Over the last decade, the Endoscopic Endonasal Approach (EEA) has revolutionized skull base neurosurgery. The endonasal approach has anatomical and technical advantages over traditional skull base approaches for the treatment of selected lesions. EEA is not only minimally invasive but also maximally effective for the treatment of a wide variety of skull base lesions. Meticulous knowledge of the skull base anatomy as seen from the endoscopic perspective is critical to apply endonasal endoscopic surgery in a safe and effective manner.

The Surgical Neuroanatomy Lab (SNL) at the University of Pittsburgh has a dual educational and research role aiming to improve surgical techniques and outcomes by mastering knowledge of relevant surgical neuroanatomy.

At the SNL, we have pioneered anatomical work on the area of skull base endoscopy. Our goal is to continue providing landmark contributions to the skull base community. The SNL has a strong commitment in training the future generation of skull base surgeons. Over the last four years, 35 national and international neurosurgeons and ENT surgeons from 14 different countries have completed a research fellowship at the SNL devoting six months to one year of focused training in endoscopic skull base surgical anatomy.

The results of the studies performed at the SNL have been published in the most prestigious journals in the field. These results have been routinely presented in an innovative and highly effective 3D format at our world-renowned endoscopic endonasal surgery course, offered three times a year at UPMC Presbyterian. More than 600 neurosurgeons and ENT surgeons from virtually every state and 25 different countries have participated in these courses.

The main theme of the SNL is “From the Lab to the OR,” a reflection of a true translational effort to introduce novel anatomical concepts and innovative surgical techniques into real surgical practice. We are defining the intricate skull base anatomy required to perform gentle, accurate, and safe endoscopic skull base surgery, and have described novel approaches that allow more effective access to previously inaccessible or highly risky areas of the skull base.

As an example, skull base tumors located at the region of the jugular tubercle (figure 1) and foramen magnum (figure 2) are extremely complex cases to operate, and they carry high risk of lower cranial nerves dysfunction after the operation, causing swallowing and breathing difficulties with the need for permanent and/or temporary feeding and breathing tubes. Now, the studies performed at the SNL have been key to effectively and safely removing tumors from these areas by using the EEA. Because the approach is performed from the endonasal route as opposed to the posterior route, the lower cranial nerves are not manipulated and therefore are fully preserved. Patients from around the world have been successfully treated at our institution. They have returned home with no neurological deficits and their complex tumors effectively removed, demonstrating the success of translating surgical innovation from the lab to the operating room.
Adaptive ingenuity. What the rescue of the Chilean miners has in common with neurosurgery

October 13, 2012 was the second anniversary of one of the most remarkable rescues of modern times. On August 5, 2010, a cave-in at the San Jose mine in Chile trapped 33 miners 2,300 feet underground. The likelihood of survival defies logical comprehension. A resolute country had to determine if the miners were alive. Small airshafts were drilled from the surface in search for the miner’s location.

Seventeen days after the cave-in, a note came up from one of the shafts reading “Estamos bien en el refugio, Los 33” (We are well in the shelter, the 33). Against all odds, the miners had not only survived the cave-in, but also survived 17 days in extremely precarious conditions and with extremely limited resources. What followed this finding was a demonstration of human ingenuity and fraternity.

An international group gathered and began three simultaneous efforts to drill a shaft large enough to rescue “los 33”. The effort was a phenomenal success and all the 33 miners were rescued. The miners survived a total of 70 days underground. This extreme situation brought out the very best of humanity and the very best of humanity.

On September 22, the faculty dealt a devastating blow to the residents in the annual softball tournament, losing by only two runs (22-20). No severe injuries were reported and therefore no RVUs were lost.
A recent review of the endoscopic endonasal approach (EEA) for resection of pituitary adenomas at the University of Pittsburgh Medical Center between 2002 and 2011 showed that this approach—pioneered at UPMC—is a safe and effective method for removing even giant and invasive tumors.

The average follow up was 3.1 years (range three months to 9.5 years). Ninety-one (17.5%) of the patients were operated on for recurrent adenomas. An expanded approach to reach the supra-, para- and infra-sellar spaces was employed in 290 patients (55.9%). Reconstruction with a vascularized nasal septal flap was used in 238 cases (65.6%).

