

About the Brain Care Institute

The Brain Care Institute (BCI) at UPMC Children's Hospital of Pittsburgh is dedicated to developing innovative treatments and approaches for infants, children, and teens with disorders of and injuries to the brain, spinal cord, muscles, and nerves.

The Brain Care Institute is more than 200 physicians, nurses, and staff who treat more than 14,000 patients every year — patients who come to us from across the country and around the world.

What is truly innovative about the approach the BCI takes is the speed with which experts from all areas of brain care can come together and put the full force of their training, technology, and intelligence to bear upon any particular child's case.

Our system is designed so physicians and other specialists can quickly get to the heart of a problem — even the most rare — and identify the most effective treatment methods. Our top priority is to give families the confidence and comfort of knowing there is no better place in the world for them to be.

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Advances in Responsive Neurostimulation in Pediatric Epilepsy at UPMC Children's

Introduced nearly a decade ago and approved by the U.S. Food and Drug Administration (FDA) to treat specific forms of focal drug-resistant epilepsy (DRE) in adults (and other indications on an investigational basis), responsive neurostimulation (RNS) has recently begun to make its way into the realm of pediatric epilepsy treatment on an experimental or investigational basis.

The Epilepsy Center in the Brain Care Institute at UPMC Children's Hospital of Pittsburgh has been at the forefront of this evolving treatment paradigm in children with focal epilepsies that are not amenable to surgical resection or ablation, as well as children with primary generalized epilepsies that have failed to respond to other treatment modalities.



Leading the clinical and investigational uses of RNS in pediatric patients at UPMC Children's are **William Welch, MD**, a neurologist and epileptologist in the Epilepsy Center who specializes in RNS, and **Taylor Abel, MD**, who is the Surgical Director of the Pediatric Epilepsy Surgery Center at UPMC Children's.



"A large proportion of patients with primary generalized epilepsy have poor responses to, or fail medication therapies, while surgical options are very limited.

The same is the case for individuals with focal epilepsy whose seizure origin(s) are located in highly eloquent areas of the brain, such as the motor and language cortices, that would be difficult or impossible to resect without causing major deficits in function or cognition," says Dr. Welch. "RNS is beginning to open new treatment possibilities for these patients."

To date, UPMC Children's has conducted eight RNS implantation cases in pediatric patients as young as nine years of age (more are currently scheduled), with two of the first pediatric cases using an implantation approach in the centromedian nucleus of the thalamus for individuals with primary generalized epilepsies. There have only been a handful of these procedures performed worldwide, and UPMC Children's is leading the way in the clinical and investigational aspects of RNS to treat generalized forms of epilepsy.

How RNS Works

The RNS system currently approved by the FDA and employed by UPMC Children's (the NeuroPace RNS®) consists of a

Neuromuscular Program and Advances at UPMC Children's

Hoda Z. Abdel-Hamid, MD, is an associate professor in the Department of Pediatrics at the University of Pittsburgh School of Medicine. She is the director of the EMG Laboratory and the Pediatric Neuromuscular Program at UPMC Children's Hospital of Pittsburgh. Dr. Abdel-Hamid also directs the multidisciplinary Muscular Dystrophy Association (MDA) Clinic at UPMC Children's.



Dr. Abdel-Hamid earned her medical degree from Cairo University in Egypt. She completed a pediatric residency in Cairo, Egypt, and a pediatric residency at Hurley Medical Center at

Michigan State University, followed by both a child neurology residency and neuromuscular/neurophysiology fellowship at UPMC Children's Hospital of Pittsburgh and the University of Pittsburgh. Dr. Abdel-Hamid then joined the Division of Pediatric Neurology at UPMC Children's as a faculty member in 2006. Dr. Abdel-Hamid has an active research and clinical trial program at UPMC Children's, and she is an active member of several national programs and committees related to neuromuscular diseases, including the American Association of Neuromuscular and Electrodiagnostic Medicine.

