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Neurological Surgery at the National Institutes of Health

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Abstract

The Surgical Neurology Branch (SNB) in the intramural program of the National Institute of Neurological Disorders and Stroke at the National Institutes of Health has been a unique setting for academic neurosurgery for nearly 60 years. Every patient evaluated and treated in the SNB is enrolled in a clinical research protocol, which underscores a singular focus on advancing neurosurgical research and patient care. Since the inception of the SNB, this research effort has been driven by dedicated clinician-investigators and basic scientists including Maitland Baldwin, Igor Klatzo, John M. Van Buren, Ayub K. Ommaya, Richard J. Youle and Edward H. Oldfield. These and other SNB investigators have studied and advanced treatment of a number of neuropathologic processes including delineation of differences between cytotoxic and vasogenic edema, head injury, Cushing's disease, the effects of vascular endothelial growth factor in nervous system tissues, tumor suppressor syndromes, the pathophysiology of syringomyelia, mechanisms underlying cerebral vasospasm after subarachnoid hemorrhage, spinal arteriovenous malformations, mechanisms of cell death and drug delivery. Currently, SNB efforts are focused on central nervous system drug-delivery, the natural history of familial tumor syndromes, functional neurosurgery, epilepsy, vasospasm and development of chemotherapeutics for malignant glioma. Throughout its history, the SNB has also been dedicated to training neurosurgeon clinician-investigators; 22 previous fellows/staff have become Chairs of their respective neurosurgical departments. Recently, the commitment to training future neurosurgeon clinician-investigators has been further defined with the development of a residency-training program in neurological surgery approved in 2010.

Keywords

National Institutes of Health; National Institute of Neurological Disorders and Stroke; Neurological Surgery; Residency; Surgical Neurology Branch

Introduction

“The National Institutes of Health have an Intramural Program which includes a neurosurgical service. This Branch of Surgical Neurology has an active research

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program and a reasonable share of the beds in the 500-bed Clinical Center of the National Institutes of Health. The research production of this Branch of the NIH has been impressive, the men working in this center are of the highest order, and this particular 'face' of neurosurgery, which is seen by so many visitors from this country and abroad, is one which does justice to our specialty."

Eben Alexander, Jr., M.D.

1967 Presidential Address

*American Association of Neurological Surgeons*⁵

The National Institute (singular) of Health was founded in 1930 when the Ransdell Act, sponsored by United States Senator Joseph E. Ransdell (D-Louisiana) reorganized the Hygienic Laboratory of the Public Health Service (P.L. 71-357, 46 Stat. L. 585.). The organization has since been composed of two separate research programs: intramural (11% of FY NIH 2009 budget) and extramural (89% of FY NIH 2009 budget)(the intramural organizational structure is shown in Figure 1). In 1940, this intramural program moved from Washington, District of Columbia, to its permanent home in Bethesda, Maryland. The organization would be renamed in 1948 as the National Institutes of Health (NIH) through the National Heart Act (P.L. 80-655, 62 Stat. L. 464.). Two years later, on November 22, 1950, as part of the Omnibus Medical Research Act, Congress authorized the formation of the National Institute for Neurological Disorders and Blindness (NINDB) (P.L. 81-692, 64 Stat. L. 443.). The institute would be renamed the National Institute of Neurological Disorders and Stroke (NINDS) in 1968 when the National Eye Institute was formed.

In 1951, Pearce Bailey, M.D., was appointed the first Institute Director of the NINDB. Dr. Bailey was charged with oversight of clinical and basic science research in the neurosciences of the intramural program of NINDB. Since their inception, the clinical services in the intramural programs at the NIH were unique, as every patient would be recruited in the context of clinical research investigations. To lead clinical research operations on the NIH campus, Dr. Bailey hired G. Milton Shy, M.D., as the NINDB Intramural Clinical Director.⁷⁹ Dr. Shy had trained in neurology at the National Hospital for Nervous Disease, Queens Square, London and the Montreal Neurological Institute. His research focused on neuromuscular disease and he would later gain notoriety for the description of Shy-Drager syndrome.⁸²

