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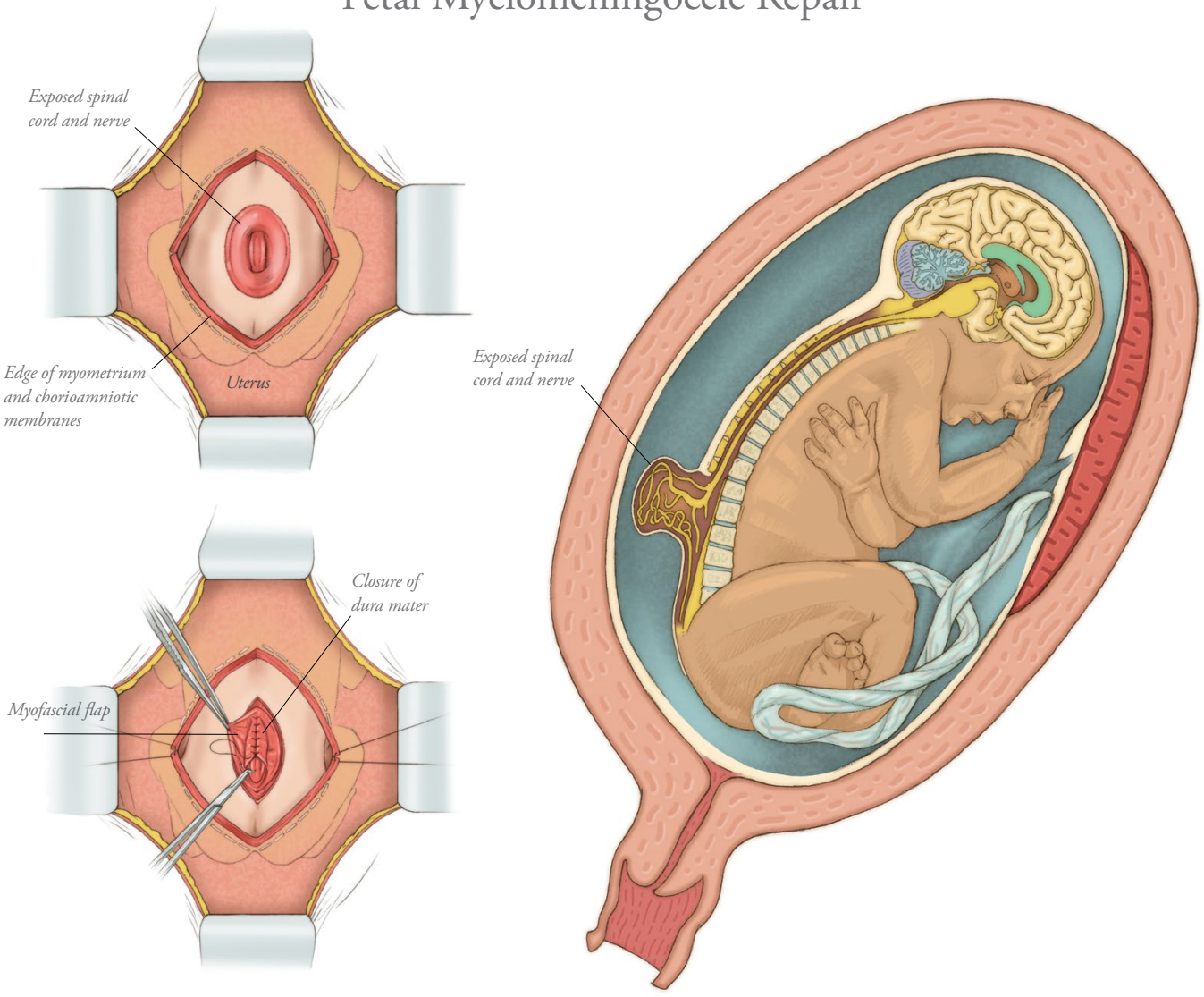
Fetal Myelomeningocele Repair



Prenatal repair of myelomeningocele is a delicate surgical procedure where fetal surgeons open the uterus and close the opening in the baby's back while still in the womb.