Dr. Abdel-Hamid evaluates patients with neuromuscular symptoms, performs neurophysiologic studies and Botox injections, orders genetic testing, and prescribes various medical and physical treatments. She follows all patients with pediatric neuromuscular disease in a multidisciplinary setting through the MDA clinic at UPMC Children's.

Dr. Abdel-Hamid leads a number of therapeutic biomedical trials for Duchenne muscular dystrophy (DMD) and collaborates with other centers and entities for the care of patients with pediatric neuromuscular disease. In the past, Dr. Abdel-Hamid has served on the executive committee of NeuroNEXT, which organizes collaborative studies to test new therapies for various neurologic diseases. Her research interests revolve around DMD, spinal muscular atrophy, and neuromuscular disease in children, including outcomes measures, new therapeutic interventions, and genetic therapies.

Neuromuscular Disease Program and MDA Clinic Growth and Expansion

Since joining UPMC Children's as a faculty member in 2006, Dr. Abdel-Hamid has expanded the scope and scale of the neuromuscular disease program at UPMC Children's. The Neuromuscular Program clinic treats all types of neuromuscular disorders, and the MDA Clinic at UPMC Children's focuses on treating all forms of muscular dystrophy — most notably DMD. The clinics provide a multidisciplinary setting for the diagnostic evaluation and follow-up care of infants and children with known or suspected neuromuscular disorders. The Muscular Dystrophy Association supports the MDA Clinic. The multidisciplinary clinic brings together neurology (Dr. Abdel-Hamid), physiatry (Jason Edinger, DO), pulmonology (Jane Taylor, MD), cardiology, genetic counseling (Deanna Steele, MGC, LCGC), social work (Amber Lewis, MSW), orthopaedics

(Ozgur Dede, MD), and physical therapy (Casey Matthews, PT, DPT), to provide collaborative diagnostic and follow-up care to children with neuromuscular disease and their families.

A year after Dr. Abdel-Hamid's arrival at UPMC Children's, she initiated an EMG-guided Botox injection program to treat patients with spasticity, dystonia, and torticollis.

"The neuromuscular program and clinic that was in place when I arrived at UPMC Children's was a smaller program run by a mentor of mine who retired. In the first year, we went from about 20 patients undergoing diagnostic testing to more than 130. The number of patients we follow and serve in the MDA clinic has since expanded to include more than 250 individuals and their families," says Dr. Abdel-Hamid.

Beyond the clinical care programs available to neuromuscular patients at UPMC Children's, Dr. Abdel-Hamid leads research and clinical trials into various neuromuscular conditions and novel therapeutics.

A History of Clinical Research

With few treatments available and still no cure for muscular dystrophy, clinical and pharmacologic research has continued to gain traction with pharmaceutical companies developing new research programs to develop and test novel therapeutics to treat neuromuscular diseases.

"In 2006, our program at UPMC Children's was part of a multicenter study on the natural history of DMD. Since that time, we have expanded the clinical research program in

pediatric neuromuscular diseases at UPMC Children's to include multiple multicenter studies in collaboration with pharmaceutical partners working on new drug therapies. Our program was part of the national multicenter study — the EXONDYS 51 study (Promovi) — that ended up deriving the first-ever FDA-approved drug to treat DMD in September 2016," says Dr. Abdel-Hamid.

More recently, Dr. Abdel-Hamid's program was part of a second drug trial that successfully achieved FDA-approval to treat another subtype of DMD — the VYONDYS 53 (Essence) study. Approved in December 2019, VYONDYS 53, developed by Sarepta Therapeutics, was approved for treating individuals with Duchenne muscular dystrophy who have a specific genetic mutation of the DMD gene that makes them amenable to exon 53 skipping treatment.

"These new trials and approved therapeutics could only happen in collaboration with pharmaceutical partners and the dedication of the patients and their families who visit the hospital weekly, and sometimes even more frequently, to take part in these ground-breaking trials," says Dr. Abdel-Hamid.

