AMERICAN BRAIN TUMOR ASSOCIATION

Metastatic Brain Tumors



American Brain Tumor Association®

Providing and pursuing answers™

ACKNOWLEDGEMENTS

ABOUT THE AMERICAN BRAIN TUMOR ASSOCIATION

Founded in 1973, the American Brain Tumor Association (ABTA) was the first national nonprofit organization dedicated solely to brain tumor research. The ABTA has since expanded our mission and now provides comprehensive resources to support the complex needs of brain tumor patients and caregivers, across all ages and tumor types, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnoses, treatments and care.

To learn more, visit abta.org.

The ABTA gratefully acknowledges the following for their review of this edition of this brochure: Minesh P. Mehta, MD (Radiation Oncology, Miami Cancer Institute, Baptist Health), Hina Saeed, MD (Radiation Oncology, Froedtert & the Medical College of Wisconsin), Manmeet Ahluwalia, MD, FACP, MBA (Medical Oncology, Miami Cancer Institute at Baptist Health South Florida), and Briea Curington (caregiver reviewer).

ABTA1223

Metastatic Brain Tumors

INTRODUCTION

This brochure is about **metastatic brain tumors**, the most common type of brain tumor in adults.

Also known as brain metastasis or secondary brain tumor, a **metastatic brain tumor forms when cancer from another part of the body spreads to the brain**.[2] Brain metastasis can present as a single tumor or many tumors.

METASTASIS refers to one tumor.

METASTASES refer to two or more tumors.

METASTASIZE is the process by which cancer cells travel from one part of the body to another.

PRIMARY SITE refers to the location of the original cancer.

Metastatic brain tumors are usually made of the same type of cancer cells found at the original tumor location or primary site. L**ung, breast, melanoma (skin**

cancer), kidney, and colon cancers, in that order, commonly spread to the brain.[1,2,3] When the primary cancer site is not found, it is called cancer of unknown primary, or CUP.[4] Researchers suggest that between 2% and 14% of brain metastases occur in patients who do not have an existing cancer diagnosis.[3,5,6]

Metastatic brain tumors are the most common type of brain tumors in adults, but account for only about 2% of brain tumors in children.[1] It is estimated that as many as 30% of adults, and between 6% and 10% of children, with cancer eventually develop a metastatic brain tumor.[1,7] Brain metastases occur equally in both men and women.[3]

When a tumor spreads to the brain, it is not called brain cancer. Rather, it is named after the part of the body where the cancer started. Lung cancer that spreads to the brain is called metastatic lung cancer, breast cancer that spreads to the brain is called metastatic breast cancer, and so on.[8,9]

SPECIFIC TYPES OF METASTASES

LUNG CANCER

- An estimated 23% to 36% of patients with lung cancer develop brain metastases.[5]
- These tumors typically occur a few months after lung cancer is found (on average, 4 months).[3] However, it is not uncommon for lung cancer to be diagnosed at the same time the brain metastasis is discovered.[7]
- When patients have metastatic brain tumors and no primary diagnosis is found, two-thirds of them will develop lung cancer.[5]
- Multiple brain metastases are common.[5,7]

BREAST CANCER

- An estimated 5% of patients with breast cancer develop brain metastases.[5]
- Metastases typically occur a few years after breast cancer is diagnosed (on average, 46 months).[5]
- These tumors are more common in women with triple-negative and HER2-positive breast cancer.[5,10]
- A single brain metastasis is more common with breast cancer than with other primary cancers.[5,7]

MELANOMA

- An estimated 7% to 10% of patients with melanoma develop brain metastases.[5]
- These tumors typically occur a few years after melanoma is found (on average, 22 to 37 months).[5]
- Multiple brain metastases are common.[5,7]

KIDNEY/RENAL CELL CARCINOMA

- An estimated 2% to 16% of patients with kidney cancer develop brain metastases.[5]
- Metastases typically occur about one year after kidney cancer is diagnosed (on average, 10 months).[5]
- A single brain metastasis is common.[5,7]

COLON/COLORECTAL CANCER

- An estimated 1% to 4% of patients with colon cancer develop brain metastases.[5]
- These tumors typically occur a few years after colorectal cancer is found (on average, 26 to 42 months).[5]
- A single brain metastasis is common.[5,7]

INCIDENCE

Incidence refers to how often a disease occurs. But without a national reporting system for brain metastases, estimates of its frequency vary significantly.[5] The most widely accepted estimate suggests **about 200,000 new cases are diagnosed each year** in the United States.[11]

About 60% of patients who are diagnosed with brain metastases are between the ages of 50 and 70 years,[3] with a peak incidence at 60 years of age. [5]

Despite not knowing exactly how often metastatic brain tumors occur, the **incidence is believed to be increasing** due to:[1,7]

- better ways of detecting small tumors using imaging in the brain,
- better treatments for primary cancers that enable cancer patients to live longer, and
- an increase in primary cancers that tend to metastasize to the brain.

The ABTA has funded research to learn more about the incidence and prevalence of these tumors.

Metastatic brain tumors are believed to occur 10 times more often than cancerous primary brain tumors.[5]

CAUSE

Metastasis occurs when cancer cells from a tumor break away and are carried to other parts of the body through the bloodstream or lymphatic system.[8] The lymphatic system helps the body get rid of toxins, waste, and other unwanted materials as well as works with the immune system to fight infection.

