Celebrating seventy-five years of neurological surgery in Pittsburgh

by Robert M. Friedlander, MD

As we celebrate 75 years of neurosurgery in the city of Pittsburgh, I wish to reflect upon what the University of Pittsburgh Department of Neurological Surgery has accomplished, and the impact it has had on neurosurgery. This milestone also provides the setting to delineate our current opportunities. As I reflect on this important milestone, four words come to mind: tradition, leadership, honor and promise.

Tradition: So much has occurred in this department that has changed the manner in which neurosurgery is practiced. This transformation of neurosurgery has been accomplished as a result of our long-standing culture of achievement and excellence. Doing all that is possible, one patient at a time, as well as developing comprehensive novel approaches to improve on what we offer the patients engenders a responsibility to deliver transformational therapies.

Leadership: We lead the path in many aspects of the practice of neurosurgery. We are the largest—and currently ranked as the most academically productive—neurosurgical department in North America. Such a coveted position comes both with pride and significant responsibilities to continue to lead the path in the practice of neurosurgery.

Honor: It is a privilege to be a doctor and an honor to be a neurosurgeon. Each one of our faculty and residents is part of the Pittsburgh neurosurgery legacy. Our faculty has been entrusted with the responsibility to train the next generation of academic leaders. Understanding the privilege of serving our patients engenders a responsibility to deliver transformational therapies.

Promise: Our faculty understand that one of their goals is to develop safer and more effective approaches for the evaluation and treatment of individuals with neurologic diseases. The development of novel therapies not only represents a challenge as we come to work every day, but we see it an opportunity to innovate. It is critical to evaluate what we do every day and ask how can we do better.

To deliver on these challenges and opportunities, we have recruited three remarkable individuals this past year. R. Mark Richardson, MD, PhD, who recently completed neuromodulatory training at the University of California, San Francisco, will be directing our adult epilepsy program as well as co-directing the functional neurosurgery program. Robert Ferrante, PhD, is a world authority in the development of novel therapeutic approaches for the treatment of neurologic diseases. Avniel Ghuman, PhD, recently completed his training in using magnetoencephalography (MEG). This technique in conjunction with the broad expertise and structural and behavioral neurosciences at our department and institution will provide an unprecedented opportunity to probe into the basic underpinnings of brain function. These three remarkable individuals are core constituents in the strategic vision to realize our mission to understand, to innovate and to teach.

To reach our short and long term ambitious goals, we are closely working with the administrations of UPMC and the University of Pittsburgh School of Medicine to develop a blueprint for a comprehensive brain institute. This entity will house a multidisciplinary effort that will enable us to continue our role as a leader in the development of novel therapies for patients with neurologic diseases. This institute will enable our faculty to work closely and develop stronger strategic partnerships with members of other clinical and basic departments and bring to fruition the developments of the therapies that will transform the care of patients with neurologic diseases. As we complete the last quarter of our first century, tradition, leadership, honor and promise will remain the guiding principles of the Department of Neurological Surgery at the University of Pittsburgh.

Neurological surgery in Pittsburgh began in 1936 with the arrival of Stuart Niles Rowe (upper left), a promising young surgeon trained under the auspices of Charles M. Frazier in Philadelphia. Rowe’s arrival marked the birth of a dedicated neurosurgical division that would become a leader in the field. His move here was prompted by a letter from Dr. L.H. Landon, Sr., the chief of general surgery at West Penn Hospital emphasizing the need for a formally trained neurosurgeon in Pittsburgh. Rowe, a Michigan native, developed a strong clinical practice based on the loosely affiliated community hospitals in the Pittsburgh area. He focused his research activities at the University of Pittsburgh and wrote several pioneering papers on the neurosurgical treatment of pain, brain abscess, and cerebral trauma. As a teacher, Rowe believed that neurosurgery training should not only teach exceptional technique, but also the critical clinical decision-making skills necessary to succeed. He preached the underlying need for thorough literature review and independent research as a means for broadening clinical knowledge.
Effective therapies developing in fight against TBI

T raumatic brain injury has reached epidemic proportions in our society. According to the Centers for Disease Control and Prevention, every year in the United States, approximately 1.7 million people sustain a traumatic brain injury (TBI). Of these, about 52,000 die, 275,000 are hospitalized and the remaining are treated and released from an emergency department.

