**Key Takeaways:**

- Brain metastases are a cancer that has spread to the brain from another area of the body.
- This occurs most commonly in lung, breast, colon and kidney cancer and melanoma.
- Common symptoms can include changes in cognitive abilities, behavior changes, unsteady gait, visual changes, difficulty finding words, headache, and seizures.
- Treatments can include surgery, radiation and some anti-cancer medications.

**What are brain metastases?**

Brain metastases happen when cancer cells from the primary site (where the cancer started) spread to the brain. This is different from a primary brain tumor. For example, a lung cancer is first formed in the lung tissue. These tumor cells can break off from the original mass in the lung and travel through the bloodstream or lymph system to other areas of the body, including the brain. This spreading of the tumor is known as "metastasis." When lung cancer metastasizes to the brain, this "brain tumor" is actually lung cancer cells.

**Primary malignant brain tumors** are tumors that start in the brain. There are an estimated 23,820 new cases yearly. Brain metastases, commonly called "brain mets," are far more common but the exact incidence of brain metastases is not known. Studies suggest brain metastases occur in about 10%-30% of patients with cancer.

It is important to understand the difference between primary brain tumors and brain metastases because they are treated differently. The media may refer to a person who died of lung cancer and brain cancer when it was lung cancer that had metastasized to the brain.

**Lung cancers** account for the highest number of brain metastases. Other cancers that commonly metastasize to the brain include melanoma, breast cancer, colon cancer, and renal cell (kidney) cancer. Although these are the most likely types to do so, any type of cancer can spread to the brain.

There has been a rise in the number of brain metastases in recent years. This may be due to better diagnosis of brain metastases using advanced imaging. People are also living longer with metastatic disease due to advances in cancer therapy.

**Signs, Symptoms, and Diagnosis**

Common signs and symptoms of brain metastases include changes in cognitive ability (memory, attention, reasoning), behavior changes, gait changes (unsteadiness), visual changes, aphasia (difficulty finding words), headache, weakness, and seizures. Report any of these to your care team immediately.

If brain metastases are suspected, your care team will order radiology studies (MRI, CT scan). A biopsy may be needed if the patient presents without a primary cancer or if there has been a long period of time between treatment for the initial primary cancer and the new symptoms.

**Treatment Options**

Treatment decisions for each patient are based on several factors, including tumor type, general health, age, presence/control of cancer outside of the brain, and number of brain metastases. Each cancer acts differently and this is important to consider when choosing treatments. For example, primary lung cancers are quite sensitive to radiation, but melanomas are not. This
Symptom Management

A danger of brain metastases is the space they take up in the brain and the pressure they put on surrounding tissue. This pressure can cause symptoms such as headaches, speech difficulties, seizures, nausea/vomiting, weakness of a limb, or visual disturbances. The goal of initial therapy is to relieve some of this pressure by decreasing swelling using medications called corticosteroids (dexamethasone, prednisone). They can be given either orally (by mouth) or through an intravenous (IV) line. Some patients may see relief of symptoms quickly after starting steroids. However, this does not mean the tumor is gone. If patients experience seizures as a result of their brain metastases, they may also receive anti-seizure medications to prevent further seizures.

Surgery

For patients with a single brain lesion, surgery may be a good option, especially if the cancer is under control in the rest of the body. However, the lesion must be in an area of the brain where it is safe to operate. Studies have shown that patients with a single brain metastasis who had surgery followed by whole brain radiation therapy (WBRT) have fewer recurrences and better quality of life than patients treated with WBRT alone. Life expectancy in these patients has also been shown to increase. However, these results do not apply to patients with radiosensitive tumors such as lymphomas, small cell lung cancer, and germ cell tumors (where surgery is generally not recommended).

Whole Brain Radiation Therapy

Whole brain radiotherapy (WBRT) is just what it sounds like – giving radiation to the entire brain. This is generally given in 10 to 15 doses (also called fractions). WBRT is often used in patients who are not candidates for surgery, or patients with more than 3 brain lesions. Many patients may receive WBRT in combination with another therapy (surgery, radiosurgery). The motivation of treating the whole brain is that there may be cancer cells in the normal-appearing brain, but not enough of them yet to form a mass or be seen by radiology studies. Thus, treatment of the whole brain attempts to kill all the cancer cells.

