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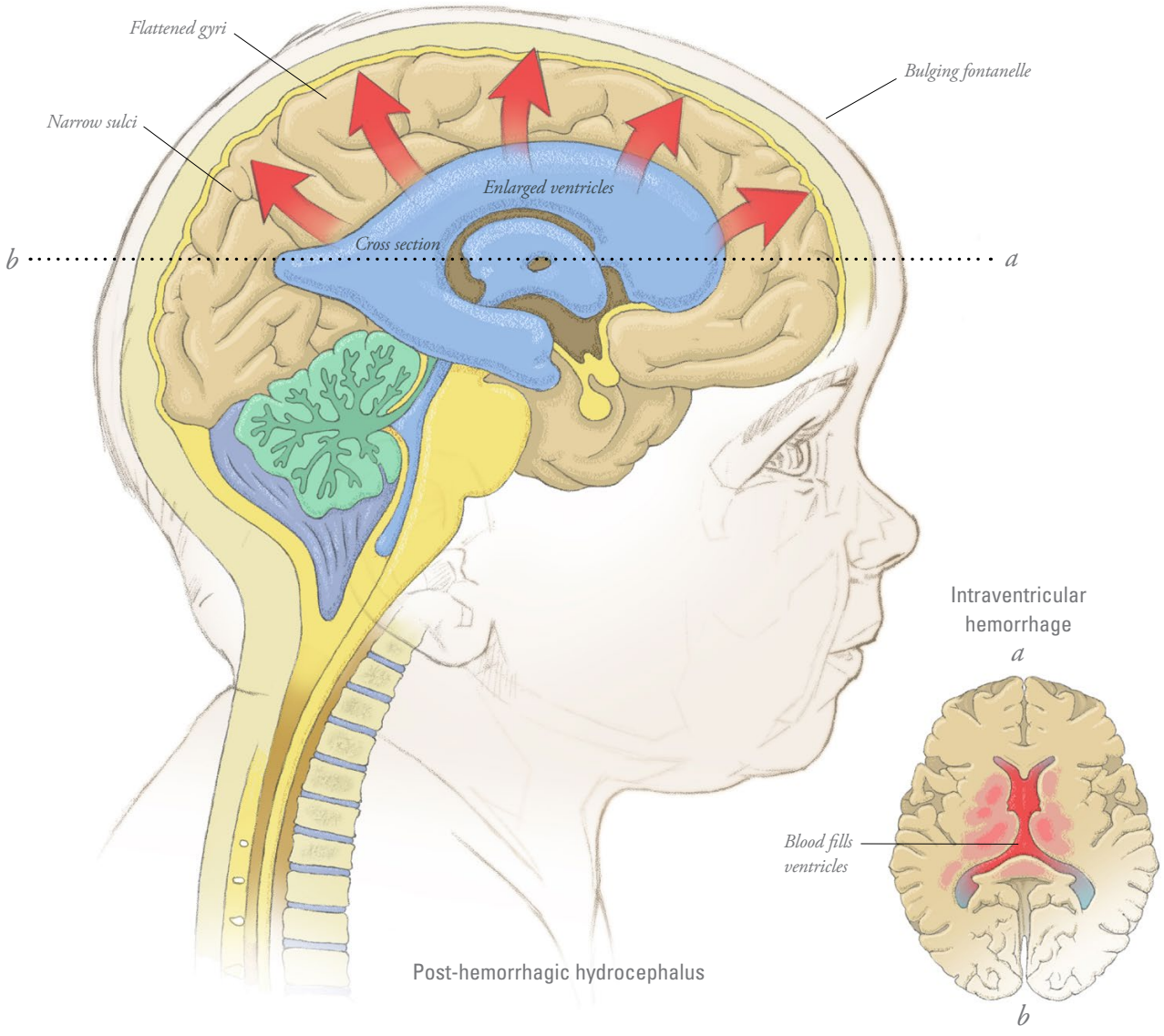
CHILDREN'S MEMORIAL HERMANN HOSPITAL

PEDIATRIC NEUROSCIENCE JOURNAL

A publication of Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth

Toward clinically safe therapies for intraventricular hemorrhage and hydrocephalus



UTHealth® Neurosciences
The University of Texas Health Science Center at Houston

Children's Memorial Hermann Hospital

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NEWS OF NOTE

It Takes an Orchestra to Play a Symphony

Great things happen when innovative people share a vision and are wholeheartedly committed to realizing it. With that in mind, we are pleased to welcome Brandon A. Miller, MD, PhD, to our pediatric neurosurgery team.

Dr. Miller has been involved in clinical medicine and basic science research simultaneously for more than 20 years. A physician-scientist, he has an interest in brain trauma and the long-term management of children with intraventricular hemorrhage and post-hemorrhagic hydrocephalus. He joins McGovern Medical School at UTHealth from the University of Kentucky Departments of Neurosurgery and Neuroscience, where he was director of the Pediatric Brain Injury Laboratory at the Spinal Cord and Brain Injury Research Center.

In this issue, you'll also read how a team of scientists led by our pediatric neurosurgeon, Manish N. Shah, MD, developed a wearable device that uses night-vision goggle technology, near-infrared light, and high-resolution detectors to image awake infants with brain disorders. Cap-based transcranial optimal tomography (CTOT) is the first whole-brain functional imaging device that does not require an infant to be put under anesthesia.

Our entire team would like to thank Jason, Kristi, and L.J. Borchardt for sharing their stories. L.J. underwent selective dorsal rhizotomy at the age of 15 with Dr. Shah, who is director of the Texas Comprehensive Spasticity Center at UTHealth Neurosciences. The family also benefited from the new pediatric inpatient unit, which opened last December at our sister hospital, TIRR Memorial Hermann.

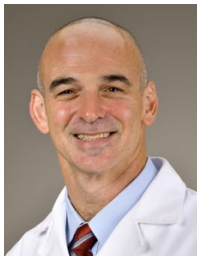
A special thanks to Hailee Nail and Alexis Shelly for sharing their experiences. Hailee was the first patient enrolled in a single-center trial of fetoscopic myelomeningocele repair using a patch made of cryopreserved human umbilical cord. Her daughter Lily was born with normal leg movement after repair of a small defect by the team of Stephen Fletcher, DO, a member of our pediatric neurosurgery team, and Kuojen Tsao, MD, co-director of The Fetal Center at Children's Memorial Hermann Hospital. Alexis, who worked on the media relations team at UTHealth, was reunited with Dr. Fletcher 30 years after her surgery for occipital encephalocele.

Four novel studies underway at UTHealth seek to improve the outlook for children with recurrent malignant brain tumors. In our research section, we also report on the work of Rachael Sirianni, PhD, and her lab team to encapsulate drugs within biocompatible and biodegradable nanoparticles that serve as carriers to prolong drug action and target specific tissue sites. Her work, funded by the National Institutes of Health, complements the research we're doing in the four single-center trials.

Our belief that unity is strength moved Children's Memorial Hermann Hospital up 10 positions in the 2020 U.S. News and World Report annual rankings of children's hospitals providing neurology and neurosurgery care in the United States. That's just the beginning.

We hope you find the articles in this issue of the Pediatric Neuroscience Journal useful in your practice. If you have questions about any of our programs, please contact us directly.

With best wishes,



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Tackling Intraventricular Hemorrhage and Hydrocephalus: A Pediatric Neurosurgeon-Scientist Joins McGovern Medical School and UTHealth Neurosciences

Brandon A. Miller, MD, PhD, FAANS, has an interest in pediatric brain injury that dates back to his time as a student laboratory technician in the Division of Pediatric Neurosurgery at Washington University in St. Louis, where he received his undergraduate degree in biology.

Brandon A. Miller, MD, PhD, FAANS

Assistant Professor,
Department of Pediatric Surgery
Division of Pediatric Neurosurgery

McGovern Medical School at UTHealth

Sixteen years later, during his pediatric neurosurgery fellowship at the same institution, he had an opportunity to delve deeper when he treated neonates who had suffered intraventricular hemorrhage (IVH), many of whom had post-hemorrhagic hydrocephalus.

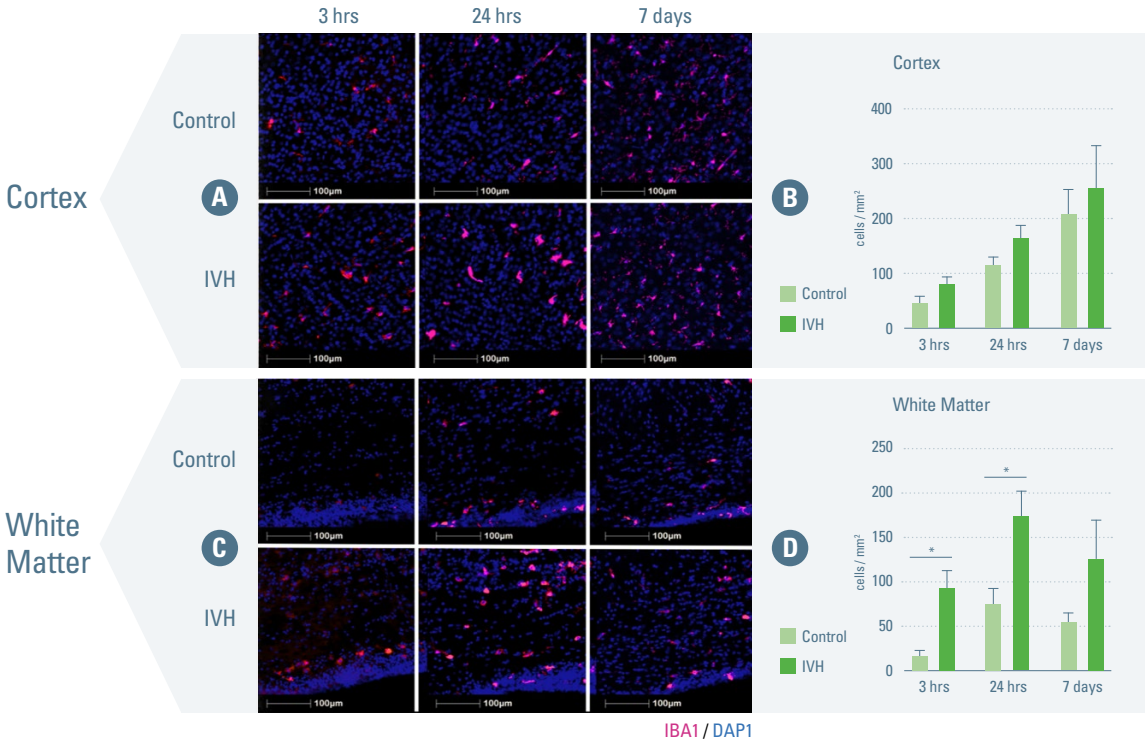
"During my fellowship, I became more interested in the long-term management of children with IVH, and I wanted to find ways to improve their care," says Miller, who joined the Department of Pediatric Surgery and the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth in July 2021 as an assistant professor. "Premature infants are at risk for IVH because the blood vessels in their brains are especially fragile. For many medical problems, there are very clear right treatment answers based on experience and the literature, and it's our job as physicians to guide patients and families to that decision. At other times, as is the case with IVH and hydrocephalus, the answers are not always clear, and it's our job to develop the best solution. That's why I do research."

Miller's research lab at McGovern Medical School is focused on ways to prevent or mitigate brain injury in intraventricular hemorrhage and post-hemorrhagic hydrocephalus. He brings to UTHealth a National Institutes of Health K08 Clinical Investigator Award focused on reversing inflammatory microphage activation as a treatment for IVH. The goal is to develop nonsurgical therapies to reduce brain injury in children with IVH.

Miller has been involved in both clinical medicine and basic science research simultaneously for more than 20 years. He joined UTHealth from the University of Kentucky Departments of Neurosurgery and Neuroscience, where he was director of the Pediatric Brain Injury Laboratory at the Spinal Cord and Brain Injury Research Center and co-director of the MD/PhD program. He received his PhD in neuroscience at The Ohio State University in 2007 and his MD from same institution in 2009. He completed residency training in neurosurgery at Emory University School of Medicine in 2016 and pediatric neurosurgery training in 2017.

"While working on my PhD, I became interested in how developing brain cells respond to injury. That work in graduate school guides my scientific research today," he says. "The developing brain is a unique organ with an increased capacity to recover. We're trying to understand how it responds to injury, and whether certain therapies may be especially effective in the developing brain. The immune cells in the developing brain play an important role in normal development, but are adversely affected by IVH and hydrocephalus. One of our goals is to reduce the deleterious affect of IVH on the brain's immune system so that normal development can continue."

In ongoing studies, Miller is testing an antioxidant therapy to reduce brain injury after IVH and in hydrocephalus. "We can treat hydrocephalus with a shunt, but even when the condition is well managed, many patients



Data from Miller's laboratory shows immune cell activation (labeled with IBA1) concentrated in the brain's white matter 3 hours and 24 hours after IVH (Panel D).

do not fully heal," he says. "We think patients with post-IVH hydrocephalus are injured by the initial brain bleed, which results in oxidative stress. Our experiments in a cell culture system of developing brain cells have shown that certain medications already approved for other purposes may reduce the harmful effects of IVH. We're continuing our work to develop clinically safe therapies for eventual clinical trials for neonates that would include long-term neurocognitive follow-up testing in NICU graduates."