There are $60 billion in estimated direct and indirect costs of TBI. More than 5.3 million people in the U.S. live with disabilities caused by TBI. Furthermore, patients, families, and caretakers must face long-term cognitive, emotional, and movement disorders that frequently complicate the lives of those who survive a TBI.

The TBI problem must be strategically addressed in order to achieve a significant impact and reduce its incidence and its short-term and long-term consequences.

TBI occurs most prominently as a result of automobile accidents as well as in sports and in the military. Injury prevention is being achieved by instituting a broad spectrum of legislative initiatives. Additionally improved protective devices have resulted in a reduction of injuries associated with these activities.

However, despite best efforts at prevention, traumatic brain injury remains a critical challenge to our society. A complementary approach of ameliorating the impact of the traumatic event is to provide the brain and the spinal cord the ability to better withstand the injury. The development of novel therapies is an important goal of research performed in our department every day. Focused and target-driven research occurs at all levels of basic science and translational medicine to develop novel therapies for this patient population.

In our laboratories, we are leading the way in the discovery of novel drugs that prevent neuronal cell death associated with brain and spinal cord trauma. As novel therapies are developed in our laboratories, we are positioned to evaluate them in humans using a highly coordinated infrastructure. All components of the therapeutic pipeline are in place and we are poised to develop effective therapies to treat these devastating and—for the most—previously untreatable diseases.

Robert M. Friedlander, MD, MA
Chairman, Department of Neurological Surgery
UPMC Endowed Professor of Neurosurgery & Neurobiology
University of Pittsburgh School of Medicine
University of Pittsburgh Medical Center

Pittsburgh Steelers James Harrison (left) and Charlie Batch (right) visited the department to learn of the novel initiatives in neurologic injury research as well as of the planning of the Pittsburgh Brain Institute.
Immunoexcitotoxicity offers new insight in brain injury related research, care

by Joseph Maroon, MD; Russell L. Blaylock, MD

Approximately 1.5 million people in the United States annually experience a traumatic brain injury (TBI). The number of unreported head injuries is much higher. Of these, a great number occur in sports-related events, professional and nonprofessional. There are approximately 100,000 to 300,000 concussions occurring in the game of football alone each year. Most sports-related head injuries are minor concussions and a significant number are repeated injuries over a relatively short period of time. It is known that football players and boxers experience thousands of subconcussive blows during a career.

Until recently, it was assumed that minor injuries resulted in few long-term neurological problems and were, in fact, characterized by a lack of neuropathological damage to the brain. Although it was recognized that a small percentage of these individuals could suffer from an array of neurological and constitutional complaints, called the post-concussion syndrome, there was little evidence of anatomical damage to explain these symptoms.

Post-concussion syndrome (PCS), post-traumatic stress disorder (PTSD), and chronic traumatic encephalopathy (CTE) are devastating neurological conditions, not completely understood in terms of their pathogenesis. There is, however, accumulating scientific evidence that physical injury as in football or other contact sports as well as some psychiatric disorders (e.g., depression and PTSD) produce a neuroinflammatory and excitotoxic response in the brain. In the case of concussions, cumulative injury may lead to progressive neurodegeneration of the brain (CTE). This process has been termed “immunoexcitotoxicity,” first observed in the “Gulf war syndrome.”

Immunoexcitotoxicity relates to an over-reaction of the resident macrophage immune protective cells in the brain (microglia). When stimulated by trauma, viruses, or other toxic substances, they normally release chemicals (cytokines and excitotoxic amino acids) that initiate a cascade of effects that, if failing to “switch off,” further leads to a series of molecular chain reactions called “excitotoxicity.” This can result in the eventual death of nerve cells. It is akin to a smoldering brush fire (inflammation) in the brain that with repeated trauma burns out of control. This process also occurs in other neurological diseases like Alzheimer’s disease, multiple sclerosis, and Parkinson’s.

