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Letter from the Director

Dear Colleagues and Friends,

Since the Cleveland Clinic Brain Tumor and Neuro-Oncology Center (BTNC) was established in 2001, we have been dedicated to best-in-class patient care, game-changing basic and clinical research and vibrant professional and patient education programs.

The BTNC continued its leadership in the field in 2009. We served a record number of patients, made significant advances in basic and clinical research and offered an impressive array of educational experiences. The innovative treatments available here, our respected research programs and extensive educational offerings are made possible though the generosity of our many donors who share our passion for improving the outcomes for patients with central nervous system tumors.

We are proud of our accomplishments in 2009 and are pleased to share them with you through this annual report. Thank you for your interest and support as we continue to make progress against these very challenging conditions.

Gene H. Barnett, MD, FACS
Director, Brain Tumor and Neuro-Oncology Center
Rose Ella Burkhardt Chair in Neurosurgery
Faculty and Key Personnel

**Neurosurgery**
Gene H. Barnett, MD, FACS  
*Director, Brain Tumor and Neuro-Oncology Center*  
*Director, Cleveland Clinic Gamma Knife® Center*  
*Rose Ella Burkhardt Chair in Neurosurgery*

Lilyana Angelov, MD  
*Head, Spinal Radiosurgery*  
*Head, Primary CNS Lymphoma Program*

William Bingaman, MD*  
Xiao Di, MD*  
Joung Lee, MD  
*Head, Section of Skull Base Surgery*

Mark Luciano, MD, PhD*  
Peter Rasmussen, MD*  
Burak Sade, MD  
Samuel Tobias, MD*  
Michael A. Vogelbaum, MD, PhD  
*Director, Center for Translational Therapeutics*  
*Brain Tumor and Neuro-Oncology Center Associate Director*

Robert Weil, MD  
*Head, Pituitary and Neuro-Endocrine Surgery*  
*Associate Director, Basic Laboratory Research*

**Radiation Oncology**
Samuel Chao, MD  
Aleck Hercbergs, MD*  
Roger M. Macklis, MD*  
John H. Suh, MD*

**Radiation Physics**
Christopher Deibel, PhD*  
Toufik Djmel, PhD*  
Gennady Neyman, PhD*  
*Head, Gamma Knife Physics*

**Neuropsychology**
Michael Parsons, PhD*

**Neuropathology**
Richard Prayson, MD*  
Susan Staugaitis, MD, PhD*

**Endocrinology**
Amir Hamrahian, MD*  
Betul Hatipoglu, MD*  
Laurence Kennedy, MD*

**Medical Oncology**
David Peereboom, MD  
*Head, Medical Oncology and Clinical Research*

Mannmeet Ahluwalia, MD  
*Head, Neuro-Oncology Outcomes*

Brian Bolwell, MD*  
Ernest Borden, MD*  
Tarek Mekhail, MD*

**Pediatric Oncology**
Kate Gowans, MD*  
Michael Leven, MD*  
Gregory Plautz, MD*  
Tanya Tekautz, MD  
*Co-Director, Pediatric and Adolescent Brain Tumor Program*

**Neuroradiology**
Todd Emch, MD*  
Thomas Masaryk, MD*  
Doksu Moon, MD*  
Paul Ruggieri, MD*  
Todd Stultz, MD*  
Andrew Tievsky, MD*

**Research**
Gene H. Barnett, MD  
*Director, Brain Tumor and Neuro-Oncology Center*

Mannmeet Ahluwalia, MD  
Peter Cohen, MD*  
James Finke, PhD*  
Candece Gladson, MD*  
Jaharul Haque, MD*  
Damir Janigro, PhD*  
David Peereboom, MD  
*Head, Clinical Research*

Gregory Plautz, MD*  
Baisakhi Raychaudhuri, PhD  
Jeremy Rich, MD, PhD*  
Susan Staugaitis, MD, PhD*  
Bruce Trapp, PhD*  
Raymond Tubbs, DO*

*Denotes secondary appointment in Brain Tumor and Neuro-Oncology Center*
Michael A. Vogelbaum, MD, PhD  
Director, Center for  
Translational Therapeutics  
BTNC Associate Director  
Ilka Warshawsky, MD*  
Robert Weil, MD  
Associate Director,  
Basic Laboratory Research  

**Nursing/Physician Assistants**  
Marcella Lupica, RN  
Brain Tumor and  
Neuro-Oncology Center  
Nurse Manager  
Cheryl Vibbert, RN  
Brain Tumor and  
Neuro-Oncology Center  
Assistant Nurse Manager  
Cathy Brewer, RN  
Gail Ditz, RN, BSN  
Carla Duvall, MSN, CNP  
Michele Gavin, MPAS, PA-C  
Betty Jamison, RN, BSN  
Kathy Lupica, MSN, CNP  
Mary Miller, RN, BSN  
Mary Murphy, RN  
Shelley Ogrin, MSN, RN, CNP  
Rachel Perez, RN, BSN  
Cathy Schiler, RN  
Sherry Soeder, MSN, CNP  
Laural Turo, RN, BSN  

**Administration**  
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Brain Tumor and  
Neuro-Oncology Center  
Administrator  
Theresa Naska  
Brain Tumor and  
Neuro-Oncology Center  
Department Manager  

Jackie Garcia  
Brain Tumor and  
Neuro-Oncology Center  
Department Coordinator  
Teresa McBride  
Brain Tumor and  
Neuro-Oncology Center  
Workleader  
Marci Ciolfi, CCRP  
Research Coordinator  
Kathy Robinson  
Research Coordinator  
Wendi Evanoff, CCRP  
Research/Database Coordinator  
Mary McGraw  
Tissue Bank Coordinator  
Kapila Navaratne  
Lead Research Technologist  
Charlotte Horner  
Patient Access Coordinator  
Jianping Li  
Systems Engineer  
Jason Gray  
Executive Director of Development  
Neurological Institute  
James Saporito  
Executive Director of Development  

**Taussig Cancer Institute**  
Millie Torres  
Patient Access Coordinator  
Cynthia Flanagan  
Gamma Knife Surgery Scheduler  
Colleen Burke  
Marketing Manager  
Jennifer Lynch  
Marketing Associate  
Molly Johnson  
Media Associate  
Martha Tobin  
Continuing Medical Education  

Angela Wojtylak/Tina Badley  
Reimbursement Specialist  
Jackie Bell  
Medical Secretary  
Janette Collazo  
Medical Secretary  
Lynette Beagle  
Medical Secretary  
Cassandra Holliday  
Medical Secretary  
Tamika Smith  
Medical Secretary  
Deborah Qualls  
Medical Secretary  

**Neurological Institute**  
Michael Modic, MD  
Institute Chair  
Fielding Epstein  
Administrator  
Daniel Tomic  
Financial Manager  
Kim Hunter, RN, MSN  
Nursing Director  

**Taussig Cancer Institute**  
Derek Raghavan, MD, PhD  
Institute Chair  
M. Frank and Margaret Domiter Rudy Institute (Distinguished) Chair in  
Translational Cancer Research  
John Sweetenham, MD  
Director, Clinical Research  
John Pellechica  
Grant Administrator  
Denise Connor  
Research Finance Manager  
Kristie Moffett  
Division Research Administrator  
Deb Johnson  
Research Accountant
Executive Summary

The Cleveland Clinic Brain Tumor and Neuro-Oncology Center (BTNC) recorded a year of accomplishments in 2009.

**Record-Setting Clinical and Financial Performance**

- 8,344 outpatient visits
- 1,039 surgical, Gamma Knife® and Novalis® procedures
- Increase of 145% in new patient visits, 389% in total outpatient visits, 34% in surgical cases and 117% in Gamma Knife cases
- Largest market share in Ohio
- 119% increase in net revenue and 41% increase in contribution margin since 2002

**Solid Research Revenue and Philanthropic Support**

- Funding through three federal grants
- More than $2.6 million in philanthropic support since 2007 and more than $16 million since inception

**Pacesetting Clinical Programs**

- Completion of AutoLITT® thermal therapy system clinical trial, following world’s first human treatment of brain tumor using the AutoLITT system in 2008
- Advanced navigation using DTI and fMRI planning and intraoperative visualizations
- Compact MRI with development of high-field interventional MRI operating room
- Leader in convection-enhanced delivery of advanced agents to brain tumors
- Second Gamma Knife Perfexion® unit in North America, performing 360 cases in 2009
- Leader in spinal radiosurgery – 95 procedures performed in 2009, more than 300 cases since program inception in 2004
- Integration of neuropsychology into clinical program

**Robust Clinical Research**

- Charter member of National Cancer Institute-sponsored Adult Brain Tumor Consortium (ABTC), commencing in 2009
- Leadership in national brain tumor organizations
- More than 65 active clinical trials

**Local, Regional, National and International Education Outreach**

- Hosted three major symposia, including the Third International Symposium on Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery
- One of only three centers worldwide certified to teach introductory Gamma Knife to new practitioners, hosting four Gamma Knife hands-on courses in 2009

**Disseminating Our Knowledge**

- Publication of 86 journal articles and book chapters

**Laboratory Research**

- Recruitment of Candice Gladson, PhD, as Head of Brain Tumor Laboratory Research in the Department of Cancer Biology, Cleveland Clinic Lerner Research Institute
- Expansion of the medical neuro-oncology program with the addition of medical oncologist Manmeet Ahluwalia, MD
- Cutting-edge basic and translational research in progress in more than a dozen laboratories
A Team Approach to Individualized Care

Established in 2001, the Brain Tumor and Neuro-Oncology Center (BTNC) is among the leading programs in the United States and the world for the diagnosis and treatment of primary and metastatic tumors of the brain, spine and nerves and research to advance the care of patients with these conditions. As part of the Cleveland Clinic Neurological Institute, the BTNC closely collaborates with Cleveland Clinic Taussig Cancer Institute to provide innovative solutions for these complex problems.

The BTNC is uniquely structured to allow our multidisciplinary team of physicians and scientists to focus almost exclusively on brain tumors and combine therapeutic approaches from multiple disciplines to create the most effective, individualized treatment for the thousands of patients who entrust their care to us each year. This structure also encourages the staff to participate in international research protocols and share information about the latest developments in the field to advance patient care.