The rate of complete removal was 65.3% in the 359 patients with non-functioning adenomas. The remission rates with EEA alone were 82.5% in 57 patients with Cushing’s disease (ACTH-secreting tumors), 65.3% in 49 patients with acromegaly (GH-secreting adenomas) and 54.7% in 53 patients with prolactinomas.

The EEA was found to offer an advantage especially in challenging adenomas such as recurrent tumors, those with suprasellar extension (figure 1) or cavernous sinus extension (figure 2). In fact, many tumors with cavernous sinus invasion, previously thought to be unresectable, were able to be completely removed (figure 3).

Outcomes were favorable and complication rates low when compared with traditional approaches. Of the 237 patients presenting with visual loss, 190 (80.2%) improved or normalized, 41 (17.3%) remained unchanged, and only six (2.5%) experienced transient visual deterioration due to postoperative apoplexy. None of these patients suffered permanent visual worsening. In addition, no patient without preexisting visual loss suffered new visual decline. These results are an improvement over microscopic transsphenoidal approaches. The collaboration with otolaryngology in the two-surgeon, four-hand endoscopic technique along with the improved visualization provided by the endoscope (wider, high definition field of view) allows for better identification of the optic apparatus, which may be part of the reason for these results.

This also likely contributes to other improvements noted with the EEA including better preservation of the pituitary gland and stalk with lower rates of postoperative pituitary dysfunction, including diabetes insipidus. Patients also had fewer nasal complications such as sinusitis and septal perforation.

All complications were evaluated including the postoperative CSF leak rate that decreased from 5% to 2.9% after the introduction of reconstruction with the naso-septal flap. Despite frequent carotid and cavernous sinus dissection, only two patients (0.3%) had an internal carotid artery injury and neither suffered a stroke as a result.

In conclusion, the EEA is a safe and effective way to surgically approach pituitary adenomas, particularly recurrent tumors, those with supra-sellar extension or cavernous sinus invasion. The remission and complication rates are comparable or favorable compared with those reported in previous series of microscopic and endoscopic approaches.

Figure 1a: Preoperative, coronal T1-weighted, postcontrast MRI showing a large, multilobular adenoma with significant suprasellar extension into the third ventricle. Figure 1b: Postoperative, coronal T1-weighted, postcontrast MRI following an endoscopic endonasal, complete resection. Figure 2a: Preoperative, coronal T1-weighted, postcontrast MRI showing a large pituitary adenoma that invades both cavernous sinuses (arrows). Figure 2b: Postoperative, coronal T1-weighted, postcontrast MRI following removal using an endoscopic endonasal approach (EEA). The arrows show that the tumor in the cavernous sinuses has been removed.

Figure 3: Table showing rates of gross total resection (GTR) based on Knosp grading (Grade 0 is no cavernous sinus invasion, Grade 4 is complete invasion with encircling of the cavernous carotid). Based on these results, many tumors with cavernous sinus invasion, especially those not involving the lateral cavernous sinus where the oculomotor nerves resides (Grade 4), can be completely removed.
A report on skull base chordomas: The largest endonasal series published

by Mary Koutourousiou, MD; Paul Gardner, MD

In the most recent issue of Neurosurgery (Sep;71(3):614-625) we published the UPMC experience using Endoscopic Endonasal Surgery (EES) for the treatment of 60 skull base chordomas. To date, the number of patients successfully treated with EES for skull base chordomas in our department is 80.

Arising from notochord remnants, chordomas are extra-axial tumors with a tendency to occur at the two extreme ends of the vertebral axis. Skull base chordomas account for <0.2% of all intracranial neoplasms and, although slow growing tumors, they are considered low grade malignancies representing one of the most difficult pathologies to treat given their location and high recurrence rates. Gross total resection (GTR) is not always possible due to the tumor extension, invasiveness and proximity to critical neurovascular structures. Although GTR provides the best long-term outlook for survival, there is still controversy regarding the optimal surgical approach. Surgical experience and technological advancements (angled endoscopes, image guidance, neurophysiological monitoring) have extended the indications of EES, so that skull base chordomas can be totally removed in most cases.