Immunoexcitotoxicity represents a new concept in medicine in the development of brain diseases and can explain the original observations of subsequent progressive brain injury (pugilistica dementia) in fighters, in other contact sports, and in injury suffered in military combat. This immunoexcitotoxic response may be enhanced by prior “priming” of the microglia by exposure to neurotoxic metals (Pb, Al, Hg, Cd, Fe), neurotoxic chemicals, (pesticides/herbicides), prior or occult infections, and brain trauma (concussions). With subsequent concussions, as in a previously primed immune allergic reaction (e.g., peanut allergy), there is an outpouring of cytotoxic chemicals that is associated with memory loss, personality changes, depression, and more—all common findings in PCS, PTSD, and CTE.

Elevated levels of the same immunoexcitotoxic chemicals (IL-1, interleukin-6, tumor necrosis factor, and excitotoxins) seen in brain trauma have now been observed in depression, obsessive compulsive disorder, and other psychiatric disorders—unrelated to physical trauma to the brain. Thus, there appears to be a continuum from traumatic concussion to PTSD to CTE—all with the underlying substrate of immunoexcitotoxicity.

We are of the opinion that there exists abundant evidence that mild, repetitive concussions can trigger immunoexcitotoxicity that in some cases can result in a progressive degeneration in a pattern seen with CTE. A number of studies have shown immune proinflammatory cytokine responses in the traumatized brain that are widespread, with more intense localization within areas of the brain also affected in Alzheimer’s disease.

Most such studies have examined acute immune effects in moderate to severe TBI, but a few are concerned with chronic immune responses as well. Likewise, there are a number of studies, both in human beings and experimental animals, demonstrating a massive acute accumulation of glutamate, aspartate, and other excitotoxins in the central nervous system (CNS) following TBI.

With neuroinflammation linked with excitotoxicity as a possible common genesis to all, preventive and therapeutic strategies with anti-inflammatory agents and glutamate receptor modulators, both pharmacologic (non-steroidal anti-inflammatory drugs (NSAIDS), tetracycline’s, etc.) and natural (Omega 3 fatty acids, vitamin D3, resveratrol, curcumin, quercetin, magnesium, luteolin, and hyperbaric O2, etc.) should be thoroughly investigated.
The treatment of recurrent glioblastoma multiforme (GBM) is challenging. Although re-irradiation is limited by the radiation tolerance of the brain, stereotactic radiosurgery can selectively boost the target tissue and the adjacent tumor border where most further recurrences develop. Several reports have described the potential efficacy and acceptable toxicity of radiosurgery for recurrent GBM.

GBMs are innately hypoxic tumors with strong endogenous expression of vascular endothelial growth factor (VEGF) which is a potent mitogen that facilitates migration, proliferation and survival of endothelial cells which are essential for tumor angiogenesis. VEGF is directly correlated with tumor growth rate, metastatic potential and poor outcome. Bevacizumab, a humanized monoclonal antibody to VEGF, inhibits angiogenesis and has been found to be active in several types of tumors such as breast, non-small cell lung cancer and colorectal cancer. A series of phase 2 trials employing bevacizumab and irinotecan demonstrated encouraging response rates, as well as improvements in time-to-progression and 6-month progression free survival in patients with recurrent malignant gliomas compared to historical controls. In the present study we evaluated the efficacy and safety of re-irradiation using Gamma Knife Stereotactic Radiosurgery (GKSR) followed by bevacizumab in a series of patients with recurrent GBM and compared outcomes to a matched cohort who underwent salvage GKSR alone.

Our experience included eight male and three female patients. The median patient age at GKSR was 62 years (range, 46-72 years). At the time of GKSR, seven patients had a first recurrence and four had two or more recurrences. The median interval from the initial diagnosis until GKSR was 17 months (range, 5–34.5 months). The median tumor volume was 13.6 cm³ (range, 1.2–45.1 cm³) and the median margin dose of GKSR was 16 Gy (range 13–18 Gy). Following GKSR, bevacizumab was administrated with irinotecan in nine patients and with temozolomide in one patient. One patient was treated with bevacizumab monotherapy. The treatment outcomes were compared to 44 case-matched controls who underwent GKSR without additional bevacizumab.

