BRAIN TUMOR TREATMENT USING IMPLANTED RADIOACTIVE WAFERS GAMMATILE THERAPY

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Introduction

The purpose of this case study is to better understand the effective treatment of brain tumors using advanced methods to improve the quality of life and surgical outcomes for our patients. In the following, we take a closer look at the use of implanted radioactive wafers during the removal of three types of commonly diagnosed brain tumors.

Background

Neoplasms (aka: tumors) occur when cells lose the ability to limit their reproduction and, as a result, grow in an uncontrolled fashion thus developing into a damaging mass that compresses and/or infiltrates surrounding normal tissue. Brain neoplasms are broadly categorized using the following three major criteria:

1. **Location**
    a. **Intramedullary/Intra-axial:** Located within the brain tissue.
    b. **Extramedullary Intradural or Extradural/Extra-axial:** Located inside the skull, but outside the brain tissue.
2. **Malignant vs Benign**
    a. **Malignant:** Prone to uncontrolled growth and diffuse spread.
    b. **Benign:** Prone to slow growth and limited spread.
3. **Cell Type**
    a. **Primary:** Composed of cells that are normally located in the brain or in the structures surrounding the brain (neurons, glia, ependyma, pituitary, pineal/germ, myelin).
    b. **Secondary:** Composed of cells from other body organs that have spread to the brain (aka: organ origin metastases).

For the purposes of this newsletter, we will focus on THREE SPECIFIC TYPES OF BRAIN TUMORS:

1. **Primary malignant intra-axial tumors:**
    a. Tumors from glial cells (gliomas)
2. **Metastatic malignant intra-axial tumors:**
    a. Breast origin
    b. Colon origin
    c. Skin origin
    d. Lung origin
    e. Other organ origin
3. **Extramedullary tumors:**
    a. Tumors from the meningeal covering of the brain (meningiomas)

Management of Brain Tumors

Once a brain tumor is diagnosed, using imaging modalities such as CT and MRI scans, a decision needs to be made regarding how to best treat the lesion(s). Options include:

1. **No treatment (AKA: conservative therapy):**
    a. Considered an option for benign tumors that are asymptomatic and are growing slowly.
    b. Considered an option for malignant tumors in individuals who will not benefit from surgery because of advanced age, widespread disease, extremely poor baseline neurologic function, and/or medical conditions that make treatment too dangerous.
2. **Medical treatment:**
    a. Chemotherapy
    b. Genetic therapy
    c. Non-chemo pharmacologic therapy
    d. Vaccine /Immuno therapies
3. **External beam radiation therapy:**
    a. Multi-fractionated therapy (radiation delivered over several individual sessions)
    b. Focused radiosurgery (radiation delivered in a single session)
4. **Surgery:**
    a. Minimally invasive needle biopsy of the lesion for diagnostic purposes followed by medical treatment (aka: image guided stereotactic biopsy)
    b. Surgical resection

The above treatment options can be used alone or in combination with the goal of improving or prolonging an individual's survival while at the same time maintaining a desired high quality of life.

For the purposes of this newsletter, we will focus on SURGICAL RESECTION (#4b).

Surgical Resection of Brain Tumors

Surgical resection of a brain tumor involves opening the skull, locating the lesion, and removing the neoplasm while disturbing the normal surrounding brain tissue as little as possible.

Risks: The risks of surgical resection include, but are not limited to, neurologic injury with sustained functional deficits, death, and infection. These risks are influenced by factors that may include: tumor location, tumor type, patient comorbidities, and patient age.

Although surgery's goal is the complete removal of a tumor, this may not be possible.

Even when complete resection is achieved (aka: gross total resection of radiographically visible neoplasm), tumor recurrence can occur when small, microscopic tumor cell remnants remain in surrounding brain or adjacent structures. These cells can continue to multiply with subsequent neoplasm regrowth. Recurrence may lead to brain injury and death.

In an effort to reduce the risk of tumor recurrence after gross total resection and to inhibit the growth of residual tumor that remains after a non-total resection, patients often undergo post-surgical adjuvant therapies which are aimed at enhancing the effects and benefits of the surgical resection.

Adjuvants include chemotherapy, non-chemo drug therapies, immune therapies and/or external beam radiation therapy. Such treatments have been shown to improve overall functional outcomes for a variety of tumor types.

Delivery of adjuvant therapies, however, is often delayed for several weeks after surgery so that the surgical incision can heal. If therapy is not delayed, then the incision may fail to heal leading to infection and its associated complications which can include neurologic injury and death.

The requisite delay in beginning adjuvant therapy means neoplastic cells can multiply during the delay period and the tumor can begin to spread and re-grow.

Use of GammaTile Therapy

Definition: GammaTile is an FDA approved device which incorporates Cesiums-131 radiation emitting seeds in an implantable/resorbable collagen-based carrier tile for immediate surgically targeted radiation therapy to achieve highly conformable radiation at the time of surgery. (Figure 1).

