



## RADIOTHERAPY TREATMENT TO BRAIN TUMOR

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### Abstract

A group of abnormal brain cells known as a brain tumor. A brain tumor is an abnormal enlargement of the brain's surrounding tissue. To improve treatment options and increase patient survival rates, early brain tumor identification is essential. It is essential to diagnose and treat brain tumors as soon as possible to avoid irreversible brain damage or the patient's death. Brain tumors can either be malignant or benign. Should a brain tumor become large enough to compress nerves, blood vessels, and other tissues, it may affect brain function. Just one-third of brain tumors started out as malignant cells. Surgery, radiation therapy, and targeted therapy are available for the treatment of brain tumors. Sixty-seven percent of cancer patients receive radiotherapy, and only a relatively small percentage of those individuals receive charged particle therapy. One potential brain tumor inhibitor that may be utilized to treat advanced cancers is being discovered. The purpose of this review is to provide comprehensive information about brain tumors, including diagnosis, treatment options, risk factors, and related symptoms. The therapy of brain tumors is discussed from a radiobiological standpoint in this review.

**Keywords:** Brain Tumor, Chemotherapy, Radiobiological, Immunotherapy.

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### Introduction

The use of science for the treatment of diseases has been an idea of interest for scientists like Newton and Galileo since the 16th century. In the 18th century, the famous Scottish surgeon, John Hunter suggested for a surgical remedy for treating cancers, which led to the birth of the modern pathological study of a tumor in the 19th century. (1) There were multiple theories proposed to explain the cause of cancer, which included popular ones such as the humoral theory, the lymph theory, the trauma theory and the infectious disease theory. It was after much research and technological advancements that the idea of viral and chemical carcinogens occurred to the scientist of the 20th century. (3)

#### Primary Brain Tumor:

A primary brain tumor is a tumor that starts in the brain. A primary brain tumor is often described as "low grade" or "high grade." A low-grade tumor generally grows slowly, but it can turn into a high-grade tumor. A high-grade tumor is more likely to grow faster. (7) Healthcare providers categorize primary tumors as glial (composed of glial cells in your brain) or non-glial (developed on or in the structures of your brain, including nerves, blood vessels and glands) and benign (noncancerous) or malignant (cancerous). Many types of brain tumors can also form in your spinal cord. (10)

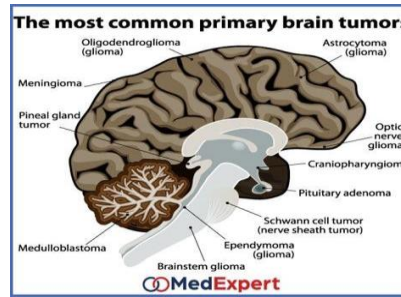


Figure no: 1

1. **Craniopharyngiomas:** These tumors usually arise from a portion of your pituitary gland. They're difficult tumors to remove because of their location near critical structures deep in your brain. Gangliocytomas, Gangliomas and anaplastic gangliogliomas: These are rare tumors that form in neurons (nerve cells).<sup>(12)</sup>
2. **Glomus Jugulare:** These tumors are typically located just under the base of your skull at the top of your jugular vein (neck vein). They're the most common form of glomus tumor.
3. **Meningiomas:** These are the most common type of primary brain tumors. Meningiomas typically develop slowly. They form in the meninges, the layers of tissue that protect your brain and spinal cord. In rare cases, a meningioma can be malignant.<sup>(12)</sup>
4. **Pineocytomas:** These slow-growing tumors form in your pineal gland, which is located deep in your brain and secretes the hormone melatonin.
5. **Pituitary adenomas:** These tumors form in your pituitary gland, which is located at the base of your brain. Your pituitary gland makes and controls hormones in your body. Pituitary adenomas are usually slow growing and they may release excess pituitary hormones.<sup>(15)</sup>
6. **Schwannomas:** These are common benign brain tumors in adults. They develop from the Schwann cells in your peripheral nervous system or cranial nerves. Schwann cells assist the conduction of nerve impulses. Acoustic neuromas are the most common schwannoma. These tumors occur on nerve your vestibular nerve (the that leads from your inner ear to your brain)

#### Secondary brain tumors:

Cancer that begins elsewhere and spreads to the brain Secondary (metastatic) brain tumors are tumors that result from cancer that starts elsewhere in your body and then spreads (metastasizes) to your brain. Secondary brain tumors most often occur in people who have a history of cancer. Rarely, a metastatic brain tumor may be the first sign of cancer that began elsewhere in your body.<sup>(14)</sup> In adults, secondary brain tumors are far more common than are primary brain tumors. Any cancer can spread to the brain, but common types include: Breast cancer, Colon cancer, Kidney cancer, Lung cancer, Melanoma.