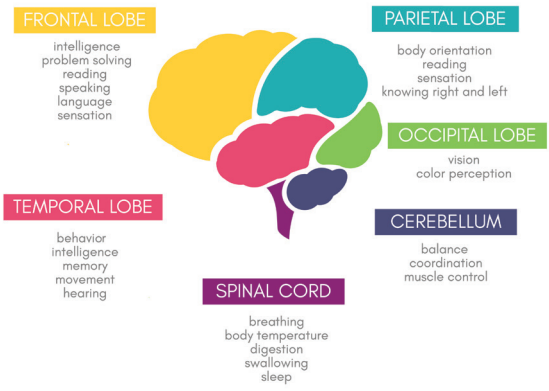
In adults, **lung, breast, melanoma, kidney, and colon cancers are the leading causes for brain metastases.**[5,7] In children, the most common sources of brain metastases are germ cell tumors, neuroblastomas, and sarcomas.

SYMPTOMS

The symptoms of a metastatic brain tumor often depend on where the tumor is located, how much cancer is in the brain, and how quickly it spreads.[3,12]

The symptoms a person may experience are linked to the location of the tumor because the lobes of the brain control different functions, such as thought and reasoning versus vision and hearing.

About 80% of metastatic brain tumors occur in the cerebrum, 15% in the cerebellum, and 5% in the brainstem.[3,7]



Functions of the lobes of the brain.

The cerebrum controls muscles as well as speech, thought, emotions, reading, writing, and learning.[13] The cerebellum controls balance for walking and standing, and other complex motor functions. The brain stem controls basic functions such as breathing, heartbeat, blood pressure, control of consciousness, and sleep.

Cancer that spreads to the brain can compress the brain and cause edema (swelling in the brain near the tumor) inside the skull, leading to **headaches, which affect about half of patients with brain metastases.**[7] It also can disrupt connections between normal brain cells, causing **seizures, speech problems, numbness, or tingling.**[8] When a tumor interrupts signals from the brain to the muscles, it can result in c**oordination problems. Cognitive changes** - those related to thinking, learning, concentrating, problem-solving, and decision-making - commonly occur.[7] Other symptoms can include **nausea or vomiting; changes in mood, behavior, or personality; vision changes; and muscle weakness.**[2,8]

Relieving symptoms will be an important part of your care and treatment plan.

DIAGNOSIS

A metastatic brain tumor may be found when the primary cancer is diagnosed or when a cancer patient begins having symptoms.[8] Doctors use different types of tests to detect brain metastases and to also learn what type of tumor it is and where in the brain it is located. These tests are often done by different specialists who are part of the healthcare team.

Different tests and history. After getting a thorough medical history from the patient, the doctor will do a physical examination.[7] **Neurological exams** test a patient's eye movements, vision, hearing, balance, coordination, and reflexes as well as cognitive skills, such as awareness, attention, speech, language, memory, and judgment. These tests, which are used to help determine which part of the brain the tumor is affecting, are typically done by a clinical neuropsychologist, a psychologist who specializes in understanding the relationship between the brain and behavior.

A **computed tomography** (CT) scan, a form of imaging, is often ordered first as it is very helpful in identifying the presence of the tumor.[8] But a **magnetic resonance imaging** (MRI) scan is the preferred test for further evaluating brain and spine tumors because it is more sensitive than CT for detecting brain metastasis and identifying important features.[7] These imaging tests can be used with or without contrast, which is a dye that makes the scanned images clearer.[14]

The doctor may recommend a **lumbar puncture**, also called a spinal tap, to look for tumor cells within the cerebrospinal fluid (CSF).[4] A lumbar puncture is done only after the pressure in the brain is relieved once the tumor is removed through surgery.[15]

The primary tumor site is identified during the history and physical exam in about 25% to 33% of patients.[7] For the remaining patients, the doctor will use other tests, such as a chest CT scan, to locate the primary cancer site. A **CT scan of the stomach and hips** as well as a **bone scan** can help determine how much metastatic disease there is.[3,7] A **positron emission tomography, or PET, scan** can be used to identify the primary tumor or find other sites of metastatic disease that can be biopsied.

Doctors are increasingly using **molecular testing** of brain metastases to determine the primary cancer and

Patient entering MRI machine.

help guide treatment.[11,16] Testing usually involves a biopsy of the brain tumor(s) and a blood test. After sending the samples to a laboratory that specializes in molecular testing, the doctor will get a report with the test results.[17]

Although imaging tests may give the doctor an educated idea of the tumor type, a **biopsy** or **surgical resection** is needed to be sure of the diagnosis.[7] This is especially true for patients with a single tumor.[3,7]

During a biopsy, the ***neurosurgeon*** (a doctor who specializes in surgery of the nervous system) surgically removes a small piece of the tumor tissue and sends the sample to a pathologist. The pathologist then examines it under a microscope and sends a pathology report indicating the tumor type to the neurosurgeon. Sometimes, the neurosurgeon may remove a larger part of the tumor and send a sample for pathology testing. This is known as a ***surgical resection***.

Ask your doctor if molecular testing can help inform your treatment options and improve your outcomes.

