

An up-to-date and essential guide to

Tools for getting organized

Understanding brain tumors

Molecular markers

Your medical team

Questions to ask

Standard-of-care treatment

Clinical trials

Alternative and complementary treatments

Common medicines for treating symptoms

“Real world” and online support groups

Insurance management

Al Musella, DPM

Eleventh
edition

Brain Tumor Guide for the Newly Diagnosed



MUSELLA
FOUNDATION
FOR BRAIN TUMOR
RESEARCH & INFORMATION

Brain Tumor Guide for the Newly Diagnosed

Eleventh edition



Brain Tumor Guide for the Newly Diagnosed

An up-to-date and essential guide to

Tools for getting organized • Understanding brain tumors

Molecular markers • Your medical team

Questions to ask • Standard-of-care treatment

Clinical trials • Alternative and complementary treatments

Common medicines for treating symptoms

“Real world” and online support groups

Insurance management

Al Musella, DPM

Eleventh edition

The Musella Foundation
for Brain Tumor Research & Information, Inc.

This book is sponsored in part by generous grants
from Genentech, Novocure, and AbbVie.



MUSELLA
FOUNDATION
FOR BRAIN TUMOR
RESEARCH & INFORMATION

About the Musella Foundation

The Musella Foundation for Brain Tumor Research & Information, Inc., is a 501(c)3 nonprofit public charity dedicated to speeding up the search for the cure of brain tumors and to helping families deal with a brain tumor diagnosis. We create and distribute educational materials, provide help matching patients to clinical trials, give emotional and financial support to brain tumor patients, support awareness and advocacy for brain tumor issues, and give grants for brain tumor research. We maintain the brain tumor information and treatment virtualtrials.com website; the co-pay assistance braintumorcopays.org website; and the fundraising walktoendbraintumors.org website.

Dr. Henry Friedman and Dr. Linda Liao reviewed and approved the contents of this guide.



Henry S. Friedman, MD, is deputy director of the Preston Robert Tisch Brain Tumor Center at the Duke University Medical Center in Durham, North Carolina. An internationally recognized neuro-oncologist, Dr. Friedman has a long-standing career in the treatment of children and adults with brain and spinal cord tumors. He has written hundreds of research articles, and his work has been showcased on several segments of the CBS program *60 Minutes*. Dr. Friedman strongly believes that there is hope for patients who are being treated for brain cancer.



Linda Liao, MD, PhD, MBA, is the chair of the Department of Neurosurgery at UCLA in Los Angeles, California and director of the UCLA Specialized Program of Research Excellence (SPORE) in Brain Cancer. She is a neurosurgeon with a clinical expertise in intra-operative functional brain mapping for resection of brain tumors. Dr. Liao's research is focused on clinical neuro-immunology, immunotherapy, and brain cancer vaccines. Her work has been published in major journals and textbooks and has been highlighted on several television shows. She is an elected member of the National Academy of Medicine.

Copyright © 2019 by the Musella Foundation for Brain Tumor Research & Information, Inc.

The Musella Foundation
1100 Peninsula Boulevard, Hewlett, NY 11557
888-295-4740 www.virtualtrials.com

Printed April 2019

All rights reserved. No part of the material protected by this copyright may be reproduced or used in any form without written permission of the copyright owner.

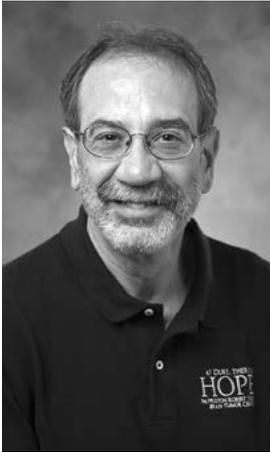
ISBN 978-0-9899740-0-4

Table of contents

INTRODUCTION by Henry S. Friedman, MD	viii
SOME NOTES ABOUT THIS EDITION	x
CHAPTER 1: What you need to know right now	1
Starting now	2
This guide and the Musella need-to-know checklist	4
The Musella Foundation need-to-know checklist	6
Survivor story #1	9
CHAPTER 2: From day one, a place for everything	11
Location, location, location	13
A personal diary	13
Major parts of the brain and associated functions	14
Legal documents	15
Power-of-attorney legal documents	15
Phone numbers	16
Second “expert” opinions	16
Survivor story #2	19
CHAPTER 3: Understanding brain tumors	21
What does histologic grade mean?	23
Types of gliomas	23
Molecular markers that define tumor entities	25
Additional molecular markers that are routinely assessed	26
How long has the tumor been there?	27
Can brain tumors be removed surgically?	28
What are the survival statistics for patients with brain tumors?	29
Survivor story #3	32
CHAPTER 4: How brain tumors are diagnosed	33
Imaging of the brain before surgery	34
All about brain scans	34
Screening for systemic malignancy	36
Obtaining the tissue sample	36
The medical team	37
What questions should I ask my medical team?	38
Survivor story #4	41
CHAPTER 5: The standard-of-care treatment of high-grade malignant glioma	45
Surgery	46
Treatment after surgery: NCCN recommendations	49
Radiation therapy	51
Chemotherapy with temozolomide	52
Alternating electric-field therapy	53
Long-term side effects	55
Survivor story #5: Ben Williams	59

CHAPTER 6: The importance of clinical trials	61
Understanding clinical trials	61
Why should you consider participating in a clinical trial?	62
When should you consider a clinical trial?	63
How do you assess a clinical trial?	64
How do you find clinical trials?	64
Treatments and the Food and Drug Administration	65
Exciting therapies under development	67
The Brain Tumor Virtual Trial	69
Survivor story #6	71
CHAPTER 7: Alternative and complementary treatments	73
The mainstream path of treatment development	73
How alternative treatments are developed	74
Survivor story #7	79
CHAPTER 8: Symptom treatment and sex and fertility issues	81
Medications for pain relief	83
Medications for swelling	84
Medications for reducing seizures	85
Medications for reducing nausea	86
Medications for improving mood	87
Medications for reducing the formation of blood clots	88
Effects of treatment and medication on sex and fertility	89
Birth control	90
Sex, surgery, and brain tumor treatment	91
Fertility	91
Survivor story #8	94
CHAPTER 9: Caregiving and support groups	95
Mind, body, soul: faith in healing and emotional wellness	95
Impairments and strategies for coping	98
Support groups	101
Survivor story #9	105
CHAPTER 10: Insurance management and financial assistance	107
The costs of cancer care	108
Understanding your insurance	109
Medicare coverage	112
Financial assistance	113
Survivor story #10	116
AFTERWORD by AI Musella, DPM	118
RECENT GRANTS MADE BY THE MUSELLA FOUNDATION	120
APPENDIX: The virtualtrials.com website of the Musella Foundation	123
ACKNOWLEDGMENTS	123
SITE MAP OF VIRTUALTRIALS.COM	124
DISCLOSURE	126

Introduction



Henry S. Friedman, MD

If you have this book in your hands, it is possible that you or someone close to you have just received one of the biggest shocks of your life: the diagnosis of a brain tumor.

And as if that shock were not enough, let me add another: You now have to make immediate and important decisions about your brain tumor treatment.

The medical team who made the diagnosis will provide advice and guidance.

But because so many options exist — what doctors to choose, where to be treated, what treatments are available, what clinical trials can be entered — you need to become as informed as possible as soon as possible in order to make the best and most rational decisions.

The goal of the *Brain Tumor Guide for the Newly Diagnosed* is to provide you, your family, and your friends with a basic primer of the “brain tumor” terrain. This book provides tools for getting organized and delivers information about brain tumors, your medical team, brain tumor treatment, clinical trials, and sources of support. This book can be a vital first resource as you begin the fight against your brain tumor, by providing context for the world of brain tumor treatment.

A special feature of this book is that it is written with explicit reference to the virtualtrials.com website run and managed by the Musella Foundation for Brain Tumor Research and Information. The virtualtrials.com website

was begun in the 1990s to list clinical trials and host online support groups for brain tumor patients. Since then, the website has grown steadily. There were over 50,000 visitors in the past year, from 217 different countries. For many people, the website has become an essential portal to brain tumor information and a place of shared experience. The website lists brain tumor centers, hosts and manages online support groups, keeps an up-to-date catalog of brain tumor clinical trials, and describes current and experimental brain tumor therapies. The website also provides links to, and actually gives, financial assistance.

A final word. Although it might feel otherwise right now, you are not alone. However difficult your next months or years will be as you fight your brain tumor, there are others who have lived through the experience and have a lot to share with you. Please reach out. There is a community that can support you — that wants to support you — beginning with the wonderfully resourceful Musella Foundation.

We wish you peace and health.

Henry S. Friedman, MD
Preston Robert Tisch Brain Tumor Center
Duke University Medical Center
Durham, North Carolina

Some notes about this edition

Internet links

This eleventh edition of the *Brain Tumor Guide for the Newly Diagnosed* contains many up-to-date Internet links to different sections of the virtualtrials.com website of the Musella Foundation and to other websites.

Due care has been taken to ensure that the Internet links are accurate. But as we know, such links are sometimes changed by the organizations that originally posted them. At the virtualtrials.com website of the Musella Foundation, a PDF version of this book is available, which is both searchable and has activated Internet links. There is also a separate webpage on which all the website links in this book are routinely kept up to date. To access that page to see a complete listing of the website links in this book, go to: www.virtualtrials.com/booklinks.cfm.

Glossary words

The page-bottom glossary definitions of some words come from the National Cancer Institute's online Dictionary of Cancer Terms, a resource with 7500 entries related to cancer and medicine. The National Cancer Institute is part of the National Institutes of Health, which is one of 11 agencies that compose the Department of Health and Human Services in the United States.

Access to the Dictionary of Cancer Terms is available at the National Cancer Institute website: www.cancer.gov/dictionary.

Survivor stories

The survivor stories in this book are real but have been edited for this book format in order to highlight general themes and the specific interests of book chapters in which they appear. You can find the full stories for these survivors — as well as stories for other survivors — at the virtualtrials.com website of the Musella Foundation: www.virtualtrials.com/survive.cfm.

The Musella Foundation is deeply appreciative of all the people who have shared their stories at our website and in this book. Please share your story, too.



What you need to know right now

Whether or not it was a loss of physical balance that led you to be diagnosed with a brain tumor (a loss of balance can be a symptom), surely a loss of emotional balance quickly followed.

Every day, more than a hundred adults will be diagnosed with a primary brain tumor and many more will be diagnosed with a cancer that has spread to the brain from someplace else in the body, such as the lung or breast. Each year, thousands of parents will hear those two devastating words — brain tumor — about one of their children.

There is no known cause of most brain tumors starting in the brain. There are indications that genetic factors or exposure to toxic chemicals or ionizing radiation may contribute to the formation of brain tumors. However, it is important to remember that you and your loved one did not do anything to cause the brain tumor and that each person and each brain is different.

There are over a hundred kinds of primary brain tumors, some very rare. However, not all types of brain tumors, or even all types of malignant brain tumors, are invariably fatal. With surgery, radiation therapy, and **chemotherapy**, some types of tumors respond very well to treatment and may even be cured. While many of the more common brain tumors, such as **gliomas**, are not typically curable, there are more long-term survivors with these brain tumors now than ever before, as new treatments have been introduced.

Chemotherapy (KEE-moh-THAYR-uh-pee): *Treatment with drugs that kill cancer cells.*

Glioma (glee-OH-muh): *A cancer of the brain that begins in glial cells (cells that surround and support nerve cells).*

.....
: To read survivor stories of people with brain tumors,
: go to: www.virtualtrials.com/survive.cfm.
:.....

You will have a lot of important decisions to make with this medical condition. You can make them yourself, or you can select a loved one or a team of loved ones to advocate for your care and treatment and to help you make important decisions. Not only will you have to make choices between treatment options presented to you, but you and your advocates may have to actively seek out options that your immediate medical team might not have access to.

Starting now

We are here to help you sort through various treatment options and to be a resource for you so that you can further understand your disease.

You must learn to question what you are told initially and, as treatment plans are put into place, to ask what qualifying factors your diagnosis and treatment plan are based upon.

You must also seek out the foremost expert advice.

Typically, your physician will have a treatment plan to discuss with you following your initial diagnosis. This plan may include a referral to a **neurosurgeon** or a **neuro-oncologist** for a consultation regarding treatment. Treatment usually consists of a number of different but reinforcing types of interventions: brain surgery to resect (that is, cut out) the tumor and obtain a tissue sample; radiation therapy; chemotherapy; alternating electric field therapy with a device called the Optune; different drugs for managing symptoms caused not only by the tumor but also by the tumor's treatment; and even enrollment in a clinical trial. This large number of different possible treatments means that you should select a group of doctors — usually associated with a single medical center experienced in treating brain tumors — that will be able to coordinate and administer the most up-to-date treatments with precision and care.

Neurosurgeon (NOOR-oh-SER-jun): *A doctor who has special training in surgery of the brain, spine, and other parts of the nervous system.*

Neuro-oncologist (NOOR-oh-on-KAH-loh-jist): *A doctor who specializes in diagnosing and treating brain tumors and other tumors of the nervous system.*

.....
: If you ever have any questions or comments, or if you have just been told :
: that you need brain surgery, please call us at the Musella Foundation at :
: 888-295-4740 at any time between 10:00 AM and 6:00 PM ET Monday :
: through Friday, and between 10:00 AM and 1:00 PM ET Saturday and :
: Sunday. You can also submit questions by means of our website. Go to: :
: www.virtualtrials.com. :
.....

In some circumstances, emergency surgery at a local hospital might be the only immediate option because of symptoms related to brain swelling caused by the tumor or because of some acute risk of brain injury. Typically, however, the good news is that there is usually sufficient time to locate the doctors who are most experienced in the treatment of brain tumors and to gather information that can assist in your decision-making process.

Most patients learn that they might have an abnormal tissue growth in their brain when they are initially evaluated by imaging at a local hospital for symptoms like headaches or seizures or speech or memory difficulties, all of which might be caused by tumors but have many other possible causes. If an abnormal brain growth is suspected, further testing by **magnetic resonance imaging (MRI)** is usually undertaken in order to get a better idea of the size, location, and impact of the brain growth and to check whether there is any cancer in other parts of the body.

Brain tumors are not diagnosed by imaging. Rather, they are diagnosed by examination of a tissue sample by a **neuropathologist**, a person trained in identifying types of cancer, if there is cancer at all, and testing tissue for cancer markers that might help choices in therapy. That tissue sample is acquired by surgery when the brain tumor is removed or — if surgery is not possible — by biopsy. A biopsy is the removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue.

Magnetic resonance imaging (mag-NEH-tik REH-zuh-nunts IH-muh-jing):

A procedure in which radiowaves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. These pictures can show the difference between normal and diseased tissue.

Neuropathologist (NOOR-oh-puh-THAH-loh-jist):

A pathologist who specializes in diseases of the nervous system. A pathologist identifies disease by studying cells and tissues under a microscope.

Brain Tumor Guide for the Newly Diagnosed

For the most accurate diagnosis and for the best treatment, the most important factor will be the experience of your medical team — that of the radiologist to identify abnormal brain growth and refer you for additional diagnostic work-up, of the neurosurgeon to remove the brain tumor and obtain a tissue sample, of the neuropathologist to examine the tissue and test for the important cancer markers that can help guide your treatment, and then, finally, of the neuro-oncologist and his or her team to consult about, select, coordinate, and administer treatment.

That type of experience across multiple medical disciplines is most often found at major brain tumor centers. The neurosurgeons and team members at these centers perform over 50 brain surgeries annually (as many as five surgeries per week at some centers) and may offer the most technologically advanced procedures with higher rates of survival. Your choice of surgeon and treatment team can profoundly affect the outcome of your care. Many of these specialized centers allow you to directly submit imaging scans — and even tissue samples, if you have progressed that far — for further examination without a referring physician. If the nearest brain tumor center is far from where you live, that is okay: the staff there should be able to coordinate some of your treatment with doctors more local to you, so that extended stays near the brain tumor center may not be necessary.

Knowing your enemy (the type of brain tumor) and having the best possible team to treat it are of course essential for this battle. But so is having the tools to employ a strategy — a strategy for life. Brain tumors can change, grow, and recur, so it is important to be organized and knowledgeable about your tumor's makeup and location, your medications and their side effects, and symptoms that you might expect throughout your treatment. It is equally important to maintain an ongoing, open dialogue with your medical care team. Physicians rarely engage one another in the type of dialogue that patients often assume is transpiring on their behalf. Being organized can assist you by ensuring that all of your team members are on the same page with current information at the time of your appointments and consultations. You and your advocate team must become your own primary-care manager.

This guide and the Musella need-to-know checklist

This guide is made available to help you understand some of the common decisions you will be facing. It will answer some of the questions frequently asked by patients and caregivers and connect you with a support community. Additionally, it will help you get organized so that you can best advocate for the quality of care you need and deserve. Most importantly, this guide provides you with information on tumor

types, the most current treatment options, and how to find major brain tumor treatment centers.

The Musella Foundation need-to-know checklist is presented on the following three pages. This short checklist of critical information is intended to provide guidance at a time when information processing might be difficult for you and your loved ones. The checklist condenses a lifetime of experience in helping brain tumor patients: it is what I would tell my loved ones if they were suspected of having a brain tumor or were newly diagnosed with one.

This guide will explain in detail the items on the checklist, and the checklist will be updated on the front page of the virtualtrials.com website as new techniques and treatments are discovered. Even if you have no time to read anything else in this guide, please read through the Musella Foundation need-to-know checklist. It will make a positive difference.

.....
: For a list of brain tumor centers by state and country, go to:
: www.virtualtrials.com/Brain_Tumor_Centers.cfm. If possible,
: all brain tumor patients should receive at least one second opinion from
: a brain tumor center.
:



The Musella Foundation need-to-know checklist

**IF YOU HAVE TIME TO READ ANYTHING IN THIS BOOK,
PLEASE READ THIS LIST**

1. Seek out the most advanced and the most specialized brain-tumor care available to you.

Many smaller and local hospital systems may offer neurosurgery and treatment for brain tumors. However, these systems do not usually have the same state-of-the-art facilities, technologies, and doctors specializing in different tumor types that large brain tumor centers have. You should find the most experienced neurosurgeon you can who specializes in surgical removal of brain tumors, and you should find the best integrated group of doctors you can, experienced in treating brain tumors, to coordinate and administer the different types of treatment your brain tumor will require. Even if that means travelling a distance from home, bear in mind that larger brain tumor centers will have (1) more advanced pathology facilities for diagnosis; (2) greater capacity for storing tumor tissue for future testing; (3) better familiarity with the latest surgical and treatment practices; and (4) more clinical trial options to offer. If your tumor is considered “inoperable,” large brain tumor centers might also offer alternatives to surgery, such as laser interstitial thermal therapy (eg, NeuroBlate), MRI-guided focused ultrasound, and stereotactic radiosurgery (eg, Gamma Knife).

2. Before surgery occurs, carefully consider various treatment options.

There are some clinical trials that require registration before surgery of a brain tumor occurs. In some trials, such as for certain types of immunotherapy, treatment begins before surgery. For trials related to custom-made vaccines, the tumor sample obtained during surgery needs to be handled in a special way. There are also treatments that can only be received at the time of surgery, such as implantation of chemotherapy-eluting Gliadel Wafers or radioactive GammaTile therapy. Discuss these and other options with your doctors before surgery.

3. Ask whether treatment with alternating electric-field therapy (the Optune device) is available.

The Optune device, which treats brain tumors by delivering alternating electric fields, is a new therapy approved by the US Food and Drug Administration (FDA) for newly diagnosed and recurrent glioblastoma (the most common type of primary brain tumor). Since the device has only been available for the past several years, some treatment centers might not yet offer it. So find the closest brain tumor center that does.

4. Insist that your tumor tissue undergoes comprehensive molecular-marker testing.

If you are treated at a major brain tumor center, the sample of your tumor tissue will be tested for molecular markers that can guide treatment choices. These markers include MGMT status, IDH1 mutation, EGFR mutation/amplification, and chromosome 1p/19q codeletion. Of these, a mutation in the EGFR gene called EGFR variant 3 (EGFRvIII) is particularly important, for this mutation can determine enrollment eligibility for several clinical trials targeting this mutation. There are two companies that offer molecular-marker testing if the hospital system where you are being treated does not: Caris Life Sciences and Foundation Medicine.

5. Ask your surgeon how your tumor tissue will be preserved.

The preservation of your tumor tissue should be discussed with your neurosurgeon before surgery. Brain tumor tissue is commonly preserved by the formalin-fixed paraffin-embedded method. A better alternative is for the tumor tissue to be flash-frozen in liquid nitrogen. One advantage of freezing is that the tumor tissue is preserved intact and can be later used to create personalized cancer vaccines. A company that freezes and preserves tumor tissue is Store My Tumor.

6. Educate yourself.

Read this guide and visit the virtualtrials.com website. In the “Learn About” section of the website, there is an archive of articles called “Noteworthy Treatments.” In the “Interact” section, there is a video library of talks and presentations on all things brain-tumor related. You can also subscribe to our “Brain Tumor News Blast,” which carries news stories about brain tumors: www.virtualtrials.com/maillist.cfm.

7. Join a real-world or online support group.

In the chapter on support in this book, the importance of support groups is emphasized, and there is a list of real-world support groups. On the virtualtrials.com website, you can immediately join several online support groups, where you can connect with people who would be more than pleased to share their knowledge and experience. Find these groups and more in the “Resources” section of the website. One of the most popular of the groups is the “Braintumor treatments group.”

8. Request, record, organize and keep all brain-tumor–related documents and information.

Request all documents related to your diagnoses and treatment, including all pathology reports, and keep these documents organized in a binder. This binder can also contain whatever notes you take along the way. You may also consider making audio recordings (eg, on your cell phone) of appointments with your doctors for future reference and review. It might also be good to bring a friend or family member with a good memory to all medical appointments.

9. Designate a support team.

Receiving a diagnosis of brain tumor is an exceptionally emotional and confusing situation. Unless you are especially skilled and motivated to do your own medical research, it may be best to designate a friend or family member to research treatment options and all things tumor-related on your behalf. Please give this person this book to read and direct him or her to the virtualtrials.com website. Another person might be designated to relay news to your larger network of family and friends.

10. Upgrade your insurance and know that some financial support is available.

Upgrade to the best medical insurance that you can afford. If you are enrolled in Medicare, seek out the best supplemental policy you can afford but avoid Medicare Advantage Plans because they limit the choice of doctors. The Musella Foundation runs a co-pay assistance program for people with insurance to help with expenses related to the Optune device and several common chemotherapy treatments. For people without insurance, the Musella Foundation offers a Drug Discount Card that gives discounts for prescription and nonprescription medications.

Survivor story #1

It started with small things in 1999, mostly visual. My wife thought I was experiencing a stroke.

I called my doctor at home on a Sunday. He had a scan set for Wednesday, my wife and I saw the neurologist and neurosurgeon on Thursday, and surgery was on the following Tuesday. I had glioblastoma. I received radiation and chemotherapy as well as stereotactic radiation. I was very fortunate to be at a teaching hospital.

I had a recurrence in 2001 with successful resection during which Gliadel Wafers were implanted.

In 2002, they thought I had another recurrence, but it was only scar tissue and radiation necrosis.

I am currently a 19-year survivor of glioblastoma. I still deal with several medical issues associated with my tumor treatment, including some loss of peripheral vision and neuropathy in my right foot, which affects my balance. Most important to me are conversations I have with brain tumor patients and their caregivers. On average, I talk to two or three patients in a given month. I always point them to the virtualtrials.com website as the best resource for all things brain tumor. I do not give medical advice, but I do answer questions as best I can. What I hear quite often is the hope they feel when they meet someone who has survived glioblastoma for as long as I have. I make sure they know that there are many long-term survivors and that there is hope based on new treatments and research.



Brain Tumor Guide for the Newly Diagnosed

I have learned a lot of things from my experiences; these are just a few of them:

- You will learn quickly who is comfortable and who is not comfortable in dealing with issues of mortality.
- Have someone with you to listen, ask questions, and remember. Several times the neurosurgeon told my wife that no one had ever asked him a particular question before.
- Don't fear knowledge. As my wife said many times, "There is nothing you can tell us that is worse than we can imagine."

God gave us the gift of life that brings uncertainty. When tough times hit, He can comfort us much as we can comfort each other.





From day one, a place for everything

The diagnosis of a brain tumor can leave patients and their loved ones in a mental fog, a fog so thick with questions that simply determining where to begin can be debilitating. There are ways in which you can regain control, stepping out from the fog and into the light of day. Organization is your key to obtaining the information you will need for finding the proper treatment necessary for your specific type of tumor. The following is a list of tools that have helped other brain tumor patients.

A three-ring binder can become your best friend and treatment partner, easily safeguarding and making available at your fingertips all the necessary information about your tumor type and treatment plan. Referrals to specialists or for second or third opinions are often delayed by the need to obtain records and, sometimes, by records that have been lost along the way. Maintaining your own copies of the following items will ensure that your consulting physicians have access to all of your important documents at the time of your appointment. Many people maintain these records on their computers or flash drives and occasionally print them out and store them in the binder as needed — since it is easier to carry a binder around. You should also print out a list of your current medications and allergies to store in your wallet or pocketbook in case of emergency. Items to keep in your treatment binder include:

- **Medical history.** Start with a copy of the first medical history form you are asked to fill out. This will list past medical problems, such as diabetes or heart problems, which may affect the treatment choice, as well as any allergies you have. An important allergy to note is one to either iodine or shellfish, as the dyes (contrast agents) used in some brain scans contain iodine. Having a copy of your first medical history will be helpful when you have to fill out similar forms. Keep your medical history updated as things change. You can also ask your doctor for a copy of your examination records.

Brain Tumor Guide for the Newly Diagnosed

- **Copies of imaging films and reports.** Most radiological centers today can provide you with a copy of your imaging scans on a CD that can be viewed on any computer. When you check in at the MRI radiology facility, it is very important to request a copy of the film or a CD along with the written report of the radiologist's findings. Ask BEFORE you go into the scanner, as it is easier for the staff to handle the request then than if you tell them afterward. Most office supply stores carry special three-hole vinyl pages that hold multiple CDs safely within a binder.
- **All routine laboratory reports and pathology reports from biopsies.** Different members of your medical team will benefit from receiving recent laboratory results that may have been initially ordered by another physician. Having your own personal copies of all routine laboratory reports as well as **pathology** reports from biopsies, so that they are available for review on demand, will save time, increase your own understanding, and in some cases eliminate the need for unnecessary blood work. As a bonus, if you are computer literate, keep track of lab results in an Excel spreadsheet so you can graph results over time and see how you are doing.
- **Medication at a glance.** It is important to disclose all the medications you take to your physician and care team members. Keeping an up-to-date medication record in your treatment binder (including herbal supplements and over-the-counter items) can provide a quick and clear snapshot of your daily meds at a glance, reducing the chance of error when more than one physician is involved with your care. Without this information, you may experience symptoms that are medication related or side effects of a medication that one member of your medical team may not realize you are taking, with the consequence that you may be incorrectly diagnosed or treated.