At McGovern Medical School and Children's Memorial Hermann Hospital, Miller has joined forces with the pediatric neurosurgery team, including David I. Sandberg, MD, FAANS, FACS, FAAP, professor and director of pediatric neurosurgery, who holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery; Manish N. Shah, MD, FAANS, associate professor in the Division of Pediatric Neurosurgery, William J. Devane Distinguished Professor, and director of pediatric epilepsy and spasticity surgery at McGovern Medical School, who also directs the Texas Comprehensive Spasticity Center at UTHealth Neurosciences; and Stephen Fletcher, DO, associate professor of pediatric neurosurgery. He will also collaborate with Charles S. Cox, Jr., MD, George and Cynthia Mitchell Distinguished Chair in Neurosciences, director of the Pediatric Trauma Program at McGovern Medical School and Children's Memorial Hermann Hospital, and director of the Pediatric Surgical Translational Laboratories and Pediatric Program in Regenerative Medicine at UTHealth.

"I'm excited to be part of an established pediatric neurosurgery team with a record of good outcomes," Miller says. "We've seen parallels between data from children with hydrocephalus and children with traumatic brain injury. Partnering with Dr. Cox and his pediatric trauma group will complement my research in IVH and hydrocephalus. I'm also pleased to be working at a hospital that houses one of the country's busiest Level 1 trauma centers because of my long-standing interest in neurotrauma.

"While working on my PhD, I became interested in how developing brain cells respond to injury. That work in graduate school guides my scientific research today. The developing brain is a unique organ with an increased capacity to recover. We're trying to understand how it responds to injury, and whether certain therapies may be especially effective."

"The goal of my research is better medical and surgical therapy for kids with IVH and hydrocephalus," he adds. "UTHealth physicians are conducting clinical trials that will change the future of pediatric neuroscience care. I'm excited to be practicing in an environment where scientific knowledge is being translated to clinical care that helps patients achieve the best possible quality of life."

A Pediatric Neurosurgeon Teams Up with Scientists to Develop a Novel Imaging Device for Infants with Brain Disorders

Using night-vision goggle technology, near-infrared light, and high-resolution detectors, a team of scientists and a pediatric neurosurgeon at McGovern Medical School at UTHealth have developed a wearable imaging device for awake infants with brain disorders.

Manish N. Shah, MD, FAANS

Director of Pediatric Spasticity and Epilepsy Surgery

Director of Texas Comprehensive Spasticity Center

William J. Devane Distinguished Professor

Associate Professor, Department of Pediatric Surgery Division of Pediatric Neurosurgery

McGovern Medical School at UTHealth

Cap-based transcranial optimal tomography (CTOT) is the first high-resolution, whole-brain functional imaging device that does not require an infant to be put under anesthesia.[1]

"The precise imaging we gain with CTOT helps us accurately diagnose the severity of a baby's brain injury and identify the ideal treatment to optimize quality of life throughout childhood," says Manish N. Shah, MD, FAANS, associate professor in the Division of Pediatric Neurosurgery and William J. Devane Distinguished Professor at McGovern Medical School and practitioner with UT Physicians Pediatric Surgery clinics in Memorial City and at the Texas Medical Center. Shah is also director of the Texas Comprehensive Spasticity Center at UTHealth Neurosciences.

Disorders such as cerebral palsy, birth-related stroke, and epilepsy affect an infant's brain development. In the United States, approximately 10,000 babies are born each year with cerebral palsy, and about 470,000 children have epilepsy and other seizure disorders. Before CTOT, there was no way to accurately capture brain activity to quantify the severity of these conditions without putting the infants under anesthesia for MRI or PET scans.

"Imaging helps us understand which parts of the brain are not functioning normally, which is critical for localizing a seizure focus in epilepsy and understanding brain dysfunction in neurological disease," says Shah, who holds the William J. Devane Distinguished Professorship at UTHealth and is director of pediatric spasticity and epilepsy surgery at Children's Memorial Hermann Hospital. "In addition to requiring anesthesia, MRI and PET scans are expensive. We wanted to find a new and better way to get the kind of functional brain mapping we need for diagnosis and treatment."

To create the cap, which babies can wear bedside while in a caregiver's arms, Shah teamed up with Eva Sevick-Muraca, PhD, professor and director of the Center for Molecular Imaging at the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases at UTHealth, and Banghe Zhu, PhD, assistant professor with the center, who has a broad background in instrumentation development for preclinical and clinical near-infrared fluorescence imaging studies.

"The cap is put on the child and harmless near-infrared light is passed through from one side and collected on the other side of the cap. Our sensitive detector system uses the collected light to build a 3D high-resolution picture of brain activity," Shah says. "When we know which part of the brain is not functioning, we can either remove it in infants with epilepsy who qualify for surgery, or stimulate it in children with epilepsy, cerebral palsy, Parkinson's disease, or depression. Better diagnosis yields more precise treatment and an improved outcome for the patient."

Shah took the idea of an imaging cap to Sevick and Zhu. "We needed to find a way to detect very weakly transmitted near-infrared light and avoid interference. To solve the problem, we adapted night-vision goggle technology used by the military to detect near-infrared heat signatures," says Zhu, the lead biomedical optical engineer on the project.

Sevick, who oversaw the project using technology she had previously developed for other health care applications, says the laser light is harmless for infants. "Using the light transmitted across the brain of newborns, Dr. Zhu applies a mathematical algorithm to create a map of light-absorbing hemoglobin levels, which provides clinical information about brain injury," says Sevick, the Nancy and Rich Kinder Distinguished Chair in Cardiovascular Disease Research at McGovern Medical School. "No one has ever before created an optical device sensitive enough for this kind of quick imaging across the brain. It took nearly three years of developing prototypes, trial and error, and close communication with Dr. Shah for the cap to achieve whole-brain imaging in a clinical setting. It's rare for ideas to go from bench to bedside so quickly and successfully. Success requires a physician who is patient with the quirks of engineers and at the same time maintains a primary focus on clinical care."

The device opens the door for physicians and researchers to revolutionize diagnosis and treatment of movement disorders such as cerebral palsy. "Our next step is to make an even higher resolution device and continue collecting data from children with strokes and epilepsy to better understand the diseases," Shah says.

The project was funded by grants from the Memorial Hermann Foundation and a Men of Distinction award given to Shah for excellence in community achievement. In a new study funded by an R21 grant from the National Institute of Neurological Disorders and Stroke, co-principal investigators Shah and Sevick, along with Zhu, are assessing fluorescence-based cerebrospinal fluid in an animal model using the whole-brain optical imaging technology. The study, which is funded for two years, began in October 2020.

"I envision this becoming a larger study that will help us understand how cerebrospinal fluid flows in various animal models of hydrocephalus and eventually in humans," Shah says.

[1]*Zhu B, Sevick-Muraca EM, Nguyen RD, Shah MN. Cap-Based Transcranial Optical Tomography in an Awake Infant. IEEE Transactions on Medical Imaging. 2020 Nov;39(11):3300-3308.*

Manish N. Shah, MD, holds the patient while the Cap-based Transcranial Optical Tomography captures whole-brain imaging in minutes.

A Fresh Start for L.J. After Selective Dorsal Rhizotomy

Cerebral palsy is the most common cause of motor disability in childhood, according to the U.S. Centers for Disease Control and Prevention, with symptoms ranging from a mild gait abnormality to severe total body involvement. Regardless of the level of disability, the natural history of untreated cerebral palsy (CP) may be marked by progressive deterioration.

Manish N. Shah, MD, FAANS

Director of Pediatric Spasticity and Epilepsy Surgery

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William J. Devane Distinguished Professor

Associate Professor, Department of Pediatric Surgery Division of Pediatric Neurosurgery

McGovern Medical School at UTHealth

"Children are quite variably affected, but even mild untreated CP leads to painful contraction of the muscles. Prolonged muscle contraction causes spasticity. Every time the child has a growth spurt, it produces hip, knee, and ankle pain," says Manish N. Shah, MD, FAANS, associate professor in the Division of Pediatric Neurosurgery at McGovern Medical School at UTHealth and director of the Texas Comprehensive Spasticity Center at UTHealth Neurosciences. "L.J. Borchardt came to us as a minimally affected 14-year-old who could walk on his own, but he had pain and some activity limitations. He met all the criteria for success in selective dorsal rhizotomy (SDR): the spasticity was limited to his legs, he had good trunk control and no previous orthopedic procedures, he could tolerate physical and occupational therapy, and he had strong family support."

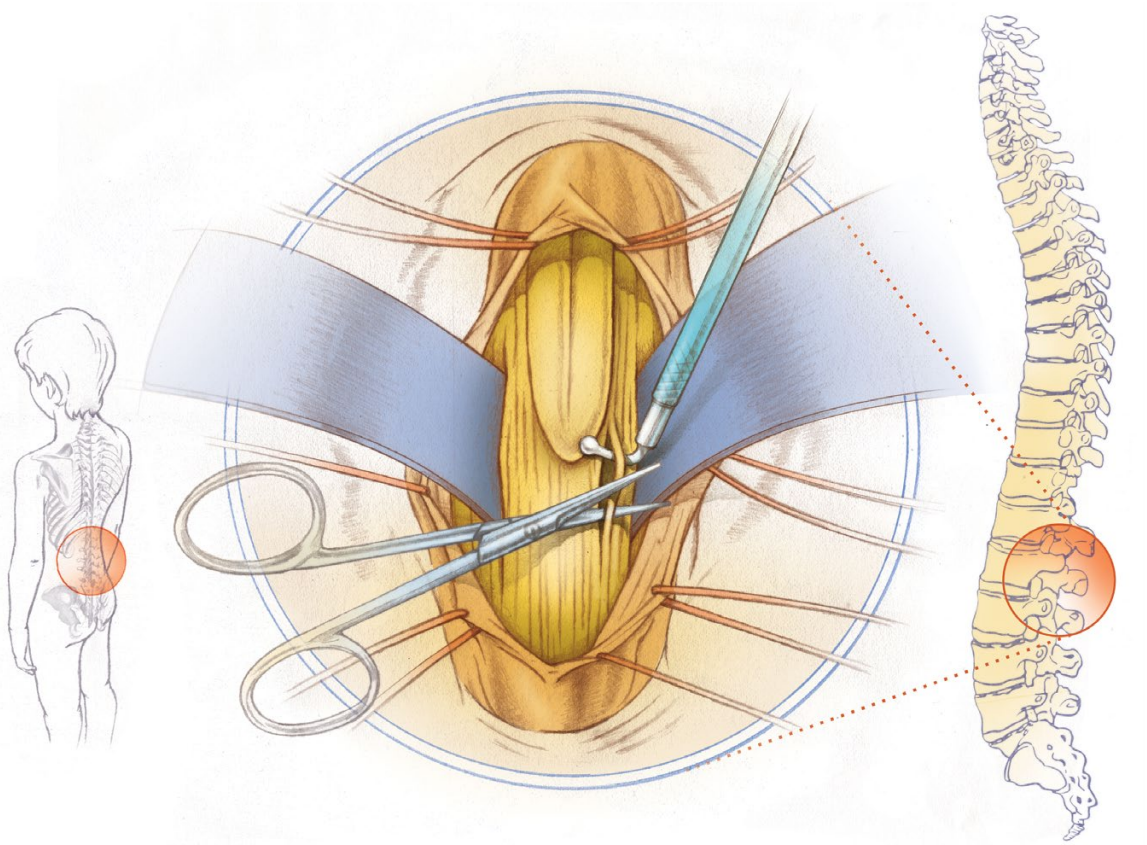
The neurosurgical procedure selectively sections problematic nerve roots in the spinal cord. Performed on well-selected patients with the right surgical hands, SDR provides an immediate permanent reduction in spasticity and offers children who follow a program of intensive postoperative therapy the potential to walk independently.

"L.J. has always been very high functioning, but his right knee was starting to turn in, causing some pain," says his mother Kristi Borchardt. "The more research we did, the more we understood that the taller he grew, the more the spasticity would keep him from turning his knee out. The twisting would continue, and later in life he would have more pain and would likely need assistance with mobility."

The Borchardts came to Shah through Dallas neurologist Janice Brunstrom-Hernandez, MD, an outspoken advocate for people with cerebral palsy who lives with CP herself and faces many of the same challenges her patients face. It was Dr. Jan, as her patients call her, who suggested SDR surgery for L.J.

"After our initial meeting with Dr. Jan, we began our research," Borchardt says. "When you hear about SDR and learn what the surgery involves, you realize that it's a huge life decision. L.J. was headed toward adulthood with pain and mobility issues. We read about other patients with CP who had the surgery, and they all said they wish they had done it earlier. Dr. Shah connected us with a mom, dad, and daughter who were willing to talk with us about their experience. Their daughter was the same age as L.J., with a similar level of CP. She told us that the surgery had changed her life, and that it would change ours as well. Having that conversation made a huge difference for us as a family."

Patients who undergo SDR must commit to intensive therapy for a year following the surgery. "Typically children with spasticity become weak. Most are already in physical and occupational therapy for cerebral palsy," says Shah, who holds the William J. Devane Distinguished Professorship at UTHealth and is director of pediatric spasticity and epilepsy surgery at Children's



Selective dorsal rhizotomy (SDR) is a neurosurgical procedure that selectively destroys problematic nerve roots in the spinal cord and is most often done in children to relieve the symptoms of spastic diplegia or spastic hemiplegia.

Memorial Hermann Hospital. "L.J. was using his spasticity and stiff muscles and joints to walk. If we took the spasticity away, he would have to relearn how to walk using a normal gait pattern. At the Texas Comprehensive Spasticity Center, we've been able to reduce drastically the work our patients have to do in therapy. We use a single incision at one level of the spine and cut 75 to 80 percent of the nerve rootlets. Most neurosurgeons use longer incisions and cut only about 30 percent of the rootlets. Evidence shows that this 30-percent approach often fails in the long term, with a return of the spasticity. It's a one-shot procedure with no room for revision if it fails."