The BTNC has been a member of the prestigious New Approaches to Brain Tumor Therapy (NABTT) consortium, now the Adult Brain Tumor Consortium (ABTC), since 2000. The primary objective of this National Cancer Institute-sponsored consortium is to improve the therapeutic outcome for adults with primary brain tumors while sharing clinical and laboratory data to facilitate laboratory research on new treatments. To qualify for membership, an institution must possess strong clinical and research programs for adult brain tumors, expert multidisciplinary clinical teams, extensive laboratory and clinical resources, and the ability to conduct high-quality, clinically relevant trials.

With the support of our dedicated donors, we continue our commitment to innovation in patient care, research and education, focused on bringing potentially groundbreaking therapies from the laboratory to patient care as rapidly and safely as possible.

Clinical and Financial Performance – 2009

2009 continued the BTNC’s strong positive trend in clinical volume and financial growth.

Growth in Patient Volume

Between 2001 and 2009, the BTNC experienced a 145 percent increase in new patient volume, a 389 percent increase in total outpatient visits, a 34 percent increase in surgical cases, and a 117 percent increase in Gamma Knife cases.

In 2009 BTNC physicians recorded 8,344 outpatient visits and performed 1,039 surgical, Gamma Knife and Novalis procedures. BTNC physicians began performing Novalis radiosurgery in 2004, beginning with three cases. In 2009, our physicians performed 95 of these cases.

Growth in Market Share

The BTNC maintains the highest market share in the “Cuyahoga County,” “21-county” and “state of Ohio” markets and continues to increase dominance over its closest competitor. In 2009, BTNC physicians cared for more than 4,200 patients.

Beyond the local and regional markets, the BTNC is a national and international referral center, drawing patients from 41 states and 14 countries. BTNC physicians also work closely with neurosurgeons at Cleveland Clinic Florida to provide services for patients. Cleveland Clinic’s medical concierge service helps to coordinate the details of bringing patients from Florida to Cleveland for care. The special requirements of international patients are handled through Cleveland Clinic’s Global Patient Services program.
Generous supporters have contributed nearly $2.7 million to the BTNC since 2007 as gifts, pledges and estate bequests. This foundation of philanthropic support is essential to the innovative treatment, educational efforts and research that are the BTNC’s hallmarks.

In addition to financial support, friends also contribute their time and invaluable service as members of the Neurological Institute and Taussig Cancer Institute National Leadership Boards. In collaboration with physicians and healthcare professionals and the development team, the Leadership Boards drive efforts to increase awareness and provide opportunities for friends to support priority research and clinical initiatives.

The Brain Tumor and Neuro-Oncology Center extends deep appreciation to our Partners in Neuro-Oncology, each of whom has donated $1 million or more over their lifetimes to support our programs.

Melvin H.* and Rose Ella* Burkhardt
Robert W. and Kathryn B. Lamborn
Alfred* and Norma Lerner
Mr. and Mrs. Lucius B. McKelvey
Ms. Karen Wilson
*deceased

**Benefactors**

The Brain Tumor and Neuro-Oncology Center is pleased to acknowledge the following friends whose giving in support of our mission totals $1,000 or more.

Advanced Health Media
Allos Therapeutics, Inc.
Anheuser-Busch Companies, Inc.
Asset Planning Company
B & B Investments
Mr. John Bachey
Mr. and Mrs. R. William Bailey Jr.
Baker & Hostetler
Mr. Philip A. Baskin
Mr. and Mrs. Al Bleggi
Carol Bollo and Associates
Melvin H.* and Rose Ella* Burkhardt
Butzel Long Attorneys & Counselors
Mr. Perry J. Celsi
The James & Coralie Centofanti Charitable Foundation
Central Distributors of Beer, Inc.
Mrs. Barbara Chan
Nanda Channaiah
Mr. and Mrs. John R. Colina
Mr. and Mrs. Edward DeBartolo Jr.
Thomas N. Detesco, MD
Elekta Instruments, Inc.
First Medical Associates
Continuing a Family Tradition

For the Burkhardt family, supporting brain tumor research is an honored tradition. The late Rose Ella and Melvin Burkhardt developed an interest in the research of Gene Barnett, MD, BTNC Director, when he was treating Mrs. Burkhardt for a brain tumor. The result was the Rose Ella Burkhardt Chair in Neurosurgery in 1993 and the Melvin H. Burkhardt Chair in Neuro-Oncology Clinical Research, which Mr. Burkhardt established after his wife’s death.

Mr. Burkhardt was equally generous with his time, serving as a member of the former Brain Tumor Institute Leadership Board. He was recognized as a Distinguished Fellow, Cleveland Clinic’s highest honor, and was the inaugural recipient of the George W. Crile, Sr. Award for his foresight and long-term philanthropic support of Cleveland Clinic.

Mrs. Burkhardt’s daughter Karen Colina Wilson has continued the family’s extraordinary legacy with an annual golf tournament to support the BTNC and an exceptionally generous gift that led to the naming of the Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center.

Inspired by her family’s long-standing interest, Ms. Wilson recently created the Karen Colina Wilson Endowed Chair in Pediatric Brain Tumor Research to support the work of Tanya Tekautz, MD.
Endowed Chairs

The following endowed chairs holders in the Brain Tumor and Neuro-Oncology Center are entrusted with stewarding funds generated by gifts from generous benefactors.

Gene Barnett, MD, FACS
Director, Brain Tumor and Neuro-Oncology Center
The Rose Ella Burkhardt Chair in Neurosurgery

Tanya Tekautz, MD
Brain Tumor and Neuro-Oncology Center
The Karen Colina Wilson Endowed Chair in Pediatric Brain Tumor Research

Michael Vogelbaum, MD, PhD
Associate Director, Brain Tumor and Neuro-Oncology Center
The Robert W. and Kathryn B. Lamborn Chair for Neuro-Oncology

Robert J. Weil, MD
Director of Laboratory Research, Brain Tumor and Neuro-Oncology Center
The Melvin H. Burkhardt Chair in Neuro-Oncology Clinical Research

Noel W. Jackson, DDS, and Sheri L. Snider, DDS
Ms. Jeanne Johnston
Kuboff & Associates, Inc.
Lakeshore Utility Trailer, Inc.
Mr. and Mrs. Robert Lamborn
Mr. and Mrs. Alfred Lerner
Mr. and Mrs. Benedict W. Lupo
Lyons Consulting Group
Mr. and Mrs. Keenan J. Malec
Mansour, Gavin, Gerlack & Manos Co., LPA
Mr. and Mrs. Lucius B. McKelvey
Medtronic, Inc.
Mr. and Mrs. Samuel H. Miller
Moda America LLC
Mr. and Mrs. Nicholas Modarelli
Dennis M. Moody, DDS
John C. Moyers Consulting Services, Inc.
Mr. and Mrs. Steve Nadherny
North Olmsted City Schools
Oakwood Healthcare System
Mr. and Mrs. Donald L. Oberholtzer
Omega Laboratories, Inc.
Mrs. Jodi O'Neill
Owens-Illinois, Inc. Fund
Mr. and Mrs. Robert S. Partain
R. E. Professionals, Inc.
Ms. Tracy Ross, CPA
Ms. F. L. Rumble
Mr. Wayland J. Russell
Schoolcraft College
Mr. and Mrs. Eric Seres
Mr. Patrick J. Smithbauer
David S. Stein Foundation
Mrs. Barbara Styles Stevens
Mr. and Mrs. Joseph Sylvester
Mr. John R. Telich Sr.
Mr. and Mrs. Laurence J. Trotter
Mr. and Mrs. Robert M. Venrose
Mr. and Mrs. John G. Whitman
Ms. Karen Wilson
Mr. and Mrs. Robert J. Wright
Dr. John C. York II, and
Ms. Denise DeBartolo York

*deceased
Clinical Care

The BTNC’s multidisciplinary team of specialists, most of whom treat only patients with brain tumors, works together to deliver an individualized treatment plan for each patient. The availability here of cutting-edge investigational treatments, coupled with our routine use of molecular and chromosomal testing to guide individual patient management, help position the BTNC at the forefront of individualized care and the molecular genetic management of brain tumors.

Brain tumors are extremely complex lesions, often requiring the use of several different types of therapy. To ensure that our patients receive the optimal treatment for their diagnoses, the BTNC offers a comprehensive range of treatment options.

Medical Neuro-Oncology

Our medical neuro-oncologists manage chemotherapy and biologic therapy for patients with malignant brain tumors. As new treatments are developed, they determine the best option for each patient at each disease stage with the goal of enhancing quality of life and extending survival. Our team members are respected authorities in the use of conventional anti-tumor drugs as well as leaders in the testing of new agents targeted at specific tumor molecules (growth modifiers).

Neurosurgery

Pioneers in computer-assisted stereotactic techniques for brain tumors since the mid-1980s, BTNC surgeons extended the scope of operable brain tumors by using techniques such as frame or frameless stereotaxy (to provide a fixed frame of reference to assist with computerized navigation for locating brain tumors), laser surgery, skull base techniques, microsurgery, endoscopic surgery, computer-assisted rehearsal of surgery, intraoperative MRI, radiation implants and radiosurgery. The development of precision surgical navigation systems by Cleveland Clinic’s Center for Computer-Assisted Neurosurgery has resulted in substantial reductions of wound and neurologic morbidity, length of surgery, hospital costs and length of stay for many brain tumor surgeries. The ability to plan and navigate using specialized imaging techniques such as diffusion tensor imaging (DTI) fiber tracking and functional MRI (fMRI) allows us to see the critical brain pathways and surface regions, making brain tumor surgery even safer – and expanding the scope of surgical treatment.