TREATMENT

Traditionally, the most common treatment options for metastatic brain tumors are surgery and radiation therapy.[2,3,12] Patients who have surgery may be treated with radiation therapy to improve local disease control.[18] However, targeted therapy and immunotherapy are increasingly being used and are showing promise in helping some patients with metastatic brain tumors.[8,12,18] Chemotherapy is not often used to treat brain metastases because the blood-brain barrier prevents many drugs from reaching the brain.[8,12]

The goals of treatment may be to relieve symptoms, improve functioning, prolong life, or provide comfort.[4]

Specific treatment approaches will depend on:[2,4,8]

- Type of primary cancer diagnosed
- Brain metastasis tumor size and location
- Number of brain metastases
- Symptoms
- How far the cancer has spread
- Genetic changes found in the cancer cells
- The patient's age, overall health, and treatment preferences
- Previous treatments
- Prognosis

SURGERY

Surgery is often considered as a first option for treating brain metastases if there is one large tumor causing symptoms, the number of tumors is limited, all or most of the tumor(s) can be safely removed, there is diagnostic uncertainty, the cancer is controlled, and the patient

is in good overall health.[3,8,18] Surgery also may be recommended if there is a single tumor and the cancer has not spread to other parts of the body.[4] Some tumors can be removed completely, while others may be reduced in size.

Advances in surgery are making it a safer option for a growing number of people with brain metastases.[18,19]

Laser interstitial thermal therapy (LITT), also called laser ablation, is a minimally invasive surgical technique that allows surgeons to precisely target and treat the tumor with a high temperature laser. It has shown some promise for patients with difficult to reach tumors that do not respond to radiation therapy.[20]

Image-guided surgery and ***intraoperative ultrasound*** are two techniques that can help more accurately identify margins around the tumor for surgical removal. Functional navigation can help the neurosurgeon distinguish the tumor from areas of the brain that control functioning, enabling the doctor to avoid harming those areas.[21]

When a tumor cannot be reached surgically, ***stereotactic biopsy***, which uses a computer and a 3-dimensional scanning device to help guide the removal of tissue for a biopsy, may be helpful.[18]

Major risks of surgery include worsening of neurologic symptoms, infection, hemorrhage (loss of blood from damaged blood vessels), and peri-operative stroke.[18]

To learn more, read the ABTA's Surgery brochure.

It's important to weigh the benefits and risks of surgery as well as other treatment options.

RADIATION

Radiation therapy is often given following surgery to improve local control.[18] It is also used upfront in many patients when surgery is not feasible.[3] Types of radiation therapy commonly used to treat brain metastases are **whole-brain radiation therapy** (WBRT) and **stereotactic radiosurgery** (SRS). Sometimes both types of radiation are used.

Whole-brain radiation therapy involves treating the entire brain with radiation. When people have lesions deep in the brain or many lesions throughout the brain, WBRT is often recommended.[4,8] WBRT also is recommended for treating cancer cells that have spread into the cerebrospinal fluid (CSF) surrounding the brain, this is known as ***leptomeningeal disease***.

Patients being treated with WBRT have an overall response rate, which means the tumor is either destroyed or significantly reduced, between 40% and 60%.[18] Breast cancer and lung cancer tend to respond to WBRT more than melanoma or kidney cancer. Small, solid tumors are more likely to respond to WBRT than large, necrotic, or cystic tumors.

Common side effects of WBRT include fatigue, hair loss, and an increased risk of neurocognitive decline that may reduce a person's quality of life.[18] The treatments are given daily over a course of weeks to reduce side effects.[8]

To help protect cognitive function, it is recommended that patients receive a technically advanced form of WBRT known as ***intensity-modulated radiation therapy*** that avoids the hippocampus, an area of the brain that, when injured, is associated with cognitive decline.[22] This advanced method of radiation has been shown in studies to better preserve brain function.[23] Additionally, a drug called memantine has been shown to protect cognitive function from damage during WBRT.[22]

Stereotactic radiosurgery is a form of radiation therapy that focuses high-dose x-rays aimed only at the area with the cancer.[4] This method can help lessen side effects caused by the treatment.[12] SRS is often given as a single high dose of radiation, but may also be given over two to five medium-dose fractions for targets that are larger in size or near critical normal tissues, such as the brainstem or the eye.[18]

SRS is becoming the preferred treatment for patients with a limited number of brain metastases.[18] **Patients with brain metastases are increasingly being treated with SRS as studies show it is associated with less cognitive decline than WBRT with no difference in survival.**[18,24] However, intensity-modulated radiation therapy and memantine, two more recent developments, also have been shown to lead to less cognitive decline.[22,23]

Patient undergoing SRS treatment with Gamma Knife®.

Common side effects of SRS are mild nausea, dizziness or vertigo, seizures, or new headaches.[18] Radiation necrosis (death of healthy tissue caused by radiation therapy) is the most common delayed complication, and occurs in about 10% of patients. It can happen anytime from six months to several years following treatment. Treatment options for radiation necrosis include corticosteroids and bevacizumab[25,26] as well as LITT.[27,28]

Brachytherapy is a type of radiation therapy in which radioactive material (or seeds) are placed either in or near a tumor. The radiation primarily affects the tissue closest to the radioactive seed, thus minimizing radiation exposure to healthy tissue away from the tumor. Brachytherapy shows some promise for controlling brain metastases.[29,30,31]

Any substance that makes tumor cells easier to kill with radiation therapy is known as **radiosensitizers or radioenhancers**. The use of radiosensitizers combined with WBRT is being studied in the treatment of brain metastases.[32,33]

To learn more, read the ABTA's Conventional Radiation Therapy and Stereotactic Radiosurgery brochures.

SRS is becoming the preferred treatment for patients with a limited number of brain metastases[18] because it reduces the risk of cognitive decline compared to WBRT. Talk to your radiation oncologist about the different types of radiation therapy and which one might be right for you.