From April 2003 to March 2011, 60 patients (male:female ratio of 2.3:1; median age of 41 years) underwent EES for primary (n=35) or previously treated (n=25) skull base chordomas. The overall rate of GTR of skull base chordomas was 66.7% (82.9% in primary and 44% in previously treated cases) (figure 1). The most important limitations for GTR were tumor volume >20 cm³ (p=0.042), previously treated disease (p=0.002) and tumor location in the lower clivus with lateral extension (p=0.022) due to infiltration of the more complex anatomy of the craniocervical junction and the fact that this region is approaching the caudal limit of the approach. The learning curve had the most significant impact on GTR, increasing the success rate to 88.9% (92.6% in primary cases, 63.6% in previously treated) during recent years compared with the 36.4% GTR of the early years (p<0.0001).

The most frequent complication was cerebrospinal fluid (CSF) leak (20%) resulting in meningitis in 3.3%, rates that are equivalent to open surgical approaches for chordoma. The rate of postoperative CSF leak has decreased to 15.8% in recent years after the evolution of the vascularized nasoseptal flap for skull base reconstruction. Internal carotid artery injuries occurred in two cases and they were successfully managed intraoperatively resulting in only a Horner’s syndrome in one case where the carotid was sacrificed without any further neurological impairment. Neurologic complications included new cranial neuropathies (6.7%) and long tract deficits (1.7%). There was no operative mortality in our series.

The mean follow-up was 17.8 months (range 1-71 months). During this period, in the group of 35 primary chordomas, 21 patients (60%) remain free of disease, five (14.3%) have stable or even decreased residual tumor after radiation therapy and, among nine (25.7%) with tumor progression, five underwent reoperation. In the group of 25 previously treated cases, 10 patients (40%) are free of disease, four (16%) have stable residual tumor and 11 (44%) showed recurrence with nine being reoperated. The mean recurrence free period was 14.4 months (range 3-57 months). As expected, patients who underwent a GTR of the chordoma had a lower recurrence rate (20% vs 60%). In total, six patients died due to disease progression.

Despite the lack of consensus on the optimal treatment of skull base chordomas, the best surgical treatment should facilitate GTR while minimizing complications. Over the last decade, EES, in large part developed in our department, has gained ground in the field of skull base chordoma surgery with excellent outcomes. As a result, EES may represent the single most promising approach for total resection of skull base chordomas when applied by experienced surgeons.

Figure 1: Gross total resection of a giant skull base chordoma in a 43-year-old patient with headache, partial right VIth and XIlth cranial nerve palsy. Upper: Preoperative sagittal and axial T1-weighted MRIs show a large heterogeneous skull base lesion extending from the planum sphenoid sinus to the level of first cervical vertebra. The mass destroys the sellae and the clivus, extends into the suprasellar cistern occupying the sphenoidal sinus, ethmoid cells and nasopharynx, invades the cavernous sinuses, encases both internal carotid arteries (arrows) and the basilar artery (arrowhead), compresses the brainstem and extends laterally to the petrous apices. Lower: Postoperative sagittal and axial T1-weighted MRIs after a staged EEA that combined transcervical, transellar, transplanum, bilateral transpterygoid and bilateral transcavernous approaches. The surgical defect was reconstructed with a vascularized nasoseptal flap (arrowheads). The pons and medulla are totally decompressed and the cavernous sinuses are free of tumor. The patient showed improvement of the VIth nerve palsy while the XIlth nerve palsy remained unchanged.
Quality of life improving with advances in endoscopic endonasal surgery

by John R. de Almeida, MD; Shirley Y. Su, MD; Eric Wang, MD; Carl H. Snyderman, MD

With new technology and increased experience, the indications for endonasal approaches for neurosurgical tumors have grown considerably over the last decade. Many of these new techniques have been pioneered at the Center for Cranial Base Surgery at UPMC. Proponents of this approach cite the potential for improved visualization and comparable outcomes with decreased morbidity. In particular, endoscopic endonasal surgery (EES) avoids the need for brain retraction and minimizes manipulation of uninvolved vessels and nerves.

In patients undergoing EES, the profile of morbidity changes based on the approach. In a longitudinal study of patients who had EES for cranial base tumors at UPMC, 98% of all patients had nasal crusting one month after surgery. The extent and duration of nasal crusting depends on the extent of surgery as well as the type of reconstruction.