The BTNC was one of the first sites in the world to apply intraoperative MRI with the PoleStar N20® to neurosurgical procedures. Intraoperative MRI can provide critical navigational guidance and monitoring for tumor resection (surgical removal). In conjunction with the Imaging Institute and neuroradiology, we are developing a new high-field (1.5 Tesla) interventional MRI suite/operating room that will help us expand the use of real-time MRI techniques.
Radiosurgery

A team of neurosurgeons, radiation oncologists, radiation physicists and radiation therapists offers both traditional and innovative treatments. In 1989, Cleveland Clinic’s radiosurgery program was the first in Ohio to treat patients with state-of-the-art noninvasive ablative therapy, using a modified linear accelerator. Since 1997, a number of technologies have been introduced, including Gamma Knife, intensity-modulated radiotherapy (IMRT), intraoperative radiation therapy (IORT), brachytherapy and image-guided radiation therapy (IGRT). These technologies may control lethal tumors for longer periods than conventional radiation therapy, decrease the potential side effects of radiation therapy, and benefit patients whose general health may not be sufficient to withstand a lengthy microsurgical procedure.

Gamma Knife

Gamma Knife Perfexion radiosurgery focuses 192 gamma rays at multiple points throughout the tumor. The shape of the radiation field conforms to the shape of the tumor to concentrate the radiation’s destructive potential in the tumor and minimize damage to surrounding normal tissue. Because of this precise focusing ability, aggressive high-dose radiation can be delivered to stabilize, shrink or destroy some lesions – even those deep in the brain. Gamma Knife is ideal for small tumors and requires only a single one- to two-hour treatment.

In 2009, we performed 360 Gamma Knife radiosurgery cases for a number of indications, our most productive year ever. In addition, we presented a number of papers at various meetings, highlighting our center’s results.

Novalis

Novalis is an image-guided system for radiosurgery and fractionated conformal radiosurgery, which is the delivery of repeated low doses of radiation to the brain and tumor. This technology allows treatment of lesions near critical structures, such as the optic nerve, and re-treatment for some patients who have undergone conventional radiotherapy.

At Cleveland Clinic, Novalis is used for larger malignant or benign tumors. In the BTNC, physicians use Novalis not only for treating brain tumors but also for treating tumors outside the brain, particularly primary and metastatic spinal tumors that are difficult to treat due to their proximity to critical structures. Since 2007, the BTNC has been one of the busiest spine radiosurgery programs in the nation using the Novalis platform.

Local Therapies

In 2008 the BTNC was first in the world to use a new laser-based system in humans for minimally invasive treatment of a brain tumor. The AutoLITT (laser interstitial thermal therapy) system uses a special, high-precision laser probe to coagulate tumors with the heating process monitored by computer and thermal MRI techniques. Dr. Barnett led the first clinical trial of this system in collaboration with University Hospitals Case Medical Center and the
Case Comprehensive Cancer Center. Preliminary results suggest that this technology could offer the benefits of conventional surgery to some patients with inoperable tumors or spare patients more invasive interventions. These results formed the basis for FDA approval of the AutoLITT system in 2009.

Shrinking-Field Radiation Therapy

In malignant glioma (brain tumors) tumor cells can be found centimeters away from the primary tumor mass. The mass itself often can be removed surgically, but this does not remove tumor cells that have spread beyond it, and as many as 80 to 90 percent of tumor recurrences occur within 2 cm of the site of tumor removal.

The shrinking-field technique of radiation therapy was developed to provide the highest radiation dose to the area around the site where the tumor was removed. The BTNC continues to pursue advances in other localized and regionalized therapies to treat the margins of the tumor removal area, as well as tumor-infiltrated brain that is distant from the cavity.

Convection-Enhanced Delivery

The BTNC is a leader in the clinical development of convection-enhanced delivery (CED), a technique that uses temporary catheters to deliver chemotherapy drugs to areas of the brain that are infiltrated by tumor. CED permits treatment with agents that would be too toxic to the body if delivered conventionally.

Although early trials of this technique have shown evidence of efficacy, Phase III clinical trial evidence does not exist to support this approach. CED remains in an early stage of development, and the BTNC is participating in the development of new types of catheters and drugs to optimize efficacy of this approach. BTNC physicians also are involved in clinical trials related to CED, and the BTNC has hosted the only international symposia focused on this treatment.

BTNC Associate Director Michael Vogelbaum, MD, PhD, is developing new drugs and devices for CED in the Center for Translational Therapeutics and is collaborating with Cleveland Clinic Innovations on bringing a novel CED catheter to the FDA to make it available for new CED clinical trials. Dr. Vogelbaum is Founding President of the Society for CNS Interstitial Delivery of Therapeutics, the first international organization dedicated to research in this technique.
A Family’s Expression of Gratitude

When James and Joyce Gagliarducci’s son John was diagnosed with a glioblastoma brain tumor at the age of 34, his parents’ first reaction was astonishment.

“We were at a loss because no one in our family has had cancer,” Mrs. Gagliarducci says.

Their second reaction was determination to find the best treatment for him. “We have good hospitals here [in St. Louis] but we didn’t know about their cancer care,” Mrs. Gagliarducci explains, the memories still fresh after almost 17 years. “Then a business associate of my husband’s suggested Cleveland Clinic from his experience.”

During the next three years, John and his parents made the long trip to Cleveland more times than Mrs. Gagliarducci can remember as he underwent surgery, radiation and chemotherapy. As trying as the situation was, meeting Gene Barnett, MD, Director of the Brain Tumor and Neuro-Oncology Center, early on in John’s treatment helped sustain the family through the experience, Mrs. Gagliarducci says. “We knew we could call him at any time if we or John had questions or needed to talk.”

Although she has forgotten many of the details of her son’s experience, she vividly recalls John’s positive outlook. “He never gave up hope,” she remembers.

It was that spirit and Dr. Barnett’s dedication that led the Gagliarduccis to establish the John Gagliarducci Brain Tumor Fund after losing their son in 1994. “We wanted to fund Dr. Barnett’s research so that some day there will be a cure and no one will have to go through what our son did,” Mrs. Gagliarducci says.

Three years after John’s death, Mr. Gagliarducci died from esophageal cancer. Sustained through this second loss by her close and loving family, Mrs. Gagliarducci drew on her own inner strength and determination to face the future. She views the research fund that she and her late husband established as an appropriate tribute to both her son and her husband, and she continues to be faithful in its support.

“I believe it’s what they both would want me to keep doing,” she says. “To me, it represents hope for the future.”

"Mrs. Gagliarducci has been a faithful partner with the BTNC for many years. Donors like her help support our educational, research and other departmental activities."

– Gene Barnett, MD, Director, BTNC
**Specialized Clinical Programs**

**Pediatric and Young Adult Brain Tumor Program**

A multidisciplinary clinic for children and adolescents with brain tumors takes place twice weekly. Patients can see program Co-Directors Tanya Tekautz, MD, and Bruce Cohen, MD, on the same day, and other team members are consulted as necessary. Each child’s care team consists of a physician, a nurse practitioner and a registered nurse, and a pediatric anesthesiologist is available for sedation to reduce the anxiety of neuro-imaging for our young patients. Neurosurgeons and radiation oncologists are available as needed. During 2009, the program recorded 856 pediatric outpatient visits.

Chemotherapy and radiation therapy are supervised by the patient’s care team. The nurse practitioner/RN team handles follow-up calls at home to ensure the efficacy of pain control and other medical issues, which results in fewer emergency room visits.

Since 2004, our pediatric patient volume has grown more than 200 percent from 413 to more than 855 outpatient visits.

**Section of Metastatic Disease**

**Surgery**

Surgery plus whole brain radiotherapy has been shown to be more effective than radiotherapy alone for patients with a single brain metastasis. Even in patients with multiple brain metastases, surgical resection leads to survival comparable to those patients with single resected lesions. Pioneers in contemporary computer-assisted neurosurgery, BTNC neurosurgeons routinely use minimal access techniques to remove one or more brain metastases, with minimal morbidity and short hospital stays. BTNC clinical researchers are investigating the role of intraoperative chemotherapy or radiotherapy after resection in the hope of obviating the need for whole brain radiotherapy.

Today, surgery may be part of a comprehensive management plan that includes other techniques to treat additional brain metastases not amenable to radiotherapy. Beyond radiotherapy, staged therapy options include stereotactic radiosurgery, intra-arterial chemotherapy with or without blood-brain barrier disruption, and newer systemic chemotherapies.

**Cranial Radiosurgery**

Brain metastases is the most common indication at the BTNC for Gamma Knife. Because these tumors are typically small and spherical, and because they displace, rather than infiltrate, normal brain tissue, the Gamma Knife is our preferred strategy to treat these tumors. Radiosurgery can be used to treat tumors that are inaccessible by conventional surgical techniques, and results from radiosurgery appear comparable to those achieved by surgery plus radiation therapy.

So-called “radio-resistant” tumor types (e.g. melanoma or renal cell carcinoma that has metastasized to the brain) also respond to Gamma Knife. Neurologic morbidity is low when dosing is prescribed at levels set by the Radiation Therapy Oncology Group, and cognitive side effects are minimal because the treatment is confined to small brain regions.

In addition to Gamma Knife radiosurgery, the Department of Radiation Oncology offers other stereotactic radiation options with the Novalis Brain-LB unit and Synergy-S unit. The department has been designated a “Center of Excellence” in the use of Novalis.

Treatment with Novalis is indicated for those patients with metastatic brain tumors that are not ideal for Gamma Knife radiosurgery. In addition, Novalis can be used for metastases outside the brain such as metastatic spinal tumors and prostate and lung cancers.
Chemotherapy

Systemic chemotherapy-sensitive cancers often take refuge in the brain, despite systemic control, because most commonly used chemotherapies have difficulty penetrating the blood-brain barrier. Depending on the type of tumor, available treatment options include hormone therapies; capecitabine; methotrexate; lapatinib; patupilone, which belongs to a new class of cytotoxic drugs; and temozolomide, a relatively new oral agent. More intensive treatment includes the use of chemotherapy injected directly into the carotid vertebral arteries.

As the molecular characterization of various tumors improves, investigational drugs that target specific molecular pathways may play an increasing role in the management of brain metastases. The use of these small targeted molecules to treat a variety of malignancies is an exciting area of BTNC clinical and laboratory research.