The Decision to Wait a Year

The surgery was originally scheduled for 2020, but at age 14, L.J. was not ready to make the commitment to postoperative therapy. He had been in therapy for four years when he was younger and more recently, was working out at a gym with a professional trainer.

"There's a huge difference between the response of a teenager and a much younger child," says Jason Borchardt, L.J.'s father. "A seven-year-old might participate in therapy willingly because you asked, but a teenager has to decide for himself to make the commitment. We had many conversations about the potential outcome and how much of a life-changing experience it could be for L.J. By the time he was 15, his mind was made up and he was ready."

Shah took L.J. to the OR at Children's Memorial Hermann Hospital in February 2021. After a three-day stay at the hospital, he was transferred to TIRR Memorial Hermann's pediatric inpatient unit.

"Thanks to the expertise of the TIRR Memorial Hermann team, children who undergo SDR surgery are walking sooner and less painfully," says Shah, the leading neurosurgeon in the area for selective dorsal rhizotomy. "We have high hopes for these kids. If we can treat them at the appropriate time, we can reduce the societal burden of CP enormously. They can become independent, have careers and families, and enjoy a huge improvement in quality of life."

Three Weeks at TIRR Memorial Hermann

L.J. was admitted to the new pediatric inpatient unit at TIRR Memorial Hermann on February 11, 2021, under the care of pediatric physiatrist Stacey Hall, DO, assistant professor in the Department of Physical Medicine and Rehabilitation at McGovern Medical School. "TIRR Memorial Hermann exceeded all of my expectations, which already were very high," Jason Borchardt says. "The detail they put into his care

was amazing. He did physical therapy, occupational therapy, recreational therapy, and music therapy. They did a fabulous job of finding out what his interests are and using them to design a rehab program especially for him."

Hall says SDR patients follow a standard protocol, which the therapy team personalizes to their interests. "L.J. loved being outdoors and had a passion for archery and bow hunting," she says. "We created a program that would make his rehabilitation meaningful and more fun. For instance, we worked on his posture while he held a bow and arrow. He used our Nerf gun to practice shooting at different targets. During his three-week stay, he advanced from shooting from a wheelchair to target practice in a standing position."

"L.J. has always been very high functioning, but his right knee was starting to turn in, causing some pain. The more research we did, the more we understood that the taller he grew, the more the spasticity would keep him from turning his knee out. The twisting would continue, and later in life he would have more pain and would likely need assistance with mobility."

The Borchardts were impressed with their son's rehabilitation program. "In music therapy, they worked on his posture while he was playing the guitar," Jason Borchardt says. "Recreation and music therapy added so much to their incredible physical and occupational therapy programs. The Child Life specialist provided emotional support and made sure the kids were involved and happy. She bounced in and out of his therapy sessions. One time he was doing lunges, and she was doing them with him. That kind of interaction makes a huge difference. The whole team is top notch. You can tell they really care about their patients. As happy as we were to be going home, it was hard to leave and very emotional because of the relationships we formed and how far he came in such a short period of time. You can't help but love people like that."

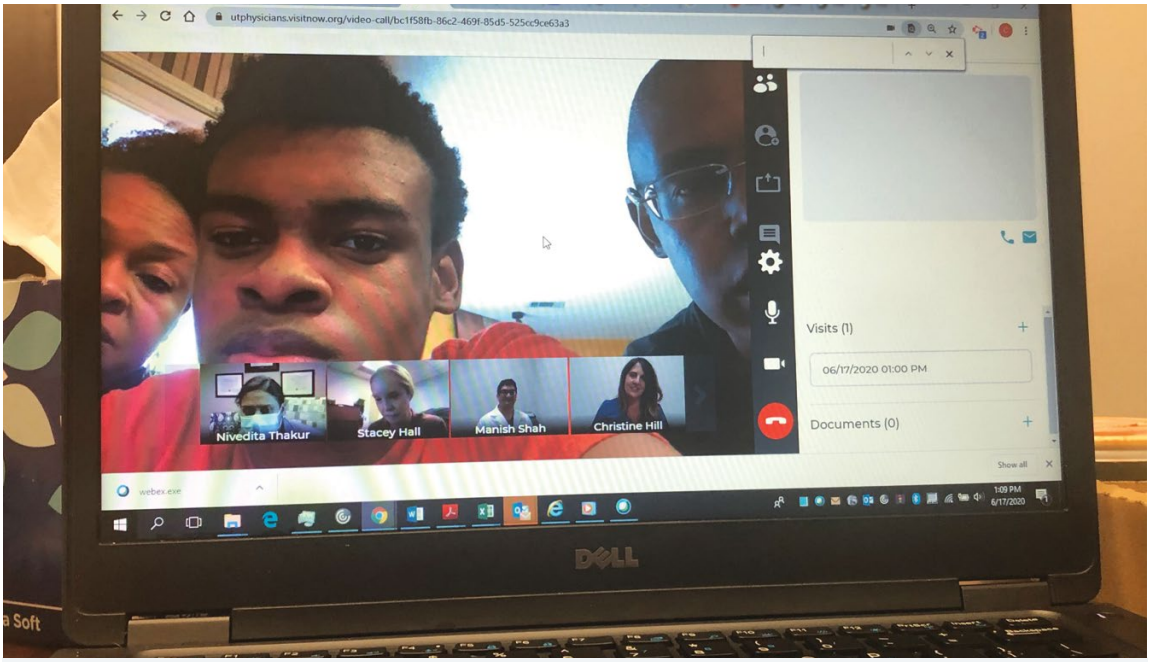
Hall also commends the TIRR Memorial Hermann team. "We all have the same priority of taking care of our patients and their families and making them part of our care team," she says. "After admission, we do an initial family and patient meeting and discuss goals and expectations of care, and goals for discharge, so that we're all on the same team working toward the same goals."

The pediatric inpatient team provides the framework for rehabilitation, but it's the patients who do the work. "L.J. is a remarkable young man. He's a hard worker with an exceptional spirit. He's smart and dedicated, and he gave 100 percent every single day," Hall says. "He's our dream patient. He did an amazing job."

L.J.'s current goals are to walk unassisted and join the TIRR Memorial Hermann Peer Program. The Peer Program provides encouragement to individuals who have been hospitalized recently and share similar life circumstances or challenges. They provide support and encouragement, help with skills training, and share information about resources.

"Dr. Shah and his staff were outstanding as well," Jason Borchardt says. "Christy Hill is a rock star. She has been available and helpful for the last two years through our scheduling, waiting, and rescheduling. All the way around, it's been a great experience, and I recommend it to any parent with a child with cerebral palsy."

Shah says TIRR Memorial Hermann is a good match for the care provided at the Texas Comprehensive Spasticity Center. "We are not a surgery factory. Each child with cerebral palsy has different needs. We have many, many happy families, thanks to the outstanding help of Christy Hill, our clinical coordinator, who is a highly trained physical therapist with expertise in cerebral palsy. We offer patients a successful, dedicated team with 100 percent follow-up. Now we have the new pediatric inpatient unit at TIRR Memorial Hermann, which is a big coup for the children of our region."



Texas Comprehensive Spasticity Center Offers Families a One-Stop Multidisciplinary Experience – Virtually

Resources available at McGovern Medical School at UTHealth have given physicians an opportunity to communicate with their patients in new, more convenient ways.

At the Texas Comprehensive Spasticity Center at UTHealth Neurosciences, a multidisciplinary team sees children with spasticity, movement disorders, or cerebral palsy, whose parents typically take them to multiple providers for different opinions before making a treatment decision. Since its inception, the team has gathered specialists together to provide carefully coordinated care in a single location.

"We were already at the forefront of virtual care in following patients who have undergone selective dorsal rhizotomy, many of whom come from surrounding states," says Manish N. Shah, MD, FAANS, associate professor in the Division of Pediatric Neurosurgery and director of the Texas Comprehensive Spasticity Center. "When UTHealth implemented InTouch to minimize our risk of exposure to the virus, it allowed us to continue our group evaluations with multiple clinicians on a video call, each safely in their own space, with parents at home with their child. Many of our kids are medically fragile. Some use wheelchairs or require transport by ambulance. It's a challenge for parents to get to physician offices under the best of circumstances. Virtual visits are especially valuable now."

Virtual visits via InTouch also allow home therapists and home nurses to share their input during the video call. "The pandemic has done that one small favor for us – advanced our video capability. We have found it to be very helpful, and families from out of town appreciate not having to drive to Houston and stay in a hotel," Shah says.

Christine Hill, PT, clinical coordinator at the Texas Comprehensive Spasticity Center, points to an additional benefit. "It's difficult for children to move freely in a small exam room," she says. "If we can see them active at home, we can better evaluate their ability to crawl and walk. Parents can take their kids outside, and we can watch them play when they don't know they're being observed. It gives us a broader look at them in motion."

Once Shah and his colleagues determine that a child would benefit from a virtual visit, Hill works with parents to schedule it. "They download the InTouch app from the app store, and our office sends them an invitation with a link for a secure HIPAA-compliant patient visit," she says. "They click the link, and we initiate the visit. We also can add other participants, including family members, multiple physicians, and the home care team."

Toward a Safe Method of Minimally Invasive Myelomeningocele Repair

Oklahoma resident Hailee Nail, 19, is the beneficiary of more than a decade of research conducted at The University of Texas Health Science Center at Houston (UTHealth) and The Fetal Center[1] at Children's Memorial Hermann Hospital.

Ramesha Papanna, MD, MPH

Associate Professor, Department of Obstetrics, Gynecology, and Reproductive Sciences

Director, Fetal Intervention Fellowship

McGovern Medical School at UTHealth

Stephen Fletcher, DO

Associate Professor, Department of Pediatric Surgery Division of Pediatric Neurosurgery

McGovern Medical School at UTHealth

Nail delivered her daughter, Lily, vaginally at 39 weeks of pregnancy on Dec. 8, 2020, as the first patient enrolled in a single-center trial of fetoscopic myelomeningocele repair of small defects at McGovern Medical School at UTHealth.

The study is led by Ramesha Papanna, MD, MPH, and Stephen Fletcher, DO, associate professor in the Division of Pediatric Neurosurgery at McGovern Medical School at UTHealth. Papanna is an associate professor of maternal-fetal medicine who is internationally recognized for his research on improving outcomes following fetal intervention and investigating methods for the prevention of preterm delivery. "Our primary outcome measure for the fetoscopic patch study is successful surgical closure of the spina bifida defect with a watertight patch that approximates native tissue and allows for the natural growth of the spinal cord," Papanna says. "The procedure differs from in-utero repair, which requires a large incision on the uterus and delivery by cesarean section. Instead, we repair the spina bifida defect in two layers through three small incisions in the uterus using a fetoscope, a high-resolution camera, and tiny surgical tools. The first layer is closed using the NEOX® Cord 1K patch as a meningeal patch placed over the spinal cord, followed by a second layer of primary closure of the skin. Mothers undergo vaginal delivery, unless there is an obstetrical indication for delivery by C-section."

Developed by Amniox Medical, Inc., a subsidiary of TissueTech, Inc., a biotechnology company in Florida, the NEOX Cord 1K patch is cryopreserved human umbilical cord (HUC) and amniotic membrane manufactured by devitalizing all living cells while retaining the extracellular matrix and growth factors/cytokines within. Extensive laboratory and clinical research on a number of ocular indications has shown that birth tissue that includes amniotic membrane and umbilical cord helps manage inflammation in wounds, facilitates cell proliferation, and creates an environment for tissue regeneration.

The study, the first to use a meningeal patch to cover the spina bifida defect, will enroll 15 patients ages 18 and older, who, like Hailee Nail, have a singleton pregnancy, a defect of 4 centimeters or less, and no preterm birth risk factors. Participants also must meet other study qualifications.

A digital image of the fetal repair site is captured immediately after the repair, and three blinded reviewers assess repair efficacy after birth. Reviewing neurosurgeons are Arthur Day, MD, McGovern Medical School and UTHealth Neurosciences in Houston; Bradley Edward Weprin, MD, UT Southwestern Medical Center in Dallas; and John Honeycutt, MD, Cook Children's Health Care System in Fort Worth.

Patients referred to UT Physicians, the clinical practice of McGovern Medical School, and The Fetal Center at Children's Memorial Hermann Hospital who intend to undergo open in-utero spina bifida repair will be offered and screened for the alternative minimally invasive approach. Women who participate in the study must agree to deliver at Children's Memorial Hermann Hospital.

[1]Located within the Texas Medical Center, The Fetal Center is affiliated with Children's Memorial Hermann Hospital, McGovern Medical School at UTHealth, and UT Physicians.

Lily Nail was delivered Sept. 1, 2020, at Children's Memorial Hermann Hospital with a back that looked normal, no hindbrain herniation, and normal leg movement.

"We published promising preclinical data and rigorously tested our techniques before taking fetoscopic repair to humans," Papanna says. "Our research is changing the way we approach spina bifida to improve closure, reduce scar tissue formation, reduce neurological deficits, and improve function. With this trial we hope to show that the cryopreserved human umbilical cord patch optimizes long-term outcomes for these kids."

Designing a Regenerative Patch for Open In-Utero Repair

Initially, the NEOX Cord 1K was used as a skin patch when primary skin closure of the spina bifida defect was not possible. Made from donated HUC of healthy newborns, the patch has been used for the repair of large defects in three cases performed by UTHealth surgeons at Children's Memorial Hermann Hospital. All cases were approved by the U.S. Food and Drug Administration Expanded Access Program, The Fetal Center at Children's Memorial Hermann Hospital, and the UTHealth Institutional Review Board prior to surgery. Patients underwent surgery performed by KuoJen Tsao, MD, professor of pediatric surgery at McGovern Medical School and co-director of The Fetal Center at Children's Memorial Hermann Hospital, and Stephen Fletcher, DO, associate professor of pediatric neurosurgery at the medical school. All patients have good lower-extremity motor and sensory function and two have been able to walk.