CHEMOTHERAPY

In general, **chemotherapy has not been shown to be as helpful as surgery or radiation therapy** for treating metastatic brain tumors.[4] That is because most chemotherapy medications are unable to cross the blood-brain barrier to treat the tumors.[3,12] As a result, chemotherapy is rarely used to treat brain metastases,[8] although there are certain exceptions.

When chemotherapy has been used to treat brain metastases from lung cancer, breast cancer, and melanoma, two to three drugs are used in combination with WBRT.[3]

Common side effects of chemotherapy include fatigue, nausea and vomiting, mouth sores, hair loss, loss of appetite, and diarrhea.[12,14]

To learn more, read the ABTA's Chemotherapy brochure.

TARGETED THERAPY AND IMMUNOTHERAPY

Targeted therapies and immunotherapies have been shown to benefit some patients with brain metastases.[8,34,35] These options appear to work best for patients with limited, small volume (which refers to the amount of cancer present) disease.

Targeted therapies refer to drugs that block the growth and spread of the tumor by interfering with specific molecular targets (certain proteins) that are involved in the growth and spread of cancer cells.[12,36]

Currently, there are only a few targeted therapies that will reach the brain tumor at high enough concentrations to stop the cancer cells from growing and spreading. **The doctor can run molecular tests to identify which proteins can be blocked to help determine the best targeted therapy for each patient.** The proteins in brain metastasis may be different from those in the primary tumor, so it is important to get a biopsy or resection of both the primary tumor and, in some situations, the brain metastasis to determine the best treatment.[11]

The following targeted therapies, by themselves or in combination, have shown some promise for treating certain specific brain metastases:

- Alectinib, brigatinib, ceritinib, crizotinib, erlotinib, gefitinib, and osimertinib for brain metastases from lung cancer.[3,10,12]
- Lapatinib, neratinib, trastuzimab, and tucatinib for brain metastases from breast cancer.[10,12]

- Dabrafenib, trametinib, and vemurafenib for brain metastases from melanoma.[3,12]
- Sorafenib and sunitinib for brain metastases from kidney cancer.[3]
- Larotrectinib and entrectinib for tropomyosin receptor kinase fusion-positive brain metastases no matter the type of primary cancer.[37,38]

Scientists are conducting research studies to identify more proteins and new treatments to target them.[39]

Immunotherapies refer to drugs that enlist the body's own immune system to fight the tumor. Some types of immunotherapy only target certain cells of the immune system, whereas others affect the immune system in a general way.

Immunotherapies that have shown promise in treating brain metastases from lung cancer and melanoma are ipilimumab, nivolumab, and pembrolizumab.[12]

Ask your doctor if molecular testing can help identify a targeted therapy or immunotherapy to treat your tumor.

SINGLE OR LIMITED BRAIN METASTASES

Surgery is often the first option used to treat brain metastases when the primary cancer is treatable and under control, and the patient has a limited number of brain tumors (typically 1 to 3).[8,18] Patients who have one large metastatic brain tumor with edema and pressure inside the skull resulting from a growing tumor (known as mass effect or intracranial pressure) have experienced rapid symptom relief and local control following surgical resection.[18] Local control refers to stopping the cancer from

growing beyond the original tumor site. If the tumor cannot be reached surgically, stereotactic biopsy may be indicated.

Following surgery, patients may have radiation therapy to improve local control.[18] For patients with a single metastatic brain tumor or limited number of tumors, surgery is often followed by SRS. Sometimes, SRS may be performed prior to surgery.

For patients who have a few metastatic brain tumors that are smaller than 3 cm (the size of a grape), studies support using SRS alone to initially manage the tumors. Patients with tumors up to 3 cm in size have had local control rates of about 70% at one year following treatment, according to clinical trials.[18]

Patients with breast, colon, and kidney cancers more commonly have a single metastatic tumor as compared with other primary tumors.[7]

MULTIPLE OR EXTENSIVE BRAIN METASTASES

In general, **most patients with multiple tumors would not undergo surgical resection**. However, there are certain exceptions. National Comprehensive Cancer Network experts recommend surgery when one or a few dominant lesions are responsible for causing increased pressure in the brain leading to significant symptoms, followed by SRS, for patients with multiple – typically 4 or more – brain metastases, who function well and are able to perform normal daily activities and have low tumor volume.[40] Patients with multiple large tumors, high tumor volume, and radiation-resistant tumors may require WBRT.[18,41]

SRS is increasingly being used to treat multiple brain metastases as there is a growing body of evidence to suggest that SRS reduces the harmful effects of treatment

compared with WBRT.[41,42] While trials support the use of SRS for up to 4 brain metastases, some doctors will treat more than 4 tumors in one SRS session.[18] These patients receiving SRS alone, without WBRT, have a higher risk of tumors coming back elsewhere in the brain. Some of these patients may benefit from receiving WBRT in addition to SRS.[43]

Patients with lung cancer and melanoma tend to have multiple metastases.[7]

SPINAL METASTASES

Metastases to the spine are most often caused by breast cancer, lung cancer, and prostate cancer.[43] These metastatic tumors usually involve the bones of the spine – the vertebrae – and then spread to the spinal cord.