Spinal Radiosurgery

Metastatic bone pain is the most common pain syndrome encountered in cancer patients, developing in 60 percent to 85 percent of patients with solid tumors. When the metastases involve the spine, disabling pain and destruction of the vertebral body can occur, leading to spinal instability, compression of the spinal cord or nerve roots and, ultimately, neurological dysfunction and paralysis. Early detection and appropriate intervention are essential to minimize these consequences.

Cleveland Clinic’s Stereotactic Spine Radiosurgery (SRS) program was established in 2006 as the first spine radiosurgery program in Ohio. It is regarded as one of the premier programs in the country routinely offering outpatient spine radiosurgery using Novalis technology. Novalis results in rapid, effective pain and tumor control with minimal risk of side effects.

Spine Tumor Board Guides Treatment Selection

Making the right treatment recommendation for spine tumor patients can be complex and requires an integrated approach. Under the direction of Lilyana Angelov, MD, Head of Spinal Radiosurgery, a multidisciplinary Spine Tumor Board includes members of the Center for Spine Health; the BTNC; Departments of Radiation Oncology, Neuroradiology, Pathology, Surgical Pain Management and Hematology/Oncology; and fellows, residents, nurses and physician assistants from multiple disciplines. Since its inception three years ago, the Spine Tumor Board has provided treatment recommendations for more than 1,033 patients.
Stereotactic spinal radiosurgery has revolutionized the treatment of malignant primary and metastatic spine tumors and many benign tumors as well. Our experience with radiosurgery, either alone or in combination with other therapies, demonstrates that this treatment is an effective option for patients with spine lesions. To date, we have treated more than 300 spine tumors, with more than 85 percent of patients having tumor-associated pain experiencing clinically significant relief and achieving local tumor control in 90 percent of patients with a single outpatient noninvasive treatment.

Other options available here for the treatment of spine tumors include open surgical procedures, minimally invasive surgery, vertebral augmentation, conventional chemotherapy and radiation therapy, surgical pain management interventions, palliative care and a variety of clinical trials.

Center for Neurofibromatosis and Benign Tumors

Von Hippel Lindau syndrome is a rare genetic disease that is characterized by benign tumors in the central nervous system, adrenal glands, kidneys and pancreas. The BTNC created the multidisciplinary von Hippel-Lindau virtual clinic in 2005 to coordinate comprehensive care for patients with this condition. Specialists in genetics, neuro-oncology, urology, gastroenterology, hematology/oncology, ophthalmology and endocrine surgery collaborate to provide patient education, surveillance and disease management to maximize quality of life for these patients.

Section of Skull Base Surgery

Surgeons in the section employ innovative skull base techniques that reduce or eliminate the need for brain retraction, minimizing injury to the brain, cranial nerves and blood vessels.

From Impression to Impact

When a friend of Robert and Kathryn Lamborn was undergoing treatment at Cleveland Clinic, the couple had the opportunity to meet BTNC Director Gene Barnett, MD. The experience of their friend’s treatment at the BTNC and meeting Dr. Barnett left a lasting impression that stayed with the Lamborns even after their friend’s death.

Together, the couple decided that supporting brain tumor research would be a fitting tribute to their dear friend and have the potential to impact patients’ lives.

“Dr. Barnett explained what he’s doing in research, and I was impressed,” says Mr. Lamborn. “I wanted to be sure that whatever we gave went to support his research efforts.”

The Lamborns established the Robert W. and Kathryn B. Lamborn Chair for Neuro-Oncology through a planned gift. Their endowed chair supports neuro-oncology research at the discretion of Michael Vogelbaum, MD, PhD, BTNC Associate Director.

The Lamborn’s farsightedness and generosity will help ensure the continuation of the BTNC’s important research into the genetics and cellular biology of brain tumors, brain tumor formation and promising new therapies and surgical techniques.
BTNC endoscopic neurosurgeons work closely with endoscopic sinus surgeons in Cleveland Clinic’s Head and Neck Institute to provide minimally invasive surgical management for skull base malignancies and pituitary region tumors.

Our Section of Skull Base Surgery is internationally recognized as one of the largest programs specializing in the management of meningiomas, evaluating more than 200 new meningioma patients annually. Among these, approximately 50 percent of patients are treated with surgery and 15 percent with Gamma Knife radiosurgery or conventional radiation.

In addition to its large clinical volume, the Section of Skull Base Surgery is one of the most productive programs internationally in the area of meningioma clinical research. Research reports from the section are published in leading professional journals.

**Pituitary and Neuro-Endocrine Center (PNEC)**

The PNEC has shown continuous growth since its inception in 2002, fostered by a close working relationship among members of the BTNC and the departments of Endocrinology, Diabetes and Metabolism; Neurological Surgery; Neuro-Ophthalmology; and Radiation Oncology. This close relationship has led to the development of highly integrated clinical care pathways that define the pre-hospital, perioperative and postoperative care for patients with secretory and non-secretory pituitary tumors. New clinical care pathways have eliminated the routine use of perioperative steroids, permitting the accurate determination of postoperative pituitary adrenal activity and decreasing length of stay, with equal patient outcomes.

Additionally, the PNEC’s collaborative structure has supported the development of a prospective IRB-approved database that provides for detailed preoperative endocrine testing, including Cortrosyn stimulation, for comparison to postoperative findings.

**Neuropathology**

Neuropathologists Richard Prayson, MD, Section Head, and Susan Staugaitis, MD, perform intraoperative consultations and final pathologic diagnoses on more than 600 brain and pituitary tumor specimens each year. More than 450 of these specimens have been digitally captured for discussion at the BTNC patient management conferences. All glioma specimens are evaluated by a panel of ancillary immunohistochemical and molecular tests.

**Neuropsychology**

Over the past year, the understanding of the cognitive consequences of brain tumors and their treatments has expanded. The involvement of Michael Parsons, PhD, ABPP, a staff neuropsychologist appointed to the BTNC, has focused clinical and research attention on these issues. Brief cognitive evaluations are integrated into the surgical program of all patients with cognitive concerns, and many receive baseline screenings prior to treatment. This proactive approach lays the groundwork for coping with cognitive problems in the event they arise. Our patients feel that we are not only caring for their medical needs but also have concern for the cognitive and emotional consequences of brain tumors and their overall quality of life.

Innovative research programs have sprung from the collaborative relationship between neuropsychology and the BTNC. Samuel Chao, MD, a radiation oncologist, and Dr. Parsons have initiated an important study that will use advanced brain imaging...
techniques and thorough cognitive assessment to understand the consequences of brain radiation. The study aims to identify individual differences that predict who will be at risk from brain radiation and what factors protect people from those risks.

Neuroradiology

The Sections of Neuroradiology and Magnetic Resonance Imaging within the Cleveland Clinic Imaging Institute provide a wide array of diagnostic capabilities for routine imaging studies and research projects in support of the BTNC. All MR imaging at Cleveland Clinic is managed centrally at Cleveland Clinic’s main campus with digital image transmission to other sites. This facilitates immediate comparison with prior studies on the central digital archive and makes the finalized reports and digital images available to our referring physicians through the electronic medical record.

Diagnostic imaging capabilities include routine imaging, diffusion imaging and high-resolution preoperative planning studies at all of our facilities. At main campus, we also have the capability to provide MR perfusion imaging, diffusion tensor imaging, functional MRI, MR spectroscopy and PET imaging for more advanced preoperative planning. These data can be fused with other DICOM data sets and incorporated into the stereotactic neurosurgical planning software.

Neuro-Oncology Social Work

The role of the neuro-oncology social workers is to address any psycho-social issues that may impede a patient’s treatment process in the BTNC.

Working closely with patients and families, they address issues such as financial stress, children, home care/private duty nursing, work/job issues, emotional coping, caregiver stress, and transportation logistics. Supportive counseling is provided as needed, and an oncology psychiatrist helps assess patients for psychotropic medications that may help modulate a patient’s anxiety and/or depression.

Many brain tumor patients undergo radiation therapy as part of their treatment plan. To ensure that all patients receive the support they need without duplication of services, the Brain Tumor social workers coordinate care between the outpatient neuro-oncology social worker and the Radiation Oncology social worker.

Neuro-Oncology Nursing

Nurses, physician assistants and technicians specializing in the care of patients with brain tumors are an integral part of the BTNC. Members of the nursing and physician assistant team are often the first contact for patients seeking an opinion or coming to the outpatient department for evaluation. Our dedicated team of more than a dozen registered nurses and physician assistants provides clinical expertise in caring for patients undergoing outpatient treatments, assists patients participating in clinical trials and provide one-on-one and group teaching for patients and families.
Research

Clinical Research

The BTNC is committed to the development of new and innovative treatments for patients with benign and malignant brain tumors. Our patients may elect to undergo investigational treatments or participate in clinical research projects. Experimental drug protocols include various chemotherapies and tumor growth modifiers.

The BTNC was recognized in 2004 for its role as a leader in cutting-edge treatment and research by being selected as a full member of the prestigious New Approaches to Brain Tumor Therapy (NABTT) consortium. In 2009 this consortium merged with the North American Brain Tumor Consortium to form the Adult Brain Tumor Consortium (ABTC). The ABTC, the only consortium funded by the National Cancer Institute to conduct Phase I and II trials of new treatments for brain tumors, includes 18 centers of excellence for brain tumor research.

The BTNC also participates in other prominent cooperative research groups:

- Radiation Therapy Oncology Group (RTOG)
  - BTNC Associate Director Michael Vogelbaum, MD, PhD, is Co-Chair of the Brain Tumor Committee and Chair of the Neurosurgery Committee
- Children’s Oncology Group (COG)
- International Blood Brain Barrier (BBB) Consortium.