Beyond the Promovi and Essence trials, Dr. Abdel-Hamid's program has taken part in more than 15 clinical research studies since she took over as program director. With research coordinator Jennifer Monahan, RN, the program is now looking to collaborate on additional trials, including newer gene therapy trials that are being developed.

"While we have collaborated on a number of important trials in the past, one of our goals for the future is to expand our clinical research program to include gene therapy trials that are evolving within the field. Our service area is approximately a three-hour radius around Pittsburgh. Expanding our clinical trial offerings will help patients in need and limit the amount of travel and distance required for families to take part in some of the cutting-edge clinical trials being developed," says Dr. Abdel-Hamid.



Currently Open Clinical Trials for Neuromuscular Disorders at UPMC Children's

Below is a current list of open clinical trials for various neuromuscular disorders at UPMC Children's. Referring physicians who have patients that may be candidates for enrollment in any of these trials can learn more by contacting research coordinator Jennifer Monahan, RN, at 412-692-5176 or by email at Jennifer.Monahan@chp.edu.

Additional information about each of these trials is available on the UPMC Children's website or by searching under the NCT number on the ClinicalTrials.gov website.

Dr. Abdel-Hamid is the site principal investigator for these neuromuscular disease clinical trials currently open and enrolling patients at UPMC Children's:

- **Long-term Outcomes of Ataluren in Duchenne Muscular Dystrophy (NCT03179631).** This is a multicenter, randomized trial to study the long-term effects of ataluren on dystrophin restoration and disease progression in patients with DMD who have the nonsense gene mutation.
- **Study of SRP-4045 and SRP-4053 in DMD Patients (ESSENCE) (NCT02500381).** This trial seeks to evaluate the efficacy and safety of SRP-4045 and SRP-4053 in treating DMD patients who specifically have the out-of-frame deletion mutations which are amenable to exon 45 or 53 skipping.
- **An Open-Label Extension Study for Patients With Duchenne Muscular Dystrophy Who Participated in Studies of SRP-5051 (NCT03675126).** This trial is open to previous enrollees of the Promovi trial, and its goal is to determine the safety, tolerability, and pharmacokinetics of ongoing administration via IV infusion of Promovi in patients with Duchenne muscular dystrophy.
- **Study for Dose Determination of SRP-5051, Then Dose Expansion in Patients With Duchenne Muscular Dystrophy Amenable to Exon 51-Skipping Treatment (MOMENTUM) NCT04004065.** This randomized, multicenter two-part study will assess the safety and tolerability at multiple ascending dose levels and evaluate the maximum tolerated dose of SRP-5051.

Clinical Spotlight: The Neuroimmunology Clinic — Treating Neuroimmunologic Disorders and Facilitating Smooth Transitions in Care from Child to Adulthood

Transitions from pediatric to adult care are significant for individuals diagnosed with and managing long-term, chronic disorders. A smooth, ordered, and well-timed transition from pediatric to adult providers can have a tremendous benefit for an individual's health if appropriately conducted. Suboptimal transition scenarios can lead to gaps in care, confronting individuals with lasting adverse consequences for their health, and jeopardizing confidence in their physician.

For pediatric patients diagnosed with various neuroimmunologic disorders, including multiple sclerosis (MS), optic neuritis, encephalitis, and others, the Neuroimmunology Clinic in the Brain Care Institute at UPMC Children's Hospital of Pittsburgh is working to smooth the transitionary period and study the attitudes and opinions of its patients to better meet their long-term care requirements.



Kavita Thakkar, MD, co-directs the Pediatric Neuroimmunology Clinic alongside **Gulay Alper, MD.** A unique aspect of the clinic, and one that speaks to its emphasis on transitions of care, is that Dr. Thakkar sees pediatric and adult patients with neuroimmunologic disorders at UPMC Children's and UPMC Magee-Womens Hospital, respectively.

Dr. Thakkar's dual role and dual pediatric and adult clinics afford her and her patients a seamless transition of care when the time comes to move from child to adult health care providers.