At a median of 13.7 months (range, 4.6–28.3 months) after radiosurgery, tumor progression was evident in seven patients. The median progression-free survival (PFS) was 15 months (95% Confidential Interval [CI], 6.5–23.3 months). Six-month and 1-year PFS rates were 73% and 55%, respectively. The median overall survival (OS) from GKSR was 18 months (95% CI, 10.1–25.7 months) and 1-year OS rate was 73%. One patient (9%) experienced grade III toxicity and one patient (9%) had major adverse radiation effects. Compared with patients who did not receive bevacizumab, the patients who received bevacizumab had significantly prolonged PFS (15 months vs. 7 months, p=0.035) and OS (18 months vs. 12 months, p=0.005), and were less likely to develop an adverse reaction effect (9% vs. 46%, p=0.037).

The combination of salvage GKSR followed by bevacizumab added potential benefit and little additional risk in a small group of patients with progressive glioblastoma. Further experience is needed to define the efficacy and long-term toxicity with this strategy.

**Treatment Response and Survival**

Post-treatment MRI scans were available for review on all 11 patients. The initial MRI at a median of 2 months (range: 1.5 months) after GKSR suggested tumor progression in two patients, stable disease in five patients, and partial response in four patients. Of the two patients with “progression” on the initial images, one was found to have a treatment response at the time of next follow up imaging, thus consistent with pseudoprogression (figure 1 above). The other patient did not undergo subsequent imaging due to clinical deterioration. During the median of 14 months of follow-up (range, 4.6 – 28.3 months) after GKSR, the best tumor response (based on RANO criteria) was complete response in two patients, partial response in five patients, stable disease in three patients and progressive disease in one patient. Over time, delayed tumor progression was evident in seven patients (63%). Treatment failure occurred within the radiosurgery volume in three patients and at adjacent area close to the margin of the treatment volume in two (figure 2 above). Two patients had a stable or smaller tumor compared with initial imaging but developed additional FLAIR or T2 signal change surrounding the radiosurgery target. The median PFS after GKSR was (continued on page 8)
Proceeds to benefit research at Pitt

Book tells story of patient’s dramatic recovery from traumatic brain injury

by Jim Olsen

On February 4, 2009, 19-year-old Alisha Webb lost control of her car after it slipped on black ice. In the horrific accident that followed, she suffered a potentially fatal combination of internal injuries, including a ruptured spleen, a heart contusion, multiple neck fractures, and a type of brain injury known as a diffuse axonal injury. Doctors at her local hospital successfully kept her alive, but did not expect her ever to regain consciousness.

Of all the injuries “Lish” had sustained, the doctors were most concerned about the injury to her brain. A diffuse axonal injury is one of the most common and devastating types of traumatic brain injury, according to David Okonkwo, MD, co-director of the Brain Injury Research Center at the University of Pittsburgh. “A diffuse axonal injury,” notes Dr. Okonkwo, who was not involved in Lish’s early care, “affects a larger portion of the brain than a focal injury, and is one of the major causes of unconsciousness and persistent vegetative state after head trauma.”

For an entire month, the family kept their vigil at Lish’s side in the intensive care unit, watching for any sign of consciousness, sustaining a level of hope far beyond what the medical circumstances seemed to justify. The family was grateful to those involved in Lish’s care, but immensely frustrated and at times discouraged that Lish’s initial medical team did not seem to share their optimism about Lish’s future.

On March 4, exactly one month following the accident, much to the surprise of doctors and nurses alike, Lish suddenly regained consciousness. As Lish’s grandparents, Regina and Jim Venturella, recalled, “To our utter amazement, she opened and closed her eyes on command, gave a thumbs-up and counted to five with her right hand. She didn’t utter a word, but had a huge smile on her beautiful face.”

Eventually, Lish became well enough to be discharged to a rehab facility, and shortly thereafter Dr. Okonkwo examined Lish for the first time.

A new book by Ms. Venturella, entitled It Only Took a Moment: A True Story of Tragedy, Faith and Triumph Following a Traumatic Brain Injury, tells the story of her granddaughter’s gradual recovery from a traumatic brain injury. Ms. Venturella has decided that proceeds from this book will support brain injury research at the University of Pittsburgh’s Department of Neurologic Surgery.