The use of the nasoseptal flap for reconstruction of dural defects has been invaluable in preventing CSF leaks, but results in a longer period of crusting and an increased burden of nasal morbidity. Nasal crusting typically resolves in just over three months although it can persist in a minority of patients. Other potential morbidities associated with this approach include malodorous nasal discharge, nasal blockage, loss of smell and taste, and conductive hearing loss from middle ear effusions. Aggressive post-operative nasal hygiene regimens may promote early return to function. A recent evidence-based practice guideline recommended frequent nasal debridements and saline irrigations.

These morbidities represent a shift in the morbidity profile from traditional transcranial or transfacial approaches. Arguably, these morbidities tend to be better tolerated than neurocognitive morbidities associated with significant brain retraction, although comparative studies are needed to better address this question. The emergence of EES over the last decade has spawned a surfeit of outcomes research focusing not only on functional outcomes but also on health-related quality of life. Studies comparing endonasal approaches to transcranial approaches have found clinically and statistically better results with endoscopic approaches in physical function and emotional domains (figure 1). However, these studies tend not to compare homogeneous populations and more controlled, larger scale prospective trials are needed.

One challenge of measuring quality of life is the abstract nature of this concept. The World Health Organization uses the description at left in defining the concept of “quality of life.”

Unlike other health care outcomes, there is no gold standard for measuring quality of life, and measures will vary depending on the diagnosis, treatment, and surgical approach. Endonasal and transcranial approaches may have numerous effects on physical function due to the complex anatomical relationships of the head, including vision, smell and taste, and facial sensation.

The Skull Base Inventory is a disease-specific instrument designed to capture and measure these physical domains as well as other relevant non-physical domains in both patients undergoing endoscopic as well as transcranial approaches. UPMC is part of multi-institutional trials now underway to better evaluate all of the dimensions of quality of life and to better compare quality of life of endonasal approaches to other transcranial approaches.

Quality of Life:

“An individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, standards and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychosocial state, level of independence, social relationships, and their relationships to salient features of their environment.”

- World Health Organization
Endoscopic endonasal approaches expands horizons for pediatric surgical access

by Elizabeth Tyler-Kabara, MD, PhD

Skull base pathology in pediatric patients is rare, but when it occurs, requires specialized management to avoid significant morbidity. The anterior cranial base has historically been approached via craniofacial resections. Most involve a craniotomy, a transfacial approach or a combined approach. Deep lesions may require brain retraction, heightening the risk of complications. Additional concerns in pediatric patients are that these approaches may damage growth centers in the craniofacial skeleton resulting in developmental craniofacial asymmetry.

The endoscopic endonasal approach (EEA) provides a minimally invasive alternative to conventional approaches. Improved techniques and intraoperative image guidance have extended endoscopic endonasal surgery (EES) from clival, sellar, and parasellar lesions to suprasellar pathologies as well as providing access to lesions involving the anterior, middle and posterior skull base. Recent studies underscore the safety and efficacy of EES in adults. The pediatric population has unique challenges: small working spaces, a smaller sized basicranium and incompletely pneumatized air sinuses. We describe our experience treating a variety of skull base tumors and bony abnormalities in 133 pediatric patients using EEA.

The mean age at the time of surgery was 12.7 years (range: 2-18 years), Eighty-five (63.9%) of the 133 patients were male. Skull base lesions were broadly classified as either bony abnormalities (n=21) or skull base tumors (n=112). Most tumors were benign (n=93, 83.0%). Fifty-three (47.3%) tumors were solely extradural while 59 (52.7%) were either intradural or extended intradurally. Postoperative follow-up duration ranged from one month to 122 months and was available for 128 (96.2%) patients. One-hundred, thirty-three patients were treated with a total of 171 EES procedures. Surgery in 10 patients (7.5%) employed 12 combined approaches, defined here as simultaneously utilizing both an EEA and an open craniotomy. An additional five patients underwent a Caldwell-Luc maxillary antrostomy to facilitate the EES. Seventeen patients (12.8%) presented with large tumors which were resected in a staged fashion, for a total of 43 surgeries.

