EPIDEMIOLOGY

Approximately 200,000 new cases of brain metastases are diagnosed each year in the United States. In contrast, the annual incidence of primary intracranial tumors is 73,623 with approximately 60% benign and 40% malignant. The incidence of meningioma is 27,000 and 6,000 acoustic neuromas compared to 26,000 primary malignant brain tumors. Approximately 75% of primary brain cancers are malignant gliomas.

There is no clear environmental link to brain tumors including use of cellular telephones, extremely low frequency magnetic fields or chemical exposure. Interestingly, patients with allergic conditions including asthma, hay fever, eczema and food allergies have a 40% decreased risk of glioma. Meningiomas are more common in women and there is an association with breast cancer, implicating a role of estrogen.

Prior cranial irradiation is associated with an increased risk of glioma and meningioma. There are rare familial tumor syndromes including neurofibromatosis types 1 and 2, Li Fraumeni syndrome, tuberosis sclerosis, Turcot syndrome and Cowden syndrome that are associated with genetic predisposition to glioma. Neurofibromatosis type 2 is associated with multiple meningiomas and bilateral acoustic neuromas.

DIAGNOSIS AND RADIOLOGY

Brain tumors frequently present with headache, seizure, hemiparesis, altered mental status and aphasia. Advanced cases may have signs of increased intracranial pressure including diffuse headache, ataxia, nausea, vomiting, and cranial nerve VI palsy. Rapidly progressive hemiparesis and altered mental status are more commonly associated with high grade glioma whereas seizures are more frequently seen with low grade glioma. Meningiomas are often asymptomatic and may be diagnosed on CT or MRI performed for other indications or through gradual development of neurological symptoms.

The preferred diagnostic test for a suspected brain tumor is MRI including T1 weighted spin-echo sequence, T2 fluid-attenuated invasion recovery and gadolinium enhancement. Advanced multimodal MRI available at Good Samaritan includes diffusion-weighted imaging to assess tumor cell density, dynamic contrast-enhanced and perfusion MRI to assess blood vessel growth and MR spectroscopy to assess tumor metabolism or necrosis. CT of the chest, abdomen and pelvis or whole body PET is often indicated to rule out primary tumor outside of the brain.
FOCUS ON NEUROSURGERY TECHNOLOGY CAPABILITIES
at Good Samaritan Hospital Medical Center Brain Tumor Center

THE BRAIN TUMOR CENTER AT GOOD SAMARITAN HOSPITAL MEDICAL CENTER is a highly specialized center accepting referrals from throughout the region. As a high volume center, our neurosurgeons are highly experienced and technically skilled resulting in excellent outcomes. Highlighted below are resources offered by the Brain Tumor Center, not typically available at community hospitals.

IMAGE-GUIDED MICROSURGERY USING THE BRAINLAB NEURONAVIGATION SYSTEM AND OPERATING MICROSCOPE
Fellowship trained neuroradiologists expertly interpret BrainLAB protocol MRI with thin axial slices that can more accurately delineate the precise size, shape and extent of tumor. The MRI is uploaded to the BrainLAB cranial navigation software that is available to neurosurgeons in the operating room. BrainLAB neuronavigation and use of the Operating Microscope allow our highly specialized neurosurgeons to extract tumors using minimally invasive brain surgery with optimal sparing of blood vessels, nerve fibers and functional brain circuits.

SURGICAL INTENSIVE CARE UNIT
Neurosurgical patients receive postoperative care in the state-of-the-art Surgical Intensive Care Unit that opened in December 2012. Neurosurgeons are supported by a dedicated team of neurosurgical nurse practitioners. There are future plans for a dedicated Neurosurgical Intensive Care Unit supported by neurointensivists to further enhance specialized care for brain tumor patients.

MULTIDISCIPLINARY TEAM
To achieve the best possible outcomes, patients in the Comprehensive Brain Tumor Center receive care from a multidisciplinary team of neurosurgeons, oncologists, neurologists, radiologists and pathologists who have extensive scientific knowledge on the diagnosis and treatment of brain tumors.

VARIAN TRUEBEAM™ USING THE PERFECT PITCH SIX DEGREE OF FREEDOM ROBOTIC COUCH
Good Samaritan Hospital Medical Center radiation oncologists routinely utilize MRI-based treatment planning to accurately target the tumor while avoiding normal brain. High-precision brain intensity-modulated radiation therapy is administered on the Varian TrueBeam™ linear accelerator with a robotic six degree of freedom couch that can nearly perfectly align with the patient’s position for submillimeter accuracy.
MANAGEMENT OF BENIGN BRAIN TUMORS

**Meningiomas**

Meningiomas arise from the membranes covering the brain. The most common locations are base of skull, parasellar regions and over the cerebral convexities. Meningiomas are accurately diagnosed by MRI based on location adjacent to bone, the presence of a dural tail and diffuse contrast enhancement. Most patients are over 60 years of age.