Take your treatment binder to every appointment with every doctor and request that this list be reviewed before any new medication is prescribed. You should also

Pathology (puh-THAH-loh-jee): *The description of cells and tissues made by a pathologist based on microscopic evidence and sometimes used to make a diagnosis of a disease.*

request a copy of the drug formulary — a list of covered medications — from your insurance company and keep it in your treatment binder. It may be necessary for your physician to request prior authorization for some medications. Knowing in advance about the need for prior authorization can save you time and expense.

Location, location, location

Knowing the exact location of your tumor will assist you in many ways. By researching the functions of that part of the brain, you can more clearly understand — and be prepared for — many of the symptoms you are experiencing, or might expect to experience. Ask your physician to be specific about the location. Perhaps he or she can provide you with a diagram of the brain with a penciled-in identification of the tumor site. Or use the anatomical figure of the brain on the following page in consultation with your physician (**Figure 1A** and **1B**). The top part of the figure (A) shows the major parts of the brain. The bottom part of the figure (B) shows some of the functions associated with each of the brain parts.

A personal diary

Beginning on day one, keeping a diary is very important as you review various treatment options with specialists. Recording your specific questions and concerns will help ensure that your medical team provides the answers you and your loved ones or caregivers need. You may want to create a separate section for each team member, writing down which doctor is responsible for the various aspects of your care, medication refills, routine lab work, referrals, and what was discussed at appointments. Questions can often arise after you leave an appointment, and being able to refer to these pages later may be helpful. It is critical that you maintain monthly calendar pages to record the start of new medications or therapies and any bad reactions to them. The starting times of symptoms and side effects may be difficult to recall at a later date, but it is important to distinguish their origins.

Figure 1A: Major parts of the brain

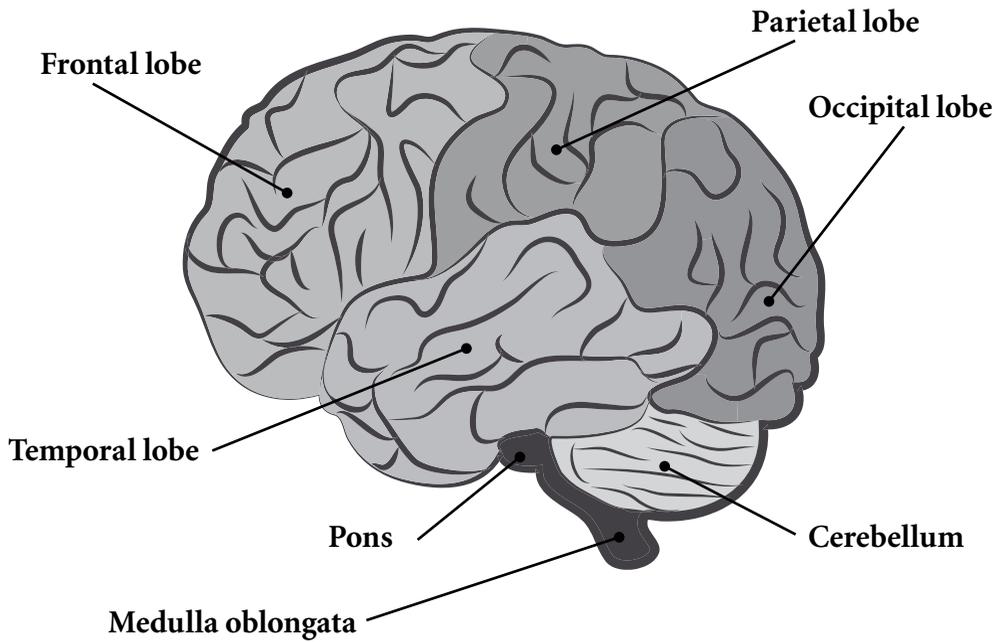
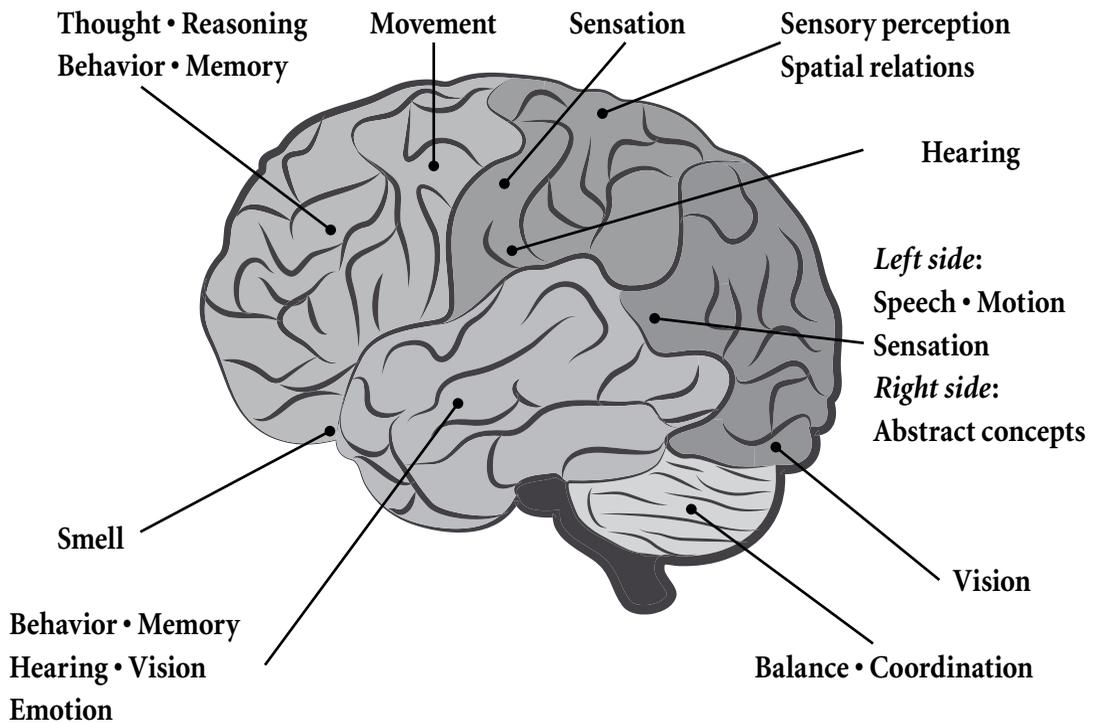


Figure 1B: Associated functions of the parts of the brain



Legal documents

Every doctor you see will ask you to sign a **HIPAA** privacy form. When you fill it out, write in that you want to specifically allow the following people to discuss details of your case with the doctor (or facility); then list by name your spouse / parents / children and maybe a friend. Then ask for a copy of the form, as the original will be kept by the physician in each case. Having the copy of the executed HIPAA form will help save time when you need to send someone to pick up reports or films or to ask questions for you. When medical personnel tell you they cannot give your children something or talk about something to anyone other than you, just have the copy of the form available for them to see, and they will have to meet your request.

2

Power-of-attorney legal documents

We all hate to think about these things, but it can save a lot of trouble later if you handle some legal matters now. An *advance directive*, also called a living will, tells your medical team what kind of care you would like to have if you become unable to make medical decisions. A *durable medical power of attorney* lets you designate who will make medical decisions for you if you are unable to. The first time you are admitted to a hospital, you will be asked if you want to fill out the forms for these legal documents, if you do not already have them in place. Do it, and ask for copies and keep them in your binder. Or search Google for “Advanced Directives in [your state]” (each state has different laws and forms). If you do already have these legal documents in place, bring them with you, and the staff will make copies for your files and return the originals to you.

It is very important to tell your family who your medical power of attorney will be and to tell them what your values are and what kinds of medical treatment you would want or not want, including breathing machines and feeding tubes, if your condition were to worsen and you were unable to communicate or were in a coma.

HIPAA (HIH-puh): *A 1996 US law that allows workers and their families to keep their health insurance when they change or lose their jobs. The law also includes standards for setting up secure electronic health records to protect the privacy of a person’s health information and to keep it from being misused. Also called Health Insurance Portability and Accountability Act and Kassebaum Kennedy Act.*

For more information about consultations with the neuro-oncology branch of the National Cancer Institute, select the tab for “Making Appointments,” then select the tab for “Patient Referrals,” after you go to: ccr.cancer.gov/Neuro-Oncology-Branch.

You may also want to consider drafting a *durable financial power of attorney*. A durable financial power of attorney designates a person of your choice to manage your finances if you become incapacitated and are unable to make financial decisions for yourself. Your financial power-of-attorney document should not contain medical directives, for these are covered in your medical power-of-attorney document. Standard durable financial power-of-attorney forms are available online or through an attorney. They are straightforward and easy to complete. If you have special circumstances, you may wish to consult with an attorney.

Phone numbers

Record the name, address, phone number, email address, and a short description of all of your important contacts. Be sure to include your family members who should be contacted in an emergency, all of your doctors, your lawyer, your financial advisor and/or insurance agent, and any clergy.

Second “expert” opinions

Because diagnosing a specific type of brain tumor is complicated, it is essential to get confirmation of a diagnosis. Second, third, or even fourth opinions should come from experts within a specific area, such as those who are experts in the removal of brain tumors: neurosurgeons performing at least 25 brain surgeries per year, or experts in neuropathology who can qualify the diagnosis of your tumor biopsy. It is estimated that as many as 25 percent of brain tumor patients will have their diagnosis changed upon further examination by a second, expert opinion, which can drastically alter not only the prognosis but also the recommended treatment plan.

If your primary brain tumor physician is not familiar with the most current treatments or clinical trials available for patients with brain tumors, request that he or she consult with one of the many major brain tumor centers and arrange for you to obtain a second expert opinion. Even if you are diagnosed by a major brain tumor

center, you may still wish to get a second opinion from another major brain tumor center to confirm your diagnosis, to confirm a treatment plan, and/or to locate a clinical trial. It is your right to have a second opinion.

A review of your MRI or CT scans, tests, and pathology reports, along with an overview of new resources and treatment programs can be obtained through many of the leading major brain tumor centers. Your physician can also consult with the National Cancer Institute (see accompanying box on previous page). They will also review your case for free. They have excellent adult and pediatric brain tumor specialists available to help you.

Most pathologists do not see enough brain tumors to allow them to make the subtle distinctions that may be necessary for diagnosis. You can also ask for a second opinion on the reading of the biopsy slides from a major center, such as the Neuropathology Division of the Department of Pathology at Johns Hopkins University Hospital (see accompanying box below), which is located in Baltimore, Maryland. There is a cost, but the process is easy — your hospital just mails the slides.

If you do need to travel for a second or third opinion, there are many organizations that provide financial assistance specifically for brain tumor patients. Please check the information on insurance and financial help in chapter 10 of this book. ●

.....
: For details about consultations by the Neuropathology Division of the :
: Department of Pathology at Johns Hopkins University Hospital, go to: :
: pathology.jhu.edu/departments/services/consults.cfm. :
:.....



Please remember

- ✓ Get organized from day #1 with a binder to keep track of everything.
- ✓ Keep an up-to-date medication record in your treatment binder.
- ✓ Know the exact location of your tumor.
- ✓ Think about and execute such necessary legal documents as an advance directive, a durable medical power of attorney, and a durable financial power of attorney.
- ✓ Recognize that brain tumors are complicated, so second, third, and fourth opinions from experts are essential for confirming diagnosis are essential.

Survivor story #2

On the night of December 25, 2012, I went to bed and had a grand mal seizure for the first time ever. The only thing I remember was waking up on a stretcher as I was being lifted into an ambulance. I failed to answer basic questions. I was confused and had no idea what was happening. I was rushed to the local hospital to undergo a CT scan. The results showed an 8-cm tumor on the right frontal lobe of my brain.

This news left my wife and me speechless. It was so much to digest. She cried, and I sat in disbelief. I was then transported by ambulance to another hospital where an MRI scan and another CT scan were performed. Unfortunately, the imaging interpretation at the first hospital was confirmed. I was told that I needed to be operated on as soon as possible. Luckily, one of the best neurosurgeons in the state was on call that night. After quick but thorough research, my family and I decided to go ahead with the surgery. My neurosurgeon and his team were able to remove the entire tumor. During recovery I had several more seizures and received the antiepileptic medication levetiracetam (Keppra). A week or so after discharge, while still recovering in bed, I received the phone call that no one wants. My pathology report was back. I had a grade 3 anaplastic astrocytoma.

My family and I were devastated. Before that first seizure my life was great. I had just turned 31 years old, I had a great job, my wife and I had just purchased our first home, and we had a beautiful one-year-old boy. Life seemed perfect, then the curve ball.

My first reaction was, Why me? What did I do to deserve this? My wife and I went to see the neurosurgeon for a follow-up appointment and he recommended a comprehensive cancer center. Our appointment came quickly. We received detailed information about my diagnosis and my treatment schedule. I did not like hearing the statistics, especially when they confirmed what Dr. Google seemed to be reporting on the Internet, but we decided to take the brain tumor head on. My treatment was



Brain Tumor Guide for the Newly Diagnosed

30 days of radiation therapy with weekends off, 6 weeks of temozolomide (Temodar) every day, and then 12 months of adjuvant temozolomide with the cycle of 7 days on, 23 days off.

The radiation therapy was difficult to tolerate near its end. Because I did not like watching my hair fall out, I shaved all my hair off. Chemotherapy, however, was not too hard to tolerate, and I went back to my job on light duty toward the end of treatment.

Throughout all this, I recognized how blessed I am. I had such an awakening. I started to take charge of my health in ways I never thought possible. I no longer procrastinated. I no longer put anything on hold. The experience gave “living life” a whole new meaning to me. I received many miracles on my journey. Although not everything was easy, especially at the beginning, I can say that my diagnosis saved me.





Understanding brain tumors

Brain tumors are classified as either primary or **metastatic**. Primary tumors are cancerous growths that arise directly from tissue in the central nervous system (CNS) — that is, from the brain and spinal cord. These tumors may spread to other parts of the brain or spine but rarely spread to other parts of the body. There are more than 120 types of primary brain tumors, which are named for the kinds of cells or parts of the brain from which they originate.

Metastatic (or secondary) tumors, on the other hand, arise from cancers that first develop in another part of the body (such as the breast, colon, kidney, lungs, or skin) and then spread to the CNS. Metastatic brain tumors are named for the location in which they originate. Secondary brain tumors are about four times more common than primary brain tumors.

Brain tumors are also classified as either benign (that is, nonmalignant) or malignant. Benign brain tumors are not cancerous. They grow slowly and rarely spread. However, benign tumors can still be dangerous. Because the brain is enclosed in a rigid container (the skull), there is no space for a tumor mass to grow. As a tumor (even a “benign” tumor) grows, it builds up intracranial pressure and compresses everything around it, and this process can lead to neurological problems and even death. Luckily, there has been a lot of progress in the treatment of benign brain tumors.

Malignant brain tumors are cancerous. They typically grow rapidly and invade surrounding healthy brain tissues. These tumors are life threatening.

Metastatic (meh-tuh-STA-tik): *Having to do with metastasis, which is the spread of cancer from the primary site (place where it started) to other places in the body.*

Brain Tumor Guide for the Newly Diagnosed

The World Health Organization (WHO) classification of tumors of the CNS is the standard and universally used diagnostic system. Published in 2016, the most recent WHO guidelines merged histology with molecular testing in order to create a “layered” integrated diagnosis. The three layers that are combined to make an integrated diagnosis are:

- **Histologic type:** This means the type of cell from which the cancer most likely originated. Cell type is normally ascertained by microscopy of stained biopsy tissue sections, **immunohistochemistry** analysis, and examination of the inner cell structure.
- **Histologic grade:** This means a description of a tumor based on how abnormal the cancer cells and tissue look under a microscope and how quickly the cancer cells are likely to grow and spread. The histologic grade is a measure of malignancy. Low-grade cancer cells look more like normal cells and tend to grow and spread more slowly than high-grade cancer cells. The histologic grading system is used for planning treatment.
- **Molecular characterization:** This means that molecular analyses are used to detect genetic mutations and **epigenetic alterations** in tumor cells. A genetic mutation is a permanent alteration in the DNA sequence that makes up a gene. Mutations range in size; they can affect anywhere from a single DNA building block to a large segment of a chromosome that includes multiple genes. An epigenetic alteration is change in the chemical structure of DNA

Immunohistochemistry (IH-myoo-noh-HIS-toh-KEH-mih-stree): *A lab test that uses antibodies to test for certain antigens (markers) in a sample of tissue. Immunohistochemistry is used to help diagnose diseases, such as cancer. It may also be used to help tell the difference between different types of cancer.*

Epigenetic alteration (EH-pih-jeh-NEH-tik ALL-teh-RAY-shun): *A change in the chemical structure of DNA that does not change the DNA coding sequence. Epigenetic alterations occur in the body when chemical groups called methyl groups are added to or removed from DNA or when changes are made to proteins called histones that bind to the DNA in chromosomes. These changes may occur with age and exposure to environmental factors, such as diet, exercise, drugs, and chemicals.*

that does not change the DNA coding sequence. Epigenetic alterations can cause changes in **gene expression**.

What does histologic grade mean?

All tumors are given a “grade,” meaning a specific classification that relates to the current speed of growth and the potential to interfere with brain function. Grading is a determination of what stage the tumor is at, or how advanced (bad) it is in its development.

Grading a specific tumor type has been described as a process that is as much an “art form” as a science and typically involves a determination made by a neuropathologist after a biopsy. Grading can be somewhat controversial depending on the size of biopsy specimen obtained. One part of the tumor may have smaller lower-grade cells, while larger more aggressive cells may be present in a different location in the tumor. Furthermore, tumors initially assigned a low grade can become aggressive in growth, changing the status of the grade even during the course of treatment. It is important to have your biopsy examined by a neuropathologist who sees a large number of brain tumors, always requesting a copy of the report for your records and comparison.

The WHO system classifies all cancers on a grade of I to IV (1 to 4). A grade of I or II designates slow-growing “benign” tumors, while a grade of III or IV designates faster growing tumors that are considered “malignant.”

Types of gliomas

In this book, we focus on gliomas, a category of CNS tumors that arise from glial cells. Glial cells are the “support cells” of the CNS, helping neurons and nerve cells do their jobs. Gliomas are the most common type of primary brain tumors. The cells of these tumors spread to other CNS tissue.

Tumors that arise from the type of glial cells called astrocytes (so named because they are star-shaped) are the most common primary malignant CNS tumors in

Gene expression (jeen ek-SPREH-shun): *The process by which a gene gets turned on in a cell to make RNA and proteins. Gene expression may be measured by looking at the RNA, or the protein made from the RNA, or what the protein does in a cell.*

adults. Based on their histological features, these tumors are classified into three categories according to the 2016 WHO system:

- WHO grade II **diffuse astrocytoma**
- WHO grade III **anaplastic astrocytoma**
- WHO grade IV **glioblastoma**

WHO grade II diffuse astrocytomas can be found anywhere within the CNS but usually occur within the cerebral hemispheres, particularly in the frontal temporal lobes. Although these tumors grow slowly and have low cell-division activity, they can infiltrate into neighboring brain structures.

WHO grade III anaplastic astrocytomas grow more quickly and aggressively than grade II astrocytomas, projecting into surrounding tissue. Unlike the cells of grade II astrocytomas, the cells of grade III anaplastic astrocytomas do not look like normal cells and are not uniform in appearance.

WHO grade IV glioblastomas are the most malignant of the diffuse astrocytomas. Glioblastomas also occur the most frequently, accounting for 60% of all astrocytic tumors. Most glioblastomas originate within the cerebral hemispheres. These tumors are aggressive, spreading into nearby regions of the brain and sometimes to the opposite side of the brain. Under a microscope, glioblastomas have a distinctive appearance that helps neuropathologists distinguish them from grade III

Diffuse (dih-FYOOS): *Widely spread; not localized or confined.*

Astrocytoma (AS-troh-sy-TOH-muh): *A tumor that begins in the brain or spinal cord in small, star-shaped cells called astrocytes.*

Anaplastic (A-nuh-PLAS-tik): *A term used to describe cancer cells that divide rapidly and have little or no resemblance to normal cells.*

Glioblastoma (GLEE-oh-blas-TOH-muh): *A fast-growing type of central nervous system tumor that forms from glial (supportive) tissue of the brain and spinal cord and has cells that look very different from normal cells. Glioblastoma usually occurs in adults and affects the brain more often than the spinal cord.*

For more information about different specific types of CNS tumors and how they are treated, visit the section on brain tumors on the website of the National Cancer Institute (NCI). The NCI is the principal agency for cancer research and training of the United States federal government. The section on CNS tumors is located at: www.cancer.gov/types/brain.

anaplastic astrocytomas. Glioblastomas are themselves classified as primary or secondary. Primary glioblastoma arises without any evidence of a precursor. Secondary glioblastoma arises from a lower-grade astrocytoma.

Not all diffuse gliomas derive from astrocyte cells. Diffuse oligodendroglial tumors display features of oligodendrocyte cells, which are another type of glial cell. Oligodendrogliomas can occur anywhere within the CNS but are primarily found in the frontal and temporal lobes of the cerebral hemispheres. WHO grade II oligodendrogliomas are relatively slow growing. WHO grade III anaplastic oligodendrogliomas are malignant but grow more slowly than grade III astrocytomas.

Molecular markers that define tumor entities

Studies have shown that molecular alterations in tumor cells (mutations in certain genes, deletions of chromosomal regions, and epigenetic changes to DNA structure) can identify distinctive characteristics of brain tumors. By testing for molecular markers in your brain tumor, your medical team can generate a genetic and epigenetic profile of your tumor cells to achieve a “layered” integrated diagnosis that can guide treatment choices.

To this end, the three molecular markers that are routinely tested for an integrated diagnosis are the following:

- **Mutations in IDH1 and IDH2:** In cancer cells, mutations in the isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) genes allow the enzymes these genes encode to interfere with cell metabolism and promote the growth of tumors. Studies have shown that IDH1 mutations are present in approximately 85% of secondary grade IV glioblastomas that originated from prior low-grade gliomas but are rarely present in primary glioblastomas. Despite being a cause of tumors, mutations in IDH1 and IDH2 are associated with longer survival.

- **Codeletion of 1p/19q:** During cell division, pieces from two different chromosomes sometimes switch places with each other. In some cases, when this rare event occurs, the chromosome pieces are jointly deleted. Codeletion of 1p/19q is an example of this type of chromosomal abnormality: part of chromosome 1 is switched with chromosome 19, and then both parts are removed. In the 2016 WHO classification, codeletion of 1p/19q serves as a diagnostic biomarker for oligodendrogliomas. Tumors that have codeleted 1p/19q are more sensitive to chemotherapeutic agents than those that lack the codeletion, and the presence of codeleted 1p/19q is associated with longer survival times.
- **H3K27 mutations:** These are mutations in histones — specialized proteins around which the DNA in our cells are wound — that can contribute to the pathogenesis of cancer and other genetic diseases. These mutations are found in most of the diffuse gliomas arising in midline brain structures, such as the thalamus, brainstem, and spinal cord. Tumors in these locations occur primarily in children but also sometimes in adults. These tumors have a grade IV classification. If your pathology report indicates that you have this mutation, please call the Musella Foundation about a new therapy that specifically targets it.

Additional molecular markers that are routinely assessed

In addition to the molecular markers above, others have been identified that are not essential but can still increase the overall reliability of a diagnosis and in some cases help guide treatment options. Two such biomarkers are described below.

- **MGMT promoter methylation:** O6-methylguanine-DNA methyltransferase (MGMT) is a DNA repair enzyme that protects cells against damage from ionizing radiation as well as from chemotherapeutic drugs that are

.....
: After his diagnosis with a rare abdominal tumor called mesothelioma, the :
: well-known evolutionary biologist and Harvard University professor Stephen :
: J. Gould wrote something of a guide to surviving exposure to survival statistics. :
: To read his famous 1985 essay "The Median Isn't the Message," go to: :
: www.cancerguide.org/median_not_msg.html. :
:.....

DNA alkylators — that is, drugs that can attach an alkyl group to DNA that stops the DNA from replicating and causes cell death. An important alkylating drug is temozolomide (Temodar), which is a standard-of-care chemotherapeutic treatment of high-grade malignant gliomas. The MGMT repair enzyme counteracts the effects of the alkyl group that has been added to the DNA by transferring that alkyl group to itself. In some people with high-grade malignant gliomas, there are decreased levels of the MGMT repair enzyme because the DNA elements that promote the production of the repair enzyme are methylated — that is, they have a methyl group attached to them that makes them less effective. That is a good thing in these people because they have lower levels of the MGMT repair enzyme that can counteract the tumor-cell-killing effects of drugs like temozolomide. The presence of MGMT promoter methylation, which can be determined by molecular testing, is thus one of the most important predictors of response to treatment with alkylating agents. The status of MGMT promoter methylation is used to guide treatment choices.

- **Epidermal growth factor receptor amplification and mutations:** Epidermal growth factor (EGF) is a protein that stimulates cell growth by binding to a receptor — conveniently called the epidermal growth factor receptor (EGFR). Many different types of cancer produce abnormally high levels of EGFRs, and when these EGFRs are stimulated by EGF proteins, they cause the cancer cells to divide and grow excessively. In up to half of glioblastomas, the EGFR gene is amplified. This means that there is an abnormally high number of copies of the EGFR gene in a cell, a situation that can lead to overproduction of the EGFR protein. Because stopping the production of excessive amounts of EGFR or preventing EGF from binding to excessive amounts of EGFR could restrain the growth of tumor cells, EGFR is a target of a number of potential therapies currently in development.

How long has the tumor been there?

Nobody really knows how long you have had your particular tumor. Slow-growing tumors can be present for years without causing any symptoms. Fast-growing tumors can occur and cause symptoms within a span of six months or less.

Can brain tumors be removed surgically?

In many cases, brain tumors can be removed by surgery. Surgery may actually “cure” some low-grade tumors. However, for high-grade tumors, surgery is not by itself a cure, but it does buy time for other treatments to work and offers a lot of opportunities. For example, a tissue sample from surgery can be used for biopsy and can undergo molecular marker and drug resistance testing. Moreover, there are some therapies that require prior surgery and removal of the tumor. One such therapy is the **Gliadel Wafer**, a dissolvable wafer impregnated with an alkylating chemotherapeutic agent that is directly implanted at the site of tumor removal.

Any tumor can theoretically be removed, but the neurosurgeon uses his or her experience to make a judgment on the risks of removal versus the benefits of removal. Each brain tumor is different, but the neurosurgeon can usually predict if — and how much — neurological damage will occur if the brain tumor is removed. Since surgery of high-grade brain tumors is not a cure, sometimes brain tumors are considered inoperable if the expected neurological damage arising from the surgery would create unacceptable problems for the patient.

In brain surgery, experience matters A LOT. Neurosurgeons who have operated on a lot of tumors can usually remove more of the tumor, with fewer side effects, than neurosurgeons who have operated on only a few tumors. They are also much more likely to have access to the latest high-tech surgical tools. In general, the more of the tumor removed, the better the outcome. That is why one of the single most important decisions you have to make is WHERE and by WHOM you will have brain surgery. A more experienced neurosurgeon may consider relatively easy what another neurosurgeon might consider inoperable.

However, keep in mind that some neurosurgeons may be overly aggressive. Discuss the expected risks of the surgery to make sure your neurosurgeon understands your views on how aggressive you want him or her to be.