"We published promising preclinical data and rigorously tested our techniques before taking fetoscopic repair to humans. Our research is changing the way we approach spina bifida to improve closure, reduce scar tissue formation, reduce neurological deficits, and improve function."

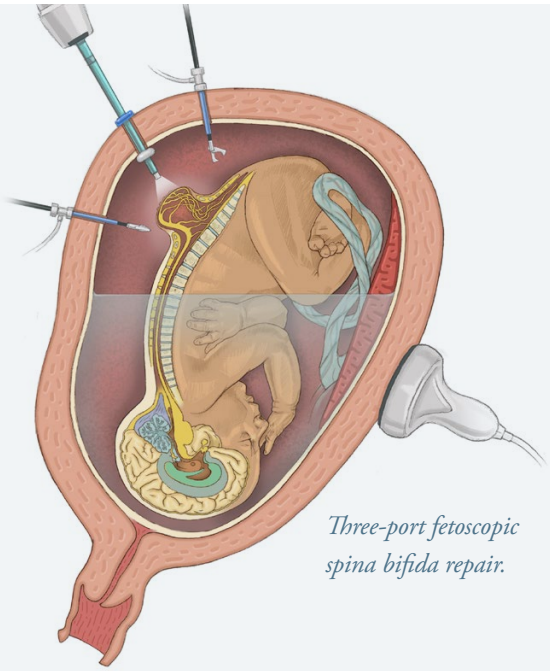
Fewer than half of the patients who undergo open in-utero spina bifida repair with a patch show improvement in spinal cord function, based on the landmark Management of Myelomeningocele Study (MOMS) long-term follow-up study. For the past decade, Papanna and Lovepreet K. Mann, MBBS, an assistant professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences at McGovern Medical School, and their research team have been working to gain greater understanding of the lack of complete benefit after fetal surgery. They tested the cryopreserved HUC patch as a meningeal patch, overlaying the spinal cord below the skin closure, to improve spinal cord function and reduce spinal cord tethering.

Preliminary data formulated in Papanna's lab led the researchers to collaboration with the industry leader in regenerative matrices, Scheffer C.G. Tseng, MD, PhD, a noted surgeon in ocular surface reconstruction, who uses human amniotic membrane and umbilical cord donated by mothers of healthy infants to repair ocular surface diseases. Tseng is the chief technology officer and co-founder of TissueTech, Inc. The research team believes that the HUC has the potential to improve the quality of life of children and families with spina bifida, which can result in paralysis, urinary and bowel dysfunction, and mental retardation.

"After investigating many types of patches in surgical animal models, we found that the HUC could promote regeneration of the protective layers around the spinal cord after surgery and improve neurological function," Papanna says. "We have compared the HUC patch to conventionally used methods in an effort to reduce scar formation and improve spinal cord function at and below the defect site."

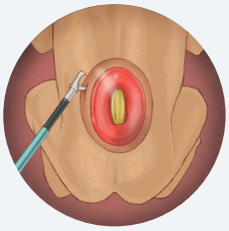
Papanna is the clinical lead principal investigator in a multicenter study of open in-utero repair of severe spina bifida using an investigational new drug version of the HUC patch, TTAX02. Developed by TissueTech, TTAX02 is nearly identical to the commercially available NEOX Cord 1K, which is widely used for chronic skin ulcers and many other indications because its innate regenerative properties facilitate faster healing. In addition to McGovern Medical School and The Fetal Center, participating centers include the University of Colorado Denver; Children's Hospitals and Clinics of Minnesota; Fetal Care Center Dallas in Medical City Children's Hospital; and the University of California, San Francisco.

Papanna's current fetoscopic research builds on his laboratory's experience with cryopreserved HUC for open in-utero spina bifida repair. His findings have been published in multiple peer-reviewed journals including the Journal of Neurosurgery: Spine,[1] Journal of Pediatric Neurosurgery,[2] Prenatal Diagnosis,[3] AJP Reports,[4] Obstetrics & Gynecology,[5] and Ultrasound in Obstetrics and Gynecology.[6]

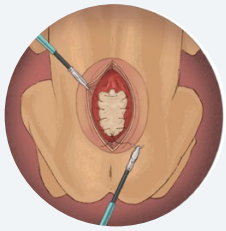


Three-port fetoscopic spina bifida repair.

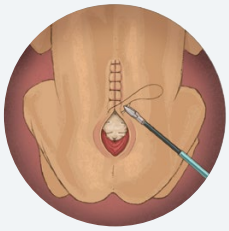
The human umbilical cord patch used by researchers at McGovern Medical School results in a spinal cord repair that appears more normal, with better function.



Neural placode dissection.

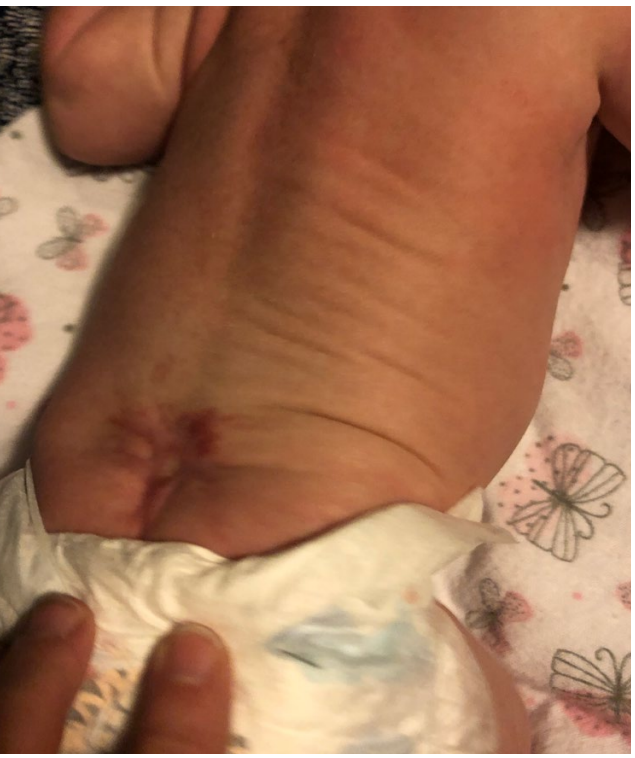


Suture close the umbilical cord as meningeal patch.



Primary closure of the skin defect.

"The HUC patch acts as a watertight scaffold, allowing native tissue to regenerate in an organized manner," Mann says. "Preclinical data have shown that the patch promotes organized cell growth, resulting in a spinal cord repair that appears more normal with better function. It also has anti-scarring and anti-inflammatory properties. Preventing the scarring could prevent spinal cord tethering, a common problem with spina bifida, which in turn can prevent further damage to the cord."



Fetoscopic repair with the human umbilical cord patch is allowing babies like Lily Nail to go full term and have normal bowel, bladder, and leg function.

Mann says the research team is focusing on further improving outcomes by pushing the boundaries of fetal wound healing through regenerative repair. "If we can make a small change and improve the quality of life for these children, we have really accomplished something," she says.

Spina bifida is the most common neural tube defect in the United States, affecting about 1,500 to 2,000 of the more than 4 million babies born in the country each year, according to the National Institute of Neurological Disorders and Stroke. Associated disorders include hydrocephalus and learning disability. An estimated 166,000 individuals with spina bifida live in the U.S.

"HUC could be a game changer for spina bifida repair," Papanna says. "Our ultimate goal is to ensure that babies born with the disorder can walk and lead normal lives. We also think HUC will lead to new paradigms in fetal wound healing for other spinal defects and repairs."

Currently, the research team is working to find ways to optimize repair in utero and new ways to deploy the patch over the defect site through less-invasive means. "We've made progress at an incredibly rapid pace," he says. "Taking an idea from the lab to human use typically takes about a decade. We've been able to reduce that time by more than half. We have a good system in place with strong collaborators, all of whom have track records of success in their fields."

"Dr. Papanna is a workhorse for UTHealth and our efforts to further research in a very fast-moving and competitive market," Fletcher says. "We see patients who come from across the country, and when I ask them why they travel so far, they say it's because of the research we're doing at UTHealth. We are leaders in the field, and we're moving forward deliberately to answer every question.

"After spending nearly 40 years in the field of neurosurgery, it seemed to me that the accepted norm for most patients with open neural tube defects was to have hydrocephalus, some degree of weakness in the extremities, and bladder and bowel disturbances," Fletcher adds. "These problems have existed alone or in combination. What a pleasure it is to see, after more than 100 of these surgeries, an increasing number of patients who have no detectable ambulation problems, no hydrocephalus and, remarkably, have normal bladder and bowel function."

Lily Nail

Hailee Nail learned her baby had spina bifida on Aug. 13, 2020, when she saw her obstetrician in Tulsa, Oklahoma, for her 20-week anatomy scan. "My OB-GYN told me that it would require surgery and gave me the names of several centers, but he said he wanted me to go to Houston," she says.

Nail arrived at The Fetal Center at Children's Memorial Hermann Hospital on Aug. 25 and went through a four-day evaluation with members of the UTHealth spina bifida surgery team. "She came to us when our study of fetoscopic repair using the NEOX Cord 1K patch had just opened," Papanna says. "She was 19, and it was her first pregnancy. Her baby had a myelomeningocele sac, which allows for easier closure of the skin. Fetoscopic repair will allow for vaginal birth, and she can have more children in the future with less concern for uterine rupture. We offered her open in-utero repair or the opportunity to enroll in the fetoscopic clinical trial."

Nail asked a lot of questions and remembers feeling well informed by Papanna and Fletcher, whose role would be to reveal the spinal cord and sew the patch in place over the small defect on Lily's lumbosacral joint. "I decided to go with

fetoscopic repair to give my daughter a better quality of life," she says.

The surgery was scheduled for Sept. 1, 2020. "They opened my abdomen vertically from the top of my belly button to midway down the pelvic bone," she says. "When they got to the uterus, they drilled three holes in order to insert two instruments and a camera. In the photos you can see the patch being placed and skin being pulled together and sewn up."

After the surgery, which took six hours, three and a half of which were devoted to the fetoscopic repair, Nail returned to Oklahoma for two months before traveling to Houston again to deliver at Children's Memorial Hermann Hospital.

"My recovery was actually really good," Nail says. "I stayed in the hospital for five days and stayed in a hotel room for two weeks after discharge. I went for an ultrasound the first week and second week, then flew home."

Lily entered the world via vaginal birth. "In the end, I had to be induced," Nail says. "Lily is amazing. Her bowel and bladder function are good. She has great leg movement and kicks a lot. I'm absolutely amazed at how awesome this team is. I'm not one for hospitals, but I loved my care before, during, and after birth."

Nail and her daughter will return to Houston at 12 months after delivery in December 2021. As participants in the clinical trial, they will be back for follow-up exams for the next six years.

"The most important thing is that we work together very well as a team and were able to close the defect," Papanna says. "Other centers are using two ports to perform a myofascial closure, moving muscle tissue over to the spinal cord and then covering it with skin. We use three ports and a high-resolution camera to place the human umbilical cord patch and suture it to create a watertight closure that helps the spinal cord grow and repair the site, reducing the potential for tethering. The myofascial closure requires a dissection cut into the fetal muscle and sometimes into the bone. This takes more time in the OR and can cause bleeding and wound healing problems, resulting in a scar. We want to avoid that. While most centers want to keep moms there for the remainder of the pregnancy, our goal, after we complete the clinical trial, is to send them home for delivery.

"The amazing thing about Hailee is that she was able to go full term with no complications during pregnancy," he says. "After we induced her, she had 24 hours of labor and then a baby. Lily's back looked totally normal, with no cerebrospinal fluid leakage. The skin had healed in the uterus, she had no hindbrain herniation, and her legs were moving. Although the HUC is based on very strong preclinical data, we need to complete the test of our methodology and compare it to the more traditional approach. We're now using it for myelomeningocele, and in the future, we hope to expand its use to the most severe form of spina bifida, myeloschisis."

After completing 12 of the 15 cases required by the Food and Drug Administration for the HUC patch feasibility study, the researchers have received approval to enroll a total of 25 patients in the fetoscopic clinical trial. All participants will be evaluated for long-term outcomes. The fetal intervention team led by Papanna also has received a $3.2 million R01 award from the National Institutes of Health to further their preclinical research on new approaches to spina bifida repair in utero.