“The University of Pittsburgh is fortunate to have access to state of the art diagnostic imaging technologies, some of which are un-

available almost anywhere else in the world,” commented Dr. Okonkwo. “Lish’s brain images at that time clearly indicated that the basic structures were reasonably intact, and given Lish’s youth and otherwise good health, we predicted then that a prolonged and thorough program of rehabilitation should yield very positive results.”

Buoyed by Dr. Okonkwo’s hopeful prognosis, Ms. Venturella (herself a retired nurse) devoted herself full time to caring for Lish and supervising her rehabilitation. During the next two years, as Lish relearned to talk, to eat, to walk and to care for herself, Ms. Venturella was her coach, advocate and constant companion.

Throughout this time Ms. Venturella met many other individuals and families who had also experienced traumatic brain injuries. She realized that Lish’s story might help other families as they put together the pieces of their own lives, and could provide hope and inspiration to help them manage the more difficult times. She began to keep detailed notes about Lish’s medical journey and eventually decided to write a book which she completed in 2011.

It Only Took a Moment is Ms. Venturella’s first book and is a moving look at Lish’s long path to recovery. In the book Ms. Venturella writes in detail about the numerous UPMC doctors, nurses and physical therapists that helped Lish along the way, as well as the family’s religious faith which sustained them throughout those many months.

After completing the book, Ms. Venturella contacted the Department of Neurologic Surgery to ask whether the proceeds might support brain injury research that could benefit other patients in the future. The department enthusiastically accepted her offer.

“We are especially grateful to Ms. Venturella commitment to support our brain research efforts in this very creative and generous way,” commented C. Edward Dixon, PhD, director of the university’s internationally recognized brain injury research programs. “Due to an increasing shortage of federal research funds, we must increasingly turn to private philanthropy to help us advance this important area of research.”

In the summer of 2011, Lish enrolled in college, a step that just two years before had seemed nearly unthinkable.

“We are forever indebted to Dr. Okonkwo,” reported Ms. Venturella, “because of all the doctors we had consulted, he was the first to predict that Lish might make a complete recovery.”

Copies of the book are available for purchase online at Barnes and Noble and Amazon. Two dollars of every book sold goes to Traumatic Brain Injury research. You can also directly contact the book’s author, Regina Venturella, at rventurella@verizon.net.
Blast TBI: Acute problem in current wars; chronic problem in survivors

by C. Edward Dixon, PhD

T

raumatic brain injury (TBI) resulting from exposure to blast energy released by Improvised Explosive Devices (IEDs) has been recognized as the “signature injury” of Operation Iraqi Freedom and Operation Enduring Freedom. Although blast injuries have long been part of combat casualty care, vulnerability of gas filled organs such as the lung has often led to fatal injuries. In modern combat, protection by body armor has increase survival with neurological damage from otherwise lethal blast exposures. As noted in a 2009 Journal of Neurotrauma article (Ling G, et al), limited estimates by the lay press and other popular media outlets report the prevalence of bTBI as approaching 40–60% of deployed U.S. warfighters. Approximately 196,000 cases of TBI reported in OIF/OEF between 2000 and 2010 (150,000 being mild and 32,000 moderate TBI). Data from surveys suggest the blast represents one of the most common mechanisms of concussion in modern warfare. Large-scale injury surveillance studies in combination with brain injury biomarker assessments are needed to better define the scope of the problem. The blast wave of increased pressure produced by an explosion is understood to be the primary mechanism of blast-related TBI, but secondary and tertiary injuries that occur when the body is struck by projectiles such as shrapnel or propelled by the explosion (table 1).

Sufferers of severe blast bTBI often exhibit complex brain injuries as revealed by cranial computed tomography, with there being evidence of acute refractory brain swelling and vasospasm. However, despite these important reports, the neuropathology of human blast TBI remains unclear across the injury spectrum.

Several techniques have been used to detect subtle brain dysfunction including neuropsychological assessments, computerized function testing and neuroimaging. TBI resulting from blast can be categorized as mild, moderate, and severe. The three severities are based on the patient’s presenting Glasgow Coma Scale (GCS). For mild TBI, the GCS is 13–15.