In recent years, new forms of SRS and advances in minimally invasive surgery have radically changed the treatment of spinal metastases.[44,45,46] **Radiation therapy continues to be the mainstay of treatment** and has been shown to be very effective in relieving pain. Specifically, SRS has been shown to offer good local control when used as either the main treatment option or following surgery.[46,47] When surgery is a treatment option, it is often a less aggressive, minimally invasive type that is linked to improved surgical outcomes and survival.

For patients with a weak spine or compressed spinal cord, surgery followed by radiation therapy is the preferred approach. Sometimes, patients may be given steroids to decrease the risk of swelling in the case of spinal cord compression.[45] ***Radiofrequency ablation***, a minimally invasive procedure, and ***vertebroplasty***, a procedure in which a special cement is injected into a fractured vertebra, also may help reduce pain.[46,47] Although targeted therapies and immunotherapies are improving both local control and patient survival for other cancers, its precise role for spinal metastases has yet to be determined.

MENINGEAL METASTASES

Meningeal metastases, also called leptomeningeal metastases, is the spread of cancer cells to the meninges (thin layers of tissue that cover the brain and spinal cord). This type of metastasis occurs most commonly with breast cancer, lung cancer, and melanoma.[47,48]

Patients with **meningeal metastases may be treated with radiation therapy alone or radiation therapy and a special type of chemotherapy called intrathecal (IT) chemotherapy**.[12,48] This type of chemotherapy is used to treat cancers that have entered the CSF. In general, chemotherapy given in pill form or intravenously cannot cross into the CSF, and therefore, is not effective in treating the cancer. Giving chemotherapy directly into the CSF allows the drug to reach the cancer and reduces the possible overall side effects caused by other forms of chemotherapy. IT chemotherapy is given either using a lumbar puncture or through a catheter with a reservoir, known as an ***Ommaya reservoir***.

In very select cases, radiation therapy is used to target the entire brain and spine, known as c***raniospinal irradiation***.[49]

Surgery may be used to relieve CSF flow blockage, but it does not play a large role in treating meningeal metastases.[48] Systemic chemotherapy is another treatment option. Both IT and systemic chemotherapy have been shown to improve survival for patients with meningeal metastases in studies.

Targeted therapy and immunotherapy are being studied for the treatment of meningeal metastases.[48] Among the targeted therapies that have shown promise in clinical trials are bevacizumab, dabrafenib, erlotinib, gefitinib, and IT trastuzumab as well as tyrosine kinase inhibitors and anaplastic lymphoma kinase inhibitors. Immunotherapy agents, such as nivolumab, ipilimumab,

and pembrolizumab, also have shown some positive results in trials.

PALLIATIVE CARE

Metastatic brain tumors and their treatments cause physical symptoms and side effects.[50] Relieving these symptoms and side effects is an important part of **supportive care**, sometimes referred to as palliative care. Palliative care is for anyone, regardless of their age, or type and stage of disease. It should be started right after a diagnosis for best results. **People who receive palliative care often have less severe symptoms, better quality of life, and are more satisfied with treatment**.[9]

The following medications may help relieve symptoms caused by the brain tumor itself or therapies to treat it:[4,51]

- Steroids, such as dexamethasone, may reduce edema
- Osmotic diuretics, such as urea or mannitol, also may reduce edema
- Anti-seizure drugs, such as levetiracetam or phenytoin, may help control seizures
- Antiemetic medications may prevent vomiting and help control nausea
- Antacids or antihistamines may control stress ulcers
- Pain medicines may relieve overall pain and discomfort

In addition to medications, palliative care may include physical and/or occupational therapy, nutritional counseling, behavioral modification/coping, relaxation techniques, and emotional and spiritual support, among others.[3,52]

Ask your doctor which treatments can be used to treat your symptoms and side effects.

CLINICAL TRIALS

Clinical trials offer individuals the chance to use new or experimental tests and treatments (meaning they have not yet been proven) before they are available to the public. It is important to understand that some of these treatments may not work or may come with severe side effects. There are several ongoing clinical trials evaluating SRS, WBRT, targeted therapies, and immunotherapies for treating brain metastases.[53] Researchers are exploring new therapies, new methods of radiation therapy, and new combinations of existing treatments.

People who want to join a clinical trial volunteer and must meet certain requirements, such as having a specific type of tumor or not having been treated with a certain therapy.[54] Most clinical trials cover treatment costs.

To learn more, read the ABTA's Clinical Trials brochure.

Talk to your doctor to see if a clinical trial is right for you.

RECURRENCE

Following initial treatment, patients should have an MRI or CT to detect a tumor that has recurred (returned) or to detect new tumors.[18] Typically, patients will be seen one month after the initial therapy and then every two to three months. For as many as half of patients with brain metastases, their tumors will return or they will develop new lesions within six months to one year following initial therapy.

Depending on the patient's overall condition, and the extent and location of the tumor, **treatment options may include surgery, SRS, or WBRT**.[18] SRS is increasingly being used to treat recurrent or new tumors that arise after initial therapy for patients who are functioning well and have stable disease. These patients are experiencing local control rates similar to those seen with initial therapy. For some patients who may not be good candidates for surgery or SRS, WBRT may be beneficial.

Surgery may be an option for certain select patients with a large recurrent brain metastasis when the primary cancer is well controlled.[18] Other techniques, such as brachytherapy and LITT, are being studied for treating recurrent brain metastases.

Talk to your doctor about the possibility of the tumor recurring and treatment options available.