"Our adolescent neuroimmunologic patients are a vulnerable patient population with respect to how and when they transition to adult care. There are many considerations

we have to take into account as providers to recognize who is most at risk for continuity of care issues, readiness for transition, level of understanding of their condition, degree of dependence on their care takers and other barriers related to their independent functioning," says Dr. Thakkar.

Challenges in Transitions of Care — Recognizing Issues and Overcoming Barriers

Abrupt changes in care or providers for vulnerable populations such as pediatric neuroimmunologic patients can lead to adverse outcomes.

Physicians need to recognize that even though a patient's age may dictate or indicate a move to adult care, pediatric patients may not yet be ready to take on the challenges and complexities of navigating their own care needs.

"You have to understand that many of these patients have never actively taken part in their health care, having family members — parents — attend to every need, even older children and adolescents. Some have no concept of how to think about or understand their long-term goals of care and then make decisions that could have lasting consequences. Some do not even know how to administer their own medications. For these and other reasons, recognizing which patients are most vulnerable to experiencing difficulty is paramount. These individuals must be transitioned slowly. They require more guidance and assurance.

Changing neurologists, sometimes after many years with the same pediatric neurologist, means it will take time for a physician who only treats adults to come to understand their new patient. These patients may be older in age, but they lack the independence necessary to manage their own health care. Physicians who do not recognize this, and have overly aggressive expectations for their patients can set up both conflict and treatment failure.

"One aspect that we pay close attention to in our clinics is how the patient's underlying disorder can affect executive function and cognition, making it that much harder for them to successfully manage their health care on their own. Having seen many of my pediatric patients in the clinic for some time, when they arrive in the adult practice, I have a good deal of knowledge about their cognitive status and the challenges it poses to these children. Developing trust and knowledge of the patient takes time. The process cannot be shortcut," says Dr. Thakkar.

Navigating the Family Dynamic

Transitions in care do not just affect the patient. They can also have far-reaching implications for the patient's family caregivers.

Abrupt or uncoordinated changes in care can leave parents and caregivers lacking the information they have become accustomed to

Pediatric Neurosurgery Division Welcomes New Surgeon

The Brain Care Institute at UPMC Children's Hospital of Pittsburgh is pleased to welcome its newest pediatric neurosurgeon, **Robert G. Kellogg, MD**. Dr. Kellogg joined UPMC Children's in September; he is an assistant professor in the Department of Neurological Surgery at the University of Pittsburgh School of Medicine.



Dr. Kellogg returns to UPMC Children's where he completed his pediatric neurosurgery fellowship in 2016. He earned his medical degree from the Indiana University School of

Medicine in 2009, and then completed his residency at Rush University Medical Center.

Clinical Areas of Focus

Dr. Kellogg's surgical work spans the spectrum of neurosurgical indications, with specific interest in the comprehensive management of spasticity and movement disorders, and craniofacial surgery. He joins

knowing about, now having to rely on their child to relay all of the information to them about their care and health. This can be a challenge for young patients in general, and particularly those experiencing cognitive issues related to their condition.

Caregiver stress and mental health are aspects of whole-family care that pediatric clinics are attuned to and work to address. Having a complete understanding of the family dynamic and any underlying issues sometimes gives physicians the ability to connect families and patients with needed resources — behavioral health referrals, social work referrals, and other needed help.

“Connecting families to other families in similar caregiving situations has proved to be beneficial. It can help families feel less alone and perhaps more able to seek other support

the highly regarded and internationally sought Spasticity and Movement Disorders Clinic at UPMC Children's. The Clinic, which provides a multidisciplinary and collaborative care approach for patients and families by integrating pediatric neurology specialists in neurodevelopmental disorders with neurosurgery, orthopaedic surgery, and physical medicine and rehabilitation, was the first program in the United States to garner Food and Drug Administration approval to study the use of intrathecal baclofen in patients.