Furthermore, while there are over 4500 neurosurgeons in the United States, only 125 (approximately) are considered experts in the removal of brain tumors, performing these delicate surgeries at least 25 times per year. Again, because choosing an experienced neurosurgeon can greatly affect the quality of tumor

Gliadel Wafer (GLY-uh-del WAY-fer): *A biodegradable wafer that is used to deliver the anticancer drug carmustine directly into a brain tumor site after the tumor has been removed by surgery.*

.....
: If you want to see brain tumor survival statistics, go to the website :
: of the Central Brain Tumor Registry of the United States: :
: www.cbtrus.org/factsheet/factsheet.html. :
.....

removal and your recovery, getting a second opinion about which neurosurgeon to choose is vital.

What are the survival statistics for patients with brain tumors?

Nobody knows how long you are going to live with your brain tumor. Statistics are a tool used for comparing treatments and for describing what has happened in the past to groups of people with your tumor type. Statistics cannot predict how long any individual person will live.

There are two important survival statistics that you will commonly see in research about brain tumors: overall survival (OS) and progression-free survival (PFS). OS is the average survival time of a group under study — such as 1 or 2 years. Just because a 1-year or 2-year survival statistic is reported does not mean that you will live for 1 or 2 years. Rather, it means that on average the people described in that particular research lived for that length of time.

PFS is reported either as the percentage of people who reach a milestone without having tumor progression — such as 6 months or 1 year — or as the average number of months before tumor progression for the entire group. Progression means tumor recurrence. The survival statistics of OS and PFS are commonly used in medical research, and you can compare treatments by looking at either number. We feel that PFS is the more important survival statistic because after people experience tumor progression, they usually move on to other treatments. In that case, relying on the OS survival statistic to evaluate a treatment may be misleading.

As you read about survival statistics, keep in mind that they fail to take into consideration many factors that are extremely important on a case-by-case patient basis — such as age, general health, tumor size and location within the brain, the extent of tumor removal by neurosurgery, and much more, including access to the care of brain tumor experts.

Surgical technologies and the ability to accurately diagnose brain tumors have improved dramatically, and ongoing clinical trials are leading the way to new and better treatments. Your ability to challenge survival statistics will greatly depend on surrounding yourself with a medical team that is not influenced negatively by such numbers.

Brain Tumor Guide for the Newly Diagnosed

Try to avoid those within the medical community who have an unfortunate and bleak outlook and may not be current in their understanding of progressive new treatments. Physicians associated with, and in consultation with, leading brain tumor medical centers are your best defense against negative survival statistics and will enhance your ability to remain positively engaged during your journey through treatment.

Look for people with your tumor type who are leading normal lives. These people prove that no tumor type is completely hopeless. Participate in online and real-world support groups, discussed later in this book, to meet others who have gone through the same medical crisis as you but are now many years out and doing well. It is important to see and acknowledge that there are people with brain tumors who do well. ●



Please remember

- ✓ Metastatic (secondary) brain tumors are about four times more common than primary brain tumors.
- ✓ The most recent WHO guidelines have merged histology with molecular testing in order to create a “layered” integrated diagnosis.
- ✓ By testing for molecular markers, your medical team can generate a profile of your tumor cells that achieves a “layered” integrated diagnosis and can help guide treatment choices.
- ✓ The single most important decision you have to make is WHERE and by WHOM to have treatment.
- ✓ Survival statistics cannot predict how long any one person will live. They are a tool for comparing treatment options.
- ✓ Find a medical team that is not negatively influenced by survival statistics.

Survivor story #3

I am now a seven-year survivor of my brain tumor. I remember being seated in the emergency department in May 2009 as a nurse pushed a sedative into my IV line to control my shaking before transporting me into the room with an MRI scanner. The CT image in front of me displayed a lesion that would later be diagnosed as anaplastic astrocytoma. At that moment, I was a 23-year-old biomedical engineer working for a medical device company, I had recently moved in with my girlfriend, and I had always been healthy. Everything changed; I become a cancer patient overnight.

The events following my diagnosis were a blur. After neurosurgery to remove the tumor performed with a procedure called an “awake” craniotomy — during which the neurosurgeon administered verbal tests to see what areas of the brain had been affected by the tumor — I began treatment, which included radiation therapy and concurrent chemotherapy with temozolomide (Temodar).

After that initial treatment, I began adjuvant therapy with temozolomide on the cycle of 5 days on, 23 days off. During adjuvant therapy I was fortunate to have no delays due to the emergence of side effects like neutropenia (an abnormally low count of a type of white blood cell).

Fast forward a year and one brain-tumor recurrence scare (a second opinion was invaluable in avoiding a second surgery), I found myself in a completely different state and city with my now fiancée starting medical school. I was looking for a job, continuing my temozolomide regimen, and trying to answer the ever present question in my mind, “What do I want to do with my life?” Ironically, I had never been much for introspection before I was diagnosed, when my perceived “time” seemed to be in oversupply. The answer I came up with is that I wanted to matter — I wanted my life to have more meaning. That sounds a little ridiculous and dramatic, but that was truly how I felt. And so over the next year I began volunteering in medical clinics and mobile hospitals in underserved neighborhoods. Eventually this culminated in my decision to become a physician and provide care to those who are diagnosed with cancer. My motivation came from a strong desire to reciprocate the heartfelt compassion and support I received during the treatment of my brain tumor.

Six years later and a score of clean MRI scans, I have graduated from medical school and am now in the last year of my residency in the field of radiation oncology. I have found fulfillment in life that I would not have had otherwise. The future is always uncertain, for cancer survivors and for everyone else, and I am still learning how to balance living for the moment with planning for the time ahead. Those diagnosed with a brain tumor may tread very different paths, but we are all survivors beginning on Day 1.



How brain tumors are diagnosed

The diagnosis of a brain tumor requires a thorough patient evaluation followed by appropriate imaging of the brain and possibly other parts of the body. If brain imaging identifies a suspicious mass in the brain, the next step is obtaining a tissue sample by surgery or biopsy for histopathologic and molecular analysis by a neuropathologist. Without examination of a tissue sample by a neuropathologist, a brain tumor cannot always be diagnosed.

The evaluation of a patient with a suspected brain tumor should include a detailed patient history, a comprehensive neurological examination, and a general examination of other body systems. Most patients with high-grade malignant gliomas will have no family history of brain tumors or identifiable risk factors for glioma.

A basic neurological examination of a patient with a suspected brain tumor should include the following activities:

- Tests for eye movement, pupil reaction, and eye reflexes
- Vision tests and examination of the optic nerve
- Hearing tests
- Tests of involuntary muscle reflexes
- Balance and coordination tests
- Tests for sense of touch using sharp and blunt objects
- Tests of facial muscles, tongue movements, and gag reflexes
- Mental status examination and memory tests

When there is a growth on the brain, symptoms can arise from excessive fluid (edema) or from increased intracranial pressure within the skull. Specific symptoms may also arise from the location of the growth. The most common presenting symptoms of high-grade gliomas include:

Brain Tumor Guide for the Newly Diagnosed

- Headache (50% to 60% of patients)
- Seizures (20% to 50% of patients)
- Focal neurologic deficits such as memory loss, motor weakness, aphasia (difficulty speaking or understanding speech), visual symptoms, and cognitive and personality changes (10% to 40%)

Focal neurologic deficits are more common with high-grade than with low-grade gliomas. In contrast, seizures are less common with high-grade than with low-grade gliomas.

Imaging of the brain before surgery

Imaging studies help to identify and localize brain masses and offer clues to what type of mass is present. They are also useful in diagnosing certain complications of brain masses, such as hydrocephalus and hemorrhage.

A brain MRI (magnetic resonance imaging) scan with contrast is often the only study required preoperatively. Patients with a contraindication to brain MRI should undergo head computed tomography (CT) with contrast.

The urgency of a neurosurgical evaluation for a suspected brain tumor depends on the clinical stability of the patient, symptom severity, and tumor size and location. Patients with large symptomatic tumors, including those with signs and symptoms of elevated intracranial pressure, require emergent evaluation and neurosurgical attention.

Patients with smaller tumors or with minimal symptoms can often be safely and effectively evaluated in the outpatient setting.

All about brain scans

Brain scans allow doctors to get an idea of what is going on inside the head. No scan is 100% accurate, and each is open to interpretation. The more experienced the doctor is at interpreting brain scans, the more confident you can be about the results of that interpretation. As mentioned elsewhere, it is a good idea to get a personal copy of the films (or a CD of them) and the radiology report. You can share these documents with your medical team to make sure they agree on the reading of the scans. Having copies of the scans will also be useful if you need a quick second opinion from another brain tumor center, or if the original scans are lost, as happens more than you would think.

Four: How Brain Tumors are Diagnosed

A CT scan (or CAT scan, a computerized axial tomogram) uses x-rays to generate a computer simulation picture of the cross section of your head. Usually, a contrast agent (a dye) is injected into your arm halfway through the test to enable the tumor to show up better. A CT scan can be readily available and much cheaper than an MRI scan. A CT scan shows some things very well, such as bleeding into the brain and signs of swelling, and it is sometimes used for planning surgery and radiation. Since CT scans use x-rays, there is a tiny risk with their use, so they are usually limited to only when they are absolutely needed, especially in children. If you are having a CT scan performed on a child, ask the radiology technician whether the level of exposure dosage can be reduced appropriately for children. On some older CT scanners, such a reduction is not possible. In such cases, you should select a different imaging facility.

An MRI scan uses magnetism and radio waves to create a “picture” of the inside of your head. It is more detailed than a CT scan and usually preferred when trying to diagnose a brain tumor. An MRI scan will find smaller tumors than a CT scan. A different contrast agent is used for MRI scans than for CT scans, so if you had an allergic reaction to the dye used for a CT scan, you can still usually use the contrast agent for an MRI scan (and vice versa). Sometimes you cannot have an MRI scan if there is any metal in your body. If there is any metal in your body, mention that when you make the appointment so they can determine whether the scanning is safe. Other than the problem with metal, and a small risk with the contrast agent, MRI scans are thought to be safe.

There are many available kinds of MRI scans. Here are some of the important ones:

- MRA (magnetic resonance angiography) shows details of the blood vessels.
- MRS (magnetic resonance spectroscopy) shows the chemical makeup of the brain, which can sometimes be used to tell the difference between radiation necrosis, normal brain, swelling, and tumor. Sometimes MRS can distinguish between low-grade and high-grade tumors, a distinction that is helpful when the best area for a biopsy is being selected. MRS can also detect whether a treatment is working much more rapidly than regular MRI can, and comparing repeated MRS scans can be especially useful for tracking tumor status. MRS is available at most brain tumor centers and is starting to become available everywhere.
- fMRI (functional MRI) measures blood flow in the brain and is used to map which areas of your brain control which functions. For example, if

the tumor is near your speech area, you will be asked to talk while the scan is performed to highlight the areas you use while talking, and to see if the tumor invades that area.

- Diffusion MRI, which measures water movement in the brain, can be used to determine how well the treatment is working.
- PET (positron emission tomography) uses a tiny amount of a radioactive substance injected into your arm. PET shows how metabolically active each area of the brain is based on how much glucose is being used. Differences in metabolic activity can help distinguish normal brain from areas affected by a brain tumor. The use of PET scans is not available everywhere, and it is expensive.

Screening for systemic malignancy

The likelihood that a lesion is metastatic should be assessed before proceeding to biopsy or surgery. Metastatic brain tumors are more common than primary brain tumors in adults. Although metastatic brain tumors usually occur in the context of known systemic cancer, they can also occur as the first sign of a systemic cancer.

If any aspect of the clinical or neurodiagnostic evaluation suggests that a brain tumor is a metastatic rather than a primary lesion, systemic evaluation, including CT of the chest, abdomen, and pelvis, should be performed.

Obtaining the tissue sample

Accurate diagnosis of a brain tumor requires an adequate tissue sample for histopathologic and molecular analysis. This sample may be obtained by open surgery or by stereotactic biopsy. Because resection is the recommended type of surgery for high-grade gliomas, patients will typically undergo biopsy at the time of operation. The patient undergoes a craniotomy (opening of the skull), and before removing the tumor, the neurosurgeon will usually obtain a frozen-section biopsy to provide a working diagnosis. This tissue sample is rapidly frozen and stained so that microscopic examination may be completed while the patient is still under anesthesia.

Following surgery, the entire resected tumor is sent to the neuropathologist for final examination, during which tissue samples are permanently preserved in paraffin.

Some patients are not candidates for surgical resection because the tumor is located next to critical brain structures, such as those responsible for the senses or for speaking, or because the patient is in poor medical condition.

Four: How Brain Tumors are Diagnosed

In these patients, a tissue diagnosis can usually be obtained by stereotactic biopsy. The tumor is localized by CT or MRI using a head-mounted frame or other system that provides three-dimensional reference coordinates. The CT or MRI images and coordinates are used to guide a needle to the tumor through a small opening in the skull. The tissue is initially examined by frozen section to confirm that the tumor has been sampled, and other tissue samples are submitted for permanent paraffin sections.

The medical team

Your medical team will include several experts experienced in different medical specialties. These different specialties might be neuro-oncology (the medical treatment of brain tumors), neurology (conditions of the nervous system, such as the brain and spinal cord), surgery, radiology (MRI/CT), radiation therapy, and pathology (the study of tissue). The make-up of your medical team will vary depending on the type and location of your tumor, and it may include experts representing a variety of different medical cross-specialties. It is essential that your medical team include experts experienced specifically in the treatment of brain tumors.

A medical (board-certified) oncologist treats many forms of cancer; however, not all oncologists are experts in treating brain tumors. As part of your medical team, your general oncologist can assist you with obtaining second opinions and researching available treatment options, but he or she should refer you to a neuro-oncologist experienced specifically in the treatment of brain tumors. Most neuro-oncologists are also neurologists, treating disorders of the nervous system (some also started as general oncologists) as well as general cancer. It is important that you establish that he or she is experienced in treating your type of tumor and is up to date on advances in both surgery and alternative treatments. If a neuro-oncologist is not available in your area, an experienced oncologist is the next best thing.

A neurosurgeon is someone who performs surgery involving the nervous system, typically specializing in one particular area or system, such as the spine. Before considering any surgical procedure, it is important to know the experience level of your neurosurgeon, opting for a second opinion (preferably) from a neurosurgeon

.....
: For breaking news about brain tumor treatments, regularly visit the news :
: page of the Musella Foundation website and subscribe to the "Brain Tumor :
: News Blast." Go to: www.virtualtrials.com/news.cfm. :
:.....

Brain Tumor Guide for the Newly Diagnosed

associated with a major brain tumor center. While some neurosurgeons also practice neuro-oncology and oversee the administration of chemotherapy treatments, most confine their practice to surgical therapy and follow-up care.

A neuroradiologist is a specialist in the area of reading MRI and CT scans involving the nervous system. Your MRI or CT scans should always be reviewed by a neuroradiologist experienced with tumors within the brain.

A radiation oncologist specializes in the administration of radiation therapy (solely and specifically) and should work in cooperation with your neuro-oncologist/surgeon to develop an appropriate course for the duration and intensity of your radiation therapy.

You should consider other specialists for complementary care throughout your treatment and recovery, such as:

- Rehabilitation specialists (physical/speech therapist, occupational therapist)
- Neuropsychologists and psychiatrists
- Endocrinologists
- Ophthalmologists (eye doctors)
- Dentists (especially important prior to chemotherapy)
- Pharmacists
- Nutritionists
- The group of doctors at your hospital of care who might undertake the tumor board review of your tumor treatment

What questions should I ask my medical team?

- What type of brain tumor do I have?
- What is the grade of the brain tumor?
- Are any additional tests needed?
- How many tumor types like this do you treat each year?
- Will the brain tumor board review my case? How often?
- Where would you recommend I get a confirming/second opinion?
- Do you have any written information about my type of brain tumor?
- How will the brain tumor affect my functioning?

Four: How Brain Tumors are Diagnosed

- What are my treatment options?
- Which treatment do you recommend? Why?
- Which clinical trials do I qualify for, and which do you recommend?
- Can you recommend an oncologist who specializes in this type of brain tumor?
- What other specialists will be part of my care?
- What is the timeline for treatment(s)?
- Where will I get the treatment?
- Will I be able to drive myself to and from treatment?
- Will my medical insurance cover this type of treatment?
- How will this type of treatment affect my work schedule?
- Will I need to apply for disability? Social Security disability?
- Will I need to take medications? If so, what kinds and how often?
- Are there any side effects? What kind?
- Are there short-term and long-term side effects?
- How can side effects be managed? By medicines? By physical therapy?
- Will my quality of life change? Will I function differently?
- Will I see a change in my personality? Appetite? Sleep habits? Memory?
- What can I expect before, during, and after treatment?
- What is the follow-up plan if this treatment doesn't work?
- How often will I need follow-up imaging scans? What kind of scans?
- Do you think I should attend a support group now? Are there any support groups nearby?



Please remember

- ✓ Get copies of your brain scans (or a CD of them) and their interpretations, and share them with other members of your medical team to ensure that they agree with the interpretations.
- ✓ Understand the different functions of the members of your medical treatment team.
- ✓ Make yourself certain that the members of your medical team are experienced specifically in the treatment of brain tumors.
- ✓ Using the questions in this book as a guide, prepare your own list of questions, being sure to ask the members of your medical team about treatment options.

Survivor story #4

My brain tumor story began in late 2006, when I suffered a series of debilitating seizures. Such symptoms would typically result in emergency treatment, but my case was complicated by the fact that I had suffered from epilepsy since childhood. It had been kept under control with medication, and by 2006 I had been seizure-free for years. Nonetheless, my physicians attributed these new seizures to my old epilepsy condition. Medication was increased but the convulsions grew progressively worse. One day in early 2007, I awoke to find the right half of my face paralyzed, with generalized stiffness on the right side of my body. My wife took me to the emergency room. I underwent a CT scan, which showed a large tumor in my left frontal lobe along the motor strip.

In February 2007, I had a total resection. Before the operation, the surgeon had requested my permission to be as aggressive as possible (permission I granted) but warned me to be prepared for deficits, including the possibility of paralysis of one side of the body. In reality, my only postoperative deficits were similar to the preoperative ones: facial paralysis, right-side weakness, and minor aphasia. These problems gradually improved in the weeks, months, and years following the operation.

I was sent home to await the pathology report, which arrived within a few days. The diagnosis was glioblastoma, a conclusion confirmed by two other laboratories, which independently analyzed the tumor tissue on paraffin slides. I received the usual prognosis for this disease: almost certain recurrence within 1 year, with slim odds of surviving more than 3 years. Molecular testing reported that the MGMT status of my tumor was unmethylated, meaning that my tumor was less likely to respond to chemotherapy with alkylating agents like temozolomide (Temodar).

I sought out therapeutic options. At that time where I lived abroad, what is now the current standard-of-care therapy for glioblastoma was not widely applied. But I found and read the famous paper by Stupp et al entitled "Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma," which showed benefit for concurrent administration of daily temozolomide during a 6-week period of radiotherapy followed by adjuvant therapy with temozolomide. I found two radiation oncologists who were willing to offer this therapy to me, and I got started immediately.

Even before the radiation phase, I had begun to read everything I could find about brain tumors, searching for ways to improve my survival probabilities. The website PubMed (www.pubmed.com), the US National Library of Medicine index of medical articles published worldwide, was an invaluable resource. At some point I stumbled on the Musella Foundation virtualtrials.com website, which also provided me with

Brain Tumor Guide for the Newly Diagnosed

substantial information about my illness. I found Ben Williams's story on that website to be particularly interesting and the logic behind his treatment approach compelling. I read Ben's book and his periodic updates, which led to an exchange of email, followed by several telephone conversations. Throughout my ordeal Ben has been an invaluable source of knowledge and support for me, as he has been for many other patients.

I was in the fortunate position of having had a total resection of my brain tumor. However, I was aware that the odds of recurrence within 1 year were extremely high, and that a recurrent tumor is more difficult to control than a newly diagnosed tumor due to its acquired resistance to first-line therapies. My goal, therefore, became that of postponing a recurrence for as long possible and to do so by all means at my disposal. The approach was along the lines of that advocated by Ben Williams: to block multiple tumor growth mechanisms by means of a "cocktail" of agents that have shown some evidence of efficacy against glioblastoma or other types of cancer.

During the 6 weeks of radiation, I had ample time to start planning for the next treatment phase. My oncologist proposed 8 28-day cycles of temozolomide on the standard schedule of drug administration on days 1 to 5 of each cycle followed by 23 days off. I had read that this schedule provided limited benefit for someone like me, whose tumor MGMT status was unmethylated. But there were some positive reports of experiments using a low-dose daily (metronomic) schedule, in which MGMT methylation status had less of an effect on patient outcomes.

Based on this argument, I lobbied my physicians to try the metronomic schedule, and they said that they would consider it. In 2007 the drug bevacizumab (Avastin) was becoming popular as an experimental treatment for recurrent glioblastoma. Bevacizumab is an anti-angiogenesis drug that inhibits the growth of new blood vessels to feed the tumor. Based on positive results from various early studies, I wanted to add bevacizumab to the proposed metronomic therapy for temozolomide. This highly anti-angiogenic approach was attractive to me because it had the potential to forestall recurrence by delaying the growth of blood vessels in the tumor area. I discussed the idea with some prominent neuro-oncologists around the world and received encouragement from many quarters. Physicians at one particular comprehensive cancer center were particularly enthusiastic and generously offered to write letters of support for my plan. With help from a researcher, I drafted a proposal for my bevacizumab/metronomic temozolomide treatment plan, which I presented to my oncologists. They were interested in seeing whether such a treatment plan could work in a case like mine. Provided that I sign a consent form, they were willing to send the proposal through the hospital's internal review board, which approved it as a one-person experiment.

Four: How Brain Tumors are Diagnosed

Things were looking good, but I wanted to pursue a more aggressive strategy. I added chloroquine to the therapy, after reading papers that showed that it improved results for chemotherapy. I likewise included verapamil, which could potentially inhibit extrusion of chemotherapy agents from cancer cells and help prevent multi-drug resistance. Another addition was aspirin (200 mg/day), mainly as a prophylactic against blood clots from bevacizumab, but it had potential anti-cancer benefits in its own right. The drug celecoxib was also included early on due to promising results from small clinical trials for brain tumors and other cancers. Before going further, I compiled a list of 60-plus agents that could potentially contribute to the therapy, which fell into three categories: (a) they had shown efficacy against some form of cancer, either in clinical or preclinical settings; (b) they had been shown to be synergistic with chemotherapy or other substances already in my therapy; or (c) they had demonstrated positive effects in building up the immune system. The list was eventually refined to 27 substances, many of which were natural supplements, for example, green tea extract, fermented papaya extract, omega-3 fish oils, resveratrol, melatonin, mushroom extracts, selenium, and so on.

With minor exceptions, my MRI scans have been clear since the summer of 2007. There were a few scares during the first 2 years, with images showing small degrees of enhancement in and around the tumor cavity. But these abnormalities, which could indicate recurrence, were likely due to radiation damage. In any case they have disappeared over time. I now get yearly MRI scans, and no changes have been noted for many years.



Brain Tumor Guide for the Newly Diagnosed

Note that if I had to go through this again, I would alter many of the details in my treatment plan based on discoveries made in years subsequent to my diagnosis. I would not, however, change my treatment approach — that is, to battle the tumor aggressively using multiple agents simultaneously, thereby inhibiting as many growth pathways as possible.

It has been over 9 years since my diagnosis without any signs of recurrence. After I have passed the 10-year survival point, I will switch from once-per-year to every-other-year MRI scans. I still believe that my approach was the most effective way to treat a glioblastoma. For other patients with brain tumors, I thus advise the following:

- Become as educated as possible about this disease and participate in formulating your treatment plan to the best of your ability.
- Make your voice heard.
- Never be afraid to ask questions or offer suggestions, based on what you have learned from other sources (including other patients).
- Finally, if you feel like your input is being ignored, find another physician who will listen to you.





The standard-of-care treatment of high-grade malignant glioma

The standard-of-care treatment of newly diagnosed high-grade malignant glioma usually consists of four different types of treatment — surgery, radiation therapy, systemic chemotherapy, and alternating electric field therapy (the Optune device). You should understand each of these types of treatment and the sequence in which they are used.

You should also understand that although this standard-of-care treatment has been found in clinical trials to extend survival time after the diagnosis of high-grade malignant glioma — sometimes considerably — nevertheless it only actually “cures” brain tumors in a relatively small number of persons.

For that reason, all persons newly diagnosed with high-grade malignant glioma should consider enrollment in a clinical trial of an experimental therapy. Clinical-trial enrollment can occur at the very start of your treatment, or it can occur later. Clinical trials and their importance are discussed in Chapter 6.

The National Comprehensive Cancer Network (NCCN) is a not-for-profit alliance of 27 leading cancer centers dedicated to improving the quality, effectiveness, and efficiency of care so that patients can live better lives. The NCCN issues *Clinical Practice Guidelines in Oncology* (NCCN Guidelines) for treatment of different types of cancer, which are regularly updated. In 2018, the NCCN issued updated guidelines for treatment of central nervous system cancers, which include anaplastic gliomas and glioblastomas. These guidelines represent a consensus — based on published medical evidence and expert opinion — about what is the best treatment for typical patients with newly diagnosed or recurrent brain tumors. As such, the NCCN recommendations represent a general standard of care, although there are variations in “standard” treatment among the participating cancer centers.

Because patients newly diagnosed with high-grade malignant glioma will be seen by multiple different medical specialists, the NCCN strongly recommends

close and regular communication among all providers across the different medical services involved — including physical and occupational therapists, psychologists, and social workers. Bear in mind that this type of interaction is more likely to occur at comprehensive cancer centers and at hospital systems with established brain tumor boards.

Surgery

Surgery is performed to improve neurological function, to obtain an exact diagnosis of the brain tumor, and to completely remove the brain tumor (the removal is often referred to as a total resection). Ideally, it will be possible to perform a maximally safe total resection of the brain tumor. But if that is not possible, a sub-total resection or a stereotactic or open biopsy will take place, in each case obtaining a sample of tumor tissue for the pathologist to examine in making a diagnosis.

Be sure to ask your surgeon for a copy of the pathology report from the procedure. Although it may be expensive to do so, you can readily get a second opinion on the reading of the pathology slides. There is a lot of interpretation put into the reading of the pathology slides, and this is the single most important diagnosis you will ever have in your life, so it may be worth the money to double-check it. Best of all, getting a second opinion will not involve any pain — and can be accomplished by mail — so there will be no need for additional travel.

For some benign brain tumors, surgery may be curative. For high-grade malignant brain tumors, surgery may relieve symptoms caused by too much pressure in the brain and allow time for other treatments to work. Malignant brain tumors can grow so fast that without surgery, other treatments might not have the time to work. Surgery is also an opportunity to try experimental treatments that require direct access to the brain.

Surgery is performed by a neurosurgeon. However, a general neurosurgeon may not have adequate experience in the removal of brain tumors and may be less informed regarding current treatment therapies. Because most neurosurgeons do not see many brain tumors, you need to find one that specializes in brain tumors. Check out the websites of potential neurosurgeons to make sure that “brain tumors” is listed as one of the main areas of expertise. An “expert” is defined as a neurosurgeon who performs a minimum of 25 surgeries per year. Typically these neurosurgeons are associated with major brain tumor centers. Studies indicate that major brain tumor centers and/or surgical teams that perform 50 or more surgeries a year achieve better survival rates with fewer complications.