PROGNOSIS

Prognosis refers to the chance of recovery or survival from a disease. A prognosis is based on statistics that look at a large group of people with the same disease over time. Keep in mind that **statistics on survival rates are estimates**. Typically, they are measured every five years, so the latest estimates may not include the most current methods of diagnosing and treating metastatic brain tumors.[55]

The prognosis of brain metastases in some patients is improving, largely due to advances in targeted therapies and immunotherapies, both of which have led to better disease control and prolonged survival.[34,35]

Recovery from brain metastases, however, is not always possible.[12] When the tumor cannot be cured or controlled, the cancer is called ***advanced*** or ***terminal***.

Hospice care offers the best possible quality of life for people who are not expected to live longer than six months. Hospice care can be provided at home or a healthcare setting. In-home hospice care requires nursing care and special equipment. Support services are available that can help individuals cope with an advanced tumor diagnosis.

Although brain metastases in many cases may not be curable, doctors can treat metastatic brain tumors to slow their growth and reduce symptoms. It is possible to live for many months or years with certain types of cancer, even after metastatic disease develops.[9]

In general, key predictors of survival are:[3,18]

- Performance status – T***he better a person can function and perform normal daily activities, the better the prognosis.***
- Controlled disease – ***The more controlled the disease, the better the prognosis.***
- Patient's age – ***The younger the patient (under the age of 65), the better the prognosis.***

Talk to your doctor about expected outcomes to get a more individualized prognosis.

FUTURE DIRECTIONS

The growing knowledge of genes and molecular markers, and their role in brain tumor development has allowed researchers to understand brain metastases in ways that are having a significant impact on both treatment and survival. But there is much more work to be done.

Knowing the molecular make-up of the tumor is an important first step in developing drugs that target and kill the cancer cells. Molecular testing is playing an increasingly greater role in helping to make that determination.

The hope is that this better understanding will lead to better and more precise treatment. Together, the medical and scientific communities, supporting organizations, and patients and their families are building on past successes toward a better cure for all people diagnosed with brain metastases.

METASTATIC BRAIN TUMORS QUESTIONS TO ASK YOUR DOCTOR

What can you tell me about my brain tumor type? Was molecular testing used to make my diagnosis?

What is my prognosis (outlook), both with and without treatment?

How many brain tumor patients with my tumor type do you treat each year?

What treatment options are available? Can treatment wait?

If radiation is recommended, what is the difference between Whole Brain Radiation Treatment (WBRT) and Stereotactic Radiosurgery (SRS)?

Is SRS available at this treatment center? If not, is SRS available in the area?

Considering the cognitive decline associated with WBRT, would SRS be better suited for me?

If WBRT is the best treatment for my tumor, how do you recommend preserving my cognitive functioning? Is hippocampal avoidance possible?

What are the goals of treatment?

What are the risks and benefits of treatment?

How do you determine if the treatment is effective? What follow-up tests are needed?

What are common treatment side effects? How will treatment affect my daily activities?

What are the possible long-term effects of having this treatment?

How do you expect my brain tumor to progress? Will it spread or come back after treatment?

Are there alternative treatment options? Would a clinical trial be right for me?

Do you recommend getting a second opinion? Whom would you recommend I consult with?

What survivorship services are available to me? To my family?

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

Educational brochures are available on our website or can be requested in hard copy format for free by calling the ABTA. Most brochures are available in Spanish, with exceptions marked with an asterisk.

GENERAL INFORMATION

About Brain Tumors: A Primer for Patients and Caregivers
Brain Tumor Dictionary*
Brain Tumors Handbook for the Newly Diagnosed*
Caregiver Handbook*

TUMOR TYPES

Ependymoma
Glioblastoma and Anaplastic Astrocytoma
Medulloblastoma
Meningioma
Metastatic Brain Tumors
Oligodendroglioma and Oligoastrocytoma
Pituitary Tumors

TREATMENT

Chemotherapy
Clinical Trials
Conventional Radiation Therapy
Proton Therapy
Stereotactic Radiosurgery*
Steroids
Surgery

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

INFORMATION

ABTA WEBSITE | ABTA.ORG

Offers more than 200 pages of information, programs, support services and resources, including: brain tumor treatment center and support group locators, caregiver resources, research updates and tumor type and treatment information across all ages and tumor types.

EDUCATION & SUPPORT

• ABTA Educational Meetings & Webinars

In-person and virtual educational meetings led by nationally-recognized medical professionals.

• ABTA Patient & Caregiver Mentor Support Program

Connect with a trained patient or caregiver mentor to help navigate a brain tumor diagnosis.

• ABTA Connections Community

An online support and discussion community of more than 25,000 members.

• ABTA CareLine

For personalized information and resources, call 800-886-ABTA (2282) or email info@abta.org to connect with a CareLine staff member.

GET INVOLVED

• Join an ABTA fundraising event.

• Donate by visiting abta.org/donate.