[1] *Mann LK, Won JH, Trenton NJ, Garnett J, Snowise S, Fletcher SA, Tseng SCG, Diehl MR, Papanna R. Cryopreserved human umbilical cord versus acellular dermal matrix patches for in-utero fetal spina bifida repair in a pregnant rat model. J Neurosurg Spine. 2019 Nov 1;1-11. doi: 10.3171/2019.7.SPINE19468. Epub ahead of print. PMID: 31675701.*

[2] *Vu T, Mann LK, Fletcher SA, Jain R, Garnett J, Tsao K, Austin MT, Moise KJ Jr, Johnson A, Shah MN, Papanna R. Suture techniques and patch materials using an in-vitro model for watertight closure of in-utero spina bifida repair. J Pediatr Surg. 2019 Jun 19;S0022-3468(19):30409-9. doi: 10.1016/j.jpedsurg.2019.05.024. Epub ahead of print. PMID: 31255327.*

[3] *Snowise S, Mann L, Morales Y, Moise KJ Jr, Johnson A, Fletcher S, Grill RJ, Tseng SCG, Papanna R. Cryopreserved human umbilical cord versus biocellulose film for prenatal spina bifida repair in a physiologic rat model. Prenat Diagn. 2017 May;37(5):473-481. doi: 10.1002/pd.5035. Epub 2017 Apr 16. PMID: 28295455.*

[4] *Papanna R, Mann LK, Snowise S, Morales Y, Prabhu SP, Tseng SC, Grill R, Fletcher S, Moise KJ Jr. Neurological Outcomes after Human Umbilical Cord Patch for In Utero Spina Bifida Repair in a Sheep Model. AJP Rep. 2016 Jul;6(3):e309-17. doi: 10.1055/s-0036-1592316. PMID: 27621952; PMCID: PMC5017885.*

[5] *Papanna R, Fletcher S, Moise KJ Jr, Mann LK, Tseng SC. Cryopreserved Human Umbilical Cord for In Utero Myeloschisis Repair. Obstet Gynecol. 2016 Aug;128(2):325-30. doi: 10.1097/AOG.0000000000001512. PMID: 27400004.*

[6] *Papanna R, Moise KJ Jr, Mann LK, Fletcher S, Schniederjan R, Bhattacharjee MB, Stewart RJ, Kaur S, Prabhu SP, Tseng SC. Cryopreserved human umbilical cord patch for in-utero spina bifida repair. Ultrasound Obstet Gynecol. 2016 Feb;47(2):168-76. doi: 10.1002/uog.15790. PMID: 26489897.*

Novel Studies Seek to Improve Outcomes in Children with Malignant Fourth Ventricular Brain Tumors

Only a very small amount of the chemotherapeutic drugs given systemically for the treatment of pediatric brain tumors actually reaches the brain, due to the blood-brain barrier's efficiency at excluding the entry of most agents that circulate in the blood. As a result, the current outlook for children with recurrent malignant brain tumors is extremely poor.

David I. Sandberg, MD, FAANS, FACS, FAAP

Professor and Director of Pediatric Neurosurgery

Dr. Marnie Rose Professorship in Pediatric Neurosurgery

Department of Pediatric Surgery and Vivian L. Smith Department of Neurosurgery

McGovern Medical School at UTHealth, Children's Memorial Hermann Hospital and Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center

Co-director, Pediatric Brain Tumor Program

The University of Texas MD Anderson Cancer Center

Most clinical trials offer systemic chemotherapy or radiation therapy, both of which have side effects and often fail in children with recurrent tumors. To address this issue, David I. Sandberg, MD, FAANS, FACP, FAAP, is leading four single-center studies at McGovern Medical School at UTHealth and Children's Memorial Hermann Hospital. All four investigate novel therapies with the potential to improve outcomes for children with fourth ventricular brain tumors, while avoiding systemic toxicity.

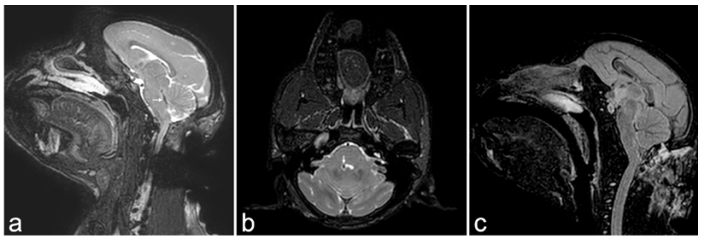
"Despite the advances we've made in pediatric neuro-oncology, we're still seeing far too many children die of malignant brain tumors. We believe we can do better," says Sandberg, professor and director of pediatric neurosurgery and holder of the Dr. Marnie Rose Professorship in Pediatric Neurosurgery in the Department of Pediatric Surgery and Vivian L. Smith Department of Neurosurgery at McGovern Medical School.

According to the American Cancer Society, about 500 children are diagnosed every year with medulloblastoma, the most common malignant brain tumor in children. Current treatments expose children to considerable toxicity, and when tumors reoccur despite treatment, survival rates are low. Sandberg is hopeful that a novel clinical trial of MTX110, a new formulation of soluble panobinostat from Midatech Pharma, will help patients overcome the devastating disease.

The clinical trial follows a successful study he led in an animal model, which demonstrated that MTX110 can be safely infused in the fourth ventricle and can achieve drug levels dramatically higher than intravenous or oral administration of the same drug. The team at McGovern Medical School found no neurological deficits after fourth-ventricle infusions in the preclinical study.

"Our objective was to test the safety and pharmacokinetics of short-term and long-term infusions of MTX110, a chemotherapeutic agent that inhibits the growth of medulloblastoma," Sandberg says. "In the animal study group there were no MRI signal changes in the brainstem, cerebellum, or elsewhere in the brain. In addition, the cytoarchitecture of the brain was preserved in all of the animals, with only mild postsurgical changes.

"We are really excited about the promising data from these experiments," says Sandberg, who is lead author of an article detailing results



MRI scan demonstrating catheter placement within the fourth ventricle of the brain for infusion of MTX-110 in an animal model developed by Sandberg.

in the Journal of Neurosurgery: Pediatrics.[1]

The pilot study, which has been approved by the U.S. Food and Drug Administration, will enroll five patients with recurrent medulloblastoma at Children's Memorial Hermann Hospital.

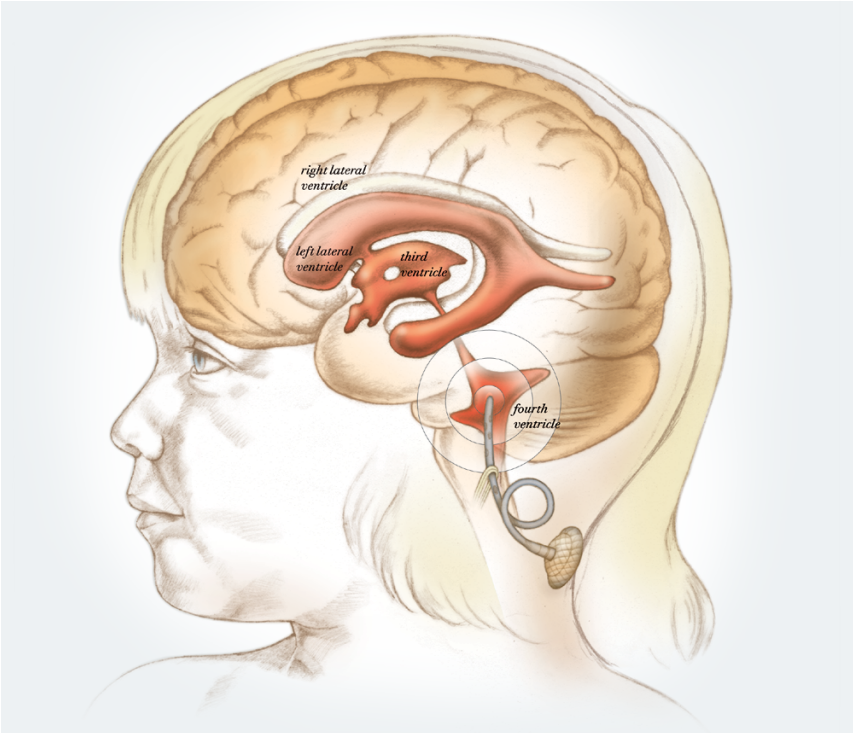
Combination Intraventricular Chemotherapy Pilot Study, Infusion of 5-Azacytidine, and Infusion of Combination 5-Azacytidine and Trastuzumab

Three additional trials of infusions into the fourth ventricle or resection cavity of children and adults with brain tumors are currently enrolling at McGovern Medical School and Children's Memorial Hermann Hospital. All three build on translational models of direct infusion of chemotherapy into the fourth ventricle of the brain in animal models, developed by Sandberg. None involve simultaneous systemic chemotherapy.

In "A Combination Intraventricular Chemotherapy Pilot Study," Sandberg and his research team are investigating combined methotrexate and etoposide infusions into the fourth ventricle in children with recurrent posterior fossa brain tumors. The trial is open to patients age 1 to 80 years with recurrent medulloblastoma, recurrent ependymoma, or recurrent atypical teratoid/rhabdoid tumors of the brain and/or spine.

"Our primary objective is to determine if combination intraventricular infusions of these two agents are safe and do not result in neurological toxicity," he says. "We are also assessing the antitumor activity of these infusions in the hope that they will yield even more robust treatment responses than those observed in previous single-agent trials."

Another trial involves infusion of 5-Azacytidine (5-AZA) into the fourth ventricle or resection cavity in children with recurrent posterior fossa ependymoma. 5-AZA is a DNA methylation inhibitor that has been infused in an animal model with no neurological toxicity while achieving substantial and sustained cerebrospinal fluid levels.



Dr. Sandberg's research involves infusions of chemotherapeutic drugs into the fourth ventricle of the brain to achieve high drug levels at the site of tumor origin and recurrence while avoiding systemic toxicity.

"Recent studies have demonstrated that DNA methylation inhibitors are logical therapeutic candidates for ependymomas originating in the posterior fossa," Sandberg says. "We've shown in the laboratory that 5-AZA kills ependymoma cells and hope to establish the safety of direct administration of 5-AZA into the fourth ventricle, and also demonstrate the clinical efficacy of these infusions. Low-dose infusions in a pilot trial we conducted showed shrinkage of some tumors in the brain. We are hopeful that higher doses and more frequent dosing can lead to even more robust responses."

The 5-AZA study is open to patients age 1 to 80 years old with recurrent ependymoma that originated in the posterior fossa of the brain.

Sandberg is also conducting a new intraventricular chemotherapy pilot study of combination 5-Azacytidine and trastuzumab infusion into the fourth ventricle or resection cavity in children and adults. The study is open to patients age 1 to 80 years old with recurrent or residual posterior fossa ependymoma.

"5-AZA has been safely infused into the fourth ventricle in our previous clinical trial," Sandberg says. "Trastuzumab is a targeted antibody therapy of interest for the treatment of ependymoma and has been safely infused intrathecally in children. As with the other trials, there will be no simultaneous systemic chemotherapy."

Using Nanotechnology for Delivery of Chemotherapeutic Drugs Directly to the Brain

In developing novel treatments, Sandberg works closely with bioengineer and research scientist Rachael Sirianni, PhD, whose research is focused on bringing novel nanomedicine approaches from the lab to the clinic to improve outcomes.

For more information about the brain tumor trials, email Bangning Yu, RN, PhD, clinical trial program manager, at bangning.yu@uth.tmc.edu, or phone 713-500-7363.

"Many drugs are available to treat brain tumors, but most do not go directly to the site where they will provide the most benefit," says Sirianni, an associate professor in the Vivian L. Smith Department of Neurosurgery and faculty member of The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences. "We're working on ways to circumvent these barriers and deliver drugs directly to the tumors."

Sirianni and her team encapsulate drugs within biocompatible and biodegradable nanoparticles, which serve as carriers to prolong drug action and target specific tissue sites. "Early on scientists discovered that nanoparticles have the capability to slide between the spaces of a tumor's vasculature and selectively accumulate within the tumor," she says. "This enhanced permeation retention enables nanoparticles to deliver encapsulated drugs preferentially to large tumors that are highly vascularized. But there are some tumors or parts of tumors that do not receive a good blood supply. Drug delivery to these tumors remains a challenge."

Pediatric brain tumors tend to metastasize along the surfaces of the brain and spinal cord. "This leptomeningeal metastasis is difficult to treat," she says. "Instead of delivering nanoparticles intravenously, we're working toward administering them directly to the cerebrospinal fluid, which moves across these lesions to deliver more drug with less overall toxicity. We're engineering nanoparticles to possess the right properties to accumulate selectively within these metastatic lesions."

Because the polymers her laboratory uses are nontoxic and readily cleared by the body, degrading over weeks to months, there is potential to design new, safer chemotherapy for patients.

In May 2019, Sirianni was awarded a five-year, $2.7 million R01 grant by the National Institute of Neurological Disorders and Stroke to design nanoparticles that can target drug delivery to leptomeningeal metastases in pediatric medulloblastoma. Her laboratory is evaluating the safety and efficacy of these new approaches and testing whether delivery of drugs from nanoparticles can reduce the radiation dose needed to treat metastases. In July 2019, she received a second five-year, $4.5 million R01 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development to study intrathecal delivery of radiation-sensitizing nanoparticles in pediatric neuro-oncology.

Many drugs succeed in preclinical models but fail in the clinical setting. Sirianni is investigating why they fail to translate to human use. "Often there's an incomplete understanding of what is limiting the drug's potential," she says. "It may be that the human tumor responds differently to a drug than it did in an animal model, or that the tumor grows differently in a human. We gather as much information about drug delivery as possible in the preclinical setting in multiple species to determine the safest and most effective dose, so that Dr. Sandberg's clinical trials are based on rigorous study of how the drug functions.

"If we understand a drug's limitations, we can engineer the nanoparticle to enhance delivery, prolong drug presence, and improve safety," Sirianni says. "When you deliver a drug to the cerebrospinal fluid moving across the brain and spinal cord, it doesn't automatically go where you want it to go. A drug might be very effective near the injection site, but maybe you want to treat a tumor further away. You have to find the drug that has the capability to do that – or engineer a drug to accomplish your goal. Through our collaboration, we're asking and answering questions that ensure that drugs are delivered to the right place at the right time in the right amount. Every scientist is doing science to improve something. As a preclinical, translational scientist, I'm grateful for the opportunity to work closely with a clinician to help identify and solve clinical problems. We expect our studies to advance new nanotechnology toward the clinic for better treatment of pediatric brain tumors."