CSF leaks were the most frequent post-operative complication, with a post-operative leak rate of 10.5% in the cohort and 12.5% in tumor cases. The literature reports CSF leaks rates after skull base surgery between 2% and 13% for transphenoidal surgery, between 13% and 29% for open skull base surgery, and between 8% and 13% in pediatric patients. Since 2008, we close skull base defects with a vascularized nasoseptal flap (n=55, 41.4%). A pericranial flap was used in a single patient, while 10 (7.5%) other defects were repaired with free mucosal grafts. Accordingly, the rate of post-operative CSF leak after 2008 was reduced from 12.5% in the tumor cases to 8.9%.

Diabetes insipidus (DI) was among the most frequent complications with transient DI in eight patients (6.0%), and permanent DI in 12 (9.0%). Other complications included infections—five meningeal, eight sinus infections, and three abscesses. Abscesses were surgically drained; other infections were medically managed. No significant difference exists between the rate of postoperative intracranial infection in our series, and those reported for open or endonasal skull base surgery in adults. Additionally, five patients (3.8%) had transient and three (2.3%) had permanent cranial nerve palsies. Angiofibromas and craniopharyngiomas were found to be associated with the highest rates of post-operative complication, accounting for 12 of 20 cases of DI and five of eight cranial nerve palsies.

The majority of patients experienced resolution (n=73, 57.0%) or improvement in impairment (n=39, 30.5%). Most tumors (n=60, 57.7%) underwent total resection (figure 1), or near-total resection (n=29, 27.9%). Nineteen patients with residual and/or malignant tumors received adjuvant therapy, 14 (13.5%) radiotherapy and five (4.8%) chemotherapy. At a mean follow-up of 22.7 months, 16 recurrences were identified, 12 of which were treated through repeat endoscopic endonasal surgery. Additionally, in our own series, we noted no growth complications similar to observations by other groups.

The introduction of EES has expanded the horizons of surgical access for pediatric patients a provides a ‘minimally invasive’ means for managing lesions with reduced morbidity. New techniques can gain popularity quickly while expertise in these new techniques is essential to achieve the best results, and it is essential that the surgeon be well versed in conventional skull base approaches as well, in order to optimize patient treatment. In our practice, the challenges have been overcome by a team comprised of adult and pediatric skull base surgeons. The significant learning curve with EES is mitigated by combining adult surgeons with greater endoscopic endonasal case volume, with pediatric neurosurgeons who are familiar with the diseases of pediatric patients and their anatomy. This combination provides for the safe management of these patients.

In this review of the 133 pediatric patients that underwent EES, the majority of patients experienced positive outcomes, comparable to those expected from open surgical approaches. Additionally, at a mean follow-up of approximately two years, no impairments were noted in the normal pediatric craniofacial development. Longer EES studies may show more favorable longer-term outcomes.
Center for Cranial Base Surgery Celebrates 25 Years

The University of Pittsburgh’s Center for Cranial Base Surgery will celebrate its 25th anniversary with a special scientific program, November 17 at the Thomas E. Starzl Biomedical Science Tower. The program is designed for otolaryngologists, head and neck surgeons, neurosurgeons, physician extenders, and nurses interested in the most recent developments in the diagnosis and management of cranial base tumors. Topics will include imaging, visual evaluation, endoscopic surgical management, radiosurgery, and perioperative management. A special banquet will also be held November 16 at the LeMont Restaurant. For more information, please contact Mary Jo Tutchko at (412) 647-8186.

In the News

• Don Crammond, PhD, was interviewed on National Public Radio’s All Things Considered, July 19, regarding studies on how the brain’s premotor cortex works.

Congratulations

• Hideho Okada, MD, PhD, received the 2012 Pitt Innovator Award from the university. This award recognizes university innovators whose research and development efforts have resulted in licenses to industry and start-up companies.

• Avniel Ghuman, PhD, received a NARSAD Young Investigator Award from the Brain and Behavioral Research Foundation.

• The research team of Elizabeth Tyler Kabara, MD, PhD, was awarded a 2012 Top 10 Breakthrough Award from Popular Mechanics magazine.

Prominent Lectures and Appearances

• Joseph Maroon, MD, was the keynote speaker at the Sixth Annual Conference in Anti-Aging and Aesthetic Medicine in Melbourne, Australia, August 17-19.