CONTACT THE ABTA

CareLine: 800-886-ABTA (2282)

Email: info@abta.org

Website: abta.org

REFERENCES

1. WHO Classification of Tumours of the Central Nervous System, 4th ed, Louis DN, Ohgake H, Wiestler OD, Cavenee WK (Eds), International Agency for Research on Cancer. Lyon, France: 2016.
2. Patient education: Brain metastases (The Basics). (2020). UpToDate. http://www.uptodate.com/home/index.html. (Accessed 7-30-20)
3. Tse V. 2018. Brain metastasis. In N Lorenzo (Ed.), Medscape. https://emedicine.medscape.com/article/1157902-overview. (Accessed 11-4-19)
4. U.S. National Library of Medicine. Metastatic brain tumor. 2018. https://medlineplus.gov/ency/article/000769.htm. (Accessed 11-4-19)
5. Ostrom QT, Wright CH, Barnholtz-Sloan JS. Brain metastases: epidemiology. Handb Clin Neurol. 2018;149:27-42.
6. Varadhachary GR. Carcinoma of unknown primary origin. Gastrointest Cancer Res. 2007;1:229-35.
7. Loeffler JS. (2020). Epidemiology, clinical manifestations, and diagnosis of brain metastases. In AF Eichler (Ed.), UpToDate. https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-brain metastases?search=metastatic%20brain%20tumor&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. (Accessed 10-31-19)
8. ASCO® answers: When cancer spreads to the brain. 2019. https:/www.cancer.net/sites/cancer.net/files/asco_answers_brain metastasis.pdf. (Accessed 10-31-19)
9. What is Metastasis? Doctor-Approved Patient Information from ASCO®. 2019. https://www.cancer.net/navigating-cancer-care/cancer-basics/what-metastasis. (Accessed 10-31-19)
10. Lin NU, Ramakrishna N. (2020). Management of brain metastases in breast cancer. In SR Vora (Ed.), UpToDate. https://www.uptodate.com/contents/management-of-brain-metastases-in-breast-cancer?search=metastatic%20brain%20tumor&source=search_result&selectedTitle=6~150&usage_type=default&display_rank=6. (Accessed 7-30-20)
11. Brastianos PK, Carter SL, Santagata S, et al. Genomic characterization of brain metastases reveals branched evolution and potential therapeutic targets. Cancer Discov. 2015;5(11):1164-77.
12. Brain Tumor: Types of treatments. Doctor-Approved Patient Information from ASCO®. 2020. https://www.cancer.net/cancer-types/brain-tumor/types-treatment. (Accessed 7-30-20)
13. Brain Tumor: Introduction. Doctor-Approved Patient Information from ASCO®. 2019. https://www.cancer.net/cancer-types/brain-tumor/introduction. (Accessed 10-31-19)
14. National Comprehensive Cancer Network. NCCN guidelines for patients®. Brain Cancer: Gliomas. Version 1.2016. https://www.nccn.org/patients/guidelines/brain-gliomas/files/assets/common/downloads/files/gliomas.pdf. (Accessed 10-31-19)
15. Healthgrades. Lumbar Puncture (Spinal Tap). 2019. https://www.healthgrades.com/right-care/brain-and-nerves/lumbar-puncture-spinal-tap. (Accessed 9-8-19)
16. Valiente M, Ahluwalia MS, Boire A, et al. The evolving landscape of brain metastases. Trends Cancer. 2018;4(3):176-96.
17. National Cancer Institute. Fact Sheet: How is genetic testing done? 2019. https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet#how-is-genetic-testing-done. (Accessed 10-31-19)
18. Loeffler JS. (2020). Overview of the treatment of brain metastases. In AF Eichler (Ed.), UpToDate. https://www.uptodate.com/contents/overview-of-the-treatment-of-brain-metastases?search=metastatic%20brain%20tumor&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. (Accessed 7-20-20)
19. Owonikoko TK, Arbiser J, Zeinak A, Shu HG, Shim H, Robin AM. Current approaches to the treatment of metastatic brain tumours. Nat Rev Clin Oncol. 2014;11(4):203-22.
20. Hardesty DA, Nakaji P. The current and future treatment of brain metastases. Frontiers in Surgery. 2016 May 25;3:30.
21. Hatiboglu MA, Wildrick DM, Sawaya R. The role of surgical resection in patients with brain metastases. ecancer. 2013;7:308.
22. Brown PD, Gondi V, Pugh S, et al. Hippocampal avoidance during whole-brain radiotherapy plus memantine for patients with grain metastases: Phase III trial NRG Oncology CC001. J Clin Oncol. 2020;38(10):1019-29.
23. Gondi V, Pugh SI, Tome WA, et al. Preservation of memory with conformal avoidance of the hippocampal neural stem-cell compartment during whole-brain radiotherapy for brain metastases (RTOG 0933): A phase II multi-institutional trial. J Clin Oncol. 2014;32(34):3810-16.
24. Brown PD, Jaeckle K, Ballman KV, et al. Effect of radiosurgery alone vs radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: A randomized clinical trial. JAMA. 2016;316(4):401-9.
25. Chao ST, Ahluwalia MS, Barnett GH, et al. (2013) Challenges with the diagnosis and treatment of cerebral radiation necrosis. Int J Rad Oncol. 2013;87(3):449-57.
26. Patel U, Patel A, Cobb C, et al. The management of brain necrosis as a result of SRS treatment for intra-cranial tumors. Transl Cancer Res. 2014;3(4):373-82.
27. Ahluwalia M, Barnette GH, Deng D, et al. Laser ablation after stereotactic radiosurgery: A multicenter prospective study in patients with metastatic brain tumors and radiation necrosis. J Neurosurg. 2019;130:804-11.
28. Lanier CM, LeCompte MC, Glenn C, et al. Laser-interstitial thermal therapy as a novel and effective treatment in radiation necrosis following stereotactic radiosurgery to the brain. Int J Rad Oncol. 2019;105(1S):S140-1.
29. Chitti B, Goyal S, Sherman JH, et al. The role of brachytherapy in the management of brain metastases: A systematic review. J Contemp Brachytherapy. 2020;12(1):67-83.
30. Schwarz SB, Thon N, Nikolajek, et al. Iodine-125 brachytherapy for brain tumours – A review. Rad Oncol. 2012;7:30.