Approximately 93% of meningiomas are benign while 5% are atypical and 2% are malignant. Small, asymptomatic meningiomas can be safely observed with serial MRIs every 6 to 12 months. Treatment is indicated for growth, symptoms or surrounding edema implying impending neurological deficit. Microsurgery is an effective option particularly when it is possible to safely remove areas of dural attachment and abnormal bone. Approximately 80% remain free of recurrence at 10 years when gross total resection is achieved compared to 20% after partial resection. If only partial resection of a benign meningioma is feasible, these patients are often closely observed with further treatment reserved for recurrence.

Radiation therapy is effective treatment for inoperable meningiomas and is often used for surgically unfavorable locations including cavernous sinus and skull base. Radiation therapy achieves 90 to 95% local control of meningiomas by arresting their growth and preventing further symptoms. While large tumors > 3 cm require 5 1/2 weeks of radiation, smaller tumors are often candidates for stereotactic radiotherapy in three to five treatments.

Combined surgery and radiation achieves 90 to 95% local control for atypical meningiomas.

**Acoustic Neuromas**

Acoustic neuromas are benign tumors involve the eighth cranial nerve, often extending into the cerebellopontine angle. Both tumor progression and treatment can impact hearing.

While small asymptomatic tumors can be observed, most eventually require treatment. Radiation therapy has emerged as the preferred treatment for many acoustic neuromas due to 90 to 95% rates of local control with a very low rate of cranial nerve injury. Approximately 75 to 90% are able to preserve useful hearing after treatment. Microsurgery is an alternative for select patients, particularly those with large symptomatic tumors.

MULTIDISCIPLINARY TREATMENT OF MALIGNANT BRAIN TUMORS

**Glioblastoma multiforme**

Glioblastoma multiforme are often diagnosed with irregular contrast enhancement with surrounding edema and mass effect occasionally resulting in brain herniation. Tumor cells can extend microscopically several centimeters away from radiologically apparent disease. The average age of diagnosis is over 60.

Despite advances in molecular profiling, glioblastoma multiforme continues to have a poor prognosis. MGMT methylation is associated with a better prognosis and response to treatment.

The primary treatment is maximal safe tumor resection with BRAINLAB navigation and use of an operating microscope. Postoperative radiation therapy to 60 Gy improves survival compared to observation. Recent research in radiation oncology has focused on reducing radiation volume and length of treatment with the goal of improving quality of life.

Good Samaritan Hospital Medical Center oncologists prescribe temozolomide during and after radiation therapy to improve survival for glioblastoma. Temozolomide is a generally well tolerated oral chemotherapy drug. With surgery followed by radiation therapy with temozolomide, approximately 10% of patients now survive 5 years. A recent randomized trial demonstrated further survival advantage when adding alternating electric field therapy to standard chemoradiation. Tumor treating electrical fields pulse through the skin and interrupt rapidly-dividing cancer cell's ability to divide.

Recurrent glioblastoma may be treated with further surgery, Avastin-based chemotherapy and/or reirradiation. The goal is extending survival while maintaining quality of life. Research into novel drug therapies including immunotherapy is ongoing.

**Low grade glioma and anaplastic gliomas**

Patients with low grade gliomas tend to have diffuse, nonenhancing masses that are best seen on T2 weighted MRI and FLAIR with hypointensity seen on T1 weighted images. Patients with low grade gliomas are typically diagnosed between ages 30 to 45 and have extensive disease. Although gross total resection is generally not feasible, maximal safe resection often guided by MRI tractography and functional MRI is recommended. Anaplastic gliomas tend to involve older patients and have contrast enhancing lesions on MRI.
Molecular testing is useful to inform prognosis and guide treatment for grade 2 and 3 gliomas. Patients with IDH mutation and 1p19q deletion tend to have the most favorable prognosis. Patients with no mutation have an intermediate prognosis. Recently, grade 2 to 3 glioma patients with only a TERT promoter mutation have been identified to have a prognosis similar to glioblastoma.

Following surgery, most patients require adjuvant radiation. Low grade gliomas are treated to 50.4 to 54 Gy while grade 3 gliomas require 59.4 Gy. A patient with low grade glioma under age 40 with a small tumor that is amenable to complete resection with no pre-operative neurological deficits can be safely followed by MRI. Chemotherapy is often recommended for grade 3 glioma and high-risk low grade gliomas, particularly with 1p19q deletion and oligodendroglioma subtype.