Welcome

Nancy Palmer, Mercy RN; Francisco Vaz Guimaraes Filho, skull base surgery fellow; Nduka Amankulor, PhD; assistant professor; Jamie Pardini, MD, visiting assistant professor; Robert Naftel, pediatric fellow; Sharon Greene, senior administrative assistant; Nicole Molchan, physician assistant; Esther Mattes, physician assistant; Barbara Kaefer, administrative aide to Drs. Elizabeth Tyler-Kabara, Stephanie Greene and Mandeep Tamber.

Devorah Willaman, Gamma Knife nurse; Mark Geminetti, Gamma Knife nurse; Jessica Hockley, physician assistant; Tara Wilson, administrative assistant to Dr. Mark Richardson; Mary Jo Labovick, administrative assistant to Drs. Johnathan Engh and Noduka Amankulor.

Personal Congratulations

Christian B. Ricks, MD, and his wife Lauren, had a baby boy (Dean Timothy) on August 1.

Special Thank You

The department would like to extend a special thank you to Douglas Kondziolka, MD, who left the department in October to take a position at New York University. Thanks for your many years of service and best wishes in all that you do.

Dedication of new research lab

Figure 1: (left to right) UPMC Physician Services Division president and chief medical and scientific officer Steve Shapiro, MD; department chairman Robert Friedlander, MD; Pittsburgh Steeler James Harrison; UPMC board chairperson Nick Beckwith; Gordon Nelson; and neurology chairman Lawrence Wechsler, MD, at laboratory dedication reception. Figure 2: Dr. Friedlander discusses laboratory research goals and results with guests. Figure 3: Juan Fernandez-Miranda, MD, demonstrates 3D HDFT technology to dignitaries. Figure 4: Robert Ferrante, PhD, with wife Autumn Klein, MD, PhD. (See story on back page)
Department dedicates new Neuroapoptosis and Translational Therapeutics Lab

The University of Pittsburgh departments of Neurological Surgery and Neurology celebrated the opening of a new laboratory, October 4, dedicated to the study of basic pathophysiological mechanisms in neurological disorders.

The Neuroapoptosis and Translational Therapeutics Laboratory, under the direction of department chairman Robert M. Friedlander, MD, will focus on acute (stroke) and neurodegenerative disease (amyotrophic lateral sclerosis and Huntington’s disease).

Understanding how the cascading effects of apoptosis—as mediated by the caspase apoptotic family—play a role in disease, is a principal direction of the laboratory. In addition, the roles of mitochondrial dysfunction and transcriptional alterations are also major foci in determining the neurodegenerative processes in brain disorders.

The strengths of the laboratory are in clinical and experimental neurosurgery and neurology. Over the past 15 years, Dr. Friedlander, and his colleague, Robert Ferrante, PhD, have developed a premier ‘bench to bedside’ translational program to better characterize the disease pathogenesis and identify novel and re-use drug agents to ameliorate acute-neurological and chronic-neurodegenerative disorders. This part of the laboratory program involves drug discovery, the application of experimental in vitro and in vivo models of disease in translational studies. Drs. Friedlander and Ferrante’s work has set the standard for others in the field. Their work in completing pre-clinical drug trials in mouse models of neurological disease has acted as a conduit of therapeutic agents for direct translation to human clinical trials in Huntington’s disease and amyotrophic lateral sclerosis patients.

Drs. Friedlander and Ferrante’s research has recently taken on a new and exciting direction in the application of stem cell investigations under the guidance and supervision of Diane Carlisle, PhD. Dr. Carlisle is a molecular biologist with significant experience in stem cell research. Dr. Carlisle will provide her expertise in developing iP-SCs from patients with neurodegenerative disease to better understand disease pathogenesis and in the development therapeutic strategies for human disease.

Yu Zhang, PhD, will play a critical collaborative and cross-over role in the lab. Dr. Zhang’s research interests include small RNA-related pathogenesis in neurodegenerative diseases, development of autologous cell-replacement therapy for Huntington’s disease, and targeted delivery of therapeutic nucleic acid to the central nervous system.

The new lab is located on the 5th floor ‘A’ wing of UPMC Presbyterian—in the corridor connecting the hospital with the University of Pittsburgh’s Scaife Hall. (See photos of the dedication on page 7.)