To broaden the scope of clinical research within the NINDB, Dr. Bailey developed several clinical programs in epilepsy. For study of the neurosurgical treatment of epilepsy, he recruited another Montreal Neurological Institute trainee, Maitland Baldwin, M.D. Dr. Baldwin had completed his neurosurgical training under Wilder Penfield, M.D., and worked extensively with him characterizing temporal lobectomy for treatment of epilepsy.⁷⁵ Given his research interests, Dr. Baldwin aptly named the newly established department, the Surgical Neurology Branch (SNB). He would serve as Branch Chief for 17 years, additionally assuming the role of Intramural Clinical Director of the NINDB from 1960 to 1971.² The SNB initially consisted only of the Section of the Chief, led by Dr. Baldwin. As he continued to recruit faculty, the Branch would grow to 7 sections by 1956.²³ These sections included the Office of the Chief, the Section on Clinical Psychology, the Section on Clinical Neuropathology, the Section on Experimental Neurosurgery, the Section on Developmental Neurology, the Section on Pain and Neuroanesthesiology and the Section on Primate Neurology.

Over the past 5 decades, the research directions of the SNB evolved with the interests of the faculty. The Branch is now composed of 7 parts including the Office of the Chief, the Biochemistry Section, the Clinical Neurosurgery Unit, the Neurosurgical Biology and

Therapeutic Unit, the Molecular Pathology Unit, the Neuropathology Unit and the Surgical and Molecular Neuro-Oncology Unit. Below we detail the history of the SNB until the current time.

Surgical Neurology Branch

Maitland Baldwin, M.D. (1953 – 1970)

Maitland Baldwin, M.D., was recruited, at the age of 35 years, to become Branch Chief in 1953 and appointed NINDS Clinical Director in 1960. As Branch Chief, he advocated the development of advanced operating facilities and was instrumental in the design and construction of the NIH operating rotunda (Figure 2). Dr. Baldwin was effective as both a leader and scientist during his tenure. His initial research focused on the pathophysiology and treatment of epilepsy. One of his first studies at the NIH was to investigate the effect on hypothermia on seizure activity.¹⁰ Previous investigators had considered the hypothermic brain to be pro-epileptic.⁶¹ Dr. Baldwin used external cooling in a primate model to determine the amount of temporal lobe stimulation necessary to produce epileptiform activity in the setting of hypothermia. Contrary to expectations at the time, he demonstrated that increased stimulation was required to produce epileptiform activity in the hypothermic brain. This observation underlies the mechanism of applying cold Ringer's lactate solution directly to the brain to arrest seizure activity evoked in awake patients by electrical stimulation mapping.⁸⁰ Similarly, Dr. Baldwin also studied extravascular cooling to treat intractable epilepsy and for protection against ischemia during tumor resection.⁷²

Dr. Baldwin was also a pioneering and talented clinical research scientist. While training at the Montreal Neurological Institute, he helped Dr. Penfield and K.M. Earle describe the pathologic changes associated with mesial temporal sclerosis, which they initially termed *incisural sclerosis*.^{20,21} Based on this finding, Dr. Penfield and Dr. Baldwin described a new approach for epilepsy surgery for temporal lobe seizures that included hippocampal resection.⁷⁵ This work provided the basis for contemporary temporal lobectomy for epilepsy. Building on this work, Baldwin continued performing epilepsy surgery and research at the NIH. However, his surgical interests remained varied. In 1956, Dr. Baldwin successfully separated conjoined twins with cephalopagus.⁹ Dr. Baldwin's 1956 case was unique at the time, not only for the survival of both twins, but because that both twins showed normal development at long-term follow-up.⁸

On February 9, 1970, Dr. Baldwin died suddenly at work from an intracerebral hemorrhage at the age of 52.⁶² His death came as a shock to his colleagues, as he had been active as a swimmer and a mountain climber and was a reservist in the Marine Corps until the time of his death.

John M. Van Buren, M.D., Ph.D. (1955 – 1978)