### Brain Metastases

Brain metastases are a devastating diagnosis most commonly seen with primary lung cancer. A subset of patients with good performance status, limited disease extent and good nutritional status can have long-term survival with effective treatment.

Surgery is particularly recommended for patients with one to two metastases, surgically accessible location, large and symptomatic tumors and when the diagnosis is unclear. For patients with one to five brain metastases measuring less than four centimeters, fractionated stereotactic radiotherapy is frequently recommended. When surgery or stereotactic radiation is possible, brain tumor control is achieved in 80 to 90% of patients.

For patients with more widespread disease, whole brain radiation is often recommended to relieve neurological symptoms. In addition to treating the brain, patients require systemic therapy administered by medical oncologists to control disease in the rest of the body. In addition to chemotherapy, Good Samaritan Hospital Medical Center medical oncologists are increasingly using immune checkpoint inhibitors to treat cancer. Finally, patients who are particularly debilitated may be better candidates for supportive care alone under the supervision of the Palliative Care service.

### RESEARCH

While patients with benign brain tumors have an excellent prognosis, patients with brain cancer benefit from research to improve outcomes. Good Samaritan Hospital Medical Center neurosurgeons, radiation and medical oncologists have a rich tradition of contributing to research for brain metastases.

In 2015, researchers at Good Samaritan developed a new technique for whole brain radiation that selectively targets brain tumors seen on MRI while reducing dose to the normal appearing brain, hippocampus and scalp. This technique has been shown to reduce hair loss from whole brain radiation while holding promise for reducing long-term neurocognitive toxicity. Results were recently published in *Technology in Cancer Research and Treatment*.

Researchers at Good Samaritan demonstrated that brain
metastases are not an independent prognostic factor relative to metastases involving other organs. In this highly predictive model, performance status, primary tumor site, extent of disease and serum albumin were the strongest predictors of survival. This model accurately identified both favorable and unfavorable subgroups of patients with metastatic disease and was recent published in PLoS ONE.

As a member of NRG Oncology, the Comprehensive Brain Tumor Center offers patients with brain and spine tumors access to federally funded clinical trials.

**FIGURE 1.** a) Stage IIIB lung cancer patient in remission presenting with a solitary 1.3 cm enhancing mass in the left frontal lobe with vasogenic edema (arrowhead). b) Image-guided microsurgery with gross total resection was accomplished, followed by stereotactic radiotherapy to 27 Gy in three fractions to the tumor bed. c) The patient remains clinically and radiographically free of recurrent cancer one year after surgery with no toxicity.

**FIGURE 2.**

a) Newly diagnosed large cell neuroendocrine lung cancer presenting with six brain metastases treated with neuronavigation with cortical and subcortical mapping and gross total resection of symptomatic 3.5 cm right frontal lobe mass. Adjuvant radiation to 30 Gy was delivered to the surgical bed and the five remaining brain metastases (red) while limiting the normal appearing brain to 25 Gy (yellow). The hippocampal avoidance region was limited to less than 10 to 15 Gy (grey) while the mean scalp dose was kept under 16 Gy (green).

b) Repeat MRI eight months after treatment confirmed complete remission of brain tumors with no memory problems.
FIGURE 3.
a) Elderly patient presented with seizure and T1 MRI with gadolinium demonstrated a 3.3 cm enhancing right frontal lobe glioblastoma multiforme (arrowhead).
b) There was surrounding edema on FLAIR MRI (star).
c) Image-guided microsurgery was performed to accomplish gross total resection. The patient received a three week course of radiation to 40 Gy with concurrent and adjuvant temozolomide (red).
d) Follow-up MRI demonstrated no recurrent disease at 6 months with excellent quality of life.
FIGURE 4.

a) 2.2 cm mass in the left cerebellopontine angle with mass effect on the pons and dural enhancement (arrowhead).
b) Fractionated stereotactic radiation to 25 Gy in five fractions was performed (red). The patient is clinically free of symptoms and follow-up MRI demonstrated no evidence of progression (not shown).

FIGURE 5.

a) 5 mm right acoustic neuroma causing hearing loss and dizziness despite Antivert.
b) Fractionated stereotactic radiation to 18 Gy in three fractions was performed (red).
c) Follow-up MRI at 17 months demonstrated no progression and the patient has objective improvement in hearing.
MEMBERS OF THE COMPREHENSIVE BRAIN TUMOR CENTER AT GOOD SAM

<table>
<thead>
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