BTNC physicians play leadership roles in numerous multicenter trials. Some of the clinical trials they are leading include:

- National Cancer Institute-sponsored NABTT Central Nervous System Consortium Phase I/II trial of BMS-247550 for treatment of patients with recurrent high-grade gliomas (David Peereboom, MD, Principal Investigator)
- Phase I/II trial of ixabepilone in patients with recurrent high-grade gliomas (Dr. Peereboom, Principal Investigator)
- Phase II trial of erlotinib and sorafenib in patients with recurrent high-grade gliomas (Dr. Peereboom, Principal Investigator)
- An RTOG Phase III study to assess the role of the monoclonal antibody Avastin in the management of newly diagnosed glioblastoma (Dr. Vogelbaum)
- International Phase III trial of radiation and/or chemotherapy for gliomas caused by a specific genetic mutation (Dr. Vogelbaum, U.S. Principal Investigator)
- RTOG Phase II study of meningiomas (Dr. Vogelbaum)
- U.S. Phase III trial of radiation and/or chemotherapy for gliomas caused by this specific genetic mutation (Dr. Vogelbaum, Co-Principal Investigator)

Additional clinical research programs include:

1. First-in-man clinical study of the use of the Monteris AutoLITT System (laser interstitial thermal therapy) for treatment of recurrent/progressive glioblastoma, led by BTNC Director Gene Barnett, MD
   - Dr. Barnett is Principal Investigator on this study, the first application of AutoLITT for brain tumors in humans
2. Erlotinib/temozolomide and postoperative radiation for newly diagnosed glioblastoma multiforme (GBM)
   - This study, led by Dr. Peereboom, was the first to combine erlotinib with standard therapy for patients with newly diagnosed glioblastomas.
Research (continued)

Studying Brain Tumors in Ohio Residents

The BTNC is participating in a groundbreaking, prospective study of primary benign and malignant brain tumors in Ohio residents led by Principal Investigator Jill Barnholz-Sloan, PhD, Assistant Professor, General Medical Sciences (Oncology), Case Comprehensive Cancer Center. With Dr. Barnett as Principal Investigator at Cleveland Clinic, the study is enrolling patients from these sites and others in Ohio. The study will characterize brain tumor subtypes using genetic and environmental exposure information and associate these with clinical outcomes with the goal of correlating the type of brain tumor with the prevalence of mutations in key brain-tumor genes. This is the first prospective study of the genetics of brain tumors and outcomes in the state of Ohio.

3. Intraoperative radiation therapy for solitary brain metastases
   - Robert Weil, MD, is conducting this Phase I/II study utilizing INTRABEAM, a novel delivery system for radiation therapy that allows the precise delivery of radiation therapy directly into the tumor cavity and allows the patient to postpone the need for whole brain radiation.

4. Convection-enhanced delivery (CED) of anti-tumor agents
   - This program uses the slow, continuous infusion of agents targeting malignant glioma that otherwise cannot be delivered to the brain or are too toxic to other organs for systemic delivery.

5. Brain metastases trials
   - Dr. Weil is Cleveland Clinic’s principal investigator on a Department of Defense Center of Excellence grant for the eradication of breast cancer brain metastasis. He and Dr. Peereboom have activated a study in which a breast cancer chemotherapy drug is given prior to surgical removal of a breast cancer brain metastasis. The tumor sample is then assayed for drug concentration to assess the drug’s entry into the metastatic tumor.

6. Sunitinib with delayed whole brain radiation therapy
   - This multicenter study is evaluating sunitinib as adjuvant therapy for patients with one to three brain metastases who have received stereotactic radiosurgery.

7. Complementary and alternative medicine in patients with newly diagnosed brain tumors
   - Glen Stevens, DO, PhD, is conducting a National Institutes of Health-funded trial of complementary and alternative medicine using an herbal preparation as adjuvant therapy to minimize brain edema in these patients.
8. Tumor-treating fields
   - Dr. Weil is the local principal investigator of this novel, noninvasive means of using applied electromagnetic fields to treat recurrent glioblastoma.

9. Stereotactic radiosurgery
   - This RTOG study compares stereotactic radiosurgery alone vs. stereotactic radiosurgery and whole brain radiation in the management of brain metastases.

10. Primary CNS lymphoma
    - This RTOG study is assessing the addition of rituximab, methotrexate and temozolomide to the management of primary CNS lymphoma.

11. Brain metastases from non–small-cell lung cancer
    - This RTOG study is assessing the role of erlotinib and temozolomide in the management of brain metastases from non–small-cell lung cancer.

12. Cognitive dysfunction and whole brain radiation
    - A Phase III RTOG study is testing the use of memantine to prevent cognitive dysfunction in these patients.

Clinical Research Administration

The BTNC’s clinical research infrastructure is fully integrated with Cleveland Clinic Taussig Cancer Institute. Ranked among the top 12 cancer programs in Ohio by U.S. News & World Report’s 2009 “Best Hospitals” survey, Taussig Cancer Institute is affiliated with Case Western Reserve University and University Hospitals Case Medical Center. This relationship integrates BTNC’s outstanding cancer researchers and large cancer referral network with the Case Comprehensive Cancer Center.

The Case Comprehensive Cancer Center, northern Ohio’s only National Cancer Institute-designated comprehensive cancer center, combines cancer research activities of the largest biomedical research and health care institutions in Ohio – Case Western Reserve University, Cleveland Clinic and University Hospitals of Cleveland – into a unified cancer research center under single leadership. With this integration, the Case Comprehensive Cancer Center has strengthened its scientific programs, expanded opportunities for disease-focused research, and enhanced access and ability to serve the entire population of Northeast Ohio and beyond.

The BTNC has two dedicated research nurses and is in the process of hiring a third nurse for the program. The nurses manage all clinical trials, including patient consent, monitoring and follow-up. These nurses are part of the Cancer Center program and are backed up by other Cancer Center research nurses. The program oversees and manages all regulatory matters, IRB submissions and all data collection/CRF transcription responsibilities through the dedicated BTNC study coordinators. Clinical trials also may require tissue procurement or research blood collections, which are coordinated by BTNC’s Tissue Bank Coordinator. BTNC also utilizes an internal database to track protocol status, patient accrual and adverse events.

Basic Research

Central to the BTNC’s clinical success is our commitment to better understanding the causes and mechanisms of tumor development through innovative basic research. Basic science research efforts focus on identifying the genetic, cellular and molecular biology of malignant and benign brain tumors; investigating the mechanism of tumor formation; and exploring new therapeutic developments for brain tumor treatments. The BTNC relies on philanthropic support to continue its leadership in basic research.
Basic Research Highlights

**Gregory Plautz, MD**
- Development of immunotherapy for malignant glioma using vaccines formed by fusing tumor cells with dendritic cells
- Characterization of the tumor antigen profile of brain tumor stem cells to look for common glioma antigens, which would make development of a standardized glioma vaccine possible
- Investigation of the potential for dendritic cell/tumor cell fusion vaccines and tumor-sensitized T cells to cure established brain tumors

**Michael Vogelbaum, MD, PhD**
- Investigation of alterations in DNA repair mechanisms that may improve the chemo- and radio-sensitivity of malignant gliomas

  *with Baisakhi Raychaudhuri, MD*

- Examination of the role of NFkappaB and IL-8 in malignant gliomas

  *with Jose Valerio, MD*

- Production of tumor-specific toxicity in malignant gliomas by modified small interfering RNA molecules

  *with Cliff Robinson, MD*

- Development of a novel assay for MGMT function

BTNC Leading Stem Cell Study

In 2009 the Adult Brain Tumor Consortium designated the BTNC as the lead institution for a clinical trial of a gamma secretase inhibitor that targets tumor stem cells. The clinical trial will include laboratory correlative studies performed in the laboratory of Jeremy Rich, MD, PhD, Chair of the Department of Stem Cell and Regenerative Medicine.
Center for Translational Therapeutics

Vogelbaum Laboratory

The BTNC’s Center for Translational Therapeutics, directed by Dr. Vogelbaum, performs pre-clinical testing of promising anti-cancer agents that may be useful in treating malignant brain tumors. One of the center’s goals is to accelerate the lengthy and expensive process of testing new drugs targeted against brain tumors and to safely move these drugs into clinical trials as quickly as possible for the benefit of patients.

The center works with pharmaceutical companies and other medical institutions to identify, obtain and test new compounds. The center’s efforts, including an international search for all potential brain tumor-relevant therapies, have yielded several promising agents for testing.

Because many new therapeutic agents cannot penetrate the central nervous system, center researchers are exploring alternative delivery methods such as convection-enhanced delivery (CED).

In collaboration the Department of Biomedical Engineering of Lerner Research Institute, they are evaluating alternative formulations using nanotechnology, which may enhance the distribution of potential therapeutic agents within the brain.

The center has several research projects under way on drugs that are designed to be effective against malignant gliomas based on tumor molecular and genetic makeup. The center’s first translational clinical trial was a Phase II trial of erlotinib (Tarceva®) that showed an encouraging rate of tumor responses and disease stabilization. In combination with work done in preclinical models, this clinical trial raised important questions regarding the ability of the drug to penetrate the blood-brain barrier. As a result, the center launched a follow-up trial in which patients undergo a tumor biopsy while receiving the drug. By analyzing the effects of erlotinib on tumor tissues, researchers will be able to determine whether response to this drug depends primarily upon its ability to reach its intended target in the tumor.

The center also works closely with other laboratories at Cleveland Clinic to help develop novel therapeutics that may have application for patients with malignant brain tumors. The center has evaluated methods for improving immune response to gliomas and expanded the understanding of the role of a specific protein that controls the expression of genes involved in immune responses and cell death in regulating glioma cell migration. Center researchers also are exploring the use of a new drug that may sensitize gliomas to the drug temozolomide and are investigating the role of a newly defined gene that affects new blood vessel formation in tumors.

Weil Laboratory

Gliomas and Glioblastomas

The Weil Laboratory continues its work in brain tumor genomic and protein profiling to yield a richer understanding of how these tumors may develop, progress and respond to therapy, especially with respect to finding new targets.

Additional work continues on deciphering the internal genetic and protein differences among malignant gliomas, using a variety of molecular genetic and proteomic methods.

Brain Metastasis

Support from the Melvin H. Burkhardt Chair in Neuro-Oncology Clinical Research permitted preliminary work in the proteomics of breast cancer metastasis that supported a successful grant application. Dr. Weil is Cleveland Clinic’s Principal Investigator on a five-year, $17 million Department of Defense Center of Excellence multicenter grant to study central nervous
system metastasis in breast cancer patients. Cleveland Clinic received nearly $2.7 million of the total funding to support a clinical trial and proteomics research to identify proteins involved in brain metastasis.