Select Publications and Further Reading

Khavanin N, Ruge J, Vicari F, Belin E, Kellogg R, Steinberg J. Parasitic *Rachipagus* Conjoined Twin: Case Report and Literature Review. *J Neurosurg Pediatr*. 2018; 22(3): 313-316.

services. It can help them look at the situation with their child more objectively over time,” says Dr. Thakkar

Improving The Clinic and the Transition Process

Data being collected by Drs. Thakkar and Alper will ultimately help shape the evolution and expansion of how the clinic functions by tapping directly into patients' opinions on how best they can be supported when transitioning from pediatric to adult care.

“We have a number of projects in progress designed to gauge how best to help these patients navigate the complexities of managing their health with an underlying condition that will likely be with them for life, and in many cases slowly deteriorate or get worse over time. How we prepare our patients for this journey is crucial to their success and ours,” says Dr. Thakkar.

Kellogg R, Lee P, Deibert C, Temple Z, Zwagerman N, Bonfield C, Johnson S, Greene S. Retrospective Review of Myelomeningocele Management at Children's Hospital of Pittsburgh: a 20-year Experience. *J Neurosurg Pediatr*. 2018; 22(4): 439-443.

Kerolus M, Kellogg R, Novo J, Arvanitis L, Byrne R. Pigmented Ganglioglioma in a Patient With Chronic Epilepsy and Cortical Dysplasia. *J Clin Neurosci*. 2016; 24: 17-21.

Kellogg RG, Munoz LF. “Repair of Myelomeningocele”, Atlas of Neurosurgical Techniques-Spinal and Peripheral Nerve Surgery: 2nd Edition. Fessler RG, Sekhar L, Second eds. Thieme 2016.

More About Dr. Thakkar

Kavita Thakkar, MD, is co-director of the Neuroimmunology Clinic in the Brain Care Institute at UPMC Children's Hospital of Pittsburgh. She is an assistant professor in the Division of Neurology in the Department of Pediatrics at the University of Pittsburgh School of Medicine. Dr. Thakkar earned her medical degree from the Seth G. S. Medical College, Mumbai, India. Dr. Thakkar completed both her pediatric residency and pediatric neurology fellowship at UPMC Children's. In the Neuroimmunology Clinic, Dr. Thakkar sees patients with pediatric neurological disorders and adult neuroimmunological disorders. Her research and clinical interests focus on neuroimmunological and autoimmune disorders of the brain. In addition, Dr. Thakkar is a part of the child neurology residency education committee and is actively involved in the education of trainees at all levels.

UPMC Children's Division of Neurological Surgery Publishes Long-Term Outcomes in the Treatment of Pediatric Arteriovenous Malformations

Intracranial arteriovenous malformations (AVM) in pediatric patients represent a rare diagnosis. They are often challenging to treat in the acute phase. Simultaneously, AVM has the propensity for recurrence years after initial treatment (even though overall cases of recurrence are low), particularly those that are hemorrhagic in nature and require emergent surgical attention upon initial presentation. Hemorrhagic occurrences of AVM are more common in children than in adults, but the exact rate of incidence is not yet known. In the UPMC Children's study summarized below more than half of the cases examined were of a hemorrhagic nature.

Younger children with AVM are more likely to have a hemorrhagic presentation, and because of this, these individuals experience poorer outcomes. These younger patients may present with early hemorrhagic AVM due to increased risk factors for hemorrhage including deep venous drainage, intranidal aneurysms, or venous outflow stenosis. Mortality rates for AVM ruptures in pediatric patients is relatively high — about 20% according to current data in the literature.

The Brain Care Institute at UPMC Children's Hospital of Pittsburgh sees approximately five to 10 cases of AVM each year. It brings to bear upon these rare clinical presentations a multimodality treatment approach designed to achieve optimal long-term outcomes and preserve a patient's long-term functional independence while minimizing complications.

Outcomes from 30 Years of Pediatric AVM Surgery at UPMC Children's

Neurosurgeons from the Brain Care Institute at UPMC Children's, all of whom are faculty members of the Department of Neurological Surgery at the University of Pittsburgh School of Medicine, published long-term findings on AVM outcomes in a retrospective study spanning 30 years of surgical cases (1988-2018). The results of study were published in September in the *Journal of Neurosurgery: Pediatrics* as the cover article and was the editor's choice for this edition of the journal.