#### 2. Pathophysiology:

In the 19th century, Stephen Paget postulated the "seed and soil" hypothesis, which considers that metastatic growth depends on cancer cells (the seed) interactions with and affinity for specific distant organ tissues (the soil).<sup>(19)</sup> Paget's assertion that a nutritional microenvironment is imperative for metastatic cells to grow in distant tissues is supported by conceptual frameworks of contemporary cancer research. A more advanced understanding of the complex and multifactorial mechanisms of metastasis formation consists of three premises: first, the existence of tumor heterogeneity, including morphologically- and phenotypically- distinct profiles of cancer cells with different proliferative, angiogenic, invasive, and metastatic characteristics; second, a metastatic process that is selective for tumor cells that accomplish all the key steps of the metastatic cascade; and third, the metastatic potential of a tumor, which depends on multiple, reciprocal interactions between the primary tumor and the tumor

#### O-6 methylguanine-DNA mutations:

The gene encoding O-6-methylguanine DNA methyltransferase (MGMT) is found on chromosome 10q26. By methylating DNA base pairs, alkylating chemotherapeutic drugs such as temozolomide impair DNA replication. Active MGMT reverses the effect of temozolomide, enabling normal DNA replication to occur within a tumor.<sup>(12)</sup>

#### 2.2. Epidermal growth factor receptor:

Most signalling pathways and physiological responses, including migration, proliferation, survival, and tumor development, are activated by the epidermal growth factor receptor (EGFR). EGF, TGF- $\beta$ , heparin-binding epidermal growth factor-like factor (HB-EGF), amphiregulin (AR), betacellulin (BTC), neuregulin's (NRGs), also known as neuregulin; neu differentiation factors; glial growth factors; acetylcholine receptor inducing activity; and ephregrin

are all members of the EGF superfamily (EPR).<sup>(3)</sup>

### **3. Causes:**

At the molecular level, damage in the genes inside cells is the principal cause of cancer. The reasons for most brain cancers are undiscovered but scientific research has led to the identification of some risk factors that might lead to the development of a brain tumor.

#### **3.1. Inheritance:**

Family history with a few types of brain tumors increases the chances of being affected by a brain tumor. Syndromes responsible for this are tuberous sclerosis, Turcot syndrome, neurofibromatosis (type 1 and 2), li-Fraumeni syndrome, turner syndrome, gorlin syndrome and von hip pellindau, might be associated with hereditary genetic agents.

#### **3.2. Chemical Exposure:**

Certain chemicals used at workplaces may lead to an increased risk of brain cancer, for example, chloroform and ethylene dibromide, which are used at laboratories to conduct experiments. Studies have proven that nitrates and nitrites found in cured meats, cigarette smoke and cosmetics can lead to brain cancer.<sup>(19)</sup>

#### **3.3. Medical Record:**

Examination of viral infection and their association with brain cancer revealed that mononucleosis increases the risk of developing CNS lymphoma whereas, chickenpox is observed to decrease the chances of brain cancer. Hence, the effect on the development of brain

#### **3.4. Age:**

Incidence of BTs overall increases with age. For malignant glioma in particular, the incidence is bimodal, with highest incidence in the youngest and oldest ages. The age distribution also varies by histologic type. Embryonal tumors, a group that includes medulloblastoma and primitive neuroectodermal tumors, occur most frequently in children less than 10 years old. Incidence of pituitary tumors is also bimodal, with peaks in adolescence/young adulthood, and again in older adulthood.<sup>(12)</sup>

#### **3.5. Sex:**

Incidence of BTs varies by sex, with malignant tumors occurring much more frequently in males and non-malignant tumors generally occurring more frequently in females. This sex difference varies significantly by histology, with some histology's showing little or no variation in incidence by sex.<sup>(15)</sup>

#### **3.6. Race/Ethnicity:**

Incidence of different histology's of BTs varies by race/ethnicity. Neuroepithelial tumors, including gliomas, are much more common in individuals of European ancestry (white non- Hispanics) compared with other groups

#### **Allergic diseases:**

The relation of allergic diseases to neoplasia is controversial. In general, retrospective and descriptive studies have tended to show protective effects of asthma, hay-fever, eczema and other allergic diseases as found in the present study WCFS-IBMDNT: Many recent studies have attempted to define the characteristics of brain tumors to diagnose the illnesses. However, with a large dataset, the correlations across brain tumor characteristics