Work continues on proteomic profiling, comparing breast cancers from women who have never developed a brain metastasis with those who have. The goal is to identify a set of genes and proteins in the original breast cancer that may suggest which women may be at risk for breast cancer that will metastasize to the brain. This could lead to the development of surveillance methods to find such tumors early and, more importantly, to strategies and treatments that may prevent brain metastases.

**Pituitary Tumors**

This is an area of clinical interest in which several important publications have resulted from work done in collaboration with Lauri Aaltonen, MD, PhD, University of Helsinki, on the role of a specific gene mutation in the formation of pituitary tumors, especially familial acromegaly or early onset of these tumors.

**Comparative Effectiveness and Outcomes Research**

Dr. Weil and his colleagues continue to have great interest in this area, which overlaps clinical applications. A number of publications in leading journals already have resulted from this work.

**Gladson Laboratory**

The laboratory of Candece Gladson, MD, is investigating novel anti-angiogenic agents – substances that interfere with new blood vessel formation - that can be used specifically to target tumor blood vessels in malignant glioma tumors, such as glioblastoma and in metastatic cancers to the brain. Her laboratory collaborates with the Departments of Stem Cell Biology and Regenerative Medicine and Cell Biology, as well as with the Brain Tumor and Neuro-Oncology Center and Abbott Laboratory on this research.

In a recent study, Dr. Gladson’s team demonstrated that a fragment of the blood protein plasminogen (known as K5) causes death of cells that line the blood vessels (endothelial cells) in brain tumors. Prior irradiation of the endothelial cells sensitizes them to the death-inducing effect of K5. Furthermore, they identified a novel communication pathway between K5 and the endothelial cells that results in cell death. This communication pathway includes a conversation between K5 and two binding partners on the endothelial cell surface - GRP78 and a scavenger receptor LRP1, and a subsequent conversation between GRP78/LRP1 and an errand-running molecule, p38 MAP kinase. Prior to a clinical trial, pre-clinical studies are under way to determine whether K5 effectively and specifically kills brain tumor blood vessels.

**Haque Laboratory**

Jaharul Haque, PhD, is investigating the role of the transcription factor STAT3 in the malignant behavior of gliomas. In collaboration with Dr. Vogelbaum, this project obtained $1.6 million in NIH funding and generated multiple peer-reviewed publications.

**Brady-Kalnay Laboratory**

Susan Brady-Kalnay, PhD, and her team are investigating the role of a novel enzyme in regulating the invasion and migration of malignant glioma cells. In collaboration with Dr. Vogelbaum, this project obtained $1.9 million in NIH funding that extends through 2011.
Basic Research Laboratories (continued)

Rich Laboratory

Jeremy Rich, MD, PhD, is Chair of the Genomics Institute, a clinical neurologist and a world-renowned expert on brain tumor stem cells. His laboratory focuses on the potential role of stem cells in brain tumor development and treatment.

More than 80 years ago, neurosurgeons recognized that many brain tumors displayed characteristics of tissues from very early development. Only in the past five years has the significance of these observations been understood as cancer cells within brain tumors have been identified that share characteristics with normal stem cells.

The significance of these cancer stem cells has been supported by work from the Rich and Bao laboratories that showed that cancer stem cells are resistant to radiotherapy and stimulate the growth of blood vessels to feed the tumor, a process called angiogenesis.

Based on this background, research groups have been created under the leadership of Drs. Jeremy Rich, Shideng Bao and Jeongwu Lee in the Cleveland Clinic Department of Stem Cell Biology and Regenerative Medicine in Lerner Research Institute that are focused on brain tumor stem cells and dedicated to identifying what makes cancer stem cells so deadly.

Working in collaboration with Cleveland Clinic neurosurgeons and neuropathologists, the researchers have found that brain tumor stem cells are regulated by interactions with their local environment. They have demonstrated that the low oxygen conditions found in nearly all cancers (hypoxia) stimulate cancer stem cells to keep making copies of themselves and secrete factors that support tumor blood vessel growth. Blocking the ways these cells respond to low oxygen prevents the growth of new tumors. This finding suggests that drugs that inhibit these pathways may help attack brain cancers. In addition, these same pathways may promote cancer stem cell’s resistance to radiotherapy.

The researchers also have shown that cancer cells are plastic in their behavior and that non-stem cells can act more stem-like if subjected to low oxygen. This is very important as it means that new treatments that kill only cancer stem cells are likely to fail as other cells can step up to take their place. They also have identified two related pathways in cancer stem cells (IL6 and STAT3) that are important for these cells to grow. Both IL6 and STAT3 are useful as new drugs inhibiting these pathways are being developed that may be used to treat brain cancer patients.

These experiences may offer clues to better treatments for brain tumor patients in the very near future.
Finke Laboratory

James Finke, PhD, has been involved with investigation of the immunobiology of gliomas. Prior studies of malignant gliomas have shown that gliomas are immunosuppressive, meaning they suppress the immune system’s normal activity. Dr. Finke and other investigators propose that effective immunotherapy will likely be achieved by combining either vaccine or adoptive T-cell therapy with agents that can reduce the immune suppression.

To this end, the Finke laboratory has been working to advance the understanding of the biologic pathways that lead to immunosuppression. To date, Dr. Finke and colleagues have identified a potential mechanism for how the damage to the immune system occurs and a caspase-8 that appears to be critical to the process.

They have started examining peripheral blood T-cells from glioblastoma multiforme (GBM) patients to determine if abnormalities are present or whether the blood contains a significant number of myeloid-derived suppressor cells (MDSC) when compared with blood from healthy donors. Increased numbers of MDSC have been observed in peripheral blood of cancer patients, although no studies have been done in GBM patients. If MDSC are found to be increased in number, they will determine whether they suppress apoptosis (cell death) and if sunitinib can inhibit their suppressive activity or induce apoptosis in these cells.

Gerson/Liu Laboratory

Stanton Gerson, MD, and Lili Liu, PhD, are recognized authorities on the role of DNA repair enzymes in mediating tumor cell resistance to chemotherapy. In collaboration with Dr. Vogelbaum, they are evaluating the roles of certain biologic pathways in mediating the chemoresistance of gliomas. Multiple laboratory projects are ongoing.

Center for Cerebrovascular Research

Under the direction of Damir Janigro, PhD, the center is investigating proteomic markers for brain metastases in patients with lung cancer. The center collaborates with the Departments of Pulmonary Medicine and Hematology/Oncology and the Section of Neuroradiology on this research.

In a recent prospective study, center researchers determined that 65 percent of lung cancer cases followed at Cleveland Clinic over a five-year period had small vessel ischemic disease (SVID) by MRI. The presence of SVID appeared to correlate with a decreased incidence of brain metastases compared with those who did not have SVID.

The center also studied serum from lung cancer patients with SVID on MRI and with or without brain metastases. Researchers were able to identify a specific protein as a marker of brain metastases that was not elevated in the presence of SVID.
A Decade of Giving

Faithful, dedicated and tireless are just a few of the adjectives that could describe Cindy and Larry Trotter. For more than a decade, Mr. and Mrs. Trotter have partnered with Cleveland Clinic to provide outstanding care to patients in Ohio, Florida and around the world.

The couple’s generosity directly benefits the research efforts of BTNC medical oncologist David Peereboom, MD, and Jaroslaw Maciejewski, MD, PhD, Department Chair, Translational Hematology and Oncology Research, Taussig Cancer Institute.

The Trotters make continuing gifts to The Scott Hamilton CARES Initiative and the Inherited Colorectal Cancer Fund and help fund the research of Joseph Crowe Jr., MD, Director of Cleveland Clinic’s Breast Services and holder of the Lula Zapis Endowed Chair to Support Breast Cancer Research. In 2005, they provided funding to purchase a gene sequencer.

Mr. and Mrs. Trotter are as generous with their time and talents as with their financial resources. They are on the Taussig Cancer Institute National Leadership Board and Cleveland Clinic Florida’s Leadership Board, serve as vice chairs of Cleveland Clinic’s Campaign Executive Board and chaired the 2008 Cleveland Clinic Florida benefit. In 2004, Mrs. Trotter launched the Women’s Health Leadership Board, now called the OB/GYN & Women’s Health Institute Leadership Board.

In appreciation of their extraordinary leadership, Mr. and Mrs. Trotter have been inducted into the 1921 Society, whose members’ cumulative giving totals $1 million or more, and the Pyramid Legacy Society, a group of more than 1,200 friends and alumni worldwide who are helping to secure Cleveland Clinic’s future through their estate plans.
Continuing Medical Education/Professional Education

As part of our mission to advance brain tumor treatment and research through collaboration and education, the BTNC and the Department of Neurosurgery coordinated and hosted three major symposiums in 2009, including the Third International Symposium on Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery held in Orlando, Fla. The symposium attracted more than 150 participants and featured national and international leaders in brain-, spine- and body-targeted stereotactic radiation modalities and techniques.

The BTNC hosted a dual symposium in Cleveland on pituitary disease management for physicians and patients in April 2009, attracting more than 125 participants to both programs. In September, the 2009 Neuro-Oncology – Current Concepts symposium was held in Cleveland and addressed advances in imaging, molecular biology, surgery, radiotherapy, chemotherapy and alternative therapies in the care of patients with central nervous system tumors. More than 50 physicians participated in the event. A collaborative event with the Society for CNS Interstitial Delivery of Therapeutics was held in conjunction with the Neuro-Oncology symposium that provided insight into the latest technological developments regarding medical devices, therapeutic agents, imaging methods and imaging agents in the field of targeted delivery of drugs to the central nervous system. An additional 50 people attended that program.

The BTNC continues to be a major force in physician education on the Gamma Knife. In 2009, BTNC conducted four hands-on Gamma Knife radiosurgery training courses for more than 30 people.