The investigation examined the long-term outcomes of AVM treatment in a cohort of 212 patients. The main objective of the analysis was to determine if outcomes varied by

treatment choice — surgical approaches, endovascular techniques, radiosurgical options, including gamma knife radiosurgery. **Stephanie Greene, MD**, director of vascular neurosurgery at the Brain Care Institute at UPMC Children's, was the senior author of the study designed to uncover potential variations in long-term outcomes from different treatment approaches.

"Our center has one of the longest histories in the United States treating AVM with all of the modern techniques at our disposal: embolization, gamma knife radiosurgery, and open microsurgery. Going back to cases from 1988 to roughly the present day afforded us the ability to uncover disparities in outcomes by treatment modality and to obtain a clear picture of how these long-term survivors have fared across a range of outcomes, including postoperative complications and the incidence of recurrences," says Dr. Greene.

Much was uncovered in the study that analyzed outcomes in a cohort of 212 patients with a mean age of 11.3 years at presentation and who were followed for a mean duration of 79.7 months. A key finding was that the chosen treatment modality did not impact outcome.

"Long-term patient outcomes are best when the full clinical armamentarium is at our disposal. We can select the best possible treatment for any case that presents itself because we have the clinical capabilities and technologies to leverage against the various complexities and challenges that AVMs present," says Dr. Greene.

Eighty-five percent of patients in the study cohort exhibited good long-term outcomes based on functional independence measures. Only six mortalities were found during the study in the postoperative period. Three of the mortalities were the result of unrelated medical conditions. Of the remaining three (1.4% of the total study cohort), one case was the result of an AVM hemorrhage after a treatment refusal by the family; one case was attributed to AVM hemorrhage three years subsequent to a gamma knife procedure; and the third mortality occurred 15 years after a gamma knife surgery and was caused by an AVM hemorrhage.

Factors Influencing Poor Outcomes

Of the 212 individual cases analyzed in the study, 14.6% were deemed to have poor long-term outcomes. Poor long-term outcomes were more strongly associated with a higher mRS score at the time of presentation, a higher Spetzler-Martin grade, hemorrhage requiring a decompressive craniotomy, or a lack of treatment.

“The sicker a patient is when he or she presents, and the more complex their AVM is provides a good indicator for long-term prognosis and outcomes,” says Dr. Greene.

Important Findings About AVM Recurrence

An additional important finding from the analysis relates to AVM recurrence. The study found a total of five cases of recurrence (representing 3% of all cases), with a mean recurrence time of 9.5 years. Recurrence also was associated with hemorrhagic cases treated with only craniotomy.

“What this suggests, of course, is that we need to closely monitor these patients and perform follow-up imaging at regular intervals to ensure we identify recurrences as early as possible,” says Dr. Greene.

Hemorrhagic Cases

While hemorrhagic cases increase the risk for recurrence in patients, the study did not find that hemorrhagic AVM cases influenced poorer long-term outcomes in general; however, younger children — under the age of 10 — with hemorrhagic presentations did fare worse in long-term outcomes.

More About Dr. Greene

Stephanie Greene, MD, associate professor of neurological surgery, is the director of vascular neurosurgery and director of perinatal neurosurgery in the Brain Care Institute at UPMC Children’s Hospital of Pittsburgh. Dr. Greene earned her medical degree from Albany Medical College in New York, followed by residency at the Harvard Medical School/Children’s Hospital of Boston/Brigham & Women’s Hospital

program, and a pediatric neurological surgery fellowship at Seattle Children’s Hospital through the University of Washington School of Medicine. Dr. Green’s clinical and research interests are focused on vascular neurosurgery with particular emphasis on arteriovenous malformations, fetal neurosurgery, myelomeningocele, and MoyaMoya syndrome. Dr. Greene joined the Brain Care Institute at UPMC Children’s in 2009.