[1] *Sandberg CJ, Kharas N, Yu B, Janssen CF, Trimble A, Ballester LY, Patel R, Mohammad AS, Elmquist WF, Sirianni RW. High-dose MTX 110 (soluble panobinostat) safety administered into the fourth ventricle in a nonhuman primate model. J Neurosurg Pediatr. 2020 May 1:1-9.*

Pediatric Neurosurgeon Reunites with Former Patient-Turned-Colleague After Three Decades

When Kathy Shelly recalls the planning involved in scheduling her 20-week anatomy ultrasound so that her husband, Don Shelly, could also attend the appointment 31 years ago, she says she's grateful she was not alone. The couple was told that their baby, who they would soon learn was a girl, would likely never walk, talk, or have a meaningful life.

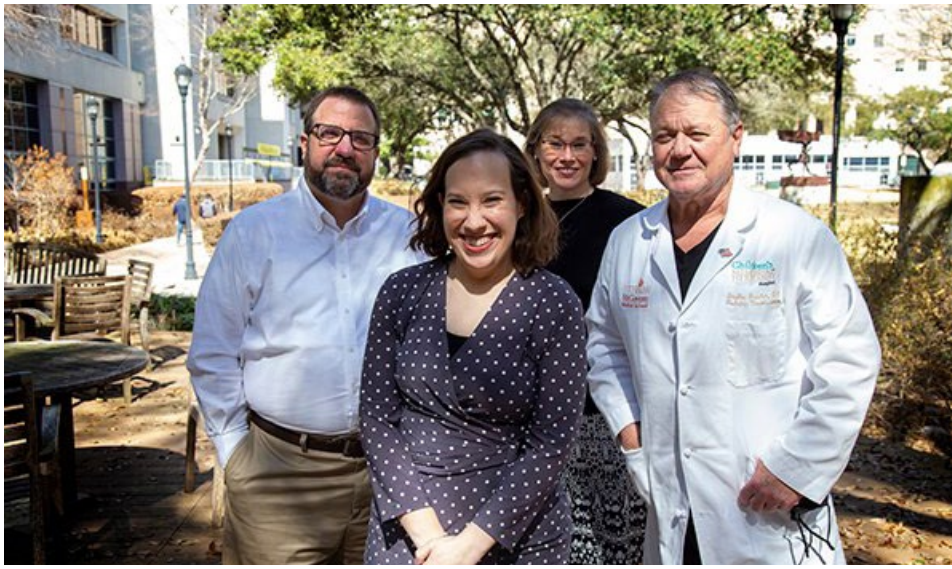
Alexis Shelly had an occipital encephalocele, a rare congenital neural tube defect manifested as a gap in her occipital bone through which brain matter protruded. Advised by their obstetrician to terminate the pregnancy, the couple sought the advice of Stephen Fletcher, DO, associate professor in the Division of Pediatric Neurosurgery at McGovern Medical School at UTHealth, who agreed to operate.

"There were no guarantees that the surgery would succeed or that Alexis would meet her developmental milestones," Fletcher says. "But we wanted to try."

Shelly underwent her first surgery at the age of five weeks at Children's Memorial Hermann Hospital, during which Fletcher folded the herniated portion of her brain into the skull. "Many surgeons consider the excess tissue nonfunctioning, but my aim is to keep as much of the brain tissue as intact as possible," he says.

Like many occipital encephalocele patients, Shelly developed hydrocephalus shortly after the surgery, and Fletcher placed a ventriculoperitoneal shunt nine days later to divert excess cerebrospinal fluid into the abdomen. She underwent her third neurosurgery to replace the shunt at the age of four months, and by the time she was 19 months old, she was walking and talking.

Her parents enrolled Shelly in dance classes to improve her coordination, and she fell in love with it. "I remember watching her at one of her recitals years ago and thinking, 'Here is my baby, who was told she'd never be able to walk or talk, dancing through life,'" Kathy Shelly says.



Together with her parents, Shelly reunited with Fletcher outside of McGovern Medical School at UTHealth for the first time in nearly three decades.

Shelly met all of her developmental milestones, making the A-B honor roll in high school and graduating from Houston Baptist University in 2012 with a degree in journalism. Shortly after she turned 30, Shelly joined the Media Relations team at UTHealth, covering neuroscience and promoting the work of the pediatric neurosurgeon who saved her life. When Fletcher recognized her name after their first email correspondence, he was thrilled. "To hear from a patient three decades later who exceeded every expectation was a wonderful surprise."

When Shelly reunited with Fletcher in person, she expressed her gratitude. "Thank you feels so insignificant, but there are no other words, just thank you," she said.

News of Note

Children's Memorial Hermann Hospital Moves Up in U.S. News Rankings of Pediatric Neuroscience Programs

Children's Memorial Hermann Hospital moved up 10 positions in the 2020 U.S. News & World Report annual rankings of children's hospitals providing neurology and neurosurgery care in the United States. The rankings are based on a detailed clinical survey that includes scores in patient care, patient safety, outcomes, nursing, advanced technology, and reputation.

The annual Best Hospitals specialty rankings are meant for patients with life-threatening or rare conditions who need a hospital that excels in treating complex, high-risk cases. The survey's strict eligibility criteria ensure that only hospitals that regularly treat complex cases are included.

"It's an incredible accomplishment to move up 10 places in the U.S. News rankings," says David I. Sandberg, MD, FAANS, FACS, FAAP, professor and director of pediatric neurosurgery, who holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery in the Department of Pediatric Surgery and Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. "We're honored to be recognized. Our primary motivations have always been excellent care for our patients, meaningful research that moves pediatric neuroscience forward, and training and mentoring new physicians. It's terrific that the word is getting out nationally about the great work we're doing."

In neuroscience, McGovern Medical School and Children's Memorial Hermann Hospital are noted for their pediatric epilepsy, spasticity, and fetal neurosurgery programs, as well as innovative brain tumor research. In the 2020 Best Hospitals survey, Children's Memorial Hermann was ranked excellent in advanced clinical services offered, commitment to best practices and quality improvement, nurse staffing, low infection rates, adoption of health information technology, and enlisting families in structuring care.

"We also ranked very high in our success rate in controlling epilepsy and survival after surgery," says Manish N. Shah, MD, FAANS, associate professor in the Division of Pediatric Neurosurgery, William J. Devane Distinguished Professor, and director of pediatric epilepsy and spasticity surgery at McGovern Medical School, who also directs the Texas

Comprehensive Spasticity Center at UTHealth Neurosciences. "Our track record of successful outcomes in epilepsy surgery is a big component of the ranking. All of our surgical patients were seizure-free, based on our 2018 case data and one-year delayed postoperative outcome assessment."

Manish N. Shah Receives UTHealth Benjy F. Brooks, MD, Outstanding Clinical Faculty Award

Manish N. Shah, MD, FAANS, associate professor of pediatric neurosurgery and William J. Devane Distinguished Professor at McGovern Medical School at UTHealth, is the 2020 recipient of the Benjy F. Brooks, MD, Outstanding Clinical Faculty Award. Shah is director of the Texas Comprehensive Spasticity Center at UTHealth Neurosciences.

"I was surprised and thrilled to receive this award," he says. "Who knew one could get an award for such an intrinsically rewarding and fun activity like teaching?"

Established in 1991 by the Alumni Association of McGovern Medical School, the Benjy Brooks award is presented by McGovern Medical School's Student Surgical Association to recognize individuals "who complement and enhance the education program by serving as role models for students." The award is named in honor of Benjy Brooks, MD, the first board-certified woman pediatric surgeon in the United States, who joined the McGovern Medical School faculty in 1973 and remained active in the life of the medical school until her death in 1998. Medical students may nominate faculty or residents for the award.

Shah molds his teaching philosophy around the words of poet Rabindranath Tagore who wrote, "A teacher can never truly teach unless he is still learning himself. A lamp can never light another lamp unless it continues to burn its own flame." He credits his parents with guiding him down the path he has been on. "My mother, Mayuri, is a retired pediatrician who taught me about service, and my father, Narendra, taught me about lifelong scholarship," he says. Throughout the COVID-19 quarantine, Shah and his father have spent 30 minutes each day learning Sanskrit together.

"I can name all of my teachers from kindergarten onwards, and they all had a meaningful impact on my career choice," says Shah, who joined the faculty at McGovern Medical School in 2014. "I learned a great deal from my mentors in medical school, and in residency and fellowship. I also continue to learn from the outstanding students, residents, and faculty here at McGovern."

Manish N. Shah, MD, FAANS

Pediatric Neurosurgeon-Scientist Joins McGovern Medical School and Memorial Hermann

Brandon A. Miller, MD, PhD, FAANS, has joined the Department of Pediatric Surgery and Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. Miller, who is certified by the American Board of Neurological Surgery with Specialization in Pediatric Neurosurgery, has clinical interests in intraventricular hemorrhage (IVH), post-IVH hydrocephalus, neurotrauma, and spina bifida.

He received his PhD in neuroscience at The Ohio State University in 2007 and his MD from the same institution in 2009. He completed residency training in neurosurgery at Emory University School of Medicine, followed by a fellowship in pediatric neurosurgery at Washington University in St. Louis and

Brandon A. Miller, MD, PhD, FAANS

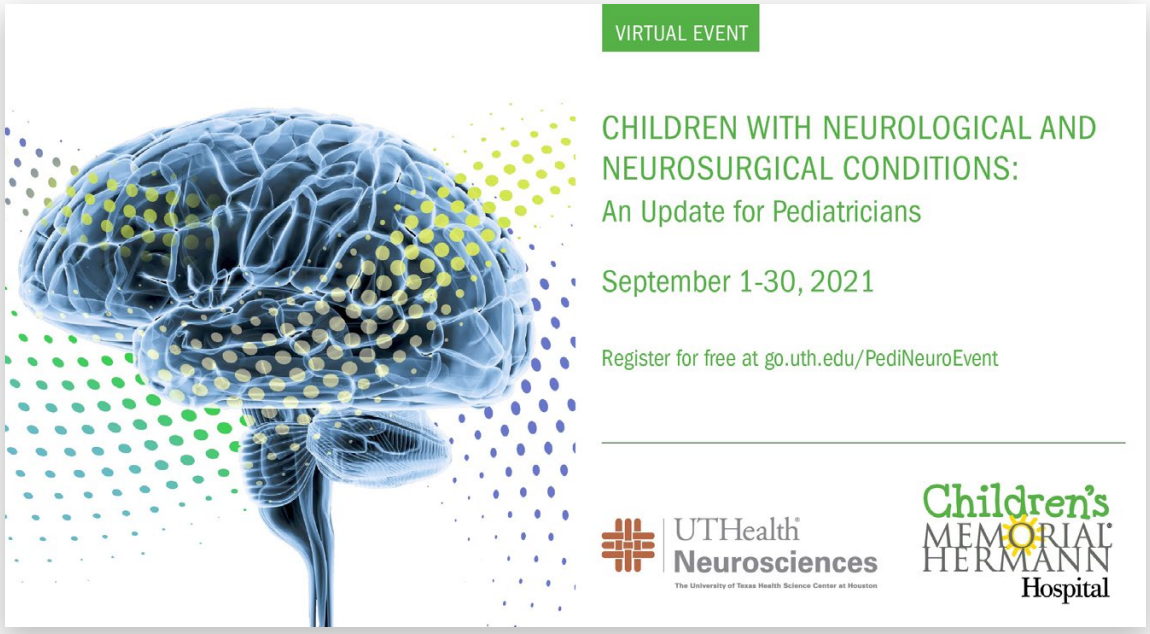
St. Louis Children's Hospital. He joins UTHealth Neurosciences and Children's Memorial Hermann Hospital from the University of Kentucky Departments of Neurosurgery and Neuroscience, where he was director of the Pediatric Brain Injury Laboratory at the Spinal Cord and Brain Injury Research Center and co-director of the MD/PhD program.

Miller is an avid researcher with interests in IVH and hydrocephalus. He is the principal investigator on a National Institutes of Health K08 Clinical Investigator Award focused on reversing inflammatory microphage activation as a treatment for IVH. He has received numerous recognitions and awards for his research, is the author of numerous peer-reviewed articles, and regularly serves as a reviewer for journals and grant review committees. Miller, who joins McGovern Medical School as an assistant professor, has a strong interest in trainee mentoring, international medicine, and treating medically underserved populations. He is an active member of the American Association of Neurological Surgeons, Congress of Neurological Surgeons, and the Hydrocephalus Association.

2020 Pediatric Neuroscience Symposium Recap

"Children with Neurological and Neurosurgical Conditions: An Update for Pediatricians" was the theme of the 2020 UTHealth Neurosciences Pediatric Neuroscience Symposium, a virtual CME meeting presented by specialists in pediatric neurosurgery at McGovern Medical School, UTHealth Neurosciences, and Children's Memorial Hermann Hospital Sept. 2-30, 2020. The experts updated participants from Texas, Oklahoma, Alabama, Georgia, California, Nebraska, New Jersey, and Guatemala on current advances in the management and treatment of patients with pediatric neurological conditions. More than 330 physicians, nurses, physical therapists, and occupational therapists accessed the course.

The symposium's course director was David I. Sandberg, MD, FAANS, FACS, FAAP, professor



and director of pediatric neurosurgery and Dr. Marnie Rose Professor in Pediatric Neurosurgery in the Department of Pediatric Surgery and the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. Faculty speakers were Stephen A. Fletcher, DO, associate professor in the Division of Pediatric Neurosurgery at McGovern Medical School, and Manish N. Shah, MD, FAANS, associate professor in the Department of Pediatric Surgery and director of pediatric surgery and epilepsy surgery at McGovern Medical School, and director of the Texas Comprehensive Spasticity Center at UTHealth Neurosciences.