The Department of Defense uses the definition proposed by the Mild Traumatic Brain Injury Section of the American Congress of Rehabilitation Medicine, which is the loss of consciousness (LOC), loss of memory

<table>
<thead>
<tr>
<th>Table 1. Four Categories of bTBI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
</tr>
<tr>
<td><strong>Tertiary</strong></td>
</tr>
<tr>
<td><strong>Quaternary</strong></td>
</tr>
</tbody>
</table>

preceding or following injury (amnesia), alteration in mental status at time of injury, and/or focal neurological deficit, (table 2). Mild bTBI can have initial symptoms of headache, dizziness, fatigue, mental slowing/fog, poor concentration that can be more challenging to diagnosis because symptoms can be subtle and/or hidden. The prevalence of postconcussional symptoms can also be determined by post-deployment self-report questionnaires and neuropsychological testing. Using these methods it has been reported that up to 23% of returnees reported that they had sustained a TBI; blast accounted for 79–88% of these injuries, and most had acute injury features consistent with mild TBI. Recent studies suggest that blast mechanism is clinically significant in concussions resulting in loss of consciousness, but not those involving only altered consciousness. Moderate-severe bTBI can result in alterations in memory (short-term), attention (complex tasks, distractibility), information processing, and executive functions (e.g. planning, organizing, multi-tasking, and strategizing.

Another approach to diagnosis mild TBI is based on measurement of biologic substances (e.g. proteins) that are released into the body after a TBI. Recent studies measuring biomarkers in CSF and serum from patients with severe TBI have demonstrated the diagnostic, prognostic, and monitoring potential. Department of Defense-funded research to evaluate serum biomarkers acutely in mild TBI patients in progress under the direction of myself and Dr. David O. Okonkwo.

TBI can lead to immediate, long-lasting and debilitating impairments in cognition, psychological health, and sensorimotor abilities. Recent post-mortem studies on athletes suggest that repeated concussive or mild TBIs are a risk factor for the long-term development of chronic traumatic encephalopathy (CTE) and possibly other neurodegenerative pathologies and conditions as well. TBI exposure has been observed to be a significant environmental risk factor for development of neurodegenerative disorders such as Parkinson’s disease and Alzheimer’s disease. Although there appears to be a correlation between repeated mild TBI and development of CTE, little is known about the mechanisms underlying this conversion from acute injury to chronic pathology and symptomatology. Less is known about the effects of a single exposure to TBI and its chronic consequences. With approximately 196,000 cases of TBI reported in OIF/OEF, the study of the long-term effects of TBI as it relates to the sequelae of neurological events following single or multiple exposures to trauma warrants investigation that targets the effects of long-term injury and the means to repair these injuries after they have been chronically established.

<table>
<thead>
<tr>
<th>Table 2. Severity of Traumatic Brain Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glasgow Coma Scale</strong></td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

Due to flying debris and bomb fragments. Targeting.

Another approach to diagnosis mild TBI is based on measurement of biologic substances (e.g. proteins) that are released into the body after a TBI. Recent studies measuring biomarkers in CSF and serum from patients with severe TBI have demonstrated the diagnostic, prognostic, and monitoring potential. Department of Defense-funded research to evaluate serum biomarkers acutely in mild TBI patients in progress under the direction of myself and Dr. David O. Okonkwo.

TBI can lead to immediate, long-lasting and debilitating impairments in cognition, psychological health, and sensorimotor abilities. Recent post-mortem studies on athletes suggest that repeated concussive or mild TBIs are a risk factor for the long-term development of chronic traumatic encephalopathy (CTE) and possibly other neurodegenerative pathologies and conditions as well. TBI exposure has been observed to be a significant environmental risk factor for development of neurodegenerative disorders such as Parkinson’s disease and Alzheimer’s disease. Although there appears to be a correlation between repeated mild TBI and development of CTE, little is known about the mechanisms underlying this conversion from acute injury to chronic pathology and symptomatology. Less is known about the effects of a single exposure to TBI and its chronic consequences. With approximately 196,000 cases of TBI reported in OIF/OEF, the study of the long-term effects of TBI as it relates to the sequelae of neurological events following single or multiple exposures to trauma warrants investigation that targets the effects of long-term injury and the means to repair these injuries after they have been chronically established.