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

Children's Memorial Hermann Hospital

In This Issue

Celebrating Firsts

For every hour we spend with patients, we spend many more in detailed preparation for that first meeting. During the exam, we ask questions, listen closely, and consider every diagnostic possibility. Afterward, we review our treatment options as a team. When we have executed successful surgical solutions, we're not afraid to marry them in new procedures that advance pediatric neuroscience. In this issue of the Pediatric Neuroscience Journal, you'll read about home runs with three patients.

Faith Hagler was the first baby in Texas to undergo in-utero spina bifida repair after the results of the Management of Myelomeningocele Study (MOMS) were published in the New England Journal of Medicine in 2011. The Haglers, residents of Dallas, learned about the MOMS trial during their internet search for the best treatment for their daughter, and their maternal-fetal medicine specialist referred them to The Fetal Center at Children's Memorial Hermann Hospital in Houston. Faith, now 9, is a shining star who performs song-and-dance routines at her church and is on the honor roll at her elementary school.

We're also grateful to the Guidry family of Louisiana and the Medlins of Texas for sharing the stories of their daughters, who were born with unicoronal craniosynostosis. Both babies underwent an innovative surgery that produced excellent outcomes after their families trusted our team to provide them with the very best care. Using CT scans, Dr. Manish N. Shah, a pediatric neurosurgeon, and Dr. Phuong Nguyen, a plastic/craniofacial surgeon, designed a 3D model and fine-tuned the surgery the day before they took each patient to the OR.

Three novel studies underway at UTHealth seek to improve the outlook for children with malignant fourth ventricular brain tumors. In our Research section, we also report on the work of Dr. Rachael Sirianni 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 complements the research we're doing in the two single-center trials for fourth ventricular brain tumors.

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

With best wishes,

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Faith in a Tiny Patient: The First Fetal Myelomeningocele Repair in Texas

Picture the most creative, self-assured 9-year-old you can imagine. Her songs and dance moves come straight from Ariana Grande. She loves bright colors and runs to the mirror to check every outfit. She performs at church, is on the honor roll at her elementary school, and reads at a higher level than her third-grade class. She has the attitude of an actress, the energy of an entertainer, and the million-dollar smile of a model. Her goal is to be a superstar dancer and actress, or maybe a teacher.

Ramesha Papanna, MD, MPH

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

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KuoJen Tsao, MD

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Like all babies, Faith Hagler's story begins before she was born. But unlike others, her history was complicated by a prenatal diagnosis of myelomeningocele – spina bifida – at 20 weeks of gestation. Born on the Fourth of July, 2011, Faith was the first child to undergo in-utero surgery for spina bifida repair in Texas.

Spina bifida is a complex and permanently disabling birth defect involving incomplete development of a portion of the spinal cord and associated nerves, as well as the surrounding spinal bones and overlaying muscle. At birth, the incompletely developed portion of the spinal cord protrudes through the open skin.

Infants born with spina bifida are at risk for a range of associated conditions, including hydrocephalus, which may require placement of a ventriculoperitoneal (VP) shunt to relieve pressure inside the skull caused by excess fluid on the brain. They are prone to life-threatening infections and may suffer loss of sensation or paralysis below the level of the spinal cord defect, as well as ambulatory problems, deformities of the hips, and lower back pain, leading to lifelong disability.

"We were devastated when we learned our baby had spina bifida," says Colette Hagler, a resident of Dallas. "Our emotions were all over the place. We had gone for a routine ultrasound to find out the gender, and the radiologist noticed an abnormality. When we learned of the possibility of spina bifida, my husband and I started doing research online."