Reference

McDowell MM, Agarwal N, Mao G, Johnson S, Kano H, Lunsford LD, Green S. Long-Term Outcomes of Pediatric Arteriovenous Malformations: The 30-Year Pittsburgh Experience. *J Neurosurg Pediatr.* 2020; 26: 275-282.

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neurostimulator device implanted under the scalp and within the skull and is connected to two electrodes. These electrodes can be placed in various locations, either on the surface of the brain or within deep structures. The RNS system continuously monitors an individual’s brain activity, and over time “learns” what a patient’s epileptiform discharges look like. When the beginning of a seizure is detected by the device based on recognition of the epileptiform discharge pattern, it conducts a small electrical current to the electrodes to disrupt propagation or prevent a seizure from occurring.

For the first month after implantation, the device records a patient’s seizure activity so that it can be programmed to recognize an individual patient’s seizure patterns. After the initial “learning” period, the responsive stimulation is then switched on. It can be tuned or adjusted over time.

“Every patient is different. Some may experience immediate reductions in their seizure activity, and others may take some time for effects to gradually build over a

period of months or years. It is generally the case that efficacy will increase over time, although how quickly or to what degree the device will be able to control a patient’s seizures does take time to develop,” says Dr. Welch.

Details From the First RNS Implantation at UPMC Children’s

The first RNS implantation completed at UPMC Children’s was performed on a 16-year-old young man with drug-resistant generalized primary epilepsy in May 2020. This individual was not a candidate for surgical resection due to the generalized nature of his epilepsy, and he experienced poor control of his seizures through multiple drug therapies, with many absence seizures each day.

“Our first RNS implantation patient was only the fifth pediatric patient in the world to have RNS implantation using an approach that places the device into the centromedian nucleus of the thalamus,” says Dr. Abel. “With its connections to the broader cerebral cortex and brain functions, the

centromedian nucleus of the thalamus is of great interest as an area to target with neuromodulation techniques for patients with generalized epilepsies.”

In this particular case, the patient experienced a marked reduction in seizure activity almost immediately upon the device being switched on after the initial learning period.

“Our patient’s seizure burden was reduced drastically in a very short time,” says Dr. Welch. “His overall course since implantation has been good, and we all are pleased with his progress to date.”

Clinical Trial Development

Drs. Welch, Abel, and colleagues currently are in the planning phases for a safety and feasibility trial of centromedian nucleus RNS implantation for primary generalized epilepsy in pediatric patients. This would be the first trial of its kind to rigorously test RNS use in pediatric epilepsy patients and report on safety and feasibility outcomes.

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At present, the UPMC Children's team is confident that RNS could be implanted in children as young as six years of age; however, in its initial series of patients, the youngest individual has been nine years old. With younger children, growth factors must be taken into consideration such that the

device implantation does not interfere with or compromise skull growth and development.

"The big question that we have right now revolves around safety for RNS in pediatric patients, and in particular with younger children who have thinner skulls. The

literature published so far points to RNS being a safe option, but we need more and better data. Our center is well-positioned and powered through our robust case volume and technological and surgical capabilities to launch such a trial," says Dr. Abel.

Affiliated with the University of Pittsburgh School of Medicine and ranked among the nation's best children's hospitals by *U.S. News & World Report*.



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About UPMC Children's Hospital of Pittsburgh

Regionally, nationally, and globally, UPMC Children's Hospital of Pittsburgh is a leader in the treatment of childhood conditions and diseases, a pioneer in the development of new and improved therapies, and a top educator of the next generation of pediatricians and pediatric subspecialists. With generous community support, UPMC Children's Hospital has fulfilled this mission since its founding in 1890. UPMC Children's is recognized consistently for its clinical, research, educational, and advocacy-related accomplishments, including ranking 15th among children's hospitals and schools of medicine in funding for pediatric research provided by the National Institutes of Health (FY2019) and ranking on *U.S. News & World Report's* Honor Roll of America's Best Children's Hospitals (2020–21).