Shah spoke on advances in the treatment of craniosynostosis and updated therapists and pediatricians on cerebral palsy treatments. Sandberg presented on the management of hydrocephalus and arachnoid cysts and gave an update on pediatric brain tumors for pediatricians. Fletcher presented on the neurology and surgical treatment of pathological conditions at the craniocervical junction and the neurology of urology.

Comments on the course were overwhelmingly positive from participants. The 2021 symposium will be held virtually in September; visit **go.uth.edu/PediNeuroEvent** for more information and to register.

Report on the 2020 Virtual Run for the Rose

Children's Memorial Hermann Hospital and UTHealth Neurosciences at McGovern Medical School were proud sponsors of the 18th Anniversary Run for the Rose, held as a virtual event to prevent the spread of COVID-19.

Last year's participants were asked to pick their perfect date and time between Nov. 15 and Dec. 6, 2020, to complete a 5K run or walk beginning at their own starting line, or to get creative by choosing to dance, hike, bike, or take a Zumba class. Funds raised by Run for the Rose support brain cancer research at The University of Texas MD Anderson Cancer Center and McGovern Medical School at UTHealth, as well as neuroscience research and the Pediatric Palliative Care Program at Children's Memorial Hermann Hospital.

The run is sponsored annually by the Dr. Marnie Rose Foundation, which has supported brain cancer research and pediatric health initiatives in Houston since 2003. To date, the foundation has given nearly $7 million to Children's Memorial Hermann Hospital, MD Anderson Cancer Center, and UTHealth. At McGovern Medical School, funds support cutting-edge research and treatment for children with brain tumors, a cause close to Dr. Marnie Rose's heart.

Selected Publications

January 2020 through April 2021

Bagić A, Funke M, Burgess RC. The Wisdom and Vision from the ACMEGS Inaugural Decade. Journal of Clinical Neurophysiology. 2020 Nov;37(6):471-482.

Bagić A, Funke M, Kirsch HE, Tenney JR, Zillgitt AJ, Burgess RC. The 10 Evidence-Supported Indications for MEG in Epilepsy Surgery: An Illustrated Compendium. Journal of Clinical Neurophysiology. 2020 Nov;37:483-497.

Bartal MF, Bergh EP, Tsao K, Austin MT, Moise KJ, Fletcher SA, Sibai BM, Papanna R. Low Transverse versus Midline Abdominal Skin Incisions for in utero Spina Bifida Repair. Fetal Diagnosis and Therapy. 2021 Feb 16;1-9.

Brown HM, Murray S, Northrup H, Au KS, Niswander LA. Snx3 is important for mammalian neural tube closure via its role in canonical and non-canonical WNT signaling. Development/ 2020 Nov 19; 147(22):dev192518.

Chung EP, Cotter JD, Prakapenka AV, Cook RL, DiPerna D, Sirianni RW. Targeting small molecule delivery to the brain via intranasal administration of rabies virus glycoprotein (RVG29) modified PLGA nanoparticles. Pharmaceutics. 2020;12(2):93 IF = 4.7.

Cook IA, Wilson AC, Peters JM, Goyal MN, Bebin EM, Northrup H, Krueger D, Leuchter AF, Sahin M; TACERN Study Group. EEG Spectral Features in Sleep of Autism Spectrum Disorders in Children with Tuberous Sclerosis Complex. Journal of Autism and Developmental Disorders. 2020 Mar;50(3):916-923.

CreveCoeur TS, Yahanda AT, Maher CO, Johnson GW, Ackerman LL, Adelson PD, Ahmed R, Albert GW, Aldana PR, Alden TD, Anderson RCE, Baird L, Bauer DF, Bierbrauer KS, Brockmeyer DL, Chern JJ, Couture DE, Daniels DJ, Dauser RC, Durham SR, Ellenbogen RG, Eskandari R, Fuchs HE, George TM, Grant GA, Graupman PC, Greene S, Greenfield JP, Gross NL, Guillaume DJ, Haller G, Hankinson TC, Heuer GG, Iantosca M, Iskandar BJ, Jackson EM, Jea AH, Johnston JM, Keating RF, Kelly MP, Khan N, Krieger MD, Leonard JR, Mangano FT, Mapstone TB, McComb JG, Menezes AH, Muhlbauer M, Oakes WJ, Olavarria G, O'Neill BR, Park TS, Ragheb J, Selden NR, Shah MN, Shannon C, Shimony JS, Smith J, Smyth MD, Stone SSD, Strahle JM, Tamber MS, Torner JC, Tuite GF, Wait SD, Wellons JC, Whitehead WE, Limbrick DD. Occipital-Cervical Fusion and Ventral Decompression in the Surgical Management of Chiari-1 Malformation and Syringomyelia: Analysis of Data From the Park-Reeves Syringomyelia Research Consortium. Neurosurgery. 2021 Jan 13;88(2):332-341.

Farach LS, Richard MA, Lupo PJ, Sahin M, Krueger DA, Wu JY, Bebin EM, Au KS, Northrup H; TACERN Study Group. Epilepsy Risk Prediction Model for Patients With Tuberous Sclerosis Complex. Pediatric Neurology. 2020 Jul 29;113:46-50. Online ahead of print.

Fischer GM, Vaziri Fard E, Shah MN, Patel RP, Von Allmen G, Ballester LY, Bhattacharjee MB. Filamin A-negative hyaline astrocytic inclusions in pediatric patients with intractable epilepsy: report of 2 cases. Journal of Neurosurgery Pediatrics. 2020 Mar 27:1-7. Online ahead of print.

Fotso C, Sandberg DI. Spontaneous Resolution of Large Subdural Hematoma with Midline Shift: A Case Report. Child's Nervous System. 2021;37:703-705.

Fowler MJ, Cotter JD, Knight BE, Sevick-Muraca EM, Sandberg DI, Sirianni RW. Intrathecal drug delivery in the era of nanomedicine. Advanced Drug Delivery Reviews. 2020;165-166:77-95.

Goulding DS, Vogel CR, Gensel JC, Morganti JM, Stromberg AJ, Miller BA. Acute Brain Inflammation, White Matter Oxidative Stress and Myelin Deficiency in a Model of Neonatal Intraventricular Hemorrhage. Journal of Neurosurgery Pediatrics. 2020 Aug 28;1-11.

Goulding DS, Vogel CR, Pandya CD, Shula C, Gensel JC, Mangano FT, Goto J, Miller BA. Neonatal Hydrocephalus Leads to White Matter Neuroinflammation and Injury in the Corpus Callosum of Ccdc39 Hydrocephalic Mice. Journal of Neurosurgery Pediatrics. 2020 Feb 7;1-8.

Grayson LE, Peters JM, McPherson T, Krueger DA, Sahin M, Wu JY, Northrup HA, Porter B, Cutter GR, O'Kelley SE, Krefting J, Stone SS, Madsen JR, Fallah A, Blount JP, Weiner HL, Bebin EM; TACERN Study Group. Pilot Study of Neurodevelopmental Impact of Early Epilepsy Surgery in Tuberous Sclerosis Complex. Pediatric Neurology. 2020 Apr 14:S0887-8994(20)30118-1. Online ahead of print.

Guillen Sacoto MJ, Tchasovnikarova IA, Torti E, Forster C, Andrew EH, Anselm I, Baranano KW, Briere LC, Cohen JS, Craigen WJ, Cytrynbaum C, Ekhilevitch N, Elrick MJ, Fatemi A, Fraser JL, Gallagher RC, Guerin A, Haynes D, High FA, Inglese CN, Kiss C, Koenig MK, Krier J, Lindstrom K, Marble M, Meddaugh H, Moran ES, Morel CF, Mu W, Muller EA 2nd, Nance J, Natowicz MR, Numis AL, Ostrem B, Pappas J, Stafstrom CE, Streff H, Sweetser DA, Szybowska M, Walker MA, Wang W, Weiss K, Weksberg R, Wheeler PG, Yoon G, Kingston RE, Juusola J. De Novo Variants in the ATPase Module of MORC2 Cause a Neurodevelopmental Disorder with Growth Retardation and Variable Craniofacial Dysmorphism. American Journal of Human Genetics. 2020 Aug 6;107(2):352-363. Epub 2020 Jul 20.

Gupta A, de Bruyn G, Tousseyn S, Krishnan B, Lagae L, Agarwal N; TSC Natural History Database Consortium. Epilepsy and Neurodevelopmental Comorbidities in Tuberous Sclerosis Complex: A Natural History Study. Pediatric Neurology. 2020 May;106:10-16.

Hale AT, Adelson PD, Albert GW, Aldana PR, Alden TD, Anderson RCE, Bauer DF, Bonfield CM, Brockmeyer DL, Chern JJ, Couture DE, Daniels DJ, Durham SR, Ellenbogen RG, Eskandari R, George TM, Grant GA, Graupman PC, Greene S, Greenfield JP, Gross NL, Guillaume DJ, Heuer GG, Iantosca M, Iskandar BJ, Jackson EM, Johnston JM, Keating RF, Leonard JR, Maher CO, Mangano FT, McComb JG, Meehan T, Menezes AH, O'Neill B, Olavarria G, Park TS, Ragheb J, Selden NR, Shah MN, Smyth MD, Stone SSD, Strahle JM, Wait SD, Wellons JC, Whitehead WE, Shannon CN, Limbrick DD; Park-Reeves Syringomyelia Research Consortium Investigators. Factors associated with syrinx size in pediatric patients treated for Chiari malformation type I and syringomyelia: a study from the Park-Reeves Syringomyelia Research Consortium. Journal of Neurosurgery Pediatrics. 2020 Mar 6:1-11. Online ahead of print.

Hebert L, Hillman P, Baker C, Brown M, Ashley-Koch A, Hixson JE, Morrison AC, Northrup H, Au KS. Burden of rare deleterious variants in WNT signaling genes among 511 myelomeningocele patients. PLoS One. 2020 Sep 24;15(9):e0239083. eCollection 2020.

Hillman P, Baker C, Hebert L, Brown M, Hixson J, Ashley-Koch A, Morrison AC, Northrup H, Au KS. Identification of novel candidate risk genes for myelomeningocele within the glucose hemeostasis/oxidative stress and folate/one-carbon metabolism networks. Molecular Genetics & Genomic Medicine. 2020 Sep 22:e1495. Online ahead of print.

Iqbal F, Ballester LY, Akash N, Sandberg DI, Bhattacharjee MB. 5-Year-Old Girl with Worsening Seizure Disorder. Brain Pathology. 2020;30(3):717-718.

Johnson BV, Kumar R, Oishi S, Alexander S, Kasherman M, Vega MS, Ivancevic A, Gardner A, Domingo D, Corbett M, Parnell E, Yoon S, Oh T, Lines M, Lefroy H, Kini U, Van Allen M, Grønborg S, Mercier S, Küry S, Bézieau S, Pasquier L, Raynaud M, Afenjar A, Billette de Villemeur T, Keren B, Désir J, Van Maldergem L, Marangoni M, Dikow N, Koolen DA, VanHasselt PM, Weiss M, Zwijnenburg P, Sa J, Reis CF, López-Otín C, Santiago-Fernández O, Fernández-Jaén A, Rauch A, Steindl K, Joset P, Goldstein A, Madan-Khetarpal S, Infante E, Zackai E, Mcdougall C, Narayanan V, Ramsey K, Mercimek-Andrews S, Pena L, Shashi V, Schoch K, Sullivan JA, Pinto E Vairo F, Pichurin PN, Ewing SA, Barnett SS, Klee EW, Perry MS, Koenig MK, Keegan CE, Schuette JL, Asher S, Perilla-Young Y, Smith LD, Rosenfeld JA, Bhoj E, Kaplan P, Li D, Oegema R, van Binsbergen E, van der Zwaag B, Smeland MF, Cutcutache I, Page M, Armstrong M, Lin AE, Steeves MA, Hollander ND, Hoffer MJV, Reijnders MRF, Demirdas S, Koboldt DC, Bartholomew D, Mosher TM, Hickey SE, Shieh C, Sanchez-Lara PA, Graham JM Jr, Tezcan K, Schaefer GB, Danylchuk NR, Asamoah A, Jackson KE, Yachelevich N, Au M, Pérez-Jurado LA, Kleefstra T, Penzes P, Wood SA, Burne T, Pierson TM, Piper M, Gécz J, Jolly LA. Partial Loss of USP9X Function Leads to a Male Neurodevelopmental and Behavioral Disorder Converging on Transforming Growth Factor β Signaling. Biological Psychiatry. 2020 Jan 15;87(2):100-112. Epub 2019 Jun 29.

Khatua S, Cooper LJN, Sandberg DI, Ketonen L, Johnson JM, Rytting ME, Liu DD, Meador H, Trikha P, Nakkula RJ, Behbehani GK, Ragoonanan D, Gupta S, Kotrotsou A, Idris T, Shpall EJ, Rezvani K, Colen R, Zaky W, Lee DA, Gopalakrishnan V. Phase I Study of intraventricular infusions of autologous ex-vivo expanded NK cells in children with recurrent medulloblastoma andependymoma. Neuro-Oncology. 2020;222(8):1214-1225.

Lopez-Rivera V, Sheriff FG, Sandberg DI, Blackburn S, Dannenbaum M, Sheth SA, Day AL, Chen PR. De novo thalamic arteriovenous malformation in a boy with a brainstem cavernous malformation. Journal of Clinical Neuroscience. 2020;76:226-228.

Madsen JR, Boyle TP, Neuman MI, Park E, Tamber MS, Hickey RW, Heuer GG, Zorc JJ, Leonard JR, Leonard JC, Keating R, Chamberlain JM, Frim DM, Zakrzewski P, Klinge P, Merck LH, Piatt J, Bennett JE, Sandberg DI, Boop FA, Hameed MQ. Diagnostic Accuracy of Non-Invasive Thermal Evaluation of Ventriculoperitoneal Shunt Flow in Shunt Malfunction: A Prospective, Multi-Site, Operator-Blinded Study. Neurosurgery. 2020;87(5):939-948.