### **4. Brain imaging:**

The main goal of computerized brain tumor diagnosis is to obtain important clinical information regarding the tumor presence, location, and type. The information obtained through clinical imaging can guide and control any future interventions and thus leads to the correct diagnosis and treatment of the tumor.<sup>(17)</sup>

#### **Single-photon emission computed tomography:**

Similar to a gamma camera, SPECT is a nuclear medicine tomographic imaging technique utilizing gamma rays that provide three-dimensional (3D) information. SPECT has a rather poor spatial resolution of 8–10 mm, but is more sensitive and somewhat cheaper, and SPECT is available at every nuclear medicine department. At present the quantization of tissue function

#### **4.1. Types of brain tumor:**

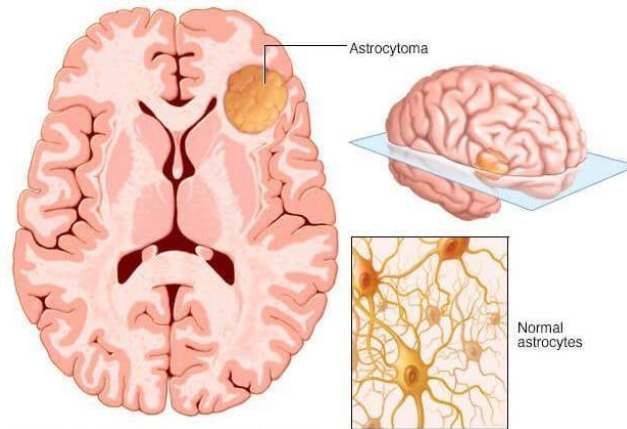
The brain plays an important role in the body by controlling voluntary and involuntary processes. It is highly necessary to maintain a healthy brain to live longer. But some factors like environmental and genetic factors tumors in the brain can be developed. These tumor causes the damage in healthy tissues and increases the pressure in the brain.<sup>(13)</sup> Thus, some tissues may get pushed against the skull.

### **5. According to WHO (World Health Organization) brain tumors are classified as:**

1. Glioblastoma
3. Oligodendroglioma.

#### **1. Astrocytoma:**

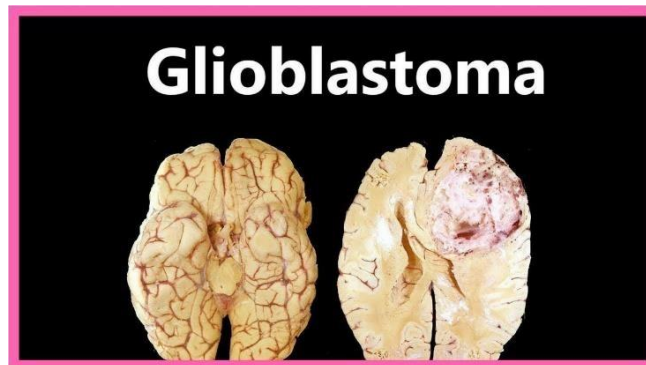
Astrocytoma tumors arise from the supportive glial cells of the brain. About 7% of the primary brain tumor are astrocytoma. A star-shaped tumor that begins in the brain is called astrocytoma. In adults, astrocytoma most often arises in the cerebrum, wherein in children it occurs in the brain stem.<sup>(12)</sup>



**Fig 2 Astrocytoma**

**2. Glioblastomas:**

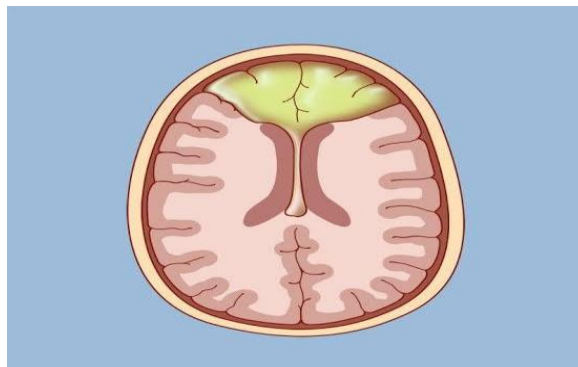
Glioblastomas (GBMs) is the most common and primary aggressive brain tumor. Glioblastoma is shown the Figure 6. Glioblastoma accounts for 45.6% of primary malignant brain tumors. Typical molecular changes in glioblastoma include mutation in gene-regulating receptor tyrosine kinase (RTK) / phosphoinositide 3-kinase (PI3K), p53, and retinoblastoma protein (RB) signalling. Secondary glioblastoma is a kind of glioblastoma that develops in younger people when a previous malignancy, such as grade II astrocytoma or anaplastic astrocytoma, somatically mutates into a glioblastoma.