.....
: The National Comprehensive Cancer Network (NCCN) is a not-for-profit
: alliance of 27 of the leading cancer centers in the United States. The NCCN
: publishes evidence-based, consensus-driven guidelines for the treatment of
: different types of cancers, including guidelines for the treatment of brain
: tumors in the document entitled “Central Nervous System Cancers.” The
: standard-of-care treatment for high-grade glioma that is described in this book
: derives from the most recent version of this guideline, dated March 20, 2018.
: To access this guideline, go to: [www.nccn.org/professionals/physician_gls/
: pdf/cns.pdf](http://www.nccn.org/professionals/physician_gls/pdf/cns.pdf). You may have to register before downloading the guideline.
:

“Brain surgery” sounds like a very scary thing. It is. But as previously mentioned, it is now much safer and easier than ever. Moreover, the goal of a maximally safe resection is now more often reached with the help of intraoperative imaging or by means of fluorescence-guided visualization of tumor tissue, which represents an important advance. During surgery, it is sometimes extremely difficult to distinguish tumor and infiltrated tissue from surrounding healthy brain. An oral drug called aminolevulinic acid (Gleolan) is now available for causing tumor cells to become fluorescent — that is, to light up under a microscope with a special blue light — thereby helping neurosurgeons remove as much tumor as possible without harming healthy tissue.

There are still some brain tumors that are too dangerous to remove because of their size or location, but the limits to what is possible are shrinking every year. If you are told that your tumor is inoperable, or that a total resection of the brain tumor is not possible, get another opinion.

While surgery of the brain tumor is essential, even a total resection will not remove all the brain tumor cancer cells. For that reason, other treatments are needed. So even before surgery, you need to be preparing with your medical team a list of options for postsurgical treatment. Here are some of the things you should request and/or ask about even before surgery occurs:

- Before surgery, double-check that the testing of your tumor tissue will involve molecular markers. As noted in chapter 3, there are molecular markers in brain tumors that can indicate drug resistance and thus influence choices about postsurgical treatment. In addition, specific genetic mutations can determine eligibility for specifically targeted immunotherapy trials or for drugs that are approved for types of cancer other than brain tumors.

Brain Tumor Guide for the Newly Diagnosed

Major brain tumor centers routinely perform molecular-marker testing of tumors, but you should ask anyway. Caris Life Sciences (www.carislifesciences.com) and Foundation Medicine (www.foundationmedicine.com) are companies that can perform a complete genetic and mutational testing of your tumor. Although this service is expensive, some insurance companies do cover the cost.

- Before surgery, find out how your brain tumor tissue will be preserved after extraction. If the specimen will not be immediately used either to create a custom-made vaccine or to serve for molecular-marker testing, ask if the specimen can be frozen for future use if needed, and ask about the costs involved.
- Before surgery, ask about personalized vaccine therapy, which requires a tumor sample.
- Before surgery, ask about clinical trials that require registration even before surgery occurs.
- Before surgery, ask about the possibility of implantation of Gliadel wafers within the brain tumor cavity during surgery. Gliadel wafers are implanted as adjuvant local chemotherapy for the treatment of newly diagnosed high-grade malignant brain tumors and recurrent glioblastoma. After implantation, Gliadel wafers dissolve, eluting the chemotherapeutic drug carmustine to treat residual cancer cells immediately after surgery. In the NCCN guidelines, Gliadel wafers are considered optional for patients who receive a maximally safe resection. Be aware that implantation of Gliadel wafers during surgery may make you ineligible for some clinical trials further on in your treatment, so plan ahead.

Most long-term survivors of high-grade malignant glioma have had multiple surgeries. Usually, surgery will not be as bad as you expect. The worst part may just be worrying about it the night before. There are risks to surgery anywhere in the body, but surgery today is much safer and easier than it was even 10 years ago. Serious side effects are much less common than they used to be, so don't let horror stories from the past bother you. Problems do still occur but not as frequently as in the past.

Laser ablation therapy

Laser ablation therapy is a relatively new yet proven minimally invasive technology that uses precise, high-intensity laser energy to destroy tissue in the brain, while

Five: The standard-of-care treatment of high-grade malignant glioma

limiting injury to healthy tissue. This type of treatment can be used with lesions in many locations in the brain, near the surface or deep inside. During the procedure, doctors use MRI to guide the laser device precisely to the lesion. The procedure has been used with thousands of patients and has been shown to be successful in reducing or removing diseased tissue. The technical name for the procedure is Laser Interstitial Thermal Therapy (LITT). LITT is not part of the usual standard-of-care treatment, but you should know about it.

Unlike traditional brain surgery, LITT does not require a large opening in the head. Instead, physicians make a small hole in the skull, about as big around as a pencil. While the head is secured in place, they guide a small laser device (probe) through that hole precisely into the lesion. The probe delivers laser light energy to heat up and destroy the lesion — a process called ablation. The precise nature of the procedure helps to lessen the likelihood of harm to nearby healthy brain tissue.

LITT might be prescribed when a brain tumor is situated in a place that could be difficult to treat with conventional surgery without harming the brain and the person's ability to function. The LITT tool that is most commonly used is the NeuroBlate system (Monteris Medical, Plymouth, MN), and information about it can be found at the following website: www.monteris.com.

Treatment after surgery: NCCN recommendations

In the NCCN guidelines, treatment of newly diagnosed high-grade malignant glioma is determined on the basis of three different characteristics: (1) age (≤ 70 years versus >70 years), (2) performance status, and (3) methylated (favorable) versus unmethylated (unfavorable) O6-methylguanine-DNA methyltransferase (MGMT) promoter status. Performance status is measured by the **Karnofsky Performance Status** (KPS) test, an assessment tool for functional impairment commonly used for

Karnofsky Performance Status (kar-NOF-skee per-FOR-munts STA-tus): A standard way of measuring the ability of cancer patients to perform ordinary tasks. The Karnofsky Performance Status scores range from 0 to 100. A higher score means the patient is better able to carry out daily activities. Karnofsky Performance Status may be used to determine a patient's prognosis, to measure changes in a patient's ability to function, or to decide if a patient could be included in a clinical trial. Also called KPS.

cancer patients. Patients with a KPS score ≥ 60 can handle most of their own needs with occasional assistance. The KPS score can be used to guide consideration of treatment options.

The recommended NCCN treatments for newly diagnosed glioblastoma are broken out for patients ≤ 70 years of age in **Table 1** (see page 56) and for patients >70 years old in **Table 2** (see page 57). As you will see in each of these tables, there are several treatment options geared to MGMT promoter status and KPS score.

For every category of patient, enrollment in a clinical trial is recommended. The next most common treatment recommendation after surgery consists of:

- Standard radiation therapy
- Oral chemotherapy with temozolomide (Temodar) during radiation therapy (when it is called concomitant therapy) and then after radiation therapy (when it is called adjuvant therapy).
- Alternating electric field therapy (the Optune device) after radiation therapy (as an adjuvant therapy).

Standard radiation therapy starts a few weeks after surgery and takes place 5 days per week for 6 weeks. Concomitant daily treatment with **temozolomide** starts at the same time as radiation therapy.

After the 6-week course of radiation therapy and temozolomide is completed, and then a 4-week break for recovery, treatment with temozolomide and with alternating electric field therapy can commence. For patients with high-grade malignant glioma, temozolomide is usually given for six 28-day cycles of adjuvant therapy, with the drug administered on days 1 to 5 of each 28-day cycle. The Optune is a battery-operated device worn on the scalp that delivers alternating electric fields that disrupt the division of tumor cells. The device is intended to be worn for up to 18 hours per day.

If this standard-of-care treatment is not offered to you, you should ask why not. If cost is the barrier to receiving any part of this standard-of-care treatment, contact us. The Musella Foundation has a co-payment assistance program that may be able to help you in some circumstances with your out-of-pocket expenses.

Temozolomide (teh-moh-ZOH-loh-mide): *A drug used to treat certain types of brain tumors. It is also being studied in the treatment of other types of cancer. Temozolomide damages the cell's DNA and may kill cancer cells. It is a type of alkylating agent. Also called Temodar.*

Five: The standard-of-care treatment of high-grade malignant glioma

The virtualtrials.com website hosts a video library, with up-to-date videos from medical and patient brain tumor conferences that cover all aspects of brain tumor treatment, from radiation therapy to the latest chemotherapeutic drugs. To view a menu of these videos and to start watching them, go to: www.virtualtrials.com/video.cfm.

Radiation therapy

Radiation therapy is typically performed (under the care of a radiation oncologist or neurosurgeon) after surgery or in cases where surgery is not an option due to the location or size of the brain tumor. The tumor and a small margin around the tumor are usually targeted by a powerful beam of radiation.

Because tumor cells reproduce much more frequently than normal brain cells, they are more affected by radiation than normal cells. The radiation disrupts the DNA of the cells that are reproducing. Compared to tumor cells, normal cells are also better able to repair damage caused by radiation.

The NCCN recommendations mention two different types of radiation therapy — standard and hypofractionated. The term hypofractionated means that the total dose of radiation is divided into large doses and treatments are given once per day or less often. Compared with standard radiation therapy, then, hypofractionated radiation therapy is provided over a shorter period of time (fewer days or weeks), and it is often given to frail patients or to the elderly.

Standard radiation therapy requires a few minutes of treatment five times per week for 6 weeks, together with concomitant administration of temozolomide. Side effects of radiation, which can range from mild to severe, include skin burning and peeling, swelling (edema), diarrhea, and nerve damage.

- For help paying for medications, two resources are available:
- NeedyMeds, a nonprofit information resource devoted to helping people in need find assistance programs to help them afford their medications and costs related to health care: www.needymeds.org.
 - The Musella Foundation co-pay assistance program can help patients pay for one or more of the following treatments: bevacizumab (Avastin), Gliadel wafer, temozolomide (Temodar), and the Optune device: www.braintumorcopays.org.

Stereotactic radiosurgery

Although no “knife” or incision is used to expose the brain during stereotactic radiosurgery (SRS) but rather a precise high-dose beam of radiation, SRS is considered “surgical” because of the degree of change that takes place after the procedure. Although not part of the standard-of-care treatment, it is good to know about SRS.

SRS can involve one treatment session or several (fractionated) sessions over a period of several days or weeks, assisted by computer-aided planning. SRS delivers a much higher dose of radiation to the target than conventional radiation therapy. For some low-grade tumors, SRS can be curative. SRS is also sometimes used as a boost at the end of standard radiation therapy or for small tumor recurrences.

Many different manufacturers have developed devices for administering SRS. Some of the notable brands are Gamma Knife, Novalis System, Linac, and Cyberknife. Each SRS device has its own advantages and disadvantages. Just know that if you are told your tumor is too large or the wrong shape for SRS, get another opinion from a doctor who uses a different type of SRS device.

Chemotherapy with temozolomide

Chemotherapy is the use of drugs to kill tumor cells. Chemotherapy drugs work in several ways, each unique to the type of treatment recommended, by (1) destroying the tumor’s DNA directly; (2) restricting the tumor cell’s ability to divide, grow, and invade healthy tissue; or (3) blocking the blood supply to the tumor itself and inhibiting the growth of new blood vessels that would otherwise feed the tumor.

Temozolomide is an alkylating agent. These drugs damage the DNA of cancer cells to keep them from making more copies of themselves. Treatment with the combination of radiation therapy plus concomitant and adjuvant temozolomide has been found to improve survival in all patient groups, even elderly patients. As a concurrent treatment with radiation therapy, temozolomide is administered daily. After the 6-week course of radiation therapy is completed, a 4-week interval follows in order to allow recovery, during which no treatment takes place. Then adjuvant temozolomide is administered for six cycles of 28 days, with the drug given on days 1 to 5 of each 28-day cycle.

For alkylating agents like temozolomide and like carmustine (the chemotherapeutic agent used in the Gliadel wafer), methylation of the promoter of MGMT is a

Five: The standard-of-care treatment of high-grade malignant glioma

major favorable prognostic factor, and it is found in approximately 35% to 45% of patients with grade III and grade IV gliomas. That is, if you have an MGMT-methylated tumor, temozolomide (or carmustine) is more likely to provide a greater magnitude of progression-free and overall survival than if you have an MGMT-unmethylated tumor. Consequently, if you are among the majority of patients with an MGMT-unmethylated tumor, you should seriously consider enrollment in a clinical trial because it is likely that you will derive less benefit from standard-of-care treatment.

Please note that different treatment durations of adjuvant temozolomide are sometimes used rather than the standard six cycles of 28 days. For example, some doctors use temozolomide for specific time periods such as 12, 18, or 24 months, while others use it until it stops working or causes side effects or until the tumor is either completely gone or sufficiently stable.

Temozolomide is administered orally. The common side effects of chemotherapy include nausea, weakness and fatigue, dehydration, and low white blood cell counts, which increase the risk of infection. Because a simple cavity or early gum infection (gingivitis) can quickly escalate into an acute infection for a patient undergoing chemotherapy, you should obtain a thorough dental examination prior to beginning chemotherapy and follow up frequently with your dental care team.

Alternating electric-field therapy

The Optune is a wearable battery-operated device that has recently been approved by the Food and Drug Administration (FDA) for the treatment of newly diagnosed glioblastoma. The device is approved for use in combination with temozolomide adjuvant therapy after concurrent radiation therapy and temozolomide treatment are completed. The Optune device has also been approved by the FDA for treatment of recurrent glioblastoma.

The Optune device delivers alternating electric fields (also called tumor-treating fields) through four insulated transducer arrays. These arrays are worn on a shaved scalp and are connected with a battery-operated electrical-field-generating device, which can be carried as a travel case or backpack. The transducer arrays can be worn continuously for 3 to 4 days before they need to be removed for hygienic care of the scalp, re-shaving of hair, and reapplication with a new set of arrays. Loose-knit wigs, hats, or other head coverings can all be worn over the arrays. The illustration on the opposite page depicts a man wearing Optune arrays while opening the Optune travel case/backpack.

.....
: For a full overview of Optune, with frequent updates, visit the Optune :
: website: www.optune.com. Because Optune is a new treatment, this :
: website can help you find doctors in your area who are certified in its use. :
.....

Alternating electric fields selectively disrupt the division of cells by delivering low-intensity, intermediate-frequency alternating current. These alternating electric fields affect only dividing cells; non-dividing cells are spared. Since alternating electric fields do not enter the bloodstream like drugs, they do not affect cells in other parts of the body.

A large randomized controlled trial has been conducted to compare the use of the Optune device plus adjuvant temozolomide versus the use of adjuvant temozolomide alone in patients with newly diagnosed glioblastoma who had received radiation therapy along with concurrent temozolomide. The FDA actually stopped this trial early because there were clearly evident increases in progression-free and overall survival in the group treated with Optune device plus temozolomide compared with the temozolomide-only group.

The FDA stated that all of the patients in the trial should be allowed to benefit from Optune treatment. This FDA action might be the first time ever that a brain tumor trial was stopped early because a treatment was found to be so clearly effective.

Doctors must be trained and certified to prescribe the Optune device. The device is intended to be worn continuously for at least 18 hours per day, and a shaved scalp must be maintained for the duration of therapy. If that seems burdensome, recent studies clearly indicate a dose-response curve with alternating electric-field therapy: patients who have the highest compliance (>90%) in



*The Optune array and carry case / backpack.
Courtesy of Novocure, Inc. © Novocure 2016.
All rights reserved.*

Five: The standard-of-care treatment of high-grade malignant glioma

wearing the device for ≥ 18 hours per day have the best outcomes, including, in one subanalysis, a 5-year survival rate approaching 30%.

The most common side effects seen with use of the Optune device are mild-to-moderate scalp irritation and headache. Because the Optune device has to be worn practically continuously, it is for some patients a disturbingly constant reminder of the disease. Patients who choose not to use the Optune device should therefore not feel guilty about seeking other treatments.

Long-term side effects

In the past, the consequences of long-term side effects were never a big concern because people with newly diagnosed high-grade malignant gliomas did not live long enough for them to be a concern. Fortunately, there has been a steady rise in the number of long-term survivors of brain tumors, largely due to the success of the standard-of-care treatment described in this chapter. Now long-term side effects have to be considered when choosing a treatment.

Radiation therapy can cause vascular injury and increase the risk of stroke. Unfortunately, stroke is fairly common among long-term survivors of brain tumors and can be either completely asymptomatic or completely devastating, depending on the location. The possibility of stroke can be reduced by managing risk factors. Please talk to your doctor about stroke risk. Another long-term side effect of radiation therapy is cognitive loss, which varies with the dose of radiation and the volume and location radiated. Cognitive loss is nearly universal with whole brain radiation. These side effects can be minimized by limiting the treatment to only the site of the tumor and a small margin around the tumor.

Chemotherapy is often associated with long-term infertility, but you can offset this side effect by freezing sperm or eggs before chemotherapy begins. Fertility may be the last thing you are worried about now, but what happens if you want kids in a few years and cannot have them? Think about it.

There are also rare cases of myelodysplasia or “preleukemia” conditions related to chemotherapy, particularly in association with alkylating agents like temozolomide. So although the optimal duration of temozolomide treatment remains unknown, staying on the agent forever could increase the associated risk. More research is needed on this question. ●

Table 1: NCCN treatment recommendations for patients with newly diagnosed glioblastoma who are ≤ 70 years of age

Glioblastoma Plus age ≤ 70 years	NCCN Recommendation
Good performance status (KPS ≥ 60) + methylated MGMT promoter status	Consider clinical trial (preferred for eligible patients) <u>OR</u> Standard brain RT + concurrent TMZ and adjuvant TMZ with or without alternating electric field therapy
Good performance status (KPS ≥ 60) + unmethylated or indeterminate MGMT promoter status	Consider clinical trial (preferred for eligible patients) <u>OR</u> Standard brain RT + concurrent TMZ and adjuvant TMZ with or without alternating electric field therapy <u>OR</u> Standard brain RT alone
Poor performance status (KPS < 60)	Fractionated brain RT with or without concurrent TMZ or adjuvant TMZ <u>OR</u> TMZ <u>OR</u> Palliative / best supportive care

KPS = Karnofsky Performance Status; MGMT = O6-methylguanine-DNA methyltransferase; RT = radiation therapy; TMZ = temozolomide (Temodar)

Five: The standard-of-care treatment of high-grade malignant glioma

Table 2: NCCN treatment recommendations for patients with newly diagnosed glioblastoma who are >70 years of age

Glioblastoma Plus age >70 years	NCCN Recommendation
Good performance status (KPS ≥60) + methylated MGMT promoter status	Consider clinical trial (preferred for eligible patients) <u>OR</u> Fractionated brain RT + concurrent TMZ and adjuvant TMZ <u>OR</u> Standard brain RT + concurrent TMZ and adjuvant TMZ with or without alternating electric field therapy <u>OR</u> Standard brain RT + concurrent TMZ and adjuvant TMZ <u>OR</u> TMZ <u>OR</u> Fractionated brain RT alone
Good performance status (KPS ≥60) + unmethylated or indeterminate MGMT promoter status	Consider clinical trial (preferred for eligible patients) <u>OR</u> Fractionated brain RT + concurrent TMZ and adjuvant TMZ <u>OR</u> Standard brain RT + concurrent TMZ and adjuvant TMZ with or without alternating electric field therapy <u>OR</u> Standard brain RT + concurrent and adjuvant TMZ <u>OR</u> Fractionated brain RT alone
Poor performance status (KPS <60)	Fractionated brain RT alone <u>OR</u> TMZ <u>OR</u> Palliative / best supportive care

KPS = Karnofsky Performance Status; MGMT = O6-methylguanine-DNA methyltransferase; RT = radiation therapy; TMZ = temozolomide (Temodar)



Please remember

- ✓ Consider entering a clinical trial.
- ✓ The current standard-of-care treatment for newly diagnosed high-grade malignant glioma consists of 4 different treatments, depending on patient and tumor characteristics: (1) surgery; (2) radiation therapy; (3) systemic chemotherapy with temozolomide during radiation therapy and then after; and (4) alternating electric field therapy (the Optune device) after radiation therapy.
- ✓ If the standard-of-care treatment is not offered to you, ask why not.
- ✓ Find an expert neurosurgeon specializing in brain tumors.
- ✓ If you are told that your brain tumor cannot be maximally resected or is inoperable, seek a second opinion.
- ✓ Before surgery takes place, ask about molecular-marker testing, enrollment in clinical trials, custom-made vaccines, and implantation of Gliadel Wafers.
- ✓ Use the Optune website to find doctors who are trained in administering the device.

Survivor story #5: Ben Williams

At the age of 50, I had surgery for glioblastoma on March 31, 1995, after an MRI scan in the emergency room the preceding day. The tumor was located in my right parietal cortex and was very large (it was approximately 180 cc and described as the “size of a large orange”). My neurosurgeon later told me that I would have been dead within two weeks had I not had the surgery when I did.

During the first two months after my diagnosis, I spent many hours on the Internet and in our medical school library, learning all that I could about possible treatment options. While I initially entertained boron neutron capture therapy, gene therapy, and radiation-loaded monoclonal antibodies as much more promising than conventional treatment, I finally rejected all of these based on likely problems of various sorts. I therefore opted for conventional chemotherapy but in combination with other agents that seemed likely to improve the effectiveness of chemotherapy over that which typically occurs.

All of my MRI scans since chemotherapy have been free of any sign of tumor. Throughout my first year of treatment I added various nutritional supplements that can be obtained at most health food stores. The inspiration for the various treatments and health food commodities I have opted for has come from many different sources. Much of it came from my own research on Medline, sometimes after hearing about a treatment in passing from participants in an online support group. I also found the webpage of the Musella Foundation as a source of leads to follow up on.



Brain Tumor Guide for the Newly Diagnosed

My treatment philosophy has been very similar to the treatment approach that has developed for AIDS. Both HIV and cancer involve biological entities that mutate at high rates, so unless a treatment is almost instantaneously effective, the dynamics of evolution will create new forms that are resistant to whatever the treatment may be. However, if several different treatments are used simultaneously (instead of sequentially, which is typically the case), any given mutation has a much smaller chance of being successful.

A second feature of my treatment philosophy is that any successful treatment will need to be systemic in nature, since it is impossible to identify all of the extensions of the tumor into normal tissue.

*Ben Williams, a 24-year survivor of glioblastoma, is the author of the 2002 book **Surviving Terminal Cancer: Clinical Trials, Drug Cocktails, and Other Treatments Your Oncologist Won't Tell You About**. At the virtualtrials.com website, he has posted various updates of this book as well as a 2017 update of the long report entitled "Treatment options for malignant gliomas." To access these important sources, go to: www.virtualtrials.com/williams.cfm.*





The importance of clinical trials

Clinical trials offer experimental treatments that may provide new inroads for extending life expectancy and improving quality of life. Understanding the current availability of clinical trials requires time and due diligence. We hate to say this, but some doctors are reluctant to refer you to other treatment centers. You must search out for yourself the appropriate clinical trials available for your specific tumor type, always advocating in your own best interests toward a cure.

A clinical trial is the best way of trying experimental therapies, for the doctors will watch you very carefully for signs of side effects. But there is another way for terminally ill patients to gain access to an experimental treatment in the United States. That is the Right to Try law, which allows terminally ill patients access to experimental drugs and devices. The Right to Try law is discussed below in the section about treatments approved by the US Food and Drug Administration (FDA).

People in clinical trials seem to do better than people who choose not to participate. And once a cure is actually found, the first people to get it will be those in the clinical trial for it. Cures have been found for other types of cancer, and it will happen for brain tumors, someday soon it is hoped.

Understanding clinical trials

Clinical trials have a designation — phase I, phase II, or phase III — that is based upon the specific types of questions that are being asked about the treatments in question. These clinical trial phase designations are defined by the FDA in the Code of Federal Regulations.

Brain Tumor Guide for the Newly Diagnosed

- In a phase I trial, a new drug or treatment is studied in a small group of people (20 to 80 patients or volunteers) for the first time to evaluate its safety, determine a safe dosage range, and identify potential side effects.
- In a phase II trial, the study drug or treatment is given to a larger group of people (100 to 300 patients) and further assessed for effectiveness and safety. The dosage of medication may be increased to determine toxicity levels.
- In a phase III trial, the study drug or treatment is given to large groups of people (300 to 3000 patients) to confirm its effectiveness within a sizable population, monitor side effects and toxicity levels, compare it with standard treatments, and further determine safety.

Statistics are used to try to make sense of the trial results. A number is calculated called the significance level. The number usually chosen as the benchmark is 0.05, which means that there is a 95% chance that the effect seen in the trial was caused by the treatment and not by chance alone. Conversely, this means that if you run 100 trials of a worthless drug, about 5 of those trials may report success even though there is none. This is why multiple trials are needed, and it is best if they are conducted by different centers.

The FDA will approve a drug that is better than standard treatment, or is at least as good as standard treatment, if it has fewer side effects. Once a treatment is approved by the FDA, everyone can get access to it, not just those in clinical trials.

Why should you consider participating in a clinical trial?

Clinical trials provide access to some of the newest and most promising treatments for diseases that have no cure. In many cases, these trials, guided by experts, may represent your best possible chance for survival or for a better quality of life. By participating in a clinical trial, you help researchers take one small step, or even a giant leap, closer to a cure. Aside from helping yourself, your experiences can support advances in the state of the art in the field, leading to improved treatments for others in the future.

In Chapter 5, we discussed the brain cancer guidelines developed by the National Comprehensive Cancer Network (NCCN), the not-for-profit alliance of 27 leading cancer centers. For every patient category in the NCCN guidelines, enrollment in a clinical trial is recommended for those who are eligible.

Another advantage to enrolling in a clinical trial is the cost. Brain tumor treatments are very expensive. In general, the experimental treatment used in a clinical

trial is free to you. There may, however, be charges for associated costs of treatment — such as surgery, doctor’s consultations and visits, MRI scans, and blood tests — so ask about costs and what your insurance will pay and what your out-of-pocket expenses will be. If you have no insurance, there may be clinical trials available that cover all the costs.

When should you consider a clinical trial?

The decision of when to participate in a clinical trial should be discussed with your medical team. Some patients and physicians feel more comfortable exhausting possibilities with the standard-of-care treatment first. Others choose right away to participate in trials from the onset of diagnosis. You may wish to discuss certain points of progress (or lack of progress) with your medical team as a guideline to help you with your decision. Obviously, if you have a low-grade tumor for which good treatments are available, you will be less likely to try something experimental.

If you have a high-grade malignant tumor and the expected outcome of the standard-of-care treatment is not acceptable to you, it is easier to make the decision to try something experimental. Clinical trials have their own sets of eligibility requirements that might include the age range of participants, location of the tumor, grade and/or type of tumor, the presence of specific molecular markers, or the requirement of a specific degree of stabilization as a trial enrollment criterion. Some clinical trials are conducted specifically for treatment of recurrent tumors rather than treatment of newly diagnosed tumors. Whether or not you decide to wait or move forward, it is important to research available trials early for your specific type of tumor and to know in advance if, or when, you might qualify. Be especially careful not to miss trial-entry deadlines. Some trials require that you sign up for them before surgery. Others require that you sign up before radiation therapy ends. One thing to keep in mind is to plan ahead and think through a large range of contingencies.