John M. Van Buren, M.D., Ph.D., was appointed Acting Chief of the SNB in 1970 and was made Branch Chief in 1972. Dr. Van Buren was also a trainee of Dr. Penfield from the Montreal Neurological Institute, with a similar interest in epilepsy. His research focused on neuroanatomy, and with help from others in the Branch he furthered the study of operative neurosurgical anatomy. Consistent with Dr. Baldwin's and his own research interests in epilepsy, Dr. Van Buren's work focused initially on describing the structures of the temporal lobe. While many early anatomic studies were based on cerebral lesions and their neurologic consequences, Dr. Van Buren had opportunity to study the results of planned lesions made by temporal lobectomy. This was advantageous in anatomical study, as these lesions were neither expansile (neoplasms) nor widespread (projectiles). Specifically, Dr. Van Buren used this data to further define the location of the temporal horns and the optic radiations within the temporal lobe.^{6,85} He demonstrated, among other points, that the optic radiations were

spatially separated as they traveled through the temporal lobe. Among his trainees was George A. Ojemann, M.D., who would go on to a distinguished career in neurosurgery, making several critical contributions to the surgical treatment of epilepsy. Later, Dr. Baldwin began clinical work at the NIH on surgery for movement disorders, including thalamotomy for Parkinson's disease.⁸¹⁻⁸⁶ However, his most lasting discoveries related to movement disorders were a result of his research interest in neuroanatomy. In 1972, Dr. Van Buren and R.C. Borke published the most detailed stereotatic atlas on the human thalamus to date.⁸⁵

Igor Klatzo, M.D. (1956 – 1970)

Many investigators in the SNB were not, or are not, neurosurgeons. Several pathologists and basic scientists have held positions within the Branch and they have provided unique perspectives on neurosurgical pathology and treatment. Igor Klatzo, M.D., who was a pathologist by training, made several important neuroscience contributions. Dr. Klatzo, like many others in the early history of the SNB, had trained at Montreal Neurological Institute with Dr. Penfield. He was recruited by Dr. Baldwin in 1956 to head the Neuropathology Section within the SNB, where he would stay until the NINDB granted him his own laboratory in 1968.¹ Dr. Klatzo studied the blood-brain barrier and cerebral edema. In 1967, he was the first to propose 2 distinct forms of cerebral edema: cytotoxic and vasogenic.³³ Dr. Klatzo was also a strong influence on Donlin M. Long, M.D., Ph.D., who studied at the NIH from 1966 to 1967. Dr. Long made critical contributions in the understanding of cerebral edema, including establishing the anatomic basis of vasogenic edema in brain tumors.⁴⁶ He would eventually become the Chair of Neurosurgery at Johns Hopkins University. Dr. Klatzo was also instrumental in defining the pathology of the prion disease, Kuru, along with David C. Gajdusek, M.D., also of the NINDB.³⁴ Dr. Klatzo described the pathologic changes as similar to those found in Creutzfeld-Jakob disease. The work on Kuru led to a Nobel Prize for Dr. Gajdusek.

Ayub K. Ommaya, M.D. (1960 – 1978)

Ayub K. Ommaya M.D. was one of the most prolific neurosurgeons to work in the SNB. Ommaya trained under Joseph B. Pennybacker M.B., Ch.B., at Nuffield College in London and joined the SNB in 1960. From 1974 to 1978, he held the position of Branch Chief. In 1966, he developed the first coma scale, although it would not become widely used.⁷² Dr. Ommaya also achieved several firsts in collaboration with John L. Doppman, M.D., and Giovanni Di Chiro, M.D., of the NIH Department of Radiology. Together, the 3 pioneered the field of spinal angiography.¹⁴ In 1968, the 3 also reported the percutaneous embolization of a spinal cord arteriovenous malformation using stainless steel pellets, providing one of the first reports of interventional neuroradiology.¹⁹ Dr. Ommaya also worked to clarify etiologies of non-traumatic cerebrospinal fluid rhinorrhea. ⁶⁸⁻⁷⁰ In 1976, he worked with Sir Godfrey N. Hounsfield to define the spatial and density resolution of computed tomography (CT).⁷¹ In the report, they provided initial results on linear attenuation coefficients of different cranial structures, which have become the basis of our modern understanding of density on head CT (Hounsfield units).

Dr. Ommaya is perhaps best remembered for his development of the eponymous Ommaya reservoir. In 1963, he published the first description of a subcutaneous device allowing repeated, sampling of cerebrospinal fluid and sterile intraventricular injection of drug (Figure 3).⁶⁹ The reservoir allowed physicians to avoid repeated lumbar or cisternal punctures. In the initial report, Dr. Ommaya alluded to the successful use of the device in 2 patients with cryptococcal meningitis. Shortly, thereafter, he expanded the series to 4 patients and formally presented the first clinical results with the device.⁹¹ Dr. Ommaya continued to study the device while at the NIH and co-authored a New England Journal of

Medicine study with Robert J. Ratcheson, M.D., describing the results in 60 cases.⁷⁸ The Ommaya reservoir is still used broadly in present day practice.

