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 are the spread of a primary tumor to the brain. This is different from a primary brain tumor. Differing between these two types of brain lesions is a common source of confusion for many people. For example, a lung cancer is first formed in the lung tissue, but tumor cells can break off from the original mass 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 a 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. They are actually quite rare, with an estimated 23,800 new cases in 2017. Brain metastases, commonly called "brain mets," are far more common. The exact incidence of brain metastases is not known. Studies suggest brain metastases occurs 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, in actuality, it was lung cancer that had metastasized to the brain.

Among tumor types, lung cancers account for the highest number of brain metastases, with 25% of patients being affected at some time in their disease course. 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 could 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 and also because people are living longer with metastatic disease due to advances in cancer therapy. Unfortunately, in most cancers, once a person develops brain metastases, the tumor is not curable. With current treatments, patients can live from months to years, depending on the number of brain metastases, the type of tumor, and the amount of cancer present in the rest of the body.

It is important to remember that not all cancers are equal. Some are more aggressive and/or less susceptible to treatments than others. For this reason, prognoses vary greatly from tumor to tumor and person to person. This is also important to consider when choosing treatments. For instance, primary lung cancers are quite sensitive to radiation, but melanomas are not. This does not change once the tumor spreads to the brain. In turn, treatment decisions vary based on the primary (original site) tumor type.

In terms of chemotherapy, researchers have known for years that many of the chemotherapy agents commonly used are not able to cross the blood-brain barrier. This means the medications are not able to penetrate the brain, and therefore cannot effectively kill cancer cells in the brain. Because of this, most chemotherapy agents, are not very effective at treating brain metastasis, even if they are working well elsewhere in the body. For most patients, treatment of brain metastases centers around surgical and radiation techniques. We will review the various treatments available and the relevant supporting data.
Signs, Symptoms and Diagnosis

Common signs and symptoms of brain metastases include changes in cognitive ability (memory, attention, reasoning), behavior changes, gait ataxia (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 obtain radiology studies (MRI, CT scan). A biopsy may be needed, especially 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 that may be associated with brain metastases.

Treatment Options

Symptom Management

The 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 on the brain tissue by decreasing swelling using medications called corticosteroids (dexamethasone, prednisone). They can be given either orally 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.

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.

Surgery

For patients with a single brain lesion, surgery may be a good option, especially if the tumor 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. A study of patients with a single brain metastasis randomized to whole brain radiation therapy (WBRT) alone vs. surgery followed by WBRT found that patients treated with surgery and 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), and is often used in patients with poor prognostic factors, 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 just not enough of them yet to form a mass and 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 be achieved in half of the patients. Patients with tumors that are more sensitive to the effects of radiation fare better (lung and breast, for example) than those with relatively radioresistant tumors (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®) and other linear accelerator-based treatments). 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. To take you back to high school chemistry, 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 to converge on the tumor, 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 location of 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.

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 blood stream, but cannot enter the brain. As a result, the brain is a safe haven for cancer cells that "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 demonstrated that in those who have not already received a large amount of chemotherapy 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 indicate 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 in combination with capecitabine for metastatic breast cancer, erlotinib and gefitinib for non-small cell lung cancer, and vemurafenib for metastatic melanoma. Ipilimumab, nivolumab, and pembrolizumab are immunotherapy medications used to treat non-small cell lung cancer and melanoma. More to come on these treatments for brain metastases.

Preventing Brain Metastases with WBRT: Prophylactic Cranial Irradiation
Small cell lung cancer is associated with a very high risk for brain metastases; approximately 50% of patients develop lesions within two years of diagnosis. For this reason, researchers looked at utilizing whole brain radiation 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. PCI is the standard of care for patients with limited-stage small cell lung cancer who have complete remission after local therapy. Studies are ongoing to assess any benefits of this practice in other tumor types.

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.

OncoLink is designed for educational purposes only and is not engaged in rendering medical advice or professional services. The information provided through OncoLink should not be used for diagnosing or treating a health problem or a disease. It is not a substitute for professional care. If you have or suspect you may have a health problem or have questions or concerns about the medication that you have been prescribed, you should consult your health care provider.