Having some types of treatments might disqualify you from later trying certain experimental therapies. In such a case, you will usually not have enough real data to make an informed decision. In the old days, it was an easy decision — the standard-of-care treatment provided so little hope that you had nothing to lose. But the current standard-of-care treatment has progressed to the point where you now have a difficult decision to make about when to enter a clinical trial, as the standard-of-care treatment does help some people for a long time.

How do you assess a clinical trial?

The best way to evaluate if a clinical trial is right for you is to speak with your primary physician, your neuro-oncologist or surgeon, and other members of your medical team, including those to whom you have turned for second opinions. You might also contact one of the major brain tumor centers for additional insight into a specific clinical trial. You should also consult with the physician in charge of the trial. It is always helpful to know how earlier trials of the proposed treatment came out. Lastly, it is important to ask any physicians not in favor of your participation: Why not? What would they recommend instead, and why?

Although individual cases are meaningless statistically, the experiences of others may help give you enough information to choose between two treatments that are otherwise a toss-up. You can find these individual experiences in the online support groups, in real-world support groups, and in the results of the Brain Tumor Virtual Trial, a study run by the Musella Foundation (see below).

How do you find clinical trials?

You can find listings for clinical trials at the virtualtrials.com website of the Musella Foundation, at the National Cancer Institute website, and at the registry of clinical trials run by the US National Institutes of Health and called clinicaltrials.gov.

- At the virtualtrials.com website of the Musella Foundation, under the tab “Find a Treatment,” clinical trials can be sorted in multiple ways: by country, by state, by tumor type, by the date the clinical trial was listed, and by the number of participating centers. You can also use key words — such as a name of a cancer center or the name of a doctor — to search for specific clinical trials. The Musella Foundation can also be directly called at 1-888-295-4740. To access the “Find a Treatment” tab, go to: www.virtualtrials.com.
- The National Cancer Institute is not specific to brain tumors, but it does maintain a powerful clinical-trials search engine. In addition to allowing you to search by cancer type, location, and other variables, it also allows you to search by the type of trial (that is, whether it is a phase I, phase II, or phase III trial). To access the National Cancer Institute clinical-trial search engine, go to: www.cancer.gov/clinicaltrials/search.

Six: The importance of clinical trials

- Clinicaltrials.gov is the world's largest clinical trials database, currently holding registrations from over 130,000 trials from more than 170 countries. You can search for trials by condition, intervention, sponsor, location, and type of trial. To access this resource, go to: www.clinicaltrials.gov.

Treatments and the Food and Drug Administration

When considering clinical trials, it is useful to understand the difference between approved and experimental treatments.

In general, there are two general classes of treatment: (1) those approved by the FDA specifically for brain tumors on the basis of evidence from clinical trials; and (2) experimental treatments, sometimes with drugs approved by the FDA for other types of cancers or other diseases, and sometimes with drugs not yet approved at all by the FDA.

Currently, only a small number of drugs and devices have been approved by the FDA specifically for the treatment of brain tumors. More than 30 years ago, the alkylating chemotherapeutic agents carmustine (BCNU) and lomustine (CCNU) were approved nonspecifically for “brain tumors.” In 2003, the FDA approved the Gliadel Wafer (biodegradable wafers impregnated with carmustine) for treatment of newly diagnosed high-grade malignant glioma, and in 2005 it approved temozolomide (Temodar) for that same indication. For the treatment of recurrent glioblastoma, the FDA approved the Gliadel Wafer in 1997 and **bevacizumab** (Avastin) in 2009. More recently, the FDA approved alternating electric field therapy with the Optune device in 2015 for treatment of newly diagnosed high-grade malignant glioma and, earlier in 2011, for treatment of recurrent glioblastoma.

But even if an FDA-approved drug is not approved specifically for “brain tumors,” your medical team is still able to prescribe it for your brain tumor. When doctors prescribe a drug for a therapeutic purpose other than the one approved by the FDA, it is called “off-label” prescribing. Many drugs commonly used for brain

bevacizumab (beh-vuh-SIH-zoo-mab): *A drug used alone or with other drugs to treat certain types of cervical, colorectal, lung, and kidney cancer, and glioblastoma. It is used under the brand name Avastin to treat these cancers. Bevacizumab binds to a protein called vascular endothelial growth factor (VEGF). This may prevent the growth of new blood vessels that tumors need to grow.*

The virtualtrials.com website of the Musella Foundation has separate sections, each with extensive information, about several of the key brain tumor treatments. Be sure to visit each of the following sections for the latest updates about these treatments:

- Gliadel wafer: www.virtualtrials.com/gliadel
- Immunotherapy: www.virtualtrials.com/Immunotherapy_treatments.cfm
- Optune device: www.virtualtrials.com/optune
- Temodar (temozolomide): www.virtualtrials.com/temodar
- Toca 511 & Toca FC: www.virtualtrials.com/tocagen/tocagen.cfm

tumors are prescribed off label. Although the use of these drugs by your medical team is legal, and the drugs are easily available, you might nonetheless have trouble getting your insurance company to pay for off-label usage of a drug because it will argue that such off-label treatment is experimental. In such cases, know that you can fight the insurance company's denial. You should enlist your neuro-oncologist to help get the drug approved by your insurance company.

The Right to Try law

In 2018, the US Congress passed the Right to Try law, allowing terminally ill patients to try experimental therapies (drugs and devices) that have completed phase I FDA testing but have not yet been approved by the FDA. Before the federal law was approved, 41 states had passed Right to Try laws.

To be eligible for a right to try a drug that is not approved for any use, a patient must meet the following conditions: (1) be diagnosed with a life-threatening disease or condition; (2) have exhausted approved treatment options; (3) be unable to participate in a clinical trial involving the eligible investigational drug, as certified by a doctor; and (4) give written informed consent regarding the risks associated with taking the investigational treatment. To request a drug or device under the Right to Try law, the patient, the patient's representative, or the patient's physician has to send a letter to the director of compassionate use or to some other designated representative at the drug or device manufacturer to discuss options for access to the drug or device.

Please note that drug and device companies are not required to provide treatments to patients under Right to Try laws. Each company is responsible for devel-

oping its own processes and procedures for approving Right to Try requests. It is reasonable that companies should not be forced to provide treatments when they do not think the treatments are appropriate or when they have limited supplies of the treatments apart from their use in clinical trials. In addition, doctors who do not think that a treatment will be helpful have no obligation to request a Right to Try treatment for a patient.

Exciting therapies under development

Gene therapy / viral therapy

Gene therapy is the insertion of a gene (usually by having it carried by a virus) into a cell in order to replace a defective cell gene or to install a new gene that can cause the cell to produce a protein for fighting a tumor. Gene therapy trials for brain tumors have not yet yielded exciting results. However, there is renewed interest in gene therapy because of the phase III Toca 5 clinical trial, which is being undertaken by the company Tocagen. Toca 5 is a randomized trial of Toca 511 and Toca FC versus standard-of-care treatment in patients with recurrent high-grade glioma.

- **How Toca therapy works.** Toca therapy requires the use of two drugs, Toca 511, which is injected into the tumor, and Toca FC, which is taken orally. Toca 511 is a virus designed to infect brain tumor cells only, while leaving normal cells alone. When the Toca 511 virus infects a tumor cell, it adds a gene to the cell. This gene, in turn, encodes for an enzyme that can selectively convert the antibiotic drug Toca FC into toxic chemotherapy (called 5-FU) in the tumor. After Toca 511 virus injection, the antibiotic Toca FC drug is then given orally every few weeks, and it kills the tumor cells that have enough copies of the enzyme to convert Toca FC to 5-FU. Tumor cells infected with the Toca 511 virus that do not yet produce enough enzyme for this purpose can serve as reservoirs that will continue to spread the infection. With every ingestion of the Toca FC antibiotic, the process starts over again and is repeated until the entire tumor is potentially gone.

Immunotherapy / vaccine therapy

Immunotherapy, including vaccines, is one of the most exciting areas of research for cancer in general and for brain tumors in particular. A large number of different immunotherapy clinical trials for brain tumors are currently underway. Immunotherapy works by enhancing the body's own immune system response against cancer cells.

There are two main types of vaccine approaches:

- **Personalized vaccines.** Personalized vaccines require that a tumor specimen be sent to a laboratory to identify tumor-specific antigens (proteins) on the surface of the tumor cells. Specific tumor antigens are combined with patient dendritic cells — a type of immune cell found in tissue — to form a personalized vaccine. These antigens stimulate an immune response, activating killer T immune cells to destroy the tumor. Results from some early vaccine trials have suggested that patients with glioblastoma receiving a personalized vaccine survive more than twice as long as patients receiving just standard-of-care treatment. Please note: If you are interested in treatment with a personalized vaccine, you must make arrangements before surgery to have the vaccine made or to have frozen tissue stored so that you can have the vaccine made later.
- **“Stock” vaccines.** Stock vaccines use a different approach. They find the most common targets on the tumors and create a vaccine against them. As an example, there is a protein called survivin in glioblastoma that prevents tumor cells from dying. Investigators have created a synthetic survivin vaccine, called SurVaxM, that stimulates the immune system to target this cancer molecule. In a phase II trial of patients with newly diagnosed glioblastoma, the addition of the survivin vaccine to standard-of-care treatment provided a survival benefit even in patients with an MGMT unmethylated (that is, unfavorable) promoter status. Other trials with SurVaxM used as an adjunctive therapy for high-grade glioma are underway. Another virus under investigation is PVS-RIPO, a man-made form of the live polio vaccine. Polio viruses can attach to and infect malignant glioma cells. Once inside the glioma cells, the viruses destroy them, causing an immune response so that other tumor cells can be recognized and destroyed by the body's immune system. Recently, the FDA granted PVS-RIPO a break-

through therapy designation as a potential treatment for patients with recurrent glioblastoma, citing evidence from an ongoing phase I trial.

The Brain Tumor Virtual Trial

The Brain Tumor Virtual Trial is a registry managed and run by the Musella Foundation. The virtual trial consists of a database of brain tumor patients, the treatments they are using, and their outcomes. Participants record the treatments that they and their medical teams decide to pursue. The Musella Foundation does not tell participants what treatments to receive; we just record the outcomes. There is no cost to participate in the virtual trial. The patient or caregiver records information on simple forms right on the virtualtrials.com website and posts an update each month. We send email reminders on the first of each month. The patient or caregiver also sends in copies of MRI reports (not the MRI films) and pathology reports so that information can be verified. Participants are able to view the ongoing results of the project.

The concept behind the Brain Tumor Virtual Trial is to identify which treatments, or which combinations of treatments, are working the best. In addition to providing greater insight for researchers about beneficial therapies in the real world, the virtual trial also supports participants in learning how to become expert managers of their own conditions. For example, participants can generate reports on the information they have entered, such as a graph of their status over time. For more information on the Brain Tumor Virtual Trial, go to: www.virtualtrials.com/brain/index.cfm. ●



Please remember

- ✓ Clinical trials may represent your best possible chance for survival or for a better quality of life.
- ✓ At the virtualtrials.com website of the Musella Foundation, there is a comprehensive list of clinical trials, which can be sorted in multiple ways, including by tumor type and the number of participating centers.
- ✓ To date, only a few drugs and devices have been approved by the Food and Drug Administration specifically for the treatment of brain tumors.
- ✓ Immunotherapy works by enhancing the body's own immune system response against cancer cells, and there are many immunotherapy trials for brain tumors underway.
- ✓ Enroll in the Brain Tumor Virtual Trail registry managed and run by the Musella Foundation, which is a database of brain tumor patients, their treatments, and their outcomes.

Survivor story #6

On September 19, 2012, I had a grand mal seizure. It was during my lunch break at work, and I was talking with a coworker when I started feeling strange. It felt as if my eyes were crossing each other. It seemed like just a minute, but the next thing I knew was that I was lying on the floor, with an emergency technician asking me whether I could see him. My co-worker was also looking down at me, and he seemed scared. I was 35 years old, the mother of two young girls, and in good health. I rarely even had headaches, let alone a seizure.

I spent several days at the local hospital. More seizures followed. A biopsy revealed that I had a grade IV glioblastoma in my left parietal lobe. Family and friends researched our options, and we selected a comprehensive cancer center as the best place for my treatment. My doctor there told me that with a tumor the size of the one I had, I should have undergone immediate surgical resection rather than first having a biopsy.

At the comprehensive cancer center, I did undergo surgery to remove as much of the tumor as possible. During surgery, the neurosurgeon placed Gliadel Wafers in the tumor cavity. After surgery, I completed 4-week radiation treatment with concomitant temozolomide (Temodar). After radiation, I continued with adjuvant temozolomide at home and had an MRI scan every 2 months.

Seven months after my first diagnosis, I had recovered well enough to run a 5K race with my family. But the adjuvant therapy with temozolomide left me feeling weak, and the MRI scans indicated that my tumor had recurred at the original site. When I was initially diagnosed, the molecular profile of my tumor indicated that it might not be as responsive as possible to alkylating agents like temozolomide because my MGMT status was unmethylated.

By fall 2013, my family and I began an intensive search for a clinical trial for me. We felt that the type of clinical trial that would offer the most hope would be one that enhanced my own immune system to



Brain Tumor Guide for the Newly Diagnosed

combat cancer cells. We searched websites, especially the listing of clinical trials on the clinicaltrials.gov website of the US National Library of Medicine, and eventually narrowed down a list of potential clinical trials.

To find a clinical trial, I needed to consider my eligibility as well as the nature of the study itself. I applied to several clinical trials and came close to entering two of them before I was accepted for a clinical trial at a comprehensive cancer center in Los Angeles that seemed the best fit for me.

My husband and I flew out there, and I underwent surgery again to remove the recurrent tumor and to have a port inserted. After cells were collected from my tumor, killer T immune cells taken from my body as well as from donors were “trained” to attack the tumor. The concept was that these modified T immune cells could be inserted every two months through the implanted port to help my body fight any residual cancer cells.

After the second resection, I returned home to await my flight back to Los Angeles for the first treatment session. I had lost vision in my right eye as a result of the second surgery, and I also had a low-grade fever, but nonetheless I was ready to proceed. I flew to California and received the first injection through the port. Unfortunately, my fever became worse, and it was discovered that meningitis had developed because my body was rejecting the implanted port. I thus had another surgery to remove the port, and the decision was made to place the modified T immune cells directly on the site of the tumor.

It took a stay in intensive care, time, and antibiotics. Luckily, after several weeks I recovered from the meningitis. I was disappointed to learn that I could not continue in the clinical trial. But my MRI scans showed no sign of tumor. The decision was made for me to go home to wait and see. I have been waiting and seeing for four and a half years. So far, my MRI scans show no sign of recurrent tumor.

The cancer and the surgeries have taken a toll. Although I am on antiepileptic drugs, I still have seizures. I have no vision in my right eye, and I have not been able to return to my former career as a mechanical engineer. But I am lucky. I am a stay-at-home mom to two wonderful girls. I can sew and work in my garden. I spend time with my friends and family and enjoy my life. I hope that sometime soon we will all have treatments that are more effective than chemotherapy.





Alternative and complementary treatments

Discussing alternative and complementary treatments is a little like discussing religion and politics. These topics are hard and emotional, there is often a lot of fear associated with them, and there can be many points of view.

This guide will give you an understanding of alternative and complementary treatments, but as with anything else, the final decision to use them must be yours.

Alternative treatments are treatments that have not yet been proven to work based on scientific testing and are used **INSTEAD** of mainstream treatments.

Complementary treatments have also not yet been proven to work but are used **IN ADDITION** to mainstream treatments. Once a treatment has been shown to work, it crosses over from “alternative”/“complementary” to “mainstream.”

The mainstream path of treatment development

When someone invents or discovers a therapy that he or she thinks might effectively treat a brain tumor, the path to the treatment’s becoming part of mainstream medicine begins with laboratory testing on cell cultures and/or on animals. If the treatment still seems promising, human trials are started. We discuss clinical trials in another section, but basically the treatment is tested on people with a brain tumor and is compared with either historical controls or with a control group.

The early stages of a trial, when only a few people are tested, cannot really show how well the treatment actually works. All phase III trials have had successful phase I and phase II trials leading up to them. However, most phase III brain tumor trials have failed to show significant benefit compared to standard treatment even though a new tested treatment looked very good in early trials. The reason for this is that the course of a brain tumor is variable. A small percentage of patients will do well no matter what treatment you give them, and the natural history is a roller coaster —

you have wild ups and downs. If you happen by chance to select a handful of brain tumor patients who happen to have the right subtype, genetics, age, resection extent, Karnofsky Performance Status score, and other prognostic factors, and are on the right track of the roller coaster at the time, they may do well in a small trial even if the treatment is not as good as the standard treatment.

The next step is to test the treatment in a large group. This is when you conduct a **randomized clinical trial**, in which patients are assigned by chance to receive treatment with either the new therapy or placebo (an inactive substance that looks just like the new therapy) or standard treatment. Then, when the two groups are compared, you get a much better feel for how the new therapy works, since all the other variables are controlled. The trials need to be repeated a few times on large numbers of patients treated before you will know if the effect is treatment related or chance related.

Statistics are used to try to make sense of the trial results. A number is calculated called the significance level. The number usually chosen as the benchmark is 0.05, which means that there is a 95% chance that the effect seen in the trial was caused by the treatment and not by chance alone. Conversely, this means that if you run 100 trials of a worthless drug, about 5 of those trials may report success even though there is none. This is why multiple trials are needed, and it is best if they are conducted by different centers.

The Food and Drug Administration (FDA) will approve a drug that is better than standard treatment, or is at least as good as standard treatment, if it has fewer side effects. Once a treatment is approved by the FDA, everyone can get access to it, not just those in clinical trials.

How alternative treatments are developed

An alternative treatment is developed when someone has an idea that a certain therapy may help a brain tumor, or the researchers notice that a brain tumor survivor

Randomized clinical trial (RAN-duh-mized KLIH-nih-kul TRY-ul):

A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial.

has tried a certain therapy. They then try the treatment on a few more brain tumor patients and see that some of them get better. (As mentioned before, some brain tumor patients are on the upswing of the roller coaster and would have been doing better even without the treatment.)

At that point, the researchers are convinced the treatment works, and they try to promote it so that more people can benefit from it. In many cases, these are the most well-meaning people with the best of motives. They saw something work in a few patients and want others to do well also. However, the difference is in the science. At this point, it would be good to follow the mainstream path and do rigorous trials of a new treatment, and if it passes the tests, the novel treatment would become mainstream and help everyone. However, that is often not the path taken. Instead, many promoters of alternative and complementary therapies skip the proof and go on to marketing. They use individual case reports or small trials to justify the treatment.

On the Internet we read about many of these types of treatments, but these stories introduce a huge new problem: selection bias. This means that you hear from and see the people who do well with a treatment but you do not see the ones who died. For example, if the standard treatment for a brain tumor has an average survival period of 18 months (and some of the experimental treatments more than double that), an alternative treatment needs to reach that point to just say it is as good as standard treatment.

Put another way: If you take 1000 patients and put them on standard treatment, you would expect 500 of them to be alive in 18 months. If you take the same 1000 patients and give them a treatment that is half as effective as standard treatment, you would expect to see 250 alive at 18 months. If you see 250 people telling you that this miracle alternative treatment worked for them, you may tend to believe them. But you are not seeing the 750 who died — they can't tell you that it didn't work for them. So, at that point, what question should you ask? If they tell you they have 250 18-month brain tumor survivors, ask out of how many that started? If it is 250 out of 250, it is a miracle. If it is 250 out of 1000, it is only half as good as standard treatment.

Frequently, those who recommend alternative treatments for serious illness will say "It doesn't hurt to try since the standard treatment does not result in a cure." This statement is erroneous, because even if the treatment itself is not toxic or dangerous, the use of such treatment often works against the science-based treatment, or sometimes is even used as a sole approach (stopping the scientific treatment that, while not curative, may extend their life and temporarily bring some relief to patients).

Also, the high cost of alternative treatment, usually not covered by health insurance, can cause serious financial pain to families and patients who desperately cling

to straws of a “cure” offered by those who sell these nonscientific treatments.

There are “red lights” to watch out for when dealing with non-scientific based treatments. The following are some of the most common “red lights” associated with alternative treatments:

- They are proprietary (available from one source or a limited number of sources) and are not available on the standard pharmaceutical market (which is subject to government supervision and regulation).
- They are expensive, and patients and their families must usually “pay up” in advance before the treatment can be started or continued. Most true clinical trials are licensed and supervised by government entities and are backed with public or private grants so that patients pay little or nothing for the treatment. Most legitimate studies are run in or by major universities or other institutions of higher learning, whereas the majority of alternative schemes are run by for-profit entities.
- The results of the alternative programs have not stood the test of review by a **peer-reviewed scientific journal** (in most cases, the data have not even been submitted to peer-reviewed scientific journals for publication). The alternative programs rely on “testimonials” by patients or former patients, and these are highly unreliable, especially when the diagnosis (of cancer) has not been based on scientific diagnostic techniques, such as pathological examination of tissue.
- There is often a tendency for the providers of alternative treatment to speak ill of traditional scientific medicine, frequently asserting that organized medicine is involved in a conspiracy to force patients to get orthodox treatment for the economic gain of the medical profession.

Brain tumor patients contact us frequently at the Musella Foundation. Many of them have tried just about every alternative treatment ever proposed for brain tumors. Some of them do well. Most do not. We track them with our Brain Tumor Virtual Trial project. Analyzing our data for this project, we found that not one of

Peer-reviewed scientific journal (peer-ree-VYOOD SY-en-TIH-fik JER-nul):

A publication that contains original articles that have been written by scientists and evaluated for technical and scientific quality and correctness by other experts in the same field.

the alternative treatments reported had any effect on the outcome of the cases.

We still keep an eye on the patients who do not join the project. The ones that use mainstream treatments do better than the ones who use alternative treatments alone. We have seen many people decline and die rapidly when refusing standard treatments. They usually change their minds near the end and start standard treatments, but of course it is too late. Unfortunately, they then blame the standard treatments for the death.

However, when it comes to complementary treatments, when you use mainstream treatments but add to them, you may see some positive results. There may be some complementary treatments that do help with treatment side effects and possibly may make treatments more effective. However, keep in mind that if you feel a complementary treatment is powerful enough to change the course of your tumor in a positive way, it is just as likely — or more so — to be able to change it in a negative way. The body is very complicated. You cannot predict what would happen if you change one thing, because one small change can upset the delicate balance of the body and have unseen consequences. The only way to tell is by trying it in a well-designed trial. Proponents may say there is no money in it so no one would fund the trial. That is not true. The Musella Foundation, as well as most of the over 100 other brain tumor foundations, fund research projects like this.

Conspiracy theories may be put to rest by these two simple thoughts: (1) there is no way the medical industry is organized enough to keep away from the public a cure that would be the biggest money maker in the world; and (2) there are many researchers who dedicate their lives to finding the cure.

Patients need to learn to ask the right critical questions:

- What exactly is this treatment?
- Who has received it?
- How many brain tumor patients have had documented responses, and how many patients have tried it?
- How are responses assessed?
- Why is it not given as part of mainstream practice in the United States?
- How was the diagnosis of brain tumor made? In some countries, MRI scans are not routine for brain tumor patients, and even if there is an MRI, there are some diseases that look similar to a brain tumor. A biopsy is the best way to tell if the diagnosis is a brain tumor and which type it is.
- Have the treatment results been published in a peer-reviewed scientific journal? If not, why not? ●



Please remember

- ✓ Alternative treatments have not yet been proved to work based on scientific testing and are used instead of mainstream treatments.
- ✓ Complementary treatments have not yet been proved to work based on scientific testing, but they are used in addition to mainstream treatments.
- ✓ There are several “red lights” to watch out for if you look at using non-scientifically based treatments — few sources for the products; an expensive cost; reliance on patient “testimonials” rather than publication of data in peer-reviewed scientific journals; and conspiracy talk.
- ✓ Learn to ask the right critical questions about alternative and complementary treatments. What is it? Who and how many have received it? How were responses assessed? Why is it not part of mainstream practice? How was the diagnosis of brain tumor confirmed? And have the treatment data been published in a peer-reviewed scientific journal?

Survivor story #7

In September 2008 I had dizzy spells and a heightened sensitivity to bright lights. Upon visiting my family doctor, he ordered blood work and asked me to wear a Holter monitor, thinking that I might have a heart problem. I was 43 years old, and other than having low blood pressure I was in good health.

On October 2, 2008, I woke up at my usual time, 6:30 AM, went about my routine, got the kids up, made breakfasts, lunches, etc., feeling fine to this point. Around 8:00 AM, I felt dizzy again and began banging into door frames and tripping as I walked from the carpet onto the hardwood floors. My daughter, 11 years old, was talking to me and I couldn't understand what she was saying. I started to panic and I was sweating. I had to get my daughter to the bus stop and figure out what was going on. I came home from the bus stop shaking and afraid. My left side went all tingly. I thought I was having a stroke.

I called my husband at work and told him I needed to go to the emergency room. He rushed home and took me to the hospital, where I was taken for an electrocardiogram right away. They told me that I had not had a stroke and that there was nothing wrong with my heart, and they were getting ready to send me home, thinking I may have had just a fainting spell. With pressure from my husband and my family doctor, I was sent for a CT scan. Soon after came the news: a 3-cm brain tumor. The tumor was located close to the surface in the left parietal region, just above my ear. We were told to go directly and immediately to the regional neurological center.

Shocked and dazed, we first picked up our children at high school and elementary school, told them what was happening, had a group cry, dropped them off at home, and then went to the center. I had surgery 5 days later. The surgeon was able to remove only about 25% of the growth as the tumor mimicked the appearance of the brain and in places he was unable to differentiate between the tumor and healthy brain tissue. While we were obviously distressed by this, the surgeon told us to take heart because in these types of cases, surgery is not the primary determinant of the final outcome. After a week in hospital I was sent home to recover and await the results of the biopsy. I was diagnosed with a grade III anaplastic astrocytoma and was referred to a cancer center for further treatment.

In the early days, we were sometimes disheartened, especially as we learned more about this disease. In particular, while the Internet can be a tremendous source of information, it can also contain information that may be misleading. One of the scarier things to read about was the statistics, which can seem very grim. I made a conscious

Brain Tumor Guide for the Newly Diagnosed

decision not to even think about statistics, and I encourage anyone going through the experience of a brain tumor to do the same, because we are not statistics.

My initial assessment at the cancer center was on October 30. My radiation oncologist and the medical oncologist felt that because I was young and strong I could handle the most aggressive treatment. On November 17 I began a treatment regimen of radiation and chemotherapy together. I had radiation treatments Monday to Friday and took a low dose of temozolomide (Temodar) 7 days a week. I had a short break from radiation over Christmas and finished this phase of treatment on January 5. Overall, I tolerated it very well. Other than losing my hair, the biggest adverse effect I felt was increased fatigue. Also the steroids I was taking to relieve headaches and pressure in my brain caused bloating and affected my sleep patterns.

After a four-week recovery period, I had an MRI that showed that the tumor had shrunk. That day I began the next phase of my treatment, which consisted of a higher dose of temozolomide for 12 months on the cycle of 5 days on and 23 days off. There was a target dose of chemotherapy toward which my doctors gradually brought me. At the lower doses, I tolerated the chemotherapy except for nausea and vomiting, but as I was brought to the target dose, my entire body became itchy, I became tired, and my level of blood platelets was greatly reduced. After a break to recover, I received again a lower dose of chemotherapy, which I remained on until my treatment finished. I have had no further treatments since then.