After his tenure with the SNB, Dr. Ommaya went on to become Professor of Neurosurgery at George Washington University and Chief Medical Advisor to the National Highway Traffic Safety Administration. He passed away in 2008 from complications of Alzheimer's disease.

Paul L. Kornblith, M.D. (1978 – 1986)

Following Dr. Ommaya's departure, Paul L. Kornblith, M.D., served as Branch Chief of the SNB. Dr. Kornblith had trained and worked on the faculty at the Massachusetts General Hospital where he focused his research on the treatment of human gliomas. He continued his work on primary brain tumors at the NIH, helping to define humoral and cell-mediated immunologic responses to gliomas.^{15,25,26} Based on this work, Dr. Kornblith showed that many patients with glioma had circulating antibody directed towards their own glioma cells and that this response was correlated with decreased tumor grade and increased patient survival.³⁵ Dr. Kornblith also continued work on the use of nitrosoureas for glioma, showing that *in vitro* glioma culture response to 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) could predict clinical response to the chemo-agent.³⁶ In addition to his role as Branch Chief, Dr. Kornblith served as acting clinical director of the NINCDS. In 1986, he left the NIH to become the Chair of Neurosurgery at the Albert Einstein College of Medicine.

Edward H. Oldfield, M.D. (1981 – 2007)

In 1986, Edward H. Oldfield became the Chief of the SNB. He would be the longest tenured Chief and would make several critical contributions to neurosurgical research while at the NIH. Dr. Oldfield received his medical degree from the University of Kentucky and entered post-graduate training in general surgery at Vanderbilt University with a year in neurology at the National Hospital for Nervous Disease, Queens Square, London. He returned to Vanderbilt where he trained in neurological surgery under Dr. William F. Meacham. Following completion of neurosurgical residency, he went into private practice in Kentucky for 1 year. After that, he joined the SNB as a research fellow and stayed on as full-time faculty. He was appointed Chief of the Clinical Neurosurgery Section in 1984 and was appointed Branch Chief 2 years later.

In the early 1980s, D. Lynn Loriaux, M.D., Ph.D. of the Endocrinology and Reproduction Research Branch began examining the corticotropin-releasing hormone stimulation test to improve diagnostic accuracy in Cushing's disease.^{13,60} Based on the promising results from this study, many patients with an equivocal diagnosis of Cushing's disease were referred to the NIH for treatment. Taking advantage of this patient base, Dr. Oldfield began to build a large series of operations for adrenocorticotrophic hormone (ACTH)-secreting pituitary adenomas, which has surpassed 1200 transsphenoidal surgeries for this disorder alone. In the process, several advancements in the treatment of these tumors have been made. In conjunction with John L. Doppman, M.D., Dr. Oldfield helped to establish the use of inferior petrosal sinus sampling for distinguishing patients with a pituitary source of elevated ACTH from those with an ectopic source, where he introduced the use of CRH during simultaneous bilateral venous sampling.⁶⁵ Dr. Oldfield also described the use of the histologic pseudocapsule during surgical resection and demonstrated that this technique could be used to reliably achieve biochemical remission in patients with these tumors.^{31,67}

In the mid-1980s neurologists in NINDS and Dr. Oldfield began collaborations for studying patients with von Hippel-Lindau (VHL) disease. Among other novel findings, this provided the initial patient population that ultimately led to the localization and mapping of the *VHL*

gene.⁴⁰ As these patients frequently develop central nervous system hemangioblastomas, many required neurosurgical consultation and treatment. Dr. Oldfield quickly established the NIH as a center for the surgical treatment of VHL-associated hemangioblastomas. This resulted in numerous series detailing the principles of hemangioblastoma resection, and led to study on the natural history of these tumors that is the basis for the current management guidelines.^{30,54,89,90}