Madsen KL, Buch AE, Cohen BH, Falk MJ, Goldsberry A, Goldstein A, Karaa A, Koenig MK, Muraresku CC, Meyer C, O'Grady M, Scaglia F, Shieh PB, Vockley J, Zolkipli-Cunningham Z, Haller RG, Vissing J. Safety and efficacy of omaveloxolone in patients with mitochondrial myopathy: MOTOR trial. 2020 Feb 18;94(7):e687-e698. Epub 2020 Jan 2.

Mao D, Reuter CM, Ruzhnikov MRZ, Beck AE, Farrow EG, Emrick LT, Rosenfeld JA, Mackenzie KM, Robak L, Wheeler MT, Burrage LC, Jain M, Liu P, Calame D, Küry S, Sillesen M, Schmitz-Abe K, Tonduti D, Spaccini L, Iascone M, Genetti CA, Koenig MK, Graf M, Tran A, Alejandro M, Lee BH, Thiffault I, Agrawal PB, Bernstein JA, Bellen HJ, Chao HT. De novo EIF2AK1 and EIF2AK2 Variants Are Associated with Developmental Delay, Leukoencephalopathy, and Neurologic Decompensation. American Journal of Human Genetics. 2020 Apr 2;106(4):570-583. Epub 2020 Mar 19.

Medina DX, Chung EP, Teague C, Bowser RP, Sirianni RW. Intravenously administered, retinoid activating nanoparticles increase lifespan and reduce neurodegeneration in the SOD1G93A mouse model of ALS. Frontiers in Bioengineering and Biotechnology. 2020;8:224 IF = 5.1.

Melin AA, Moffitt J, Hopkins DC, Shah MN, Sandberg DI, Teichgraeber JF, Greives MR. Is Less Actually More? An Evaluation of Surgical Outcomes Between Endocopic Suturectomy and Open Cranial Vault Remodeling for Craniosynostosis. Journal of Craniofacial Surgery. 2020;31(4):924-926.

Mendes MI, Green LMC, Bertini E, Tonduti D, Aiello C, Smith D, Salsano E, Beerepoot S, Hertecant J, von Spiczak S, Livingston JH, Emrick L, Fraser J, Russell L, Bernard G, Magri S, Di Bella D, Taroni F, Koenig MK, Moroni I, Cappuccio G, Brunetti-Pierri N, Rhee J, Mendelsohn BA, Helbig I, Helbig K, Muhle H, Ismayl O, Vanderver AL, Salomons GS, van der Knaap MS, Wolf NI. RARS1-related hypomyelinating leukodystrophy: Expanding the spectrum. Annals of Clinical and Translational Neurology. 2020 Jan;7(1):83-93. Epub 2019 Dec 8.

Miller BA, Spears RC, Hines TK, Alhajeri A, Fraser JF. A lumbar dural arteriovenus fistula presenting with intraventricular hemorrhage and hydrocephalus. Journal of Neurointerventional Surgery. 2020 May;12(5).

Mosher JC, Funke M. Towards Best Practices in Clinical Magnetoencephalography: Patient Practices and Data Acquisition. Journal of Clinical Neurophysiology. 2020 Nov;37(6):498-507.

Mowrey K, Koenig MK, Szabo CA, Samuels J, Mulligan S, Pearson DA, Northrup H. Two different genetic etiologies for tuberous sclerosis complex (TSC) in a single family. Molecular Genetic & Genomic Medicine. 2020 Jul;8(7):e1296. Epub 2020 May 8.

Mullarkey MP, Nehme G, Mohiuddin S, Ballester LY, Bhattacharjee MB, Trivedi D, Shah MN, Fuller GN, Zaky W, Sandberg DI. Posttreatment Maturation of Medulloblastoma into Gangliocytoma: Report of 2 Cases. Pediatric Neurosurgery. 2020;55(4):222-231. Epub 2020 Sep 3.

Nguyen RD, Kennady EH, Smyth MD, Zhu L, Pao LP, Swisher SK, Rosas A, Mitra A, Patel RP, Lankford J, Von Allmen G, Watkins MW, Funke ME, Shah MN. Convolutional Neural Networks for Pediatric Refractory Epilepsy Classification Using Resting-State Functional Magnetic Resonance Imaging. World Neurosurgery. 2021 May;149:e1112-e1122. Epub 2021 Jan 6.

Oluwafemi OO, Benjamin RH, Navarro Sanchez ML, Scheuerle AE, Schaaf CP, Mitchell LE, Langlois PH, Canfield MA, Swartz MD, Scott DA, Northrup H, Ray JW, McLean SD, Ludorf KL, Chen H, Lupo PJ, Agopian AJ. Birth defects that co-occur with non-syndromic gastroschisis and omphalcele. American Journal of Medical Genetics Part A. 2020 Sep 4. Online ahead of print.

Pandya CD, Vekaria H, Joseph B, Slone SA, Gensel JC, Sullivan PG, Miller, BA. Hemoglobin induces oxidative stress and mitochondrial dysfunction in oligodendrocyte progenitor cells. Translational Research. 2021 May;231:13-23.

Raj SR, Arnold AC, Barboi A, Claydon VE, Limberg JK, Lucc V-E M, Numan M, Peltier A, Snapper H, Vernino S; on behalf of the American Autonomic Society Statement. Clinical Autonomic Research Journal. 2021 Mar 19. Epub ahead of print.

Russo SN, Goldstein A, Karaa A, Koenig MK, Walker M. Leigh Syndrome as a Phenotype of Near-Homoplasmic m.8344 A>G Variant in Children. Child Neurology Open. 2021 Jan-Dec;8:2329048X21991382. eCollection 2021 Jan-Dec.

Sánchez Fernández I, Yang E, Calvachi P, Amengual-Gual M, Wu JY, Krueger D, Northrup H, Bebin ME, Sahin M, Yu KH, Peters JM; TACERN Study Group. Deep learning in rare disease. Detection of tubers in tuberous sclerosis complex. PLoS One. 2020 Apr 29;15(4):e0232376. eCollection 2020.

Sandberg DI, Kharas N, Yu B, Janssen CF, Trimble A, Ballester LY, Patel R, Mohammad AS, Elmquist WF, Sirianni RW. High-dose MTX110 (soluble panobinostat) safely administered into the fourth ventricle in a nonhuman primate model. Journal of Neurosurgery Pediatrics. 2020 May 1;1-9. Epub ahead of print.

Scherrer B, Prohl AK, Taquet M, Kapur K, Peters JM, Tomas-Fernandez X, Davis PE, M Bebin E, Krueger DA, Northrup H, Y Wu J, Sahin M, Warfield SK. The Connectivity Fingerprint of the Fusiform Gyrus Captures the Risk of Developing Autism in Infants with Tuberous Sclerosis Complex. Cerebral Cortex. 2020 Apr 14;30(4):2199-2214.

Schoenberger A, Capal JK, Ondracek A, Horn PS, Murray D, Byars AW, Pearson DA, Williams ME, Bebin M, Northrup H, Wu JY, Sahin M, Krueger DA. Language predictors of autism spectrum disorder in young children with tuberous sclerosis. Epilepsy & Behavior. 2020 Feb;103(Pt A):106844. Epub 2019 Dec 18.

Scott TM, Guo H, Eichler EE, Rosenfeld JA, Pang K, Liu Z, Lalani S, Bi W, Yang Y, Bacino CA, Streff H, Lewis AM, Koenig MK, Thiffault I, Bellomo A, Everman DB, Jones JR, Stevenson RE, Bernier R, Gilissen C, Pfundt R, Hiatt SM, Cooper GM, Holder JL, Scott DA. BAZ2B haploinsufficiency as a cause of developmental delay, intellectual disability, and autism spectrum disorder. Human Mutation. 2020 May;41(5):921-925. Epub 2020 Feb 7.

Sokola M, O'Connor K, Sokola B, Miller B, Neltner J, Lukins D, Khan G. Propofol Related Infusion Syndrome in a Pediatric Patient with an Intracerebral Hemorrhage. Neurology Clinical Practice. 2020 Sept 9. Epub ahead of print.

Starling CT, Nguyen Q-B D, Butler IJ, Numan MT, Hebert AA. Cutaneous manifestations of orthostatic intolerance syndromes. International Journal of Women's Dermatology. 2021 Mar 11. Epub ahead of print.

Streff H, Posey JE, Mauer CB, Krempely K, Potocki L, Northrup H. TSC1 Variant Associated With Mild or Absent Clinical Features of Tuberous Sclerosis Complex in a Three-Generation Family. Pediatric Neurology. 2020 May 4:S0887-8994(20)30148-X. Online ahead of print.

Trimble DJ, Parker SL, Zhu L, Cox CS, Kitagawa RS, Fletcher SA, Sandberg DI, Shah MN. Outcomes and prognostic factors of pediatric patients with a Glasgow Coma Score of 3 after blunt head trauma. Child's Nervous System. 2020 Nov;36(11):2657-2665. Epub 2020 May 6.

Turan N, Heider RA, Nadeem M, Miller BA, Wali B, Yousuf, Sayeed I, Stein DG, Pradilla G. Neurocognitive Outcomes in a Cisternal Blood Injection Murine Model of Subarachnoid Hemorrhage. Journal of Stroke and Cerebrovascular Diseases. 2020 Nov;(29)11:105249.

Uya A, Gautam NK, Rafique MB, Pawelek O, Patnana SR, Gupta-Malhotra M, Balaguru D, Numan MT, Hill MJ, Miller SK. Point-of-Care Ultrasound in Sternal Notch Confirms Depth of Endotracheal Tube in Children. Pediatric Critical Care Medicine Journal. 2020 Jul;21(7):e393-e398. Epub ahead of print.

Vu T, Mann LK, Fletcher SA, Jain R, Garnett J, Tsao K, Austin MT, Moise KJ Jr, Johnson A, Shah MN, Papanna R. Suture techniques and patch materials using an in-vitro model for watertight closure of in-utero spina bifida repair. Journal of Pediatric Surgery. 2020 Apr;55(4):726-731. Epub 2019 Jun 19.

Wang CY, Bonaroti A, Miller BA, Liau JL. Sagittal Synostosis Scaphocephaly Cranial Reconstruction with Spiral Cut Cranioplasty. Journal of Neurosurgery. 2021 Apr. Epub ahead of print.

Yahanda AT, Adelson PD, Akbari SHA, Albert GW, Aldana PR, Alden TD, Anderson RCE, Bauer DF, Bethel-Anderson T, Brockmeyer DL, Chern JJ, Couture DE, Daniels DJ, Dlouhy BJ, Durham SR, Ellenbogen RG, Eskandari R, George TM, Grant GA, Graupman PC, Greene S, Greenfield JP, Gross NL, Guillaume DJ, Hankinson TC, Heuer GG, Iantosca M, Iskandar BJ, Jackson EM, Johnston JM, Keating RF, Krieger MD, Leonard JR, Maher CO, Mangano FT, McComb JG, McEvoy SD, Meehan T, Menezes AH, O'Neill BR, Olavarria G, Ragheb J, Selden NR, Shah MN, Shannon CN, Shimony JS, Smyth MD, Stone SSD, Strahle JM, Torner JC, Tuite GF, Wait SD, Wellons JC, Whitehead WE, Park TS, Limbrick DD. Dural augmentation approaches and complication rates after posterior fossa decompression for Chiari I malformation and syringomyelia: a Park-Reeves Syringomyelia Research Consortium study. Journal of Neurosurgery Pediatrics. 2021 Feb 12:1-10. Online ahead of print.

Zhu B, Sevick-Muraca EM, Nguyen RD, Shah MN. Cap-Based Transcranial Optical Tomography in an Awake Infant. IEEE Trans Med Imaging. 2020 Nov;39(11):3300-3308. Epub 2020 Oct 28.

About the Children's Neuroscience Center

The UTHealth Neurosciences physicians affiliated with the Children's Neuroscience Center at Children's Memorial Hermann Hospital specialize in the evaluation, diagnosis, and treatment of children with a broad range of neurological disorders, including brain tumors, epilepsy, hydrocephalus, spasticity, spina bifida, and head injuries. Through a collaboration with McGovern Medical School at UTHealth and Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center, the team approach combines the experience of pediatric specialists and subspecialists to ensure children receive coordinated, evidence-based care that can lead to the best possible clinical outcomes.

Scope of Practice

Our affiliated, board-certified pediatric neurosurgeons are leaders in providing the most advanced treatments for a full spectrum of conditions, including:

- Arachnoid cysts
- Arteriovenous malformation (AVM)
- Brain tumors
- Cerebral palsy
- Chiari malformation
- Congenital malformations
- Craniofacial disorders, including craniosynostosis
- Epilepsy surgery
- Head and spine trauma
- Hydrocephalus
- Moyamoya disease
- Myelomeningocele and other congenital spinal anomalies (spina bifida)
- Pediatric stroke
- Peripheral nerve disorders (brachial plexus disorders)
- Spasticity
- Spinal cord tumors
- Tethered spinal cord
- Tuberous sclerosis complex
- Vascular malformations

For more information on specific clinical trials, please call 713.500.7363 or visit memorialhermann.org/childrens-neuro-research

Collaboration

Referring physicians are kept fully informed about patient progress throughout the entire evaluation and treatment process. After a patient's office visit, referring physicians will receive a summary which includes the initial diagnosis, pending tests, and treatment options.

childrens.memorialhermann.org/refer-neuro
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