**Fig 3 Glioblastoma**

**3. Oligodendroglioma:**

Oligodendroglioma is a rare form of brain tumor. The brain is made up of many supporting cells that are called glial cells. Any tumor of these glial cells is called glioma. A tumor that arises from the glial cells (oligodendrocyte cells) is called oligodendroglioma. Oligodendrogliomas vary from other glial tumors in their molecular genetic makeup. On chromosome 1p and chromosome 19q, LOH is seen often in oligodendrogliomas of all grades. (17)



**Fig. 4 Oligodendroglioma.**

## **6. Drug delivery to brain cancer:**

### **6.1 Systemic delivery:**

Currently, most antineoplastic agents for brain cancers are delivered systemically either as intravenous or oral preparations, depending on the bioavailability of the drug. Although some agents have properties that allow access to brain tumors, the limitations outlined previously impair delivery of most chemotherapies. <sup>(17)</sup>

### **6.2. Implanted therapies:**

Gliadel is a polyanhydride biodegradable polymer wafer impregnated with BCNU (carmustine) that is placed in the surgical cavity at the time of tumor debulking and results in improved survival of roughly 2 months in patients with both newly diagnosed and recurrent malignant gliomas. <sup>(8)</sup> It is well tolerated and associated adverse effects, including increased edema, cerebrospinal fluid leaks, and impaired wound healing, are rare. Used in clinical practice. Efficacy studies at the higher dose may show even more robust survival results. <sup>(17)</sup>

### **6.3. Convection enhanced delivery:**

Convection-enhanced delivery (CED) uses locally placed catheters within and around a tumor to directly infuse anticancer agents under hydrostatic pressure. This is an attractive approach for agents that are too large to cross the BBB or too toxic for systemic administration. It is a particularly attractive approach for conjugated, targeted toxin therapies, antibodies, and even whole cells. Infusion into CSF cavities restricted volume of distribution (and potentially increased toxicity) if there are CSF flow abnormalities. As these abnormalities are relatively common in patients with leptomeningeal disease, CSF flow studies should be ordered prior to initiating any CSF drug infusion. <sup>(17)</sup>

### **Exposure to radiation:**

Radiations are the only definite factor for brain cancer, even if it is responsible for a small percentage of the cases. The World Health Organisation (WHO) has recognized ionizing radiation to be a carcinogenic agent and is presently assessing the role of electromagnetic radiations from mobile phones in causing a brain tumor in adults and children. UV rays used at industries and laboratories contribute to the high risk of cancer. Patients who have previously undergone radiotherapy for the brain are more prone to developing a brain tumoring

### **Radiation therapy to brain tumor:**

Patients with primary brain tumors benefit from radiation therapy because it helps them maintain local control or prolong their progression-free life. In the treatment of primary brain tumors, radiation therapy (RT) plays a crucial role, with the majority of patients experiencing local control or prolonged progression-free survival. <sup>(8)</sup>

### **Treatment:**

Patients reported to suffer from the above symptoms of a brain tumor are recommended for the assessment of the following parameters: tumor type, grade, size, location, its complexity with the nervous system and their medical history. These assessments are conducted using various diagnosis techniques like computed axial tomography (CT), magnetic resonance imaging (MRI), electroencephalograph (EEG), perfusion MRI, functional MRI (fMRI), and magnetic resonance spectroscopy (MRS)

### **Discussion:**

The brain is responsible to control all activities of the human body. It is well-known that a disease occurred in the brain may affect human life negatively. In this paper, we proposed a new scheme to classify three types of brain tumors, namely, Meningioma, Glioma, and Pituitary tumors from MRI images. First, pre-processed is applied to images. Recent laboratory advances in primary brain tumors have shown that specific molecular signatures can predict the biological behaviour of tumors. Current brain tumor classification systems based on histology and morphology may soon be supplemented by a system based on molecular markers of tumor differentiation and progression.

### **Conclusion:**

Since x-rays were discovered in 1896 and used for tumor identification, radiation therapy has emerged as a more effective option for treating brain cancers <sup>(17)</sup>. Because x-rays are flexible, they are used in IGRT, SRT, and IMRT. The notion of an expanded Bragg peak and an ideal RBE has prompted research on heavy ions and subatomic particles, hence presenting carbon and proton ions as very accurate and efficient substitutes for x-rays. the use of radiobiology in brain tumor treatment.

### **Author contributions**

All authors are contributed equally.

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None

### **Declaration of Competing Interest**

The authors have no conflicts of interest to declare.

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