In 1994, citing the poor penetration of drugs infused directly into brain parenchyma, Dr. Oldfield along with Robert Dedrick, Ph.D., and Paul Morrison, Ph.D., proposed the use of convection to improve the distribution of locally-delivered chemo-agents.¹¹ By maintaining a small, continuous pressure gradient through a cannula inserted directly into brain parenchyma, they showed a significant increase in the volume of distribution than could be achieved by simple diffusion alone. Further work has shown that convection-enhanced delivery (CED) can produce both consistent and reliable distribution.^{47,49} Another clear advantage of CED is that it can produce a homogenous distribution across the perfused area with an exponential drop-off at the infusion margins.⁸³ This produces consistent drug concentrations within infused areas while limiting toxicity to surrounding areas. Since his initial study, Dr. Oldfield and other neurosurgeons around the world continue to improve the technique and emerging experimental and clinical applications continue to be developed.^{16,29,37,50,56}

Working with John L. Doppman, M.D., Dr. Oldfield also devoted significant attention to the study of spinal arteriovenous malformations (AVMs). Clinical research focused on both imaging and treatment of these lesions. Together they pioneered the use of magnetic resonance (MR)-imaging for diagnosis of spinal AVMs.^{18,63} Along with Ian E. McCutcheon, M.D., they used microangiography to show spinal dural AVMs to be direct arteriovenous fistulae (AVFs) and of acquired origin.⁵³ Dr. Oldfield also established the current surgical techniques for dural AVFs, showing that both cranial and spinal lesions could be effectively treated by interruption of dural venous drainage alone when the venous drainage was limited to intrathecal veins.^{3,64,84}

Dr. Oldfield also used intraoperative ultrasound and dynamic MR-imaging to determine the pathophysiology of syringomyelia associated with Chiari I malformations.^{28,66} He showed that syringomyelia in these patients was due to occlusion of the foramen magnum by the cerebellar tonsils leading to cerebrospinal fluid pressure waves acting on the surface of the spinal cord to forming a syrinx cavity. Extensive work was also performed in vascular neurosurgery in the study of vasospasm with Ryszard M. Pluta, M.D., Ph.D. Together they investigated the pathogenesis of vasospasm and demonstrated the potential for nitrite infusions for cerebral vasospasm.^{4,28,66,76} Based on this work, a Phase I study examining the safety and pharmacokinetics of prolonged intravenous sodium nitrite infusion has been completed at the NIH and lead to the use of intravenous sodium nitrite infusion for vasospasm is now being studied in a Phase II clinical trial.

For his extensive research contributions, Dr. Oldfield has received numerous awards including the Grass Medal for Meritorious Research in Neurological Science from the Society of Neurological Surgeons in 1995 and the Harvey Cushing Medal from the American Association of Neurological Surgeons in 2009. In 2007, he moved to the University of Virginia where he now holds the Crutchfield Chair in Neurosurgery.

The Surgical Neurology Branch: Current and Future Directions

Today, the SNB is led by Russell R. Lonser, M.D. Dr. Lonser completed neurosurgical residency at the University of Utah and during residency he spent more than 2 years at the NIH (1995–1998) performing a research fellowship. While at the NIH, he was strongly

influenced and mentored by Dr. Oldfield under whom he contributed original observations in the research on drug delivery and von Hippel-Lindau disease.⁴⁷⁻⁴⁸⁻⁵¹ Upon completion of residency in 2001, he returned to the NIH as faculty. In 2007, he was appointed Acting Chief of the SNB and was named Chair in 2009. Now he heads a department with 8 full-time faculty and several adjunct faculty (Table 1).

Clinical Research

Research in clinical neurosurgery remains the cornerstone of the SNB and takes place in the 234-bed Mark O. Hatfield Clinical Research Center, which opened in 2004 (Figure 5). The Branch currently maintains 12 active clinical research protocols (Table 2). Work continues on understanding the basis of the progression, the natural history, and treatment of CNS disease in VHL. Led by Dr. Lonser, a 250-patient, prospective study of the natural history of hemangioblastoma in VHL is nearing its 10th year (protocol 00-N-0140). The results will provide a more definitive management paradigm for treatment of patients with the disease, as well as permit further study of the biology of this familial neoplasia syndrome. Similarly, a prospective study of neurofibromatosis type 2 (NF-2) led by Ashok R. Asthagiri, M.D., is underway to provide insight into the biology of NF-2 as well as the timing and indications for operative management of tumors associated with this disease (protocol 08-N-0044).