31. Wernicke AG, Smith AW, Taube S, et al. Cesium-131 brachytherapy for recurrent brain metastases: Durable salvage treatment for previously irradiated metastatic disease. J Neurosurg. 2017;126:1212-19.
32. Kim MM, Parmar HA, Schipper M, et al. BRAINSTORM: A multi-institutional phase ½ study of RRx-001 in combination with whole brain radiation therapy for patients with brain metastases. Int J Radiation Oncol Biol Phys. 2020;107(3):478-86.
33. Buch L, Cho S, Salinas R, et al. Near infrared fluorescent dye localizes brain metastasis prior to dural opening and is more sensitive than white light in brain metastasis surgery. Neurooncol Adv. 2019;1(Supple 1):i9.
34. Han RH, Dunn GP, Chheda MG, et al. The impact of systemic precision medicine and immunotherapy treatments on brain metastases. Oncotarget. 2019;10(62):6739-53.
35. Lorenzo RD, Ahluwalia MS. Targeted therapy of brain metastases: Latest evidence and clinical implications. Ther Adv Med Oncol. 2017;9(12):781-96.
36. National Cancer Institute. Targeted Cancer Therapies. 2020. https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet. (Accessed 7-21-20)
37. Drilon A.(2020). TRK fusion-positive cancers and TRK inhibitor therapy. In DMF Savarese (Ed.), UpToDate. https://www.uptodate.com/contents/trk-fusion-positive-cancers-and-trk-inhibitor-therapy. (Accessed 7-20-20)
38. Drilon A. TRK inhibitors in TRK fusion-positive cancers. Annals Oncol. 2019;30 (Supple 8):viii23-30.
39. Brain Tumor: Latest Research. Doctor-Approved Patient Information from ASCO®. 2019. https://www.cancer.net/cancer-types/brain-tumor/latest research. (Accessed 10-31-19)
40. National Comprehensive Cancer Network. Central Nervous System Cancers (Version 1.2020) https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. (Accessed 7-23-20)
41. Niranjan A, Monaco E, Flickinger J, et al. Guidelines for multiple brain metastases radiosurgery. Prog Neurol Surg. 2019;34:100-9.
42. Ammirati M, Nahed BV, Andrews D, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines on treatment options for adults with multiple metastatic brain tumors. Neurosurgery. 2019;84(3):E180-2.
43. Ziu E, Viswanathan VK, Mesfin FB. Cancer, Spinal Metastasis. [Updated 2020 Jan 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441950/. (Accessed 1-26-20)
44. Tse V. 2018. Spinal metastasis. In SA Berman (Ed.), Medscape. https://emedicine.medscape.com/article/1157987-print. (Accessed 1-26-20)
45. Barzilai O, Laufer I, Yamada Y, et al. Integrating evidence-based medicine for treatment of spinal metastases into a decision framework: neurologic, oncologic, mechanicals stability, and systemic disease. J Clin Oncol. 2017;35(21):2419-27.
46. Barzilai O, Fisher CG, Bilsky MH. State of the Art Treatment of Spinal Metastatic Disease. Neurosurgery. 2018;82(6):757-69.
47. Batool A, Kasi A. Leptomeningeal Carcinomatosis. [Updated 2019 Sep 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499862/. (Accessed 1-26-20)
48. Leal T, Chang JE, Mehta M, et al. Leptomeningeal metastasis: Challenges in diagnosis and treatment. Cur Cancer Ther Rev. 2011;7(4):319-27.
49. El Shafie RA, Bohm K, Weber D, et al. Outcome and prognostic factors following palliative craniospinal irradiation for leptomeningeal carcinomatosis. Cancer Management and Research. 2019; 11:789-801.
50. Caring for a person with a brain tumor or metastatic brain cancer. Doctor-Approved Patient Information from ASCO®. 2018. https://wwwcancer.net/coping-with-cancer/caring-loved-one/caring-person-with-brain-tumor-or-metastatic-brain-cancer. (Accessed 10-31-19)
51. Tsao MN. Brain metastases: advances over the decades. Ann Palliat Med. 2015 Oct;4(4):225-32.
52. What is palliative care? From ASCO®. 2019. https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/what-palliative-care. (Accessed 10-31-19)
53. National Cancer Institute. Clinical Trials to Treat Adult Metastatic Brain Tumors. https://www.cancer.gov/about-cancer/treatment/clinical-trials/adult-metastatic-brain-tumors?pn=4. (Accessed 3-22-2020)
54. About clinical trials. Doctor-Approved Patient Information from ASCO®. 2019. https://www.cancer.net/research-and-advocacy/clinical-trials/about-clinical-trials. (Accessed 10-31-19)
55. Brain Tumor: Statistics. Doctor-Approved Patient Information from ASCO®. 2019. https://www.cancer.net/cancer-types/brain-tumor/statistics. (Accessed 10-31-19)

AMERICAN BRAIN TUMOR ASSOCIATION

8550 W. Bryn Mawr Avenue, Suite 550
Chicago IL 60631

For more information:

Website: abta.org

CareLine: 800-886-ABTA (2282)

Email: info@abta.org

American Brain Tumor Association®

Providing and pursuing answers™