A maternal-fetal medicine specialist in Dallas confirmed the diagnosis and referred her to The Fetal Center[1] at Children's Memorial Hermann Hospital in Houston. A week later, Hagler and her husband, Ivan, were consulting with KuoJen Tsao, MD, co-director of The Fetal Center and professor of pediatric surgery at McGovern Medical School at UTHealth; Stephen Fletcher, DO, associate professor of pediatric neurosurgery at McGovern Medical School; and a maternal-fetal medicine specialist on staff at the time. During their two-day visit, they also met with other members of Children's Memorial Hermann Hospital's multidisciplinary team to determine a treatment plan. The team performed the first in-utero spina bifida repair in Texas, and one of the first in the nation after the results of the Management of Myelomeningocele Study (MOMS) were published.

Tsao had begun screening patients for in-utero repair in early 2011, based on outcomes reported in a landmark study that found major benefits for fetal surgery in patients with spina bifida. The results of MOMS were published in an article that appeared in the March 17, 2011, issue of the New England Journal of Medicine. The Haglers learned of the MOMS trial during their internet search.

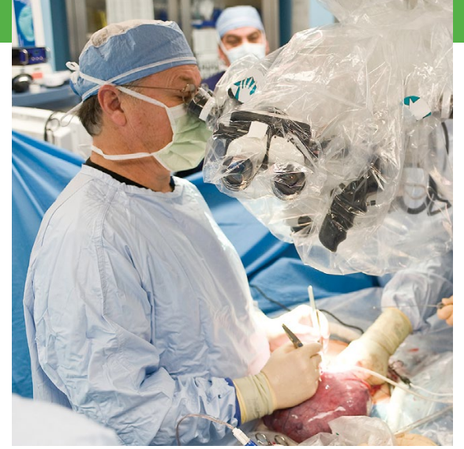
With support from the National Institutes of Health, MOMS studied the effects of fetal surgery for the repair of spina bifida to the standard-of-care surgery for the disorder after birth. The study, which followed 158 women at three hospitals, found that if a baby undergoes surgery in utero, the serious complications associated with spina bifida could be reversed or lessened. Fetal surgery decreased the need for shunting at 12 months for the infants who participated in the study, and nearly half were able to walk without crutches by age 2½.

"MOMS was the first study to show the significant benefits of surgery to unborn babies with spina bifida," Tsao says. "The study was also important because traditionally, fetal surgery was performed for lethal conditions. With the MOMS study, researchers conducted the first fetal operation for a nonlethal condition. Because of the risks involved in fetal surgery, we tend to limit heroic interventions to the most severe and life-threatening cases – those associated with high mortality and high morbidity. While myelomeningocele is associated with high morbidity, the mortality rate is relatively low."

Since the 1930s, the first step in the treatment of newborns with the condition has been to close the opening within a few days of birth. The surgery moves tissues back into their normal position and prevents further damage to and infection of the nerve tissue, but does not restore function to the already damaged nerves. The second step is usually placement of a shunt in the ventricles of the brain, which allows for drainage of the excess fluid characteristic of spina bifida, relieving pressure on the brain.

"The MOMS study was exciting because it produced greatly improved outcomes," says Fletcher, a key member of the pediatric neurosurgery team at Children's Memorial Hermann Hospital and UTHealth Neurosciences. "But in fetal surgery, there are risks to the mother and the baby, and we weigh those risks carefully."

The physician team was up front with the Haglers about the risks, which include infection, bleeding, miscarriage, stillbirth, placental abruption, uterine scar separation/rupture, preterm ruptured membranes, and preterm birth. For mothers who had prenatal surgery during the trial, the average age of delivery was 34 weeks.



Stephen Fletcher, DO, works with the fetal medicine team to perform an in-utero spina bifida repair at Children's Memorial Hermann Hospital.

Thirteen percent had a preterm birth at less than 30 weeks, one-third delivered between 30 and 34 weeks, and one-third delivered between 35 and 36 weeks, with the remainder delivering at 37 weeks or later.