CNS drug-delivery remains a focus in the SNB. While work continues on improving the accuracy and precision of CED, several actively-recruiting clinical trials using CED are ongoing. One trial uses CED to deliver IL13-PE38QQR (while monitoring distribution in real-time) for high-grade pediatric brainstem and supratentorial gliomas (Table 1). The SNB is working in conjunction with Mark Hallett, M.D., Chief of the Medical Neurology Branch and Human Motor Control Section of the NINDS to use CED to study the biology underlying Parkinson's disease. CED will be used to target the subthalamic nucleus and infuse of a temporary neuron suppressant, muscimol, in patients with refractory Parkinson's disease (protocol 09-N-0160) and comparing distribution patterns with clinical effect of neuronal suppression. Dr. John D. Heiss is investigating the effect of convective infusion of muscimol for suppression on intractable seizures. Data from this study should provide a mechanism to define seizure foci, tailor resections and predict potential complications. Collaborative epilepsy research at the NIH provided the scientific environment to detect the presence of increased expression of HHV-6 in the brain resection specimens of patients with mesial temporal sclerosis and not with neocortical epilepsy, suggesting a new pathogenic mechanism for mesial temporal sclerosis.¹⁷⁻²⁴ Preclinical investigation by Dr. Asthagiri is focused on the use of bacteriophage display to help identify endothelial motifs unique to brain tumor neovasculature which may be used to deliver systemic therapeutics in a targeted and more effective manner. Kareem A. Zaghloul, M.D., Ph.D., was recently recruited and will begin studying the mechanisms underlying epilepsy and movement disorders and their treatment.

Dr. Heiss is also continuing work on understanding Chiari I malformations and the pathophysiology of syringomyelia. Previous work by Dr. Oldfield and Dr. Heiss has revealed new insights into the development and propagation of syringomyelia related to Chiari I malformation and primary spinal syringomyelia, as well as optimal treatment. To better understand the natural history of syringomyelia and timing or need for treatment, Dr. Heiss will initiate a long-term natural history study of syringomyelia this year.

John K. Park, M.D., Ph.D. heads the Surgical and Molecular Neuro-oncology Unit. He has recently devised the NIH Recurrent Glioblastoma Scale, a pre-operative scoring system that identifies patients likely to have poor, intermediate and good relative outcomes following surgical resection of a recurrent GBM tumor. Application of this simple to use scale should be useful for counseling patients regarding their treatment options and clinical trial design.

Dr. Park is also performing clinical research on differentiating glioma recurrence from radiation necrosis using MR-imaging.

Basic Research

Four SNB faculty focus primarily on basic science research. Richard J. Youle, Ph.D., who leads the Biochemistry Section, has worked extensively on the use of immunotoxins for the treatment of brain tumors.^{38,39,57} In the past several years his interests have focused on the mechanisms of programmed cell death and the role of mitochondria in neurodegenerative diseases, including Parkinson's disease.^{32,58} Zhengping Zhuang, M.D., Ph.D., who heads the Molecular Pathogenesis Unit, investigates the pathogenesis of tumor predisposition syndromes including VHL and multiple-endocrine neoplasia type 1 (MEN 1).^{27,87,88,93} He also helped discover and develop techniques for microdissection, including laser-capture microdissection.^{22,92} Dr. Zhuang's current research involves preclinical trials of small molecule inhibitors for use against human cancers including malignant glioma.⁵² Dr. John Park's basic science research focuses on the mechanisms of chemo-resistance in intrinsic brain tumors and the differentiation of malignant glioma tumor stem cells as a treatment strategy.^{41,44,59,74} Finally, Marsha J. Merrill, Ph.D., has done substantial work on the role of vascular endothelial growth factor (VEGF) in central nervous system pathology. Previously, she and Dr. Oldfield have shown that VEGF is involved in the astrocytic response to injury and has described its role in blood brain barrier permeability in CNS tumors and in inflammatory processes.^{73,77} Currently Dr. Merrill is studying the development of VHL-associated hemangioblastomas through histopathological analyses of spinal cord and cerebellar tissue from patients with VHL.

The Residency Program in Neurological Surgery

Training in neurosurgery and neurosurgical research has long been a major focus of the SNB. Since the inception of the SNB, neurosurgical trainees from around the world have traveled to the NIH to perform research fellowships in neurosurgery. Similarly a number of residency graduates have begun their neurosurgical careers in the SNB as faculty. Many of these fellows and staff have taken leadership roles in neurosurgery and 22 have eventually become neurosurgical department chairs (Table 2). Training of medical students has also been a priority. Students are typically funded by either the NIH Clinical Research Training Program (CRTP) or the Howard Hughes Medical Institute (HHMI). Students' projects frequently lead to publications and recent trainees have been successful in the neurosurgical residency match, placing at the University of Pennsylvania, the University of Iowa, the Barrow Neurological Institute, the University of Southern California, Duke University and the NIH residency-training program.