I am now a 10-year survivor of grade III anaplastic astrocytoma. I have difficulty dealing with multiple things at the same time, and I have problems with short-term memory, which means I have to make notes for everything. This has been my "new normal," but I am not complaining.

One thing I did not mention, which I think is very important, is having a positive attitude, and for me personally, the power of faith. I was surrounded by people who kept my spirits up and always encouraged me. I thank God each day for the miracle of healing that I have received.





Symptom treatment and sex and fertility issues

In the treatment of brain tumors, not unlike the treatment of any other acute or chronic illness, a variety of medications are used to combat symptoms, such as pain, fatigue, swelling, and seizures. The medications may include antibiotics, steroids, analgesics or narcotics, and anticonvulsants. It is necessary to take responsibility for your medications to ensure your safety. As your medical team will be made up of physicians from various specialties, all of whom may prescribe different medications or alter dosages in the context of your care, it is vital that you keep ongoing and accurate (up-to-date) records in your treatment binder regarding your medications, including:

- Medications you are currently taking (including dosages) and who is responsible for monitoring you (prescribing physician) or providing refills. This information can be very helpful to any caregiver seeking information or assistance on your behalf.
- Medications you have taken in the past, noting their value (e.g., “was most helpful for sleep”).
- Medications discontinued due to negative side effects.
- Any allergic or adverse reactions, mild or otherwise, noted in RED.

You should always:

- Ask your doctors to review your list of current medications prior to prescribing something new.
- Check to ensure that the recommended drug is covered on your insurance plan’s drug formulary, or if you’ll need a prior authorization.

Brain Tumor Guide for the Newly Diagnosed

- To avoid receiving the wrong medication at the pharmacy (a growing concern), write down the specific medication and dosage as stated on your prescription before submitting it to a pharmacist and compare this information to the label on the bottle you receive to ensure it is the same drug as stated on the prescription.
- Your prescription might be filled with a **generic** substitution if your doctor did not prescribe it to be “dispensed as written.” If the medication you receive is different from what was written on the original prescription by your physician, ask the pharmacist. Also ask the pharmacist for his/her thoughts on the generic. Most generic drugs are okay to use, but for some drugs that have a very narrow effectiveness range, such as anti-seizure drugs, it may be worthwhile to pay the extra for the brand name or insist on the same brand of generic each time.

Whenever possible, having all your prescriptions filled through a single pharmacy source can be an additional safeguard against medical errors, preventing adverse drug interactions, as most pharmacies now use computer systems that automatically flag dangerous interactions based upon your previous medications. Should your physician fail to recall a particular medication that might present a problem, chances are your pharmacist will catch it. Still, asking your physician(s) to review your medication sheet in your treatment binder — each and every time a new drug is prescribed — is an important, life-saving step.

It is important that you understand the side effects and drug interactions of all the medications you are prescribed. Most of the drugs we use have very scary package inserts and list every side effect ever reported to happen in people who were taking the drugs — whether the drug caused it or not. Our point is to be aware of the most common side effects and watch for them, not to be scared away from using the drugs. Additional information regarding your medications and drug interactions can be found at websites like Drugs.com (www.drugs.com).

The following is a general list of medications commonly used to treat symptoms and/or conditions caused by a brain tumor itself, or resulting from surgery and/or other standardized treatments of brain tumors. Many of the significant/common side effects associated with a particular medication are noted, but the

Generic (jeh-NAYR-ik): *Official nonbrand names by which medicines are known. Generic names usually refer to the chemical name of the drug.*

list may be incomplete. Your physician may recommend medications not covered within this general guide. You are advised to thoroughly discuss and understand all the benefits and side effects with your physician before a prescription is issued. Physicians are often creatures of habit — ask about alternative medications and why your physician would choose the recommended medication over another.

This is a general overview. Always ask your doctor before taking anything, even over-the-counter pain medications.

Medications for pain relief

Because the brain itself does not feel pain, studies show that physicians treating patients for brain tumors often overlook pain. However, pain as a by-product of disease or due to complications from surgery or other forms of treatment is very real and deserves real attention. Headaches from brain inflammation or tension, scalp sutures, muscular pain and hairline fractures due to steroid therapy, and pressure points on arms and hips from extended bed rest require medication. Pain left untreated can slow healing, deplete emotional reserves, exacerbate depression and sleep deprivation, and detract from your quality of life.

- **Mild pain.** The lowest level of pain can usually be managed with Tylenol (acetaminophen), Advil (ibuprofen), or Aleve (naproxen). Note that aspirin can affect how fast your blood clots, which may be bad or good. Always ask your doctor about it first.
- **Moderate pain.** More powerful prescription medication, such as Percocet (the combination of oxycodone and acetaminophen) and Percodan (the combination of oxycodone and aspirin), can be taken as directed by a physician.
- **Severe pain.** Codeine, Vicodin (the combination of hydrocodone and acetaminophen), oxycodone, and stronger, morphine-type medications are typically long acting and are taken less frequently. Many also come in “patch” form for slow absorption and continuous relief. Ritalin (methylphenidate) is used to treat attention-deficit hyperactivity disorder (ADHD). If taken in small doses with pain medication, Ritalin can increase the narcotic effect (enhancing pain relief) while reducing the drowsiness commonly associated with these drugs. Ritalin has also been shown to benefit patients who suffer from fatigue. According to package

inserts for drugs that contain morphine, such drugs should not be used in patients with brain tumors. However, they are still commonly used, and the benefits may outweigh the risks when you are in severe pain. Discuss any concerns you might have with your physician.

Medications for swelling

Steroids are powerful anti-inflammatory drugs typically prescribed to reduce swelling in the brain (cerebral **edema**) before and/or after surgery, during radiation treatments, or to relieve symptoms such as memory loss and limb (arm/leg) weakness caused by brain swelling. While common, swelling can be harmful if excessive and must be controlled.

Synthetic steroids such as Decadron and Hexadrol (dexamethasone) are man-made hormones similar to cortisol, which is produced naturally by your body. Taken orally, these steroids create higher levels in the body than what is normally secreted, reducing inflammation but also causing the body to temporarily stop natural production on its own. For this reason, it is very important to “wean” yourself (cut back slowly) when stopping oral steroid therapy. Always follow your physician’s recommended schedule for reducing dosages. During this reduction period, your body will slowly come back “on line” and begin to produce normal cortisol levels again. You should never abruptly stop taking steroid medication, because in extreme cases, going cold turkey can cause sudden death, as the body is not yet ready to resume full production of cortisol on its own, a necessary and vital hormone.

While the benefits of steroids are undeniable, often unmatched by any other medication, they are not without short and long-term side effects.

Long-term side effects can include (but are not limited to) diabetes, muscle pain/weakness, osteoporosis (bone loss) leading to fractures, and susceptibility to infections. Short-term effects can include (but are not limited to) increased appetite, weight gain, and indigestion; swollen or “moon-faced” appearance; stretch marks, rash/flushing of skin, and acne; increase in blood sugar; brittle bones; depression and/or behavioral changes; anxiety and/or paranoia; and suppressed immune system.

Other oral steroidal therapies include prednisone or prednisolone. While not as strong as Decadron or Hexadrol, side effects are generally the same, although per-

Edema (eh-DEE-muh): *Swelling caused by excess fluid in body tissues.*

haps not as severe in most cases. There are nonsteroidal medications that can help with swelling, such as Avastin (bevacizumab) and Diamox (acetazolamide).

Medications for reducing seizures

Roughly 30 to 40 percent of patients will experience some level of seizure activity and require medication to reduce electrical responses in the brain. Due to the location and/or size of some tumors, many neurosurgeons will prescribe anti-seizure medication as a matter of routine before, during, and/or after surgery when the risk of seizure is considered high. In the past, all brain tumor patients were put on anti-seizure medications routinely for life, but since they can have a lot of side effects, many doctors now try to do without these drugs until seizures occur.

In some cases, a seizure will appear as something slight and quick — muscle or eye twitching, or a sense of being “out of the moment” mentally and/or physically for a brief time, or a blank stare or sudden pause without response. These are called focal seizures. For others, seizures will involve full body activity, often categorized as grand mal seizures.

Most anticonvulsants share common side effects, such as fatigue and dizziness, so for obvious reasons you may be restricted from driving a car or operating dangerous equipment while taking anti-seizure medications, even when seizures have not been documented or have subsided. Other medications and certain foods can prevent proper absorption, so frequent blood draws for proper dosage and serum levels are necessary.

Phenytoin, often prescribed under the brand name Dilantin, is a commonly used medication to prevent full-body seizures in high-risk patients. People metabolize Dilantin differently, so periodic blood levels are taken to ensure that dosages are adequate and stable. Side effects of Dilantin include muscle fatigue, dizziness, and loss of coordination, as well as tooth decay and gum problems. Regular dental checkups and extra attention to oral hygiene are advised. Long-term use of Dilantin can cause a decrease in certain nutrients, such as folic acid and calcium. Ask your physician about supplements if necessary. Dilantin can also interact with other medications, including over-the-counter drugs, birth control pills, and herbal supplements. Dilantin can also make some chemotherapy drugs less effective.

Neurontin (gabapentin) has similar side effects as Dilantin, as well as the side effects of double vision, tremors, and involuntary eye movements. While Neurontin has fewer drug interactions than Dilantin, it does interact with certain antacids, such as Maalox.

Tegretol (carbamazepine) is an anticonvulsant that is also prescribed in the treatment of manic depression and other psychiatric disorders. Effective in its ability to control grand mal seizures, Tegretol must be monitored closely with frequent blood-level measurements, since in rare cases it may suppress bone marrow production. You should report any onset of a rash to your physician immediately. Tegretol also reduces or increases the effects of many medications. Double vision, pounding or slow heart rate, and nausea are noted side effects with this drug.

Depakote and Depakene (valporic acid or valproate) are commonly prescribed for focal seizures and require periodic blood levels to ensure adequate dosage and guard against liver damage. Because Depakote interacts with many medications, make sure your physician reviews your current medication list, including over-the-counter and herbal supplements, at the time of recommendation.

Phenobarbitol (a barbiturate and strong depressant) and primidone are less frequently prescribed, as the effectiveness of other anticonvulsants can be more easily achieved without the potentially addictive qualities of these drugs.

Keppra (levetiracetam) is a newer anticonvulsant drug. Sometimes it is used alone, and sometimes for difficult cases it is combined with other drugs. Keppra does not interfere with chemotherapy drugs.

Medications for reducing nausea

Nausea is common with brain tumors, as both a part of the disease process itself and as a by-product of radiation and chemotherapy treatment. Zofran (ondansetron) is used to control nausea caused by chemotherapy or radiation. It is usually administered intravenously prior to treatment and can be taken orally after treatment, if necessary. Effective for only a few hours, Zofran is limited to nausea caused by chemotherapy and radiation only and is not to be taken for motion sickness or other generalized conditions related to nausea. While mild in nature, side effects of Zofran include headache, fatigue, diarrhea, and constipation, and the drug may exacerbate pre-existing liver disease.

.....
: To get additional information about any medication, go to the drug :
: information site Medline Plus: [www.nlm.nih.gov/medlineplus/](http://www.nlm.nih.gov/medlineplus/druginformation.html) :
: [druginformation.html](http://www.nlm.nih.gov/medlineplus/druginformation.html). Medline Plus is provided as a service of the US :
: National Library of Medicine. On this website, drugs can be looked up by :
: their brand or generic names. :
.....

Eight: Common medicines for treating symptoms

Kytril (granisetron) is similar to Zofran in both treatment administration and side effects, although it may also cause abdominal pain. It lasts up to 12 hours.

Compazine (prochlorperazine) is a commonly prescribed medication for the treatment of generalized nausea and is given orally, intravenously, or as a suppository. Compazine belongs to a family of antipsychotic agents called “phenothiazines” and may cause drowsiness, low blood pressure, dizziness, constipation, dry mouth, blurred vision, and sensitivity to light. While effective in the management of nausea, Compazine should not be used in conjunction with alcohol, may interact with other medications, and could potentially cause an irreversible condition called tardive dyskinesia — involuntary movements or twitches of the face, tongue, or arm muscles.

Anzemet (dolasetron) is a new anti-nausea drug currently being used with success. Anzemet is given prior to chemotherapy. In some patients, a combination of Anzemet and Decadron prior to chemotherapy works in cases when the older drugs do not provide enough relief.

Haldol (haloperidol) is another antipsychotic medication that is used to control nausea and has risks and side effects similar to those of Compazine. Haldol and Compazine should not be taken without a detailed discussion with your physician.

Transderm Scop contains the seasickness drug scopolamine, which can sometimes be used for nausea. Transderm Scop is a patch formulation of the drug that is applied to the skin and works for 3 days per patch. A main side effect is dry mouth, which can be a benefit when there is difficulty swallowing and too much saliva is being produced.

There are also many alternative treatments. Some patients report that acupuncture, biofeedback, and hypnosis provide nausea relief with no side effects and are much cheaper than most commonly used drugs.

Medications for improving mood

Being diagnosed with a brain tumor alone is enough to create overwhelming anxiety and stress. It is important to understand that during the course of treatment, intense and seemingly “over-emotional” reactions — such as acute depression, sexual dysfunction, sudden outbursts, and visual or audio hallucination — may be the result of medication or a condition stemming from the tumor itself, not necessarily an emotional response. It is also important to communicate about these emotional changes with your medical team in order to seek proper assistance and guidance to help you distinguish the many moods of treatment and recovery, and to help you cope.

A psychiatrist is a medical doctor who can assist with the mood-related conditions directly caused by the tumor or its treatment. Psychologists can also provide help with coping difficulties and with mild depression due to issues of long-term care, financial strain, or the stress placed upon family and other important relationships. Ask your medical team to refer you to a psychiatrist or psychologist experienced in treating brain tumor patients.

Common antidepressants include Prozac (fluoxetine), Paxil (paroxetine), and Zoloft (sertraline), all of which are from a class of drugs called selective serotonin reuptake inhibitors (SSRIs). There is also another class of antidepressant drugs that includes Cymbalta (duloxetine) and Effexor (venlafaxine); this class of drugs is called serotonin–norepinephrine reuptake inhibitors. Side effects of antidepressants may include sleepiness, tremors, diarrhea, nausea, insomnia, increased sweating, weight loss, and decreased sexual ability. Side effects may be reduced when these drugs are taken with meals; Zoloft, in particular, should always be taken with food. In some rare cases, anxiety and depression may worsen while taking antidepressants and should be reported to your medical team immediately. Don't let the risk of side effects stop you from trying these drugs. People report a remarkable increase in quality of life when these drugs work.

Herbal remedies may be of some benefit. However, herbal mixtures can adversely interact with other prescription medications and should always be discussed with your medical team for safety and adequate dosing information. If you are thinking of taking hypericin, one of the principal active compounds of St. John's wort, make sure to ask your medical team first, for hypericin can interfere with other drugs.

Medications for reducing the formation of blood clots

Brain tumor patients are at a higher than normal risk for developing dangerous blood clots. Blood clots commonly start in the legs as deep vein thrombosis (DVT). Symptoms of DVT may include pain, tenderness, swelling, discoloration of the affected leg, and skin that is warm to the touch. If you develop these symptoms, you must call your doctor and get it checked quickly. Left untreated, blood clots can break away and travel to the lungs where they may cause a pulmonary embolism, which can be rapidly fatal. Symptoms of a pulmonary embolism include sudden shortness of breath, chest pain (worse with breathing), and rapid heart and respiratory rates. If you develop any of these symptoms, you must go to the emergency room immediately.

Eight: Common medicines for treating symptoms

Medications called anticoagulants help to thin the blood and reduce clotting, the body's normal response to help stop bleeding. Heparin is an anticoagulant that is given by injection, usually for a short period of time to prevent or treat blood clots. Warfarin (commonly referred to as coumadin) is an oral medication that can be taken over a long period of time to prevent blood clots. Aspirin is a milder blood thinner, which some doctors recommend to prevent blood clots.

When you are taking anticoagulants, normal cuts and scrapes may take longer to stop bleeding or heal, and there is an increased risk of the tumor bleeding into the brain — so these drugs are double-edged swords and should be taken exactly as prescribed. Warfarin interacts with many medications and should be discussed thoroughly with your medical team before treatment. Your doctor will also order periodic blood tests to ensure that appropriate medication levels are maintained. Plavix is another commonly used drug that prevents clotting.

It is important to note that changes to your diet can have a negative effect on the blood-thinning measures of anticoagulant medication. Suddenly increasing foods such as spinach in your diet can adversely affect bleeding times. The sudden introduction of fish-oil capsules as a dietary supplement, which are full of omega-3 fatty acids, can also alter bleeding times. While there is no need to eliminate spinach and other healthy items (including supplements) from your daily routine, you are advised to maintain your normal diet and not increase or decrease items significantly or add new supplements without discussing them with your physician. This is not the time to begin a new diet for weight loss without consulting your physician.

It is always a good idea to wear a medical alert bracelet informing medical personnel that you are taking anticoagulants in the case of an emergency. They are widely available in most retail pharmacies and on the Internet, inexpensive, and an important safeguard for your health.

Of course, you should take your medicines as directed, not changing the frequency or dosage without talking to your doctor. If you need help with co-payments for drugs, please go to needymeds.org and look up each drug you take. If you cannot afford a drug, don't stop taking it. Instead, speak to your doctor about a less expensive alternative.

Effects of treatment and medication on sex and fertility

For patients undergoing treatment for a brain tumor, a decrease in sexual desire or in the ability to enjoy normal sexual activity is common. Deciphering the origin of these changes can be difficult, for many factors can be involved. While surgery

causes postoperative fatigue and temporary physical weakness, chemotherapy and radiation can greatly affect and reduce your desire for sexual stimulation because of adverse effects on hormone production. So, too, can medications prescribed for the symptoms of brain tumors, such as swelling, seizures, nausea, anxiety, and depression. Physical changes, such as hair loss and weight gain, can further undermine your sense of attractiveness and desirability, deepening the emotional separation from sexual contact. Individually or in various combinations, these side effects create in some cases a daunting puzzle that requires patience and communication to piece together.

Depression is common among brain tumor patients, a condition often controlled with antidepressant medication — for example, with selective serotonin reuptake inhibitors like Paxil or Zoloft. These medications can reduce sexual desire. A simple change in dosage or medication may help restore sexual desire and should be discussed with your prescribing physician.

While most treatment-associated dysfunction or lack of desire is temporary, being able to openly discuss difficulties and options for sexual intimacy with your partner and with your medical team can help in managing the extent of disruption and being able to resume normal sexual relations after treatment. Unfortunately, discomfort among health professionals in discussing sex with the same openness and honesty with which they discuss nausea, diarrhea, and even expectations for recovery can complicate your ability to understand — and prepare emotionally for — how treatment might affect sexual desire. For this reason, patients often find it beneficial to discuss issues of intimacy with other members of their medical team, such as counselors or neuropsychologists. These healthcare professionals will be familiar not only with the impact of brain trauma and the effects of medication but also with the emotional toll borne by the patient.

Birth control

If you take birth control pills, it is important to discuss the potential effects of your treatment with your gynecologist and with your medical team for your tumor. Chemotherapy may halt menstrual periods temporarily, but precaution against pregnancy must be maintained due to the devastating effects of chemotherapy for an unborn fetus.

Some chemotherapy medications, as well as anti-seizure drugs, can interact with the effectiveness of birth control pills. A thorough discussion with your medical care team is essential.

Sex, surgery, and brain tumor treatment

In most cases, there are few reasons why you cannot have sexual relations while undergoing radiation therapy or after surgery. However, you should always consult with your medical team regarding any precautions against strenuous activity, including sex. Both radiation therapy and surgery can result in fatigue, making any strenuous physical activity difficult. As your strength returns, normal sexual activity can resume.

Likewise, unless your medical team specifically warns you against sexual activity while undergoing chemotherapy, normal relations are limited only by the precautions associated with the drugs themselves. Because chemotherapy drugs can be transferred through sperm, in some cases they can also be harmful to sperm and also damage a fetus. Condoms should thus always be used during both intercourse and oral sex to eliminate the possibility of exposing another person either vaginally or orally to the harmful effects of chemotherapy drugs.

Because sperm can live for up to three months, condoms should be used until three months have passed since the last chemotherapy treatment. Although dry orgasms can occur naturally on occasion as men age, chemotherapy can also cause this syndrome. The lack of ejaculation during orgasm is not cause for alarm and should have no adverse effect on pleasure.

Women receiving chemotherapy must take extra precaution against pregnancy, for birth defects can result from these drugs. Discuss your method of birth control with your medical team and be sure to specifically discuss whether there might be any possible reduction in the effectiveness of your birth control pills during chemotherapy. Chemotherapy can also dry out mucus membranes within the nose, mouth, and vaginal area. Non-petroleum over-the-counter vaginal lubricants can assist with the temporary dryness associated with chemotherapy, relieving the discomfort and pain often experienced during sexual relations while on chemotherapy. Because petroleum-based products can irritate the vaginal area and also weaken condoms, they should be avoided.

Fertility

Radiation to the head, surgery, and most medications (except chemotherapy drugs) used to treat brain tumors do not pose a threat to fertility. If radiation therapy is aimed at locations other than the head, you should consult your radiation oncologist about fertility concerns prior to beginning treatment. Often, a lead apron can provide adequate protection to sex organs during radiation treatments.

Brain Tumor Guide for the Newly Diagnosed

Chemotherapy can have a real and permanent effect on fertility in men, reducing or eliminating sperm production. While this effect is reversible in most cases, it may be a number of years before sperm counts return to normal. In women, chemotherapy can temporarily halt menstrual periods, but normal menses should resume after treatments are concluded. Alkylating agents, however, can affect egg production (effects worsen for older women), so concerns regarding fertility should be discussed prior to beginning treatment.

The importance of fertility is a personal choice. While it is not always the priority of the medical team who are basing their treatment on life-saving measures, it should be discussed before beginning any form of chemotherapy. If necessary, you should insist on having that discussion.

Fertility experts can provide advice about the possibility of sperm banking for men or egg harvesting and fertilization techniques for women. Sperm banks typically suggest a minimum sperm count to be frozen for use at a later date, but a low count alone should not discourage you. A fertility expert can give guidance regarding your chances of success in the case of a low sperm count and other options available to you. Although rarely the result of brain tumor treatments, impotence can occur as a result of depression. If you experience more than the occasional sexual dysfunction that is normal with aging, you should consult your medical team about medications and other available treatment avenues. ●



Please remember

- ✓ Because your medical team will be made up of doctors of different specialties, it is vital that you take responsibility for keeping an ongoing and accurate record of the medications you are taking, including their dosage and the names of the physicians who prescribed them.
- ✓ Always ask your medical team to review your complete list of medications before they prescribe anything new.
- ✓ If possible, always fill your prescriptions at the same pharmacy to safeguard against medical errors and adverse drug interactions.
- ✓ Make yourself knowledgeable about the most common possible side effects and drug interactions of the medications you are taking.
- ✓ If you are in your child-bearing years, talk to your doctors about using birth control and consider using sperm banks or egg harvesting.
- ✓ Chemotherapy can produce birth defects. Use contraceptive protection.

Survivor story #8

In April 1989, asked by the girls' softball coach to demonstrate a slide (I had played softball in high school and college), I spent an afternoon practicing and banged my head on the gym floor. I was 27 years old at the time, living at home with my parents, recently engaged to the love of my life. My family physician told me to rest, but I was suffering migraines and was very tired.

The following Thursday I drove home from work with a friend. During the drive, I had another migraine, but this time the left side of my body was going numb. We went straight to the emergency room. In the meantime, my mother described my signs and symptoms to a neurologist, and he told her to have me carry over my CT scans to him. When he looked at them, he told me that I had a tumor that needed to be removed.

On May 2 the neurosurgeon did a craniotomy and removed a cystic astrocytoma from my right frontal lobe. I opted to not receive radiation therapy for there was no guarantee that the tumor would not reoccur. My husband to be and I wanted to start having children; our physicians felt that the tumor had been sufficiently well contained within the cyst. Wasting no time, we began trying right away to conceive a child.

In January when I went for an MRI scan, my pregnancy test was positive. Two more children followed. My neurologist retired. When I met my new neurologist, he shockingly asked whether my husband was ready to raise our children without me. He stated that no one survives the type of brain tumor I had. My husband and I were then contemplating having a fourth child, and I had mentioned that to the new neurologist. He felt we were being foolish.

That's when I discovered the virtualtrials.com website of the Musella Foundation. I went on a rampage to learn more about brain tumors than I ever cared to know. I read many articles and emails. Some made me laugh, some made me cry. It is all such real-life stuff.

I fired the neurologist and spoke with my former neurologist, telling him that I needed a physician that knew that I was going to survive. We had a fourth child.

Since the removal of the tumor 27 years ago, I am alive and well. I have added survival of a hurricane to my life's story, when Hurricane Sandy flooded my home and my four boys and I were not able to evacuate. But the fact that I had already survived a brain tumor made even that horrific storm just another day that God has blessed me with. I continue to have clear MRI scans, and my newest neuro-oncologist has called me an outlier, a designation with which I am perfectly content. I am blessed with good health and an interesting life. Indeed, overcoming a glioma has become the measure by which I readily estimate everything else that God has sent my way.



Caregiving and support groups

It is all too common: You enter your doctor's office with a list of questions, but as soon as your physician has finished his or her comments, you forget your own questions, or worse, forget or misunderstand the answers you receive. Emotions, not your brain tumor, are typically responsible. Emotional support and a second pair of ears can be of tremendous help while you navigate through a new world of tumor terminology.

Even for seemingly routine appointments, whenever possible, take a friend, loved one, or caregiver with you. Aside from taking notes of your session, if you become overwhelmed at any time during your physician's explanation of a particular treatment, necessary tests, or expected results, another person will be at hand to hear (or interpret) the details and will be able to ask questions that you might not think of at that moment.

Encourage your companion to make frequent notations or observations in your personal treatment binder and take an active role in discussing your care options. If your physician will allow recorded sessions, have your companion manage a small hand-held recording device and review the discussion afterwards with you.

In **Table 1** (see page 97) there is a list of organizations that can help provide support for caregivers, families, and loved ones.

Mind, body, soul: faith in healing and emotional wellness

While your primary physician may appear anything but spiritual in his or her approach to your brain tumor, some within the medical community are aware, and in support of, the power of prayer. Prayer, while very personal, may be empowering and proactive at times when "control" seems out of reach.

Also do not neglect the rest of your body. When facing a major problem like a brain tumor, the smaller problems sometimes get overlooked. You have enough prob-

lems to handle without having a “minor” problem blossom into a “major” problem. Be especially mindful of swelling and/or pain in the legs (which may indicate blood clots, unfortunately common with brain tumors), dental problems (some treatments may hurt the gums and teeth), and rashes (indicating allergic reactions to treatments).

Your life, as you once knew it, may change throughout the journey. Things may not seem normal, but there will be a new “normal” for you and your family. The new normal will be what you and your family make it. It will take time, but you will settle into a routine that is comfortable for you. As with anything that is lost, you will go through a grieving process. Although everyone experiences grief and loss differently, you will probably experience some of the universal steps in this process, which may include shock, denial, anger, depression, and acceptance.