Medically, Hagler was a good candidate. "The couple knew that this was our first in-utero spina bifida repair," Tsao says. "We had performed the various parts of the operation many times with other patients, but this was the first time we pulled everything together in one procedure. This was something the Haglers really wanted to do. They had done their research and had a good understanding of the risks to mom and baby."

The surgery itself was straightforward. A special stapling device was used to cut through the uterine wall and close blood vessels to prevent bleeding. Once the fetus was exposed, Fletcher closed the gap in her spine, and the team returned the one-pound baby to the uterus.

The Haglers say they relied in large part on their faith in making the decision to go forward with the surgery. "I had a lot of anxiety, especially about the anesthesia, but once I learned about the possibility of in-utero repair, I wanted to do it," Colette Hagler says. "By the time I got to Houston, I had already made up my mind. We wanted to give our baby the best chance possible."

Hagler gave birth almost nine weeks later on July 4, two weeks prior to her 34-week planned delivery date. "We named her Faith because at many points in our journey, it was faith that kept us going," she says. "When I think back about the surgery, even now, my lasting impression was of the outstanding care I received from the doctors. It was much more than a check-in, check-out relationship. It was genuine caring, and we've been singing their praises ever since."

Stephen Fletcher, DO

Associate Professor, Division of Pediatric Neurosurgery

Vivian L. Smith Department of Neurosurgery

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[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.*

Independence From Spina Bifida: Toward a Safe Method of Minimally Invasive Myelomeningocele Repair

In 2011, fetal surgeon KuoJen Tsao, MD, and pediatric neurosurgeon Stephen Fletcher, DO, were following the results of a landmark clinical trial, Management of Myelomeningocele Study (MOMS), which found that if a fetus undergoes surgery in utero to repair a spina bifida defect, serious complications could be reversed or lessened when compared to infants who underwent repair after birth. The study found that fetal surgery decreased the need for ventriculoperitoneal shunting for infants, and nearly half were able to walk without crutches by the age of 30 months.

Tsao, co-director of The Fetal Center at Children's Memorial Hermann Hospital and professor of pediatric surgery at McGovern Medical School at UTHealth, and his maternal-fetal medicine colleagues were in the process of screening patients for the study when Faith Hagler's parents, Ivan and Colette Hagler of Dallas, were referred to The Fetal Center. Based on the MOMS trial protocols, which included medical, psychological, and social criteria, the team determined that Hagler was an ideal candidate for the procedure.

After the fetal surgery, Hagler remained at Children's Memorial Hermann Hospital and delivered Faith almost nine weeks later on the Fourth of July, a date that Hagler describes as "so symbolic" of the independence her daughter has achieved since her birth. Faith began crawling at 11 months, took her first steps at 21 months, and today she's dancing.

The nine-year-old fetal surgery program at The Fetal Center continues to produce excellent outcomes with patients chosen based on the selection criteria established in the MOMS trial. The selection process for in-utero repair is based on a strict prenatal algorithm emphasizing education to prepare families to make an informed decision about treatment.

Designing a Regenerative Patch for In-Utero Repair

When skin closure of the spina bifida defect is not possible, a patch is needed. Fewer than half of the patients who undergo in-utero spina bifida repair with a patch show improvement in spinal cord function. For the past decade, maternal-fetal medicine specialists Ramesha Papanna, MD, MPH; Lovepreet K. Mann, MBBS, and their research team have been working to gain greater understanding of the lack of complete benefit after fetal surgery. They hope to improve the neurological outcomes of affected children through regenerative repair of the defect using a patch made of donated cryopreserved human umbilical cord (HUC).

"After investigating many types of patches in surgical animal models, we found that using a graft from human umbilical cord promotes regeneration of the protective layers around the spinal cord after surgery and improves neurological function," says Papanna, an associate professor of maternal-fetal medicine at McGovern Medical School. "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."