Patient Education

Kathy Lupica, MSN, CNP, facilitates BTNC’s monthly Brain Tumor Support Group for patients, families and friends. She presented at several professional and patient conferences in 2009, including the American Brain Tumor Association (ABTA) 9th Biennial Meeting for Patients, Survivors and Family Members; the annual Brain Cancer Symposium for patients and families sponsored by The Gathering Place, Cleveland Clinic and University Hospitals of Cleveland; the American Association of Neuroscience Nurses 41st Annual Education Conference and the 10th Quadrennial Congress of the World Federation of Neuroscience Nurses.

Program Development

Professional Recruitment

Candece Gladson, PhD, joined the staff in January 2009 as Head of Brain Tumor Laboratory Research in the Department of Cancer Biology, Cleveland Clinic Lerner Research Institute. The medical neuro-oncology program expanded with the addition of medical oncologist Manmeet Ahluwalia, MD, who recently completed his medical oncology fellowship at Roswell Park Medical Institution.
Fellowships

The BTNC offers two neurosurgical oncology fellowships. A two-year combined clinical and laboratory research fellowship provides exposure to the design and operation of clinical trials as well as opportunities to contribute to the neuro-oncology literature. Fellows are expected to participate in the design, IRB application process and management of new clinical trials during this fellowship and to produce clinical presentations and reports.

The second fellowship is offered through the Section of Skull Base Surgery. It offers in-depth experience in the highly specialized surgical techniques employed to access deep-seated, difficult-to-reach lesions by anatomic displacement or extensive removal of the base of the skull.

Fellows, 2002 – Present

<table>
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<tr>
<th>Program</th>
<th>Start</th>
<th>End</th>
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<td>Neurosurgical Oncology</td>
<td>07/01/2002</td>
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<td>James Evans, MD</td>
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<td>Vitaly Siomin, MD</td>
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<td>Narendra Nathoo, MD, PhD</td>
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<td>10/01/2002</td>
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<td>Lilyana Angelov, MD</td>
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<td>10/20/2003</td>
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<td>Abhay Varma, MD</td>
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<td>Dae Lee, MD</td>
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<td>Tina Thomas, MD</td>
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<td>Rongsheng Cai, MD</td>
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<td>Jose Valerio-Pascua, MD</td>
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<td>07/01/2007</td>
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<td>Zhiyuan Xu, MD</td>
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<td>Sacit Omay, MD</td>
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<td>Skull Base Surgery</td>
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<td>08/01/2004</td>
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<td>10/22/2007</td>
<td>10/21/2008</td>
<td>Jae Sung Park, MD</td>
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<td>11/01/2008</td>
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<td>Soichi Oya, MD</td>
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Marketing and Advertising Highlights

Professional and Patient Education

Managing Brain Tumors: An educational program for patients, family and friends, hosted by the BTNC in partnership with the American Brain Tumor Association on September 13, 2009. Program speakers included:

- Gene Barnett, MD – Advances in the diagnosis and treatment of brain tumors, including AutoLITT
- Samuel Chao, MD – Advances in radiation therapy
- Kathy Lupica, MSN, CNP – Symptom management and support group
- David Peereboom, MD – Clinical trials offering advanced treatment options
- Glen Stevens, DO, PhD – Treating meningiomas and schwannomas
- Tanya Tekautz, MD – Treating pediatric brain tumors
- Michael Vogelbaum, MD, PhD – Treating gliomas

Program speakers also reviewed the BTNC’s Tumor Review Board consensus process with the 85 event attendees from Ohio, Michigan, Pennsylvania, Indiana and Illinois.

National Advertising

Print Ads

- The Wall Street Journal (11/7/09 and 11/12/09)
- The New York Times (12/13/09)

Local/Regional Advertising Campaign

- TV spots on Fox Sports Ohio
- Cleveland Cavaliers games (11/28/09, 12/21/09)
- Columbus Blue Jackets games (12/31/09)
- Radio Spots on WMMS
- Cleveland Browns games 2009 season

BTNC in the News

ABC News: Cancer Treatment Kills Tumors by ‘Cooking’, New Laser Approach Attacks Remote Brain Tumors Once Unreachable with Surgery 2/19/09

The Medical News: FDA approves new laser surgery for brain tumors 5/13/09

Ivanhoe Cancer Channel: Cooking Brain Tumors – In-Depth Doctor Interview: Gene Barnett, M.D., Director of the Brain Tumor and Neuro-Oncology Center at the Cleveland Clinic, talks about a new technology that uses lasers to heat and kill a tumor from the inside out. 6/26/09, 8/26/09

Science Daily: Science News – Brain Tumor Cells Made More Responsive To Radiation 12/3/2009
Tribute to a Beloved Son

Tommy Detesco died at age 32 after 26 years of cancer treatments. His father, Thomas N. Detesco, MD, turned tragedy into a lasting legacy by establishing the Tommy Detesco Fund in 2007 to support the BTNC.

Dr. Detesco believes that BTNC physicians extended his son’s life because of the innovative technologies they are developing to treat previously untreatable brain tumors. His son benefited from leading-edge therapies such as Gamma Knife, a technique that beams gamma rays directly at tumors deep within the brain to shrink or destroy them.

The Tommy Detesco Fund supports research specifically on brain tumors in young people ages 15 to 35. “Tommy would think it would be perfectly logical that we would be doing something to help other people. He was a person who would have enthusiastically applauded this,” his father says.

Despite his long years of illness, Tommy was a young man of indomitable spirit. His family and friends continue to celebrate his life through their donations to the fund that bears his name, remembering him as a person who changed their lives for the better.
## Appendix A: Clinical Trials (Adult)