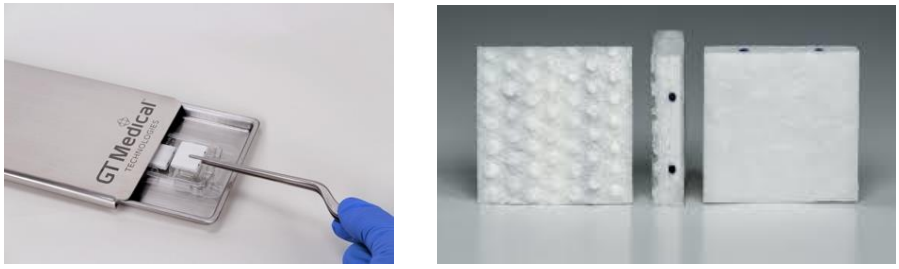

Figure 1: *GammaTiles prior to implantation*

Purpose: Like other radiation therapies, Gamma Tile Therapy works by disrupting the tumor cell replication process.

Radiation damage to the tumor cell DNA inhibits cell replication and tumor growth.

The collagen tile that contains the Cs-131 seeds keeps the radiation source in place while the radiation is being released. With a half-life of 9.7 days, the implants become biologically inert after about 10 months.

Because radiation released by the Gamma Tiles only penetrates a few millimeters into surrounding brain tissue, there is no unintended risk to the public and patients are free to participate in all normal activities (Figure 2).

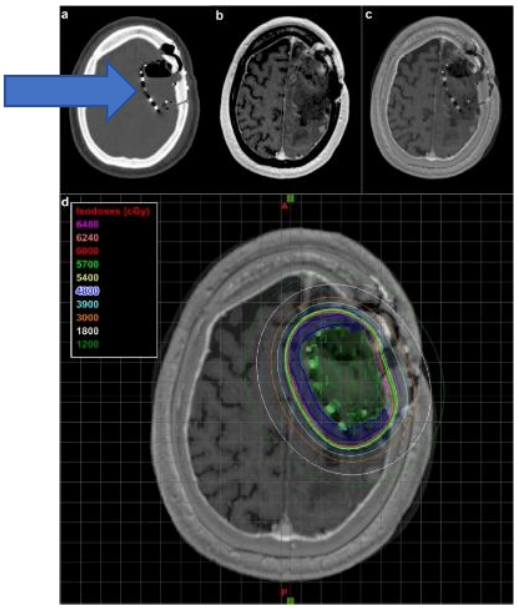

Figure 2: *This figure (left) shows an arrow pointing to the Gamma Tiles lining the wall of the brain that was next to the resected tumor. The white dots are in the wall of the tiles that line the cavity. The bottom image shows the radiation field generated by the tiles' radioactive seeds. These fields are highest in the tissue that was closest to the tumor. The radiation dose drops off very quickly the further the tissue is away from the tiles thus minimizing injury to normal brain tissue. No radioactivity is detected outside the skull.*

The placement of Gamma Tiles at the time of surgical resection means patients begin to receive radiation treatment immediately (at the time of initial tumor resection).

Immediate delivery of radiation means residual tumor cells can be destroyed before they have time to multiply and spread. **Gamma Tile implantation at surgery does not always preclude the use of traditional radiation and chemotherapy after the surgical site has healed. As a result, patients and physicians do not always need to choose between one therapeutic intervention or another.**

Results

Results following the use of Gamma Tiles are promising (1-7). As delineated below, this new treatment appears to improve functional outcomes following the surgical resection of at least three types of commonly diagnosed brain tumors:

1. **Meningioma**
   - After Meningioma resection, recurrence free rate for tumor at 2 years following Gamma Tile placement is **89%** vs **52%** with traditional treatment.
2. **Brain Metastasis**
   - After Brain Metastasis resection, recurrence free rate for tumor at 1 year following Gamma Tile placement is **83%** vs **33%** with traditional treatment.
3. **Glioblastoma Multiforme/ Other Malignant Glial Neoplasms**
   - After Malignant Glial tumor resection, median survival is **16.7** months following Gamma Tile Tx + Avastin vs **9.7** months with Avastin alone.

- Avastin is an immunotherapeutic drug that blocks a specific protein called vascular endothelial growth factor (VEGF). This blockade reduces a tumor's blood supply which in turn promotes tumor cell death.

Conclusion

Brain tumor treatment involves a complex set of decisions regarding which therapies can best prolong a patient's life span while at the same time maximizing their neurologic function and quality of life.

The use of surgery, radiation, chemotherapy, vaccines, and other medications have significantly helped improve outcomes over the last several decades.

Upon a closer look, the use of ultra-early radiation therapy using implantable wafers at the time of surgical resection may provide another means of controlling this unfortunate disease.

If you would like to learn more about Gamma Tile insertion and other treatments for brain tumors, please contact Dr. Michael Horowitz at HCA Florida First Coast Neurosurgery by calling 904-276-7336.

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