*
Ferrante Receives Gerson Scholar Award

Robert Ferrante, PhD, professor of neurological surgery at the University of Pittsburgh and co-director of the university’s Center for ALS Research, received the first annual Leonard Gerson Distinguished Scholar Award, at a special event October 6 at the Pittsburgh Athletic Association.

The award was established by Sandy Gerson Snyder in memory of her father Leonard Gerson who passed away from ALS—amyotrophic lateral sclerosis, also known as Lou Gehrig’s Disease—at age 70. The award supports educational programs for faculty and staff at the University of Pittsburgh School of Medicine as well as the community at large, with the goal of broadening horizons and pushing the boundaries of knowledge as scientists, physicians, and patients work together in the fight against ALS.

Dr. Ferrante is a leading expert on ALS research and has lectured nationally and internationally on the subject.

Henry Brem to Serve as 2011 Stuart Rowe Lecturer

Henry Brem, MD, Harvey Cushing Professor of Neurosurgery, Ophthalmology, Oncology and Biomedical Engineering and Director of Neurosurgery at Johns Hopkins Medicine in Baltimore, MD, has been selected as the 2011 Stuart Rowe Lecturer at the Department of Neurological Surgery. Brem will provide two lectures and preside over research talks given by residents at the Seventh Annual Stuart Rowe Society Research and Lectureship Day scheduled for December 7. For more information on the day’s events, please visit our website at neurosurgery.pitt.edu.

In the Media

• Robert M. Friedlander, MD, was featured in a Science Daily article October 11, discussing his research findings that showed the drug Melatonin delayed the onset of symptoms and reduced mortality in a mouse model of Huntington’s Disease.

• Walter Schneider, PhD, was featured in a CBS-TV 60 Minutes segment on autism October 23 demonstrating how High Definition Fiber Tracking can depict ‘brain wiring’ in autism patient and possibly help in diagnosis.

• Elizabeth Tyler-Kabara, MD, PhD, was featured in a CBS-TV The Early Show Health News segment on October 26 showing how research has allowed a quadriplegic to control a robotic arm through brain signals. The story was also reported in numerous other media outlets across the country, including the Pittsburgh Post-Gazette on October 11.

• David O. Okonkwo, MD, PhD, was featured in the fall 2011 edition of Pittsburgh Quarterly. In the article, Dr. Okonkwo discussed how new brain-scanning technology may allow doctors to determine extent of brain injuries and how the injuries will influence a patient’s ability to speak, walk and think.

• Joseph Maroon, MD, commented on Indianapolis Colts quarterback Peyton Manning’s neck surgery in a CNN.com article posted on September 9.

Congratulations

• Carl Snyderman, MD, MBA, earned an Executive MBA (EMBA) degree from the University of Pittsburgh Katz Graduate School of Business this past July.

• Dr. Maroon was named a recipient of the 2011 Indiana University Distinguished Alumni Service Award. The award is the highest recognition available to Indiana University alumni.

• Dr. Okonkwo was promoted to associate professor.

• Oren Berkowitz RPA-C, MSPH, successfully defended his PhD dissertation on September 27 and now has a PhD in epidemiology from the University of Pittsburgh Graduate School of Public Health.

• Cheryl Rodgers received UPMC’s Award for Commitment and Excellence in Service (ACES).

New Research Funding


• “Park Reeves Syringomyelia Research Consortium.” Funding Agency: Washington University-Park Reeves; Principal Investigator: Mandeep Tamber, MD, PhD; $110,000 per patient.

• “Safe Flexible Intracerebral Navigation with Steerable Needles.” Funding Agency: Carnegie Mellon University/ National Institute of Health; Principal Investigators: Johnathan Engh, MD; Cameron Riviere, PhD (Carnegie Mellon University); $53,048.

Avniel Singh Ghuman Joins Department

The University of Pittsburgh Department of Neurological Surgery would like to welcome Avniel Singh Ghuman, PhD, to the department as of September 2011. Dr. Ghuman will serve as director of MEG (magnetoencephalography) research.