Despite the rapid pace of advances in neurosurgery, there remains a pressing need for neurosurgical innovation.^{7,42} The scope of neurosurgical treatments continues to broaden, with indications for neurosurgery developing in increasingly prevalent diseases such as stroke and psychiatric illness.^{43,45,55} With this future in mind and the clear need for neurosurgeons who focus on technology and advancement of the field, the SNB will begin its own residency-training program in neurological surgery in 2010. In partnership with the University of Virginia, residents of the NIH-UVA program will be trained as neurosurgeon-scientists to address this need. Residents will receive clinical training in the NIH Clinical Center and the University of Virginia Medical Center and will learn basic and translational research using the resources of the NIH intramural program. A unique requirement of this program will be the design and implementation of a neurosurgical clinical research protocol during training. It is expected that graduates of this program will have the appropriate background for a career of clinical and translational research and the potential to become

leaders in academic neurosurgery with the abilities to manage the demands of this dynamic field.

Conclusions

The academic setting of the NIH has fostered neurosurgical research over the nearly 6 decades of the SNB's existence. Much of the work has been the result of dynamic and dedicated scientists who have worked and trained within the branch. Neurological surgery at the NIH is driven by the varied research interests of the current faculty.

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Biography

Figure 1.
Current organization of the National Institutes of Health, the National Institute of Neurological Disorders and Stroke, and the Surgical Neurology Branch. The Surgical Neurology Branch is part of the intramural research program of the National Institute of Neurological Disorders and Stroke, located within the National Institutes of Health campus in Bethesda, Maryland.

Figure 2.

Maitland Baldwin, M.D., chief of the Surgical Neurology Branch from 1953 to 1970, pictured with his mentor Wilder Penfield, M.D. (left, from Rowland LP: **NINDS at 50**, 2003). Dr. Baldwin was instrumental in the commissioning of the National Institutes of Health operating rotunda (right, top). Surgical department heads shown beginning construction on the NIH operating rotunda (right, bottom). Dr. Baldwin pictured controlling the steamshovel.

Figure 3.

Ayub K. Ommaya, M.D., chief of the Surgical Neurology Branch from 1974 to 1979. Original schematic illustration of the Ommaya reservoir, published in the *New Inventions* section of the *Lancet* (left, from Ommaya AK et al: **Lancet** 2:983–984, 1963). Ayub K. Ommaya, M.D. pictured with his eponymous device (from Holley J: **The Washington Post**: July 14, 2008.)

Figure 4.
Edward H. Oldfield, M.D. Chief of the Surgical Neurology Branch from 1986 to 2007.

Figure 5. The 234-bed Mark O. Hatfield Clinical Research Center, built in 2004 (top). The 1.5-tesla intraoperative magnetic-resonance imaging magnet, housed in the Clinical Center operating suite (bottom).

Table 1

Current faculty of the Surgical Neurology Branch

Position	Faculty
Chair	Russell R. Lonser, M.D.
Chief, Neurosurgical Biology and Therapeutic Unit	
Chief, Biochemistry Section	Richard J. Youle, Ph.D.
Chief, Clinical Neurosurgery Unit	John D. Heiss, M.D.
Chief, Molecular Pathology Unit	Zhengping Zhuang, M.D., Ph.D.
Chief, Surgical and Molecular Neuro-Oncology Unit	John K. Park, M.D., Ph.D.
Chief, Neuropathology Unit	Recruiting
Staff Scientist	Marsha J. Merrill, Ph.D.
Staff Clinician	Ashok R. Asthagiri, M.D.
Staff Clinician	Kareem Zaghloul, M.D., Ph.D.
Adjunct Faculty	Edward H. Oldfield, M.D.
	Anthony J. Caputy, M.D.
	Joseph C. Watson, M.D.
	John A. Jane, Jr., M.D.
	W. Jeffrey Elias, M.D.
	Donald C. Shields, M.D., Ph.D.
	Aaron S. Dumont, M.D.
	Robert Ecker, M.D.