WBRT has been reported to improve symptoms of brain metastases in 70-90% of patients, although some of this benefit is also a result of the corticosteroids. Despite this symptom improvement, recurrence is common, and control of brain metastases may only occur in half of the patients. Patients with tumors that are more sensitive to the effects of radiation respond better (lung and breast, for example) than those with tumors that are less sensitive to radiation (melanoma and renal cancers).

It is difficult to evaluate the long-term effects of WBRT, given the small number of patients that survive long-term. These effects could include dementia and a decline in cognitive and physical functioning.

Stereotactic Radiosurgery (SRS)

Stereotactic radiosurgery (SRS) is a confusing term. It is actually not surgery at all, but a highly precise administration of a large dose of radiation to the tumor site.

Unlike traditional external beam radiation, which is usually given daily over many weeks, SRS is administered in a single dose (Gamma Knife®) or up to five doses (Cyberknife®). More than one brain tumor can be treated during one session (for example, if a patient had 2 separate brain metastases, both could be treated on the same day). Treatments are administered by a traditional radiation machine called a linear accelerator, or a specialized machine such as Gamma Knife®, Cyberknife®, XKnife®, and ExacTrac®.

Gamma Knife® delivers several hundred beams of radiation from a cobalt source. Cobalt is one of the elements in the periodic table. It is the radioactive source used in this technique. The radiation beams concentrate at the point where all the beams meet (see picture). The radiation beams travel through hundreds of holes in the helmet, allowing a high dose of radiation to be delivered to the tumor while sparing the surrounding tissue from the high dose. SRS is highly dependent on accuracy and requires that the patient's head be securely stabilized using a helmet (head frame), so there is no movement during the treatment. Finally, there is a size limit for Gamma Knife; the metastases should be 3 cm or smaller.

XKnife® is a linear accelerator-based treatment. Like Gamma Knife, it requires a head frame, which will remain on the patient for the entire procedure, providing a reference for the patient's anatomy.
Cyberknife® is a form of frameless SRS using a specialized miniature linear accelerator with a robotic arm. It gets around the issue of using a frame for immobilization by using a custom mask for each patient along with skull-based tracking, allowing the robot to follow a target. Cyberknife can accommodate lesions larger than 3 cm, and can also be used to treat other types of cancer outside the brain.

Proton therapy is a newer form of SRS. Instead of using photons to target a tumor, this form of SRS uses protons. A machine called a synchrotron or cyclotron speeds up the protons, which are positively charged particles. The high energy of these moving protons can kill cancer cells. During treatment, the protons can precisely target the tumor. Proton therapy is a growing field of radiation therapy and not every cancer center has this treatment.

Your care team will assess the best radiation option(s) for you and create a patient-specific care plan to best treat your brain metastasis and control your symptoms.

Chemotherapy

It is widely believed that most chemotherapy agents are not able to cross the blood-brain barrier. In other words, they move through the bloodstream, but cannot enter the brain. As a result, the brain allows cancer cells to "escape" the chemo and make their way there. However, there are exceptions. Researchers have found that brain metastases from tumor types that are particularly sensitive to chemotherapy (for example testicular cancer, lymphomas, and small cell lung cancer) are also sensitive to chemotherapy. Research has also shown that people who have not received a large amount of chemotherapy in the past may have a greater reduction in brain metastases with chemotherapy treatment. This leads researchers to believe that there is some penetration of the blood-brain barrier by chemotherapy, just not always in effective amounts. One chemotherapy agent, temozolomide (Temodar®), is an oral medication that is capable of crossing the blood-brain barrier. This medication is used to treat primary brain tumors and metastatic melanoma lesions.

More recently, studies show that chemotherapies such as targeted therapies and immunotherapies may be useful in treating brain metastases by way of treating the primary cancer. Targeted therapies include lapatinib, capecitabine, erlotinib, gefitinib, and vemurafenib. Ipilimumab, nivolumab, and pembrolizumab are immunotherapy medications used to treat various types of cancer.

Preventing Brain Metastases with WBRT: Prophylactic Cranial Irradiation

Whole brain radiation can be used as a way to prevent future brain metastases from developing. When whole brain radiation is given as a preventive measure, it is also known by the name "prophylactic cranial irradiation" or "PCI." Studies of PCI have shown significant decreases in brain mets (from 55% to 19% at 2 years and from 56% to 35% at 3 years) and increases in overall survival. Some have suggested there may be long-term neurologic impairment from this treatment, but long-term neurotoxicity data is lacking.

Clinical Trials

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 healthcare provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Use our Cancer Types menu to find more information about primary tumor types and their treatment.