Dr. Ghuman received his undergraduate education in math and physics at The Johns Hopkins University and completed his doctoral education in biophysics at Harvard. He completed postdoctoral training at the National Institute of Mental Health prior to arriving at the University of Pittsburgh.

Prominent Lectures and Appearances

• Dr. Okonkwo was visiting professor at the University of Kentucky Spinal Cord and Brain Injury Research Center, July 22.

• Juan Fernandez-Miranda, MD, was honored guest for the First Neurooncology and Skull Base Symposium of the Colombian Society of Neurosurgery; Dr. Fernandez-Miranda was also co-director of “Anatomy and Endo-Microneurosurgical Strategies in Brain Surgery,” a hands-on course sponsored by the Spanish and Portuguese Societies of Neurosurgery.

• Douglas Kondziolka, MD, was a visiting professor at the University of New Mexico, November 9-10.

Motorcycle Ride Provides Support for ALS Research

The Second Annual Jon Obusek Memorial Motorcycle Ride to support ALS research at the University of Pittsburgh was held August 28 in White Oak, PA, and helped raise $3,500 for the university’s atrophotropic lateral sclerosis research program. Dr. Ferrante, co-director of the university’s Center for ALS Research, spoke at the event that attracted 75 area bikers.

Personal Notes

• Phillip Parry, MD, was married to Katarzyna Glab, DMD, on September 24; Christopher Bonfield, MD, was married to Stephanie Jacekso on September 17; Paul Richard, MD, was married to Viktoria Totoraitis, MD, on May 2.
(continued from page 4)

14.9 months (95% CI, 6.5 – 23.3 months). The six-month PFS rate was 73% and 1-year PFS rate was 55%. Of the seven patients with progressive tumor, two patients underwent repeat GKSR at 17 months and 23 months after initial GKSR. After repeat GKSR, they continued bevacizumab therapy to reduce the risk of ARE.

In 2009, the combination of stereotactic radiotherapy and bevacizumab was described by Gutin et al. in the management of 25 patients with recurrent malignant glioma. For 20 patients with GBM, the overall tumor response rate was 50%, and median PFS and OS of the patients were 7.3 and 12.5 months, respectively. The rationale for combining bevacizumab and radiotherapy is based on the potential radiosensitizing benefit of bevacizumab. The potential for such synergistic effects has been proposed both for the ability of anti-angiogenic agents to normalize blood vessels (thereby reducing tumor hypoxia), and for its ability to counteract the effects of radiation-induced VEGF secretion from tumor cells. More recently, Cuneo et al. analyzed the outcomes of 49 patients with recurrent GBM. Thirty three patients received bevacizumab before or after linear accelerator based radiosurgery and 16 patients underwent radiosurgery without bevacizumab. They demonstrated that patients who underwent radiosurgery followed by bevacizumab administration had significantly longer PFS and OS compared with patients who had radiosurgery without bevacizumab (median PFS, 5.2 months vs. 2.1 months; median OS, 11.2 months vs. 3.9 months). In the current study, follow up imaging demonstrated radiographic improvement (either complete response or partial response) in seven patients (64%). The median PFS after GKSR was 14.9 months. The six-month and 1-year PFS rate were 73% and 55%, respectively. The median survival from the time of GKSR was 17.9 months, and 1- and 2-year survival rate after GKSR were 73%, and 42%, respectively. The overall survival after initial diagnosis was a median of 33.2 months. We believe that our initial experience using GKSR and bevacizumab compares favorably with the results reported from other centers using a similar patient selection. The survival benefit observed in our series may in part reflect selection bias, since our patients had a favorable performance status at the time of treatment and had already shown an initial response to the first line treatment.

The North American Gamma Knife Consortium is currently planning a Phase 2 multicenter prospective study to investigate the safety and efficacy of salvage GKSR plus bevacizumab for recurrent GBM. In this trial, the border zone will be determined using MRI and MRS. We hypothesize that the addition of bevacizumab will reduce radiation toxicity in the volume treated by GKSR and will improve therapeutic effect to the solid tumor itself.