How you work through this process will be highly personal and individual. As you work through each step, you will probably have some additional feelings that may at times present conflicts for you. These emotions are many and can be unpredictable. Neither right nor wrong, they just are, and you are entitled to feel the way you do. They may include feelings of loneliness, sorrow, anger, sadness, blame, or shame, which may lead to anxiety and stress. Sometimes you will feel helpless.

To combat such emotions, concentrate on wellness and try to work through each of the feelings rather than denying them. Have a set of coping strategies that will guide you through each step. These strategies may include: (1) accept and understand your limitations, and set realistic goals; (2) get as much up-to-date expert information about your condition as you possibly can so you don't fear the unknown, and be proactive in your treatment plan; (3) take good care of yourself by eating well, getting exercise and rest, and not self-medicating with alcohol; (4) see a mental health provider if you feel it necessary, as he or she can help you handle your emotions and stress; (5) record your feelings in a journal; and (6) try exercise, yoga, massage therapy, and/or meditation.

Palliative care can be a support mechanism for you, your caregiver, and your family. It is not new, having come on the scene for patients around the 1970s. How-

Palliative care (PA-lee-uh-tiv kayr): *Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of palliative care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment. Also called comfort care, supportive care, and symptom management.*

Nine: Caregiving and support groups

Table 1: Organizations that provide support for caregivers

Organization	Website	Description
Cancer Care	www.cancercare.org	Stories and podcasts on subjects ranging from financial assistance to stress management
Caregiver Hope	www.caregiverhope.com	Advice on facing fears and embracing life changes, with stories of hope and help
Cancer Compass	www.cancercompass.com	Discussion groups and resources
Caring.Com	www.caring.com	Articles about caregiver wellness and money and legal matters, and a directory of reviewed and rated home healthcare agencies, nursing homes, and hospice facilities
Family Caregiver Alliance National Center on Caregiving	www.caregiver.org	Helps provide long-term care at home by offering national, state, and local programs to support caregivers
Lotsa Helping Hands	www.lotsahelpinghands.com	Allows you to organize family and friends for needed tasks via electronic calendars and announcements and provides resources for caregivers
National Family Caregivers Association	www.thefamilycaregiver.org	Wealth of informative tips and tools about financial and medical benefits, support groups, respite care, newsletters, and publications
National Hospice & Palliative Care Organization	www.nhpco.org	Resources for caregivers including checklists advance directives
Rosalynn Carter Institute for Caregiving	www.rci.gsw.edu/	Articles and resources just for caregivers, with message boards
Today's Caregiver	caregiver.com	Webinars, resources, support groups, caregiver stories, conferences, and even a book club
Well Spouse Association	www.wellspouse.org	Blogs, articles, and events on an array of timely pertinent subjects

For more information about hospice care, go to the following websites:

- The Hospice Foundation of America: www.hospicefoundation.org
- National Association for Home Care & Hospice: www.nahc.org
- The brain-tumor help site for hospice care, Seeking Peace:
Brain Tumor Hospice Care: brainhospice.com

ever, today it has evolved into so much more and is provided to patients for any diagnosis, at any stage of the condition and/or treatment plan. With palliative care, you, your caregiver, and your family receive emotional support, knowledge, and resources associated with your illness to ensure that your concerns about treatment, medications, side effects, and symptoms are addressed and to enable you to make the most knowledgeable decisions about your care. The first step in seeking palliative care is to ask your doctor or cancer center. Your goals will be to reestablish the quality of your life, to ease stress, and to be more in control. It will take time and patience, but you will find your comfort zone.

At some point, you may want to transition to hospice care, which can be given at home, in hospitals, nursing homes, or inpatient hospice facilities. This highly specialized concept of care — given by a partnership of family members, caregivers, and medical professionals — focuses on providing ongoing comfort, emotional support, and pain management 24 hours a day. It may also include spiritual counseling for the patient and family members. Hospice care will provide medications, equipment, and any medical supplies needed, as well as physical, speech, and occupational therapies to make you feel as comfortable as possible. You will work with an interdisciplinary team including medical professionals, social workers, home health aides, clergy members, and trained volunteers. Because most people see hospice care as marking an end of life, it is often not started soon enough. You can always opt out of hospice care if you wish to re-enter appropriate treatment or if you experience remission. Like palliative care, the main focus of hospice care is to bring quality-of-life and support services to the patient, caregivers, and family members. While palliative care may be given at any time and even through treatment, hospice care is appropriate when life expectancy is six months or less and treatments are no longer an option.

Impairments and strategies for coping

Now that you have been diagnosed with a brain tumor, you may start to experience a variety of impaired functional abilities depending on the size and location of your

brain tumor and your treatment plan. You may experience depression, memory and concentration lapses, personality and mood shifts, anxiety, insomnia, difficulties with self-care, poor balance, bowel and bladder incontinence, and conversational speech and word-finding problems. Healing and recovery from surgery and treatment are very important. When you are discharged from the hospital, make sure you are given clear instructions for caring for the surgical site, for what activities you can and can't do for a period of time, for medications and dosages, and for what to do if problems develop. Arrange your ride home from the hospital and have someone at home to help you until you feel well enough to manage on your own.

Each brain reacts differently to treatment, but you can find a way to adjust and compensate. There are strategies you can use that will help you to function and feel better and in some cases regain lost functional ability.

First and foremost, speak with your medical team about your difficulties before they become more complicated. They may prescribe some medications to ease your symptoms or refer you for physical, speech, occupational, or hyperbaric therapy sessions. Physical therapists will provide exercises that strengthen your muscles, increase your flexibility and mobility, and help you regain balance. Occupational therapists will work to strengthen small muscle control and gain functionality with self-help daily activities. Speech therapists will help in developing communication skills, vocabulary, and swallowing. Neuropsychologists will help you cope with and assess cognitive and emotional changes, as well as memory, thinking skills, problem-solving and reasoning, and perception. **Hyperbaric oxygen** therapy sessions may be recommended to aid in healing damaged tissue. Each of the therapists may also recommend adaptive devices to help you regain some degree of functional independence.

Hyperbaric oxygen (HY-per-BAYR-ik OK-sih-jen): *Oxygen that is given at a pressure that is higher than the pressure of the atmosphere at sea level. In medicine, breathing hyperbaric oxygen increases the amount of oxygen in the body. It is used in treating certain kinds of wounds, injuries, and infections. It is also used to treat carbon monoxide poisoning and other conditions in which the tissues are not getting enough oxygen. It is being studied in the treatment of some types of cancer. Hyperbaric oxygen may increase the amount of oxygen in cancer cells, which may make them easier to kill with radiation therapy and chemotherapy. It is a type of radiosensitizing agent and a type of chemosensitizing agent.*

.....
: The Musella Foundation provides a comprehensive list of “real-world” face- :
: to-face support groups, with contact numbers and email addresses, and with :
: meeting locations and schedules. To access that list to find a support group :
: near where you live, go to: www.virtualtrials.com/support.cfm. :
.....

Second, speak with your partner or family members and explain how and what you are feeling. It is important to bring people on as part of your team to support you and help make things a little easier for you. However, they need to understand what you are experiencing before they can help. The more informed they are, the better they will be able to cope, understand you, and help you set goals.

The following coping strategies have been used successfully by people in our online support group to regain quality of life. But first you must understand your strengths and weaknesses, identify or know the problems, and be willing to try a solution. At this point you may be feeling overwhelmed and confused about the changes you are experiencing. You may also feel some grief or denial for the loss of functioning. These strategies will provide the tools you and your loved ones need to help you rebuild your life.

Sometimes, the simplest solutions for what you are experiencing are organization and altering the environment. For cognitive difficulties, making notations on a legal pad, calendar, or day planner will aid memory. Include a check-off sheet or page as needed for each task completed. It will be helpful to use an alarm watch or kitchen timer to alert you of time sensitive activities. You may wish to use a weekly medicine dispenser with slots for am and pm medications. For better concentration, you may need to minimize or avoid distractions such as loud noises. Stay focused on one task at a time or alter a task by breaking it down into smaller parts. Sometimes a daily activity or time-management chart may help organize your day. Set limits and don't schedule too many activities in one day. Rest when you need to. You may find it helpful to follow a routine by keeping a consistent schedule. Keeping daily items in predetermined designated places will make them easy to find and save time locating them.

For physical safety and comfort be aware of potential dangers in and outside of the home such as clutter, fire hazards, sharp objects, hazardous household products, scatter rugs, inadequate lighting, water heater temperature, and outside hoses. Don't forget to declutter drawers and closets. Switch to plastic cups and plates when needed. You may need to install additional handrails or place brightly colored tape across steps. You may need to conserve your energy or find it safer to use assistive aids such as canes, walkers, or wheelchairs. You may also need to install grab bars

in bathroom/shower areas, use a shower seat while bathing, or purchase disposable underwear. Daily movement, which may be as simple as stretching, no matter how limited your ability, will help with improving your night's sleep, reducing negative emotions, and reducing stress, and will also help you focus.

You and your family may find it helpful to communicate with the use of word cues, picture flash cards, simple language and sentence structure, or by asking only one question at a time and repeating back information to ensure understanding. But first, make sure you are looking at the person speaking to you, so that you can focus and pick up visual cues. You may also find it helpful to play word games and puzzles.

It is important to recognize that there is no one way of doing things. You will learn to compensate for your deficits by learning new ways. Sometimes, you may feel that you have reached a plateau, but that doesn't mean that you will not progress again. You may continue to experience progress and setbacks in functioning. However, it is important to realize that when one way of doing things may no longer work for you, the strategy needs to be changed. Having patience and flexibility will be essential to your recovery. Your life will feel more normal and on track by using coping strategies that work for you.

Support groups

Support groups found on the Internet or a local support group sponsored by your hospital/regional cancer organization can often assist with nonmedical issues — such as nutrition, relationships, and/or financial concerns.

Most people are shy about joining a support group, but don't be. You will be amazed at how quickly you feel at ease, because the members know and understand what you are going through, something (hopefully) nobody else in your circle of friends knows about.

“Real-world” support groups

We urge all brain tumor patients to try out one or several support groups, whether online or “real world.” It is a very powerful experience to speak directly with people who have undergone the same passage. Real-world and even online support groups are typically facilitated by nurses or other caregivers.

If you live near a metropolitan area, you can attend a support group in person. These support groups provide community, and they can be safe places to open up and share both positive and negative emotions.

There are many online support groups with different focuses. The Musella Foundation runs and manages a number of online support groups, and it maintains a list of many other online support groups. To see what is available, go to: www.virtualtrials.com/lists.cfm.

Some cancer and dedicated brain tumor organizations provide search engines on their websites that can help you find nearby real-world support groups in your area. These organizations include:

- American Brain Tumor Association. Go to: www.abta.org.
- Cancer Care. This organization is a national leader in providing professional services to help people manage the emotional and financial challenges of cancer. Go to: www.cancercare.org.
- The National Brain Tumor Society. Go to: braintumor.org/brain-tumor-information/finding-support-coping/.

Online support groups

The Internet and social media sites offer nearly an unlimited resource for brain tumor patients, including online support groups, sometimes called “mailing lists” or “listservs,” chat groups, and message boards for sharing experiences and treatment options with others who understand what you’re going through. Although social media sites like Facebook are a good way to keep in touch with family and friends, and some brain-tumor groups are active there, be aware that Facebook is very public. So be cautious, and be sure to activate privacy settings, if you do not want information about yourself or your medical condition to be available for years to people who do not know you.

Below is a listing of online support groups that are run by the Musella Foundation:

- **Braintumor treatments group.** This is our main brain tumor online support group. Talk is limited to medical discussions about brain tumor treatments (as well as diagnoses, testing, symptoms, etc.). Discussion about all types of brain tumors is allowed: malignant, benign, primary, and metastatic. No talk of politics, jokes, religion allowed. For those, use the other groups listed below.
- **Brain Novocure group.** For people interested in the Optune device.

Nine: Caregiving and support groups

- **Braintumor community group.** A group focused on nonmedical discussion, for the types of messages that would be off-message for other groups. Humor and politics welcome.
- **Braintumor faith group.** For discussions involving faith, religion, and God among people interested in brain tumors.
- **Optic glioma group.**
- **Brainstem glioma group.** Adults and children with brainstem tumors.

There are many other online support groups for brain tumor patients that are not run or endorsed by the Musella Foundation but are listed at the virtualtrials.com website.

A word of caution: Support groups (both online and “real world”) play an important and, in many cases, vital role in helping participants maintain a positive outlook during treatment and stay up to date on the latest brain tumor issues. However, you have to be cautious and evaluate how much you can trust anything you find. There are people out there who are simply looking to make money off of your misfortune, and even people who are trying to help might inadvertently supply you with misleading information. NOTHING on the Internet or at a support group meeting should be taken as real medical advice. It is important to research anything you find and discuss it with your medical team. Chat rooms are especially susceptible to problems because they may have few participants and an insufficient number of other people with whom you can discuss the pros and cons of a treatment. On the other hand, in an online support group like the “Braintumor treatments group,” you can ask for the experiences of many people with a specific treatment and get a broader view of it.

When using the Internet, exercise common sense and discuss information with your medical team to help you make the best possible decisions about your care. To evaluate information found on a website, consider the credentials of the person posting the information, how up-to-date the site is, whether any contact information is posted on the site, and whether the claims on the site are too good to be true or sound as if something is being sold to you. ●



Please remember

- ✓ Whenever possible, go to all appointments with a friend, loved one, or caregiver to help you understand what the doctors are saying to you.
- ✓ Do not neglect the rest of your body. Do not neglect your emotional health.
- ✓ Support groups can educate you, lift you up, be a place to express both positive and negative emotions, and provide a strong sense of community.
- ✓ Many cancer organizations and local hospitals offer support groups.
- ✓ Online support groups can cover a wide variety of topics and issues. The Musella Foundation runs and manages a number of such groups.
- ✓ Nothing on the Internet or at a support group meeting should be taken as medical advice. If you have any questions, discuss them with your medical team.

Survivor story #9

In June 2000, when I was 33 years old, my life quickly changed. I began having headaches that felt as if my skull were going to explode. An MRI scan showed that my brain was hemorrhaging, and I went immediately into surgery. An acorn-sized glioblastoma tumor was found in my left temporal lobe. I was told I had less than a year to live.

I quit my job to be a stay-at-home mom, wanting to spend every precious moment with my boys. I went into conformal brain radiation. I refused chemotherapy because standard treatment at that time had seriously bad side effects and would only add a few months to my life.

In July 2004, the glioblastoma came back. I had awake surgery since the glioblastoma was located in my left temporal lobe and there was a high risk of my losing the ability to speak. After surgery I went on the 5-day, 23-week temozolomide (Temodar) schedule.

Again the glioblastoma came back, and I went into brain surgery a third time. The tumor was only the size of a “pea,” but during surgery a buffer around the tumor was removed. After surgery I again went back on temozolomide.



In March 2009, the glioblastoma came back a fourth time. This time the tumor was not even located in my brain but in the meninges (the layer of tissue that covers the brain). I went into surgery a fourth time and all “visible” tumor was removed. The brain itself looked nice and clear, no visible tumor in the brain itself. After surgery, I could not go back on temozolomide since it had quit working for me, and I did not qualify for any clinical trials because of the third reoccurrence of the cancer and my treatment history. We decided to keep an eye on the tumor with MRI scans every 2 months.

Now, fast forward to 2018, I have endured three more recurrences

Brain Tumor Guide for the Newly Diagnosed

of my brain tumor. The last recurrence was last year, when it was discovered that I had a grade 3 anaplastic pleomorphic xanthroastrocytoma (a rare type of anaplastic astrocytoma) located in my pituitary gland. Because the tumor was inoperable I went through four weeks of radiation therapy. At the end of the year, my MRI scan looked clear, with no glioblastoma or xanthroastrocytoma seen.

Over time I have experienced many deficits. Some of these have been challenging, others I have managed. Most people would never know that I am battling brain tumors. I seem normal. However, my family and good friends know I am seriously suffering in the fight.

But I love life, and I will never regret this fight: it has been well worth it. Since my last recurrence, I have had fun with my family, hugged my boys goodbye at college, celebrated holidays, and enjoyed the beauty around me. During these years, connecting with others battling brain tumors has inspired me so much. Al Musella and the virtualtrials.com website have been so helpful. Reading survivor stories is encouraging. Please don't feel it is over. Don't listen to the statistics. We can still love life and have fun even as brain tumor patients.





Insurance management and financial assistance

Some people with brain tumors are afraid that their health insurance will be cancelled because they have become sick. Others are afraid that the cost of their medical treatment during a year or over a lifetime will exceed dollar pay-out limits set by their health insurance plan, thereby depleting life savings or even bankrupting them. Others are afraid that if they lose their job — and the health insurance that goes with the job — while being treated for a brain tumor, they will not be able to find new health insurance because of the preexisting condition. Or they are afraid that they will not be able to afford the health insurance even if they can continue with their existing policy or if they do find new coverage.

The Patient Protection and Affordable Care Act (ACA), the federal law passed in 2010 that is often also referred to as Obamacare, was enacted to help displace such fears. Many national cancer organizations have evaluated the ACA. According to the American Cancer Society, for example, the ACA has helped and will help people with brain tumors in the following ways:

- Upon passage, the law immediately stopped insurance companies from dropping patients from coverage just because they got sick.
- Upon passage, the law immediately banned health insurance companies from having lifetime pay-out limits. In 2014, the law banned health insurance companies from having annual pay-out limits.
- Upon passage, the law immediately banned health insurance companies from denying coverage to children with preexisting conditions. In 2014, the law banned health insurance companies from denying coverage to adults with preexisting conditions, like cancer.
- Upon passage, the law immediately banned health insurance companies from denying coverage to patients who participate in clinical trials.

- Upon passage, the law immediately banned health insurance companies from charging patients for cancer screening tests, such as mammograms and colonoscopies.
- In 2014, the law required all states to create online health insurance marketplaces (usually called “exchanges”) so that people without insurance through employment can compare and buy coverage from health insurance companies.

With passage of the ACA, if you had health insurance through your employment, you kept your current health insurance. However, your health insurance plan now has to abide by the provisions of the ACA law, such as following the ban on lifetime and annual pay-out limits and providing free cancer-screening tests, among others.

The costs of cancer care

Even with insurance coverage, cancer care can be expensive and result in financial hardship. Many people have insurance plans with yearly deductibles, specified amounts of expenses they must pay out of pocket each year before the insurance plan will begin paying any costs. After the yearly deductible is met, insurance plans also often require co-insurance payments. For example, with a typical 80/20 co-insurance rate, the insurance plan will pay 80% of approved medical costs while the patients must pay the remaining 20% of medical costs out of pocket. Finally, many insurance plans require co-payments. A co-payment is a set fee, like \$30, that an insurance plan requires the patient to pay out of pocket each time the patient visits a physician

Consequently, taking into account deductibles, co-insurance payments, and co-payments, the amount of out-of-pocket costs for direct medical care — visits to physicians, surgery, radiation therapy, chemotherapy — can add up to a considerable amount even for patients with excellent insurance plans. But in addition to direct med-

.....
: The American Society of Clinical Oncology sponsors a website for patients :
: called Cancer.net. This website has an excellent section on financial :
: considerations related to cancer care, including a video presentation. :
: Especially relevant is the page entitled “Questions to Ask about Cost.” :
: Go to: www.cancer.net/navigating-cancer-care/financialconsiderations. :
.....

ical costs, there are also many nonmedical expenses associated with cancer treatment. These include transportation, hotels, meals, and childcare.

In a recent issue of the medical journal *Neuro-Oncology Practice*, investigators analyzed the out-of-pocket expenses for 43 patients diagnosed with malignant glioma between August 2008 and May 2012. Of these 43 patients, 35 (81%) were newly diagnosed with malignant glioma. The majority had private medical insurance, 10 (23%) had Medicare or Medicaid coverage, and 2 (5%) were uninsured. The investigators found that the monthly median out-of-pocket expense for these patients was \$1342 (remember, the median is the middle value in a set of measurements, with half the values above that middle value and half below). Within that monthly median out-of-pocket amount, the highest components were payments for medication (\$710), hospital bills (\$403), and transportation (\$327). These expenses decreased after 3 months, suggesting that expenses were reduced after the completion of radiation therapy. The investigators also found that median lost wages were \$7500 and that median lost work time was 12.8 days.

Understanding your insurance

Insurance laws vary from state to state. Also, your health insurance policy may be under state or federal guidelines depending on where you work and whether your employer is self-insured. A large employer who is self-insured is not considered an insurance company but rather writes its own policy that is in turn managed by an oversight organization, which may be a health maintenance organization (HMO) operating within your state. The self-insured policies are governed by federal laws, and even state laws such as in California — with strict HMO laws protecting consumers — are not available to those covered by self-insured federally regulated plans.

Complicating things even further, plans such as HMOs and preferred provider organizations (PPOs) often fall under different jurisdictions as well. Your human resources department at your employer can often tell you if your plan is self-insured, whether it is governed by state or by federal regulations, and the contact information for the proper agency.

Most insurance plans contain a specific list of “covered” medications and those that are excluded from coverage, called a “formulary,” and by law must provide you with a copy upon request. Many of the drugs used in the treatment of brain tumors are approved by the FDA for other conditions but are not approved for treatment of conditions associated with brain tumors. When a physician prescribes a medication

.....
: The Musella Foundation runs a co-pay assistance program for people with :
: health insurance for one or more of the following treatments: Avastin, :
: Gliadel Wafer, Temodar, and the Optune device. To find out about this :
: program, go to: www.braintumorcopays.org/index.cfm. :
.....

for a condition that falls outside the FDA-approved guidelines, it's called an "off-label" use, and in many cases is not covered.

Many states provide an appeal process for challenging an off-label denial that may assist you in obtaining coverage. You may be required (if for no other reason than your immediate need of the drug) to pay for the prescription out of pocket, as the process may take several weeks for a decision. If your employer or the insurance company will allow you to upgrade your prescription coverage to one that will allow for off-label medication coverage, you would be wise to do so now, regardless of whether or not you require such coverage at this time — it's likely you will need it in the future.

Note: Request a copy of your insurance plan's formulary and keep it in your treatment binder. Have your physician check the formulary when prescribing a new medication to ensure coverage, or perhaps select a like drug (if available) from the formulary to avoid unnecessary out-of-the-pocket expense.

Information regarding the laws that govern switching plans during treatment or "continuity of care" issues when policies change with new employment can best be answered by calling the office of your state's insurance commissioner. Many states, such as California, have specific departments for patient advocacy that can help you work through these issues, or direct you to the proper federal agency if your plan is governed by federal regulations. Such patient advocates within your state health insurance department can help you with the necessary paperwork for filing appeals or complaints when your insurance company denies coverage for specific treatments or medications.

- All communications (from making claims to general inquiries) should be in writing.
- When communicating by phone or in person, be sure to record and confirm your understanding of the conversation in a letter sent certified with confirmation of receipt, and keep a copy of the letter in your file.
- Scrutinize everything you receive from the insurance company and hospital — for example, bills, payments, and credits for mistakes — they DO happen! Do not be afraid to ask for explanations for items that are unclear or unspecified.

Ten: Insurance management and financial assistance

- Read your policy thoroughly so that you are aware of what benefits you are entitled to and what items are excluded, paying special attention to areas involving clinical trials or experimental treatments. Be prepared to ask your physician to write a letter on your behalf explaining why you should be allowed coverage for these items. It is helpful to have an “understanding” with your physician as to when consideration of experimental therapies would take place, rather than waiting for that day to arrive, only to find an unsupportive care partner.
- Health insurance companies can assign a case manager to you so that you can talk to the same person each time you call. Ask your insurance company whether you can be assigned a case manager.
- Do not hesitate to ask to deal with a “superior” of the person handling your account, and keep accurate information regarding the names of all persons (and their positions) involved with your claims.
- Before making a request, make sure that the person you are dealing with has the authority to grant it.
- Do not be intimidated.
- Do not hesitate to challenge anything that doesn’t sound right to you.
- If you are unsure about anything, check with the State Insurance Department (see above) and then, if necessary, with a lawyer. If you do not think you can afford a lawyer, you may be able to get low-cost or free legal help. Try calling the local bar association to ask about legal aid (available through nonprofit organizations in most major communities) or a local law school to ask if they have a student law clinic.
- Most states have nonprofit advocacy organizations that are dedicated to access and continuity of care issues and are able to discuss your legal rights and avenues for contesting insurance decisions on your behalf. You can search the Internet using the words: insurance denials, HMO, continuity of care, or healthcare access along with “patient advocates.” In California, Citizens for the Right to Know is an excellent resource.
- Set up and keep a file of all correspondence and phone communications relating to your claims. The file should include, but not be limited to, bills, payments, claims, letters you send, letters you receive, checks, contacts, and your policy.
- Be sure that all of your premiums are paid on time. You may have trouble getting insurance again if you let your policy lapse.
- Keep track of all of your unreimbursed medical expenses. You might be able to claim these expenses on your tax returns.

Medicare coverage

In the United States, Medicare starts at age 65 years for persons eligible to receive it. Medicare comes in several distinct parts. Part A covers hospital expenses, an optional part B covers doctor expenses and outpatient care, and an optional part D covers prescription drug expenses. Part A is free for Medicare patients, but it pays only 80% of hospital inpatient care and has a deductible. Part B charges a means-based monthly fee starting at \$135.50 in 2019 (deducted from Social Security benefits if they are being received), but it also pays only 80% of expenses and has a deductible. Parts A and B are called “original Medicare.” Part D requires enrolling in a Medicare prescription drug plan provided by a private company, which charges a monthly premium.

Because parts A and B pay only 80% of medical expenses, another part of Medicare, the missing part C, is designed to cover much of that 20% gap and lower deductible exposure. These are Medicare Advantage Plans, offered by private companies. A person must be in original Medicare before joining a part C plan. Medicare Advantage Plans often have monthly premiums (in addition to the part B premium), but many of these plans also include part D drug coverage as well as extra benefits, like vision, hearing, and dental coverage. Medicare Advantage Plans, however, typically operate with provider networks — that is, they are either HMOs or PPOs. That means that covered services will be less expensive to you as long as you see doctors or use hospitals that belong to the plan’s network.

As an alternative to Medicare Advantage Plans, Medicare supplemental insurance (Medigap) policies are available from private companies to cover the 20% gap that original Medicare leaves. There are a variety of these supplemental plans, offering different benefits. These plans generally cost more than Medicare Advantage Plans, and they are not bundled with a part D prescription drug plan, which will have to be acquired separately. But supplemental plans do not attempt to limit the choice of doctors or facilities, exposing you to more expense if you choose to use doctors or medical care centers outside a plan’s provider network.

As a brain tumor patient, you will need to seek out the best care possible for your brain tumor at a comprehensive cancer center — or at more than one center over the course of your treatment — wherever possible in the country. Consequently, if you are enrolled in Medicare, or will soon be, it might be prudent during the next annual enrollment period to seek out the best supplemental insurance (Medigap) policy you can afford because Medicare Advantage Plans are designed to limit choices to a

preferred provider network. One place to begin a search for supplemental insurance (Medigap) policies is at the website of the American Association of Retired Persons (AARP): www.aarp.com.