Table 2**Current and pending clinical protocols in the Surgical Neurology Branch**

Year	Protocol Number	Title	Status
1992	92-N-0226	Establishing the physiology of syringomyelia	Actively recruiting
2000	00-N-0089	Genetic analysis of the Chiari I malformation	Actively recruiting
2000	00-N-0140	A prospective natural history study of VHL patients with central nervous system hemangioblastomas	Actively following
2000	00-N-0158	Trial of intracerebral infusion in patients with medically intractable epilepsy	Actively recruiting
2001	01-N-0085	Establishing the pathophysiology of primary spinal syringomyelia	Actively recruiting
2003	03-N-0164	Evaluation and treatment of neurosurgical disorders	Actively recruiting
2005	05-N-0075	Evaluation of the mechanism of nitric oxide formation and pharmacokinetics of long-term intravenous nitrite infusion in healthy volunteers	Actively following
2006	06-N-0085	Two-compartment model of diffusion tensor magnetic resonance imaging (DT-MRI) for the diagnosis of glioma tumor recurrence versus radiation necrosis	Actively recruiting
2008	08-N-0044	A prospective natural history study of patients with Neurofibromatosis Type 2 (NF2)	Actively recruiting
2008	08-N-0095	Assessment of cerebral circulation and perfusion in adults after neonatal carotid occlusion	Actively recruiting
2009	09-N-0117	An open label dose-escalation safety study of convection-enhanced delivery of IL13-PE38QQR in patients with progressive pediatric diffuse infiltrating brainstem glioma and supratentorial high-grade glioma	Actively recruiting
2009	09-N-0160	Convection-enhanced delivery of Muscimol to study the pathophysiology underlying the clinical features of Parkinson's disease	Actively recruiting
2010	T-D-0026	A Phase I Study of the Intrathecal Administration of Resiniferatoxin for Treating Severe Refractory Pain Associated With Advanced Cancer	Pending
2010	T-N-0895	A Phase I Open-Label Dose Escalation Safety Study of Convection Enhanced Delivery (CED) of Adeno- Associated Virus Encoding Glial Cell Line-Derived Neurotrophic Factor (AAV2-GDNF) in Subjects with Advanced Parkinson's Disease.	Pending
2010	T-N-1355	A Prospective Natural History Study of Patients with Syringomyelia	Pending
2010	T-N-1356	Using positron emission tomography (PET) to predict intracranial tumor growth in neurofibromatosis type II (NF2) patients	Pending
2010	T-N-1455	Epilepsy Surgery	Pending

Table 3

Department Chairs in Neurosurgery with research experience in the Surgical Neurology Branch.

Research Fellow/Staff	Institution
John M. Van Buren, M.D., Ph.D.	National Institutes of Health *
Shelley N. Chou, M.D., Ph.D.	University of Minnesota *
Joseph H. Miller, M.D.	National Naval Medical Center *
Ayub K. Ommaya, M.D.	National Institutes of Health *
Robert S. Bourke, M.D.	Albany Medical College *
Eugene S. Flamm, M.D.	University of Pennsylvania *
	Albert Einstein College of Medicine
Thomas H. Milhorat, M.D.	Children's National Medical Center *
	State University of New York – Brooklyn *
	North Shore University Hospital *
Donlin M. Long, M.D., Ph.D.	Johns Hopkins University *
Robert A. Ratcheson, M.D.	Case Western Reserve University *
Howard H. Kaufman, M.D., J.D.	West Virginia University *
Thomas A. Gennarelli, M.D.	Allegheny University *
	Medical College of Wisconsin
Kalmon D. Post, M.D.	Mount Sinai Medical Center *
Eugene A. Quindlen, M.D.	University of South Alabama
Edward H. Oldfield, M.D.	National Institutes of Health *
Raymond Sawaya, M.D.	M.D. Anderson Cancer Center
	Baylor College of Medicine
Raj K. Narayan, M.D.	Temple University *
	University of Cincinnati *
	North Shore University Hospital
Karin M. Muraszko, M.D.	University of Michigan
Walter A Hall, M.D., M.B.A.	State University of New York – Upstate
Zvi Ram, M.D.	Tel Aviv Medical Center
R. Bryan Mason, M.D.	National Naval Medical Center *
Russell R. Lonser, M.D.	National Institutes of Health
Lisa P. Mulligan, M.D.	National Naval Medical Center

*
Past Chair