offers brain tumor information, related news and a blog [http://braintumor.org/](http://braintumor.org/)

**American Brain Tumor Association**

Providing comprehensive resources that support the complex needs of brain tumor patients and caregivers, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnosis, treatment and care [http://www.abta.org](http://www.abta.org)

**Brain Science Foundation**

Dedicated to finding a cure for meningioma and other primary brain tumors and to advancing the understanding of brain function as it relates to these tumors. Offers information on a variety of types of brain tumors as well as research initiatives [http://www.brainsciencefoundation.org](http://www.brainsciencefoundation.org)