Financial assistance

There are many organizations and even individuals that provide financial assistance to patients with brain tumors and their families. Miles for Hope, for example, provides flight assistance to those participating in clinical trial treatment. Other organizations might not provide direct help with expenses but can help reduce the costs associated with medical care. Angel Flight was created by a group of volunteer pilots to provide for free air transportation for medically related needs when time is important but the trip is not an emergency. The organization called Mission4Maureen has funds to cover an array of expenses, from travel for treatment, to maintaining a place to live, to paying medical bills not covered by insurance.

The Musella Foundation runs two different programs to help you with treatment costs. For people with insurance, we have a *co-pay assistance program* for one or more of the following treatments: Avastin, Gliadel Wafer, Temodar, and the Optune device.

For people without insurance, we have a *Musella Foundation Drug Discount Card* that can save everyone — not just patients with brain tumors — up to 80% or more off the cost of prescription medicines, over-the-counter medicines (that is, medicines not needing a prescription), and even prescription medicines for pets. There is no cost for the card, there is no risk in using it, and it is immediately available online, with no registration required. You take the card to your pharmacy and ask how much the prescription would cost using this card compared with how much it would cost without it. If using the card is less expensive for the prescription, then use it.

The Musella Foundation Drug Discount Card can also be used by patients who have insurance — but you cannot combine the discount this card provides with the discount your insurance provides. Sometimes the card discount will be greater than your insurance discount.

.....
: The Musella Foundation provides a Musella Foundation Drug Discount Card :
: for all patients, but especially those patients without insurance. To get the :
: card immediately, go to: www.virtualtrials.com/drug_assistance.cfm. :
.....

Table 1 provides a list of some of the organizations that can help you. As a reminder, if you receive Medicare or Medicaid benefits from the US Centers for Medicare & Medicaid services, you can also contact those agencies directly for help paying some of your health care and prescription drug costs. Call 1-800-Medicare. ●



Please remember

- ✓ It is imperative to understand the health insurance you have and the benefits it provides.
- ✓ Communicate with insurance companies in writing.
- ✓ Scrutinize everything you receive from insurance companies, and ask for explanations for things you don't understand.
- ✓ Set up and keep a file of correspondence and communications regarding claims.
- ✓ Be sure that premiums are paid on time.
- ✓ Don't be intimidated.
- ✓ There are organizations and individuals that can provide financial assistance, including the Musella Foundation.

Table 1: Organizations that can provide financial advice and support

Organization	Website	Description
Angel Flight Travel Assistance	www.angelflight.com	Arranges free air transportation for any legitimate, charitable, medically related need
CancerCare	www.cancercare.org	Offers financial assistance for cancer-related costs and co-pays, and professional oncology social workers can help guide to additional resources
Darren Daulton Foundation	www.darrendaultonfoundation.org	Provides financial assistance to those who suffer from brain cancer, brain tumors, and brain injuries
Drug Assistance Programs from Pharmaceutical Companies	www.rxassist.org	Lists pharmaceutical company programs intended to facilitate access to needed medications for patients who have financial difficulties and are not eligible for Medicare, Medicaid, or private insurance
Glenn Garcelon Foundation	www.glenngarcelonfoundation.org	Gives grants to people with primary brain tumor of any type (malignant or non-malignant)
Medicare Rights Center	www.medicarerights.org	Ensures access to affordable health care for older adults and people with disabilities
Mission for Maureen Travel Assistance	www.mission4maureen.org	Provides financial assistance to families burdened with the cost of brain cancer treatment. Financial aid is available for medical bills as well as child care, housing payments, utility bills, transportation, medication and other areas of assistance
NeedyMeds	www.needymeds.org	Maintains website of programs that help people who cannot afford medications and healthcare costs and provides a free drug discount card
Patient Advocate Foundation	www.copays.org	Provides financial assistance to patients, including those insured through plans like Medicare, for co-payments, co-insurance and deductibles required by a patient's insurer

Survivor story #10

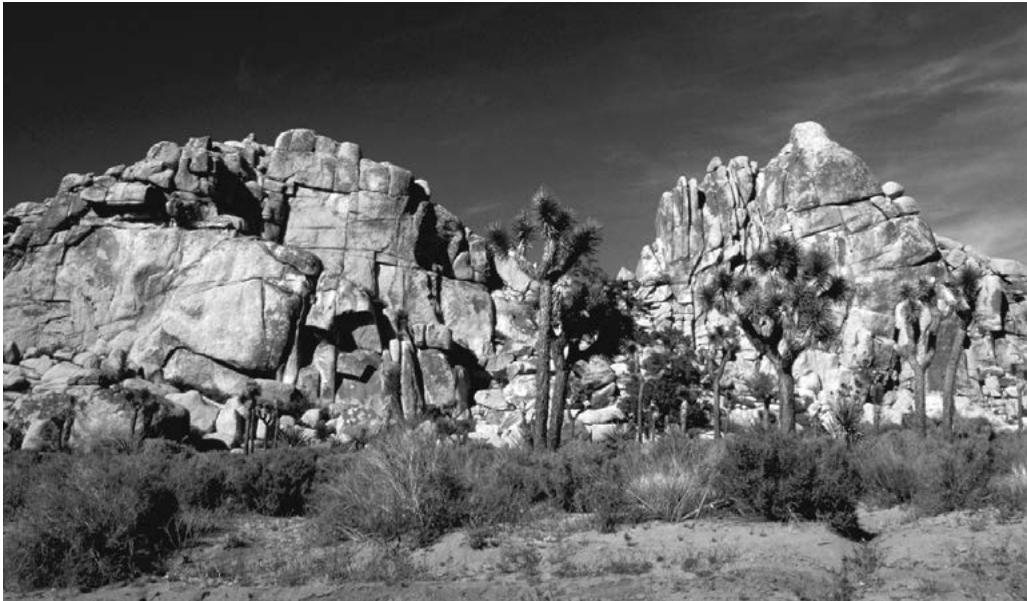
On June 1, 2005, just five weeks after the birth of my first child, I was diagnosed with glioblastoma. This malignant and deadly type of brain tumor was the size of a woman's fist. Glioblastoma patients are told that "it's not a matter of if, it's a matter of when" the tumor will come back.

I quickly underwent brain surgery to remove the glioblastoma. The problem with brain surgery is that the doctors don't know what they will find until they cut into your head and take a look. After discovering that removing the tumor could cause a loss of mobility on my left side, the surgeons removed only half of it. I was told I would be lucky to live a year. I kept telling the doctors that that couldn't be right, because I had just had my first child.

My husband and I were not going to give up easily. We hit the road to visit some prestigious cancer centers after receiving the worst possible pathology report. Both brain tumor clinics recommended that I "re-do" my brain surgery to complete the removal of the tumor. I chose one of these centers to coordinate all of my treatment. I also went on long-term disability to cover my medical bills and keep my business afloat.

In July 2005, surgeons operated again to remove the remaining tumor, a procedure that was successful.

At that time, I entered a clinical trial that involved the implantation of a drug locally at the affected areas in my brain, treatment that required a four-day stay in a neuro-intensive care unit. Most brain surgeries remove the tumor but not all the



Ten: Insurance management and financial assistance

damaged cells. The new procedure was a way to kill off the remaining damaged cells and prevent the tumor from coming back. I was lucky that my health insurance paid for the hospital stay and all expenses. Frequently, we had no idea whether our health insurance would pay for an experimental treatment if needed.

The surgeries and experimental drug procedure were a success. Nonetheless, I lost a lot of my cognitive function, and it took weeks for me to recover.

As if the brain surgeries weren't enough, my family and I moved to the location of the cancer center to receive a complete series of radiation treatment. After radiation, I then began a year of chemotherapy. I returned to work during this important recovery period. Because of my disability insurance, I didn't have to come back to work, but I love what I do. But without the disability income, I would not have been able to keep my business afloat. It was a life saver.

Now, in 2018, I have had clean MRI scans for 13 years. I attribute my success to mindset, resilience, and tenacity — all of the qualities that enabled me to see beyond a terrible diagnosis in 2005. I strive to continue to set an example to my son, my family, my peers, and my community, in hopes that I can create even a small amount of impact while I am here.



Afterword



Al Musella, DPM

In 1992, my sister-in-law Lana, a mother with four children, was diagnosed with glioblastoma. Lana had surgery and radiation, but then the first MRI scan after radiation showed that the tumor had grown even larger. This was before Temodar, the Gliadel Wafer, and Avastin were available. So the outlook for Lana was bleak. Her doctors also told her there were no clinical trials that would take her because of the size of her tumor. In fact, although they were at a major brain tumor center, they basically gave up on her. At the time, there was no centralized database of clinical trials for brain tumor patients.

But I was computer savvy. I started the first online support group dedicated to brain tumors on CompuServ and AOL. I also published a brain-tumor clinical trials database online, one of the first database-driven websites for any cancer type. Lana found that she was eligible for many clinical trials and tried two of them. She did much better than expected. She lived eight years, a survival course that was almost unheard of back then, and for most of that time she remained in good health.

In 1998, the Musella Foundation was organized as a not-for-profit charity dedicated to speeding up the search for cures of brain tumors and to helping families deal with the diagnosis of brain tumor. Ironically, my father was diagnosed with glioblastoma the very next year. We were more prepared than previously to deal with this diagnosis, but it was still a horrendous experience to go through. Because his tumor progressed so rapidly, my father died only a few months after it was discovered.

Since then, a lot has been accomplished by the Musella Foundation:

- Our virtualtrials.com website continues to expand in terms of services provided and the community served (in 2018 we had 50,000 visitors from 217 different countries).
- Our co-payment assistance program has awarded more than \$5 million in grants to over 1000 brain tumor patients in this life-saving program.

Afterword

- We created and run the Brain Tumor Virtual Trial, our study of brain tumor patients, as well as the long-term glioblastoma outcome project.
- We helped convince Medicare to pay for Temodar and for Gliadel Wafers, and we are working on getting Medicare to pay for the Optune device. We have helped accelerate FDA approval of Temodar, Avastin, and Optune for brain tumors.

Most important, we think, are the online support groups that we run. Every family that is dealing with a brain tumor should have at least one member join the “Braintumor treatments group” through our website. Joining that group allows you to communicate with more than 2600 families going through the same passage. Those who have travelled further down that road can help — and want to help — those of you starting out right now.

In the 27 years that I have been immersed in the world of brain tumors, I have seen an amazing change in attitude among brain tumor researchers. There has been an unprecedented burst of progress in identifying new approaches. I am convinced that we are in the home stretch and a cure is within sight. It is now only a matter of time and money. But although the government now funds brain tumor research at an unprecedented level, many promising projects remain unfunded. Through the Musella Foundation, we have a chance to speed up the search for a cure, by funding selected research that complements, without duplicating, research funded by the government.

To that end, we need your help. Donations to the Musella Foundation can be general or can be dedicated to specific ends, like our support for brain tumor research or our co-payment assistance program. For more details on how you can help us speed up the search for the cure, please visit the virtualtrials.com website. ●

Al Musella, DPM

Founder and President

The Musella Foundation for Brain Tumor Research and Information

Recent grants made by the Musella Foundation

Below is a listing of recent research grants made by the Musella Foundation. Since 2003, the Musella Foundation has awarded investigators with over \$4 million in 126 grants. We have helped fund the early work on some of the most promising therapies in the pipeline.

Interested investigators should call the Musella Foundation directly to discuss the project(s) for which they seek funding before submitting the formal grant application.

To see a list of all grants awarded by the Musella Foundation, please go to the grants page at the [virtualtrials.com](http://www.virtualtrials.com) website: www.virtualtrials.com/grants.cfm.

Some of the grants awarded in 2018

- \$250,000 to investigators at Oncoceutics, Inc., Philadelphia, PA, as the first payment of a \$1 million grant for the project: “Onc-201 for diffuse intrinsic pontine glioma (DIPG) and high-grade gliomas with the H3 K27M mutation.” This payment was made in collaboration with the Cure Starts Now and the Michael Mosier Defeat DIPG Foundation.
- \$50,000 to investigators at the University of South Florida, Tampa, FL, for the project: “ICA-1 treatment for glioblastoma and medulloblastoma.”
- \$50,000 to investigators at the Jackson Laboratory for Genomic Medicine, Farmington, CT, for the project: “Targeting ribonucleotide reductase for the treatment of glioblastoma.”
- \$27,000 to investigators at Dana Farber Cancer Institute, Boston, MA, for the project: “Inducing therapeutic differentiation in DIPG by reprogramming chromatin with dual HDAC/LSD1 inhibition.”
- \$25,000 to investigators at Brigham and Women’s Hospital, Boston, MA, for the project: “Targeting the actin polymerization pathway for improved treatment of glioblastoma multiforme.”

Recent grants

- \$25,000 to the DIPG Collaborative, Cincinnati, OH, to help fund research into pediatric diffuse intrinsic pontine glioma (DIPG).
- \$25,000 to investigators at Duke University Medical Center, Durham, NC, for the project: “Oncolytic poliovirus immunotherapy for pediatric medulloblastoma.”
- \$25,000 to investigators at Huntsman Cancer Institute, Salt Lake City, UT, for the project: “Exploiting the vulnerability of mutant IDH gliomas.”
- \$25,000 to investigators at Johns Hopkins Hospital, Baltimore, MD, and the NIH Neuro-Oncology Branch, Bethesda, MD, for the project: “Evaluating the pharmacokinetic and pharmacodynamics response and profile of acquired resistance to trametinib and dabrafenib in BRAF-V600E-mutated recurrent gliomas.”
- \$25,000 to investigators at the Roswell Park Comprehensive Cancer Center, Buffalo, NY, for the project: “Elucidating a novel invasion mechanism present in glioma associated mesenchymal like stem cells leading to tumor progression.”
- \$25,000 to investigators at the University of Connecticut Health Center, Farmington, CT, for the project: “Can iodine-nanoparticle-enhanced radiation therapy increase the efficacy of temozolomide therapy? A preclinical study.”
- \$25,000 to investigators at the University of Colorado School of Medicine, Aurora, CO, for the project: “Expanding preclinical work for a phase 1/2 trial of selinexor and radiation therapy in newly diagnosed DIPG and diffuse midline glioma.” This grant is from our DIPG all-in-initiative fund.
- \$12,500 to investigators at the Ann and Robert H. Lurie Children’s Hospital of Chicago, IL, for the project: “Development of a novel, selective, orally bioavailable PLK4 inhibitor for the treatment of pediatric brain tumors.”

Brain Tumor Guide for the Newly Diagnosed

Some of the grants awarded in 2017

- \$50,000 to investigators at Wake Forest University, Winston-Salem, NC, for the project: “Targeting hypoxia-inducible factors in gliomas.”
- \$50,000 to investigators at Hackensack University Hospital, Hackensack, NJ, for the project: “Potentiating radiation therapy of glioblastoma with telmisartan and immune checkpoint inhibitors.”
- \$25,000 to investigators at Oncoceutics, Inc., Philadelphia, PA, for the project: “Clinical evaluation of DRD5 as a predictive biomarker of response to the selective DRD2 antagonist ONC201.”
- \$25,000 to the DIPG Collaborative, Cincinnati, OH, to help fund research into pediatric DIPG.
- \$25,000 to investigators at the Dana Farber Cancer Institute, Boston, MA, for the project: “Defining molecular mechanisms of resistance to glioblastoma immunity using a novel CRISPR/Cas9 in vivo loss-of-function screening platform.”
- \$25,000 to investigators at the University of California, San Francisco, CA, for the project: “Targeting the glioma immune environment by creating tertiary lymphoid organs.”
- \$25,000 to investigators at the Ann and Robert H. Lurie Children’s Hospital of Chicago, IL, for the project: “Qualification of the PLK4 inhibitor CFI-400945 for future clinical trials on pediatric brain tumors: moving from the bench to the bedside.”
- \$25,000 to investigators at the Medical College of Wisconsin, Wauwatosa, WI, for the project: “Development of a low-cost vascularized integrated cranial bone flap to decrease risk of infection following cranial surgery.”
- \$25,000 to investigators at the Children’s Hospital of Philadelphia, PA, for the project: “Comprehensive genomic characterization of DIPG through a shared biorepository architecture for biospecimen collection and curation.”

Appendix. The virtualtrials.com website of the Musella Foundation

On the next two pages is a schematic site map of virtualtrials.com, the website of the Musella Foundation for Brain Tumor Research and Information.

The website is conceived to be an essential portal to the world of brain tumor treatments and organizations.

Updated weekly, the website contains a huge amount of information (which ranges in complexity from basic patient-related material to medical professional matters) and hundreds of links.

We hope you make full use of this website, including the online support groups, the co-payment assistance, the explanation of treatments, the listings of clinical trials and brain tumor centers, and more.

As noted in the first chapter of the book, we would like to hear from you. You can reach us by means of the website, or you can call us toll free at 888-295-4740 (or use our direct number 516-295-4740). The best time to call is between 10:00 AM and 6:00 PM ET Monday through Friday, and between 10:00 AM and 1:00 PM ET Saturday and Sunday.

We are located in New York State.

Acknowledgments

Brain Tumor Guide for the Newly Diagnosed was written by Al Musella, DPM.

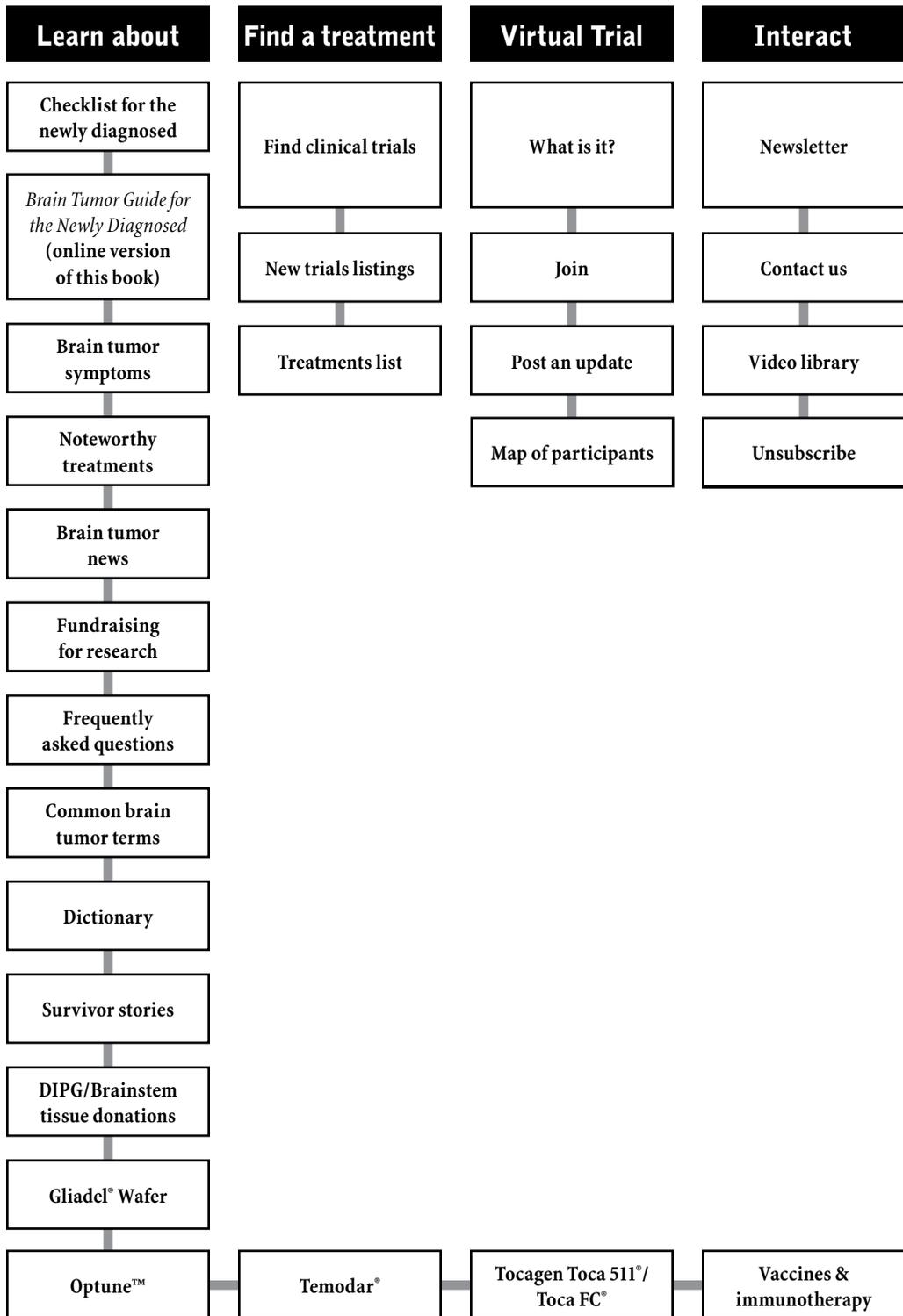
The Musella Foundation for Brain Tumor Research & Information, Inc., sponsors this book.

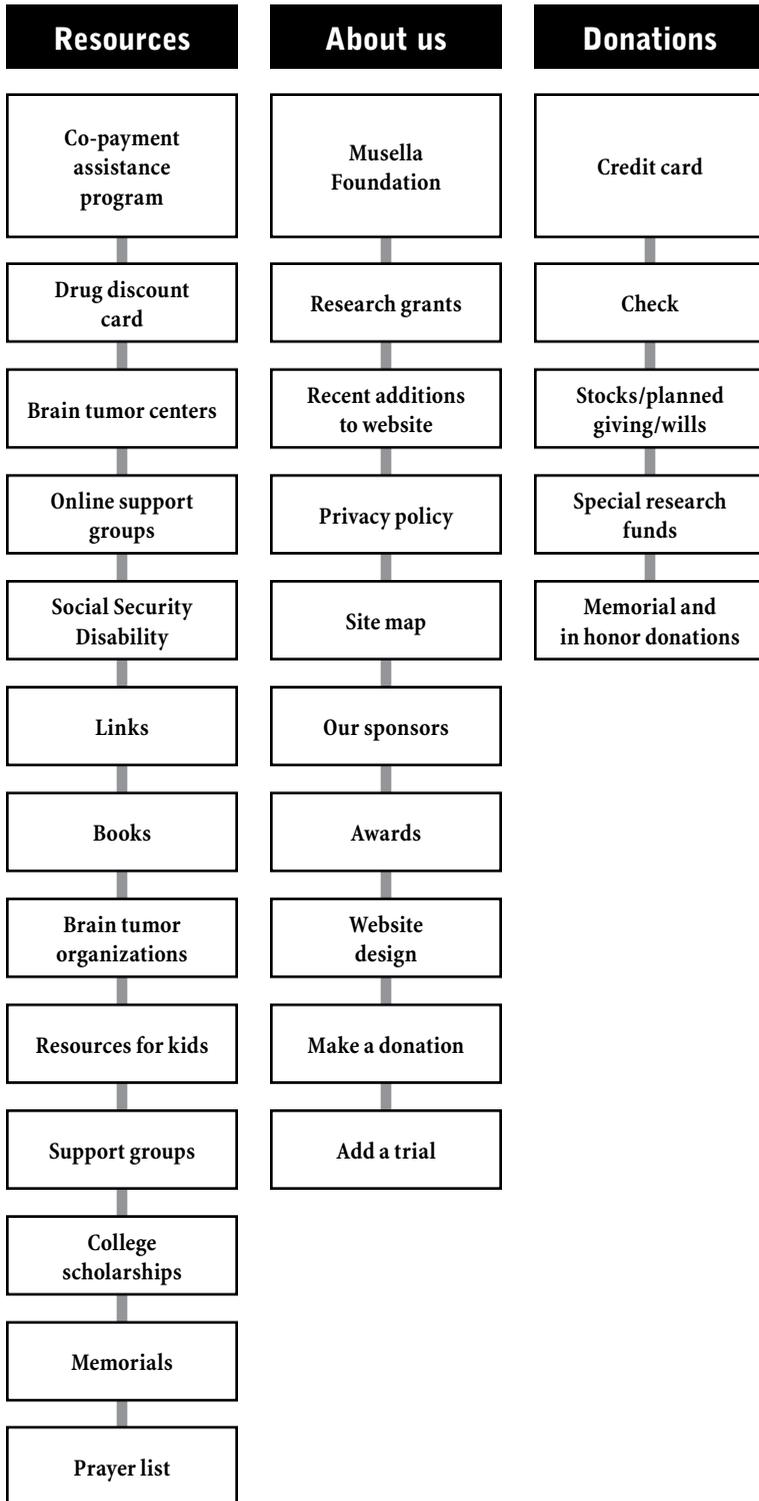
The Musella Foundation is a 501(c)(3) nonprofit public charity dedicated to speeding up the search for the cure of brain tumors and to helping families deal with brain tumors.

For brain tumor information, to join online support groups, or to make a donation, go to: www.virtualtrials.com.

All proceeds from the sale of *Brain Tumor Guide for the Newly Diagnosed* are used to fund brain tumor research.

Site map of virtualtrials.com





Disclosure

The information provided in the *Brain Tumor Guide for the Newly Diagnosed* and at the virtualtrials.com website reflects the diverse opinions of many different people, most of whom are not physicians or nurses trained to practice oncology, neuro-oncology, or neurosurgery.

The information in this book and at the website should therefore be considered simply as ideas for further exploration with your personal doctors. It is not offered as medical advice from any person at the Musella Foundation or associated with the book or website, and it should not be considered medical advice.

If you find any errors, disagree with what we say, or have suggestions to improve it, please contact us by email at musella@virtualtrials.com or phone toll free at 888-295-4740.



MUSELLA
FOUNDATION
FOR BRAIN TUMOR
RESEARCH & INFORMATION

Brain Tumor Guide for the Newly Diagnosed

IF YOU HAVE TIME TO READ ANYTHING IN THIS BOOK,
PLEASE READ THE MUSELLA FOUNDATION NEED-TO-KNOW
CHECKLIST, STARTING ON PAGE 6

Al Musella, DPM



The diagnosis of brain tumor is a life-shaking event, compounded by the need to make crucial immediate decisions. What doctors to choose, where to be treated, what treatments are available, what clinical trials can be entered — to make the most rational decisions for yourself or for a loved one, you need to become as informed as possible as soon as possible.

The goal of *Brain Tumor Guide for the Newly Diagnosed* is to provide a vital first resource with tools for organizing and engaging with a medical team and the complex array of treatment options.

Represented here in readily actionable form is the wealth of helpful and hopeful information accumulated over the past two decades by the Musella Foundation for Brain Tumor Research & Information, an organization dedicated to the cure of brain tumors.

Brain Tumor Guide for the Newly Diagnosed was written with explicit reference to the Musella Foundation's influential virtualtrials.com website that since the 1990s has served as a clearinghouse for information related to brain tumor clinical trials and treatments while hosting multiple online support groups. The Musella Foundation also awards investigators with research grants to study brain tumor treatments.

The Musella Foundation for Brain Tumor Research & Information, Inc.

1100 Peninsula Blvd, Hewlett, NY 11557

Toll Free Phone: 888-295-4740 • Direct Phone: 516-295-4740

www.virtualtrials.com



MUSELLA
FOUNDATION
FOR BRAIN TUMOR
RESEARCH & INFORMATION

ISBN-13: 978-0-9899740-0-4

5 1995



9 780989 974004