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<th>IRB</th>
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<tr>
<td>3669</td>
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<td>Protocol A: Combination Chemotherapy (Methotrexate, Procarbazine, &amp; CCNU), Intraventricular Cytarabine &amp; Methotrexate, +/- Intracocular Chemotherapy for Patients with Primary Central Nervous System Lymphoma (PCNSL) &amp; Protocol B: Combination Chemotherapy (Methotrexate, Cyclophosphamide &amp; Etoposide Phosphate) Delivered in Conjunction with Osmotic Blood-Brain Barrier Disruption (BBBD), with Intraventricular Cytarabine +/- Intracocular Chemotherapy, in Patients with Primary Central Nervous System Lymphoma (PCNSL)</td>
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<tr>
<td>CC296 CASE 1307</td>
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<td>Ohio Brain Tumor Study (OBTS)</td>
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<td>CC375 MDCC 1307</td>
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<td>GLIOGENE: An International Brain Tumor Linkage Consortium Study</td>
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<td>CC526 MONT 1307</td>
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<td>A Prospective First-in Man (FIM) Safety Trial of the AutoLITT Laser Treatment of Recurrent/Progressive Brain Tumors</td>
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<td>CC582 BRMY 1308</td>
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<td>Phase I Open Label, Multi-Center Study to Evaluate the Safety and Tolerability of CT-322 Administered in Combination with Focal Brain Radiotherapy and Temozolomide to Subjects with Newly Diagnosed Glioblastoma Multiforme</td>
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<td>CC248 RTOG</td>
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<td>NCCTG RTOG 0574: Phase III Randomized Trial of the Role of Whole Brain Radiation Therapy in Addition to Radiosurgery in Patients with One to Three Cerebral Metastases</td>
<td>Chao</td>
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<td>4204</td>
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<td>Phase II Trial of Continuous Dose Temozolomide in Patients with Newly Diagnosed Anaplastic Oligodendrogliomas and Mixed Oligoastrocytoma</td>
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<td>4347 NABTT</td>
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<td>Phase I/II Study of Oral Procarbazine in the Treatment of Recurrent High Grade Astrocytomas</td>
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<td>Phase I/II Study of Of-3 Administered on a Continuous Daily Oral Schedule in Patients with Recurrent High Grade Astrocytoma</td>
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<td>7749 NABTT</td>
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<td>Phase I Trial of Bay 43-9006 for Patients with Recurrent or Progressive Malignant Glioma</td>
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<td>7936 NABTT</td>
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<td>A Safety Run-In/Randomized Phase II Trial of EMD 121974 in Conjunction with Radiation Therapy in Patients with Newly Diagnosed Glioblastoma Multiforme NCI #: NABTT 0306 PI: Nabors</td>
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<td>8314 NABTT</td>
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<td>Phase II Trial of Talampanel in Conjunction with Radiation Therapy with Concurrent and Adjuvant Temozolomide in Patients with Newly Diagnosed Glioblastoma Multiforme</td>
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<td>CASE 1308</td>
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<td>Phase II Trial of Sunitinib as Maintenance Therapy After Stereotactic Radiosurgery in Patients with 1-3 Newly Diagnosed Brain Metastases</td>
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<tr>
<td>CC011 NABTT</td>
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<td>NABTT 0402 Identification of Hypermethylated Serum Tumor DNA in High Grade Glioma Patients and Correlation with Magnetic Resonance Imaging Finding</td>
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<td>CC038</td>
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<td>Phase I/II Study of Patients with Newly Diagnosed Primary Central Nervous System Lymphoma Treated with Methotrexate/BBBD, and Adding Rituximab (an anti CD-20 Antibody) and Carboplatin, to the Treatment Regimen</td>
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<td>Phase II Trial of Radiation Plus Temozolomide Followed by Adjuvant Temozolomide and Poly-ICLC in Patients with Newly Diagnosed Glioblastoma Multiforme</td>
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<td>CC140 NABTT</td>
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<td>Open-Label Phase I/Phase II Study of Intravenous Infusion of Tetra-o-Methyl Nordihydroguaiaretic Acid (EM-1421) in Subjects with Recurrent High Grade Glioma</td>
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<td>CC141 NABTT</td>
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<td>Phase II Trial of Erlotinib (OSI-774) and Sorafenib (BAY 43-9006) for Patients with Progression or Recurrent Glioblastoma Multiforme</td>
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<td>Phase II Trial of Patupilone in Patients with Brain Metastases from Breast Cancer</td>
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<td>CC190</td>
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<td>Phase I and II, Open-Label Multi-Center Trials of Pazopanib in Combination with Lapatinib in Adult Patients with Relapsed Malignant Glioma (Phase II)</td>
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<td>A Feasibility Assessment and a Phase I/II Trial of MLN518 for Treatment of Patients with Recurrent Glioblastoma</td>
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<td>Phase I, Open Label Study of AT-101 Plus Radiotherapy &amp; Temozolomide &amp; of AT-101 Plus Adjuvant Temozolomide for Patients with Newly-Diagnosed Glioblastoma Multiforme</td>
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<td>NABTT 2201 PHASE II Study of ANTI-CD-20 Monoclonal Antibody (Rituximab) Therapy for Patients with Refractory or Relapsed Primary Central Nervous System Lymphoma (PCNSL)</td>
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<td>Phase Ib/IIa, Multicenter, Open-label Study of AQ4N in Combination with Radiation Therapy and Temozolomide, to Evaluate the Safety, Tolerability, and Efficacy in Subjects with Newly Diagnosed Glioblastoma Multiforme</td>
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<td>CC396 NOVA 1507</td>
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<td>An Open-label, Multicenter, Phase II Study to Evaluate the Activity of Patupilone (EPO906), in the Treatment of Recurrent or Progressive Brain Metastases in Patients with NSCLC</td>
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<td>Phase II Study of R-(-)-gossypol (Ascenta’s AT-101) in Recurrent Glioblastoma Multiforme</td>
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<td>CC492 CASE 2307</td>
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<td>Phase II Trial of Rituxan/Lipinavir in Patients with Progressive or Recurrent High-Grade Giomas</td>
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<td>NVCA 1306</td>
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<td>Phase II, Multicenter, Open Label Case Controlled (Part 1), Randomized, Active Controlled (Part 2) Study of AQ4N in Combination with XRT and Temozolamide for Safety, Tolerability, and Activity in Subjects with Newly Diagnosed GBM</td>
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<td>6253</td>
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<td>Phase II Study for Patients with Relapsed Primary Central Nervous System Lymphoma</td>
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<td>Phase II Clinical Trial of Patients with High-Grade Glioma Treated with Intravenous Carboplatin-based Chemotherapy, Randomized to Treatment with or without Delayed Intravenous Sodium Thiosulfate as a Potential Chemoprotectant against Severe Thrombocytopenia</td>
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<td>Phase II Randomized Evaluation of Selective, 5-Lipoxyngease Inhibition by Boswellia serrata Herbal Medicine Approach Compared to Control as an Adjutant Therapy in Newly Diagnosed and Recurrent High Grade Giomas; NIH Grant No.1 R21 CA107277-01</td>
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<td>Evaluation of a Stress Reduction Program in Patients with Malignant Brain Tumors and Their Family Caregivers</td>
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<td>CC541 UCSF 2308</td>
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<td>Lived Experience of a Long Term Survivor with a Highly Malignant Brain Tumor</td>
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<td>4106</td>
<td>RTOG</td>
<td>Phase III Comparison of Blaife (r) to Declared Institutional Preference for Radiation Induced Skin Toxicity in Patients Undergoing Radiation Therapy for Advanced Squamous Cell Carcinomas of the Head and Neck (RTOG 99-13)</td>
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<td>6795</td>
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<td>A Phase 3 Randomized, Open-label Comparative Study of Standard Whole Brain Radiation Therapy with Supplemental Oxygen, with or without Concurrent RSR13 (efaproxiral), in Women with Brain Metastases from Breast Cancer</td>
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<td>7791</td>
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<td>RT0G 0320; A Phase III Trial Comparing Whole Brain Radiation and Stereotactic Radiosurgery Alone Versus with Temozolomide or Gefitinib in Patients with Non-Small-Cell Lung Cancer and 1-3 Brain Metastases</td>
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<td>Prospective Analysis of Wellness Following Gamma Knife for Non-Malignant Indications</td>
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<td>8208</td>
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<td>Phase II Study of Temozolomide-Based Chemotherapy Regimen for High Risk Low-Grade Gliomas</td>
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<td>CC081</td>
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<td>RT0G 0525; Phase III Trial Comparing Conventional Adjuvant Temozolomide with Dose-Intensive Temozolomide in Patients with Newly Diagnosed Glioblastoma</td>
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<td>CC238</td>
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<td>Phase I/II Study of Pre-Irradiation Chemotherapy with Methotrexate, Rituximab, Temozolomide and Post-Irradiation Temozolomide for Primary Central Nervous System Lymphoma</td>
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<td>A Randomized, Phase III, Double-Blind, Placebo-Controlled Trial of Memantine for Prevention of Cognitive Dysfunction in Patients Receiving Whole-Brain Radiotherapy</td>
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<td>4369</td>
<td>NABTT</td>
<td>Phase I Gliadel and Escalating Doses of Intravenous O6-Benzyguanine Trial in Patients with Recurrent Malignant Gliomas</td>
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<td>ACOSOG</td>
<td>Phase III Randomized Trial of the Role of Whole Brain Radiation Therapy in Addition to Radiosurgery in the Management of Patients with One to Three Metastases</td>
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<td>Phase II Trial of Tarceva In Patients with Recurrent / Progressive Glioblastoma Multiforme</td>
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### Appendix A: Clinical Trials (Adult) (continued)

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<td>7161</td>
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<td>Phase I Study of Convection Enhanced Delivery (CED) Of IL13-PE38QQR Infusion after Resection Followed by Radiation Therapy with or without Temozolomide in Patients with New Diagnosed Supratentorial Malignant Glioma</td>
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<td>CC311 CLDX 1307</td>
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<td>Phase II/III Randomized Study of CDX-110 with Radiation &amp; Temozolomide in Patients with Newly Diagnosed GBM</td>
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<td>Phase II, Multicenter, Exploratory Study, Evaluating the Treatment of Surgery Plus GLIADEL Wafer in Patients with Metastatic Brain Cancer</td>
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<td>7003</td>
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<td>Phase II Study Utilizing the PEC Intraoperative Radiotherapy Device for the Treatment of a Resected Solitary Brain Metastasis</td>
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<tr>
<td>CC126</td>
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<td>A Prospective, Multi-center Trial of NovoTTF-100A Compared to Best Standard of Care in Patients with Progressive or Recurrent GBM</td>
<td>Weil</td>
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<tr>
<td>CC385 CASE 4107</td>
<td></td>
<td>Clinical Study to Assess Entry of Chemotherapeutic Agents into Brain Metastases in Women with Breast Cancer</td>
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### Pediatric Trials: COG (Children’s Oncology Group)

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<td>ACNS0232</td>
<td>Radiotherapy vs. Chemotherapy in CNS Geminoma</td>
<td>Tekautz T; Wiersma S</td>
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<td>ACNS0331</td>
<td>RT and Chemotherapy in Medulloblastoma</td>
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<td>ACNS0423</td>
<td>Phase II Rx Radiation and Temozolomide and Temozolomide and CCNU in High Grade Gliomas</td>
<td>Tekautz T; Wiersma S</td>
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<td>ACNS0334</td>
<td>Phase III Randomized Trial for the Treatment of Newly Diagnosed Supratentorial PNET and High Risk Medulloblastoma in Children &lt;36 months old with Intensive Induction Chemotherapy with Methotrexate followed by Consolidation with Stem Cell Rescue vs. the Same Therapy without Methotrexate</td>
<td>Tekautz T; Wiersma S</td>
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<td>ANBL0531</td>
<td>Response and Biology-Based Therapy for Intermediate-risk Neuroblastoma</td>
<td>Tekautz T; Wiersma S</td>
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<tr>
<td>ANBL0421</td>
<td>Irinotecan + Temozolomide in Neuroblastoma</td>
<td>Wiersma S; Tekautz T</td>
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<tr>
<td>ACNS0121</td>
<td>Conformal RT Treatment for Ependymoma</td>
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<td>ACNS0122</td>
<td>Neoadjuvant Chemotherapy Chemo +/- Surgery for NGGCT</td>
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<td>ACNS0223</td>
<td>Carboplatin, Vincristine and Temozolomide in Gliomas</td>
<td>Wiersma S; Tekautz T</td>
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<td>ACNS0221</td>
<td>Conformal RT in Gliomas</td>
<td>Wiersma S; Hilden J; Burke M</td>
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<td>ACNS0222</td>
<td>Phase II Study of Motexafin-Gadolinium (NSC659238, IND#55563) and Involved Field Radiation Therapy for Intrinsic Pontine Glioma of Childhood</td>
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<td>ACNS0332</td>
<td>Efficacy of Carboplatin Administered Concomitantly with Radiation and Isotretinoin as Pro-Apoptotic Agent in Other Than Average Risk Medulloblastoma/PNET Patients</td>
<td>Wiersma S; Tekautz T</td>
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Appendix B: Publications

Journal Publications


Appendix B: Publications (continued)


Appendix B: Publications (continued)


Appendix B: Publications (continued)


Appendix B: Publications (continued)

Abstracts


Book Chapters


Book

Appendix C: Charts and Statistics

BTNC Procedural Volume
The Brain Tumor and Neuro-Oncology Center (BTNC) continues to grow in volume of procedures. In 2009, 455 stereotactic radiosurgery (Gamma Knife and Novalis) and 584 surgical procedures were performed, a combined 73 percent increase compared with 2001.

BTNC Patient Visits
Total outpatient visits increased by 366 percent over the past eight years. New patient visits have more than doubled since 2001.
BTNC Patient Enrollment

Over the past nine years, the number of patients on research trials has increased from 81 to 295, or 264 percent.
The Neurological Institute is one of 26 institutes at Cleveland Clinic that group multiple specialties together to provide collaborative, patient-centered care. The institute is a leader in treating the most complex neurological disorders, advancing innovations such as deep brain stimulation, epilepsy surgery, stereotactic spine radiosurgery and blood-brain barrier disruption. Annually, our staff of more than 220 specialists serves 140,000 patients and performs 7,500 surgeries. Cleveland Clinic is a nonprofit multispecialty academic medical center, consistently ranked among the top hospitals in America by U.S. News & World Report. Founded in 1921, it is dedicated to providing quality specialized care and includes an outpatient clinic, a hospital with more than 1,000 staffed beds, an education institute and a research institute.