The researchers' work is based on preliminary data formulated in Papanna's lab. Their research led them to Scheffer C.G. Tseng, MD, PhD, a world-renowned surgeon in ocular surface reconstruction, who was using human amniotic membrane and umbilical cord donated by mothers of healthy infants to repair corneas. Tseng is chief scientific officer and co-founder of TissueTech, a biotechnology company based in Miami. The research team believes that 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.

Papanna's current research builds on his laboratory's experience with cryopreserved human umbilical cord for in-utero spina bifida repair. His findings have been published in multiple leading 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]

Made of the donated outer layer of the umbilical cord of healthy newborns, the patch has been used for repairs of severe defects in cases performed at Children's Memorial Hermann Hospital. All cases were approved by the U.S. Food and Drug Administration under expanded access, by The Fetal Center at Children's Memorial Hermann Hospital, and by the UTHealth Institutional Review Board prior to the surgeries. The patients underwent fetal surgery performed by Fletcher, an associate professor of pediatric surgery at McGovern Medical School, and Tsao. All patients have good lower-extremity motor and sensory function and have been able to walk.

"The HUC patch acts as a watertight scaffold, allowing native tissue to regenerate in an organized manner," says Mann, an assistant professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences. "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."

Mann says the research team is focusing on further improving outcomes by pushing the boundaries of fetal wound healing and improving outcomes 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.

Currently, the research team is working to find ways to encourage the skin to heal inside the uterus and different ways to deploy the patch over the defect site through less invasive means. "We've made progress at an incredibly rapid pace," Papanna 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 our 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. We're moving forward deliberately to answer every question and avoid the failures that have occurred in other programs."

"After investigating many types of patches in surgical animal models, we found that using a graft from human umbilical cord promotes regeneration of the protective layers around the spinal cord after surgery and improves neurological function."

Lovepreet K. Mann, MBBS

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

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[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.*

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Clinical Trials: Advances in Regenerative Patches for Spina Bifida Repair

Open In-Utero Repair of Severe Spina Bifida Using a Human Umbilical Cord Patch

Ramesha Papanna, MD, MPH, associate professor of maternal-fetal medicine at McGovern Medical School at UTHealth, is the clinical lead principal investigator in a multicenter study of open in-utero repair for severe spina bifida using a patch made of cryopreserved human umbilical cord (HUC). The patch, developed by TissueTech, a biotechnology company based in Florida, is widely used for ocular surface repair and chronic skin ulcers because its innate regenerative properties facilitate faster healing with minimal scarring.

Papanna and his research team have used the HUC patch successfully with patients through the U.S. Food and Drug Administration's Expanded Access Program, a pathway for people with life-threatening conditions or serious diseases to gain access to investigational medical products for treatment outside of clinical trials, when no satisfactory alternative therapy options are available.

"Cryopreserved human umbilical cord has anti-scarring, anti-inflammatory, and regenerative properties that makes it an effective substrate for wound healing," Papanna says. "These unique properties may eliminate the scar formation associated with traditional spina bifida repair methods and reduce the need for future surgeries for tethered spinal cord, a complication of the disorder. Preclinical data have shown that the patch promotes organized cell growth, resulting in a spinal cord repair that appears more normal with better function."

Spina bifida is the most common neural tube defect in the U.S., 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.

In addition to McGovern Medical School and The Fetal Center at Children's Memorial Hermann Hospital, 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; the University of California, San Francisco; and Cincinnati Children's Hospital Medical Center.

TissueTech will pay for all participant hospital expenses related to research, including the patch itself, travel expenses, and a follow-up MRI at 12 months. Although funding for the study will conclude at 12 months, the primary outcome date required for the FDA to approve the patch for clinical indications, data will be collected on participating patients for 30 months.

The study is the culmination of 10 years of research conducted by Papanna and Lovepreet K. Mann, MBBS, assistant professor of maternal-fetal medicine at McGovern Medical School, and their team. The researchers found that using a graft of the human umbilical cord after surgery for spina bifida could promote regeneration of the protective layers around the spinal cord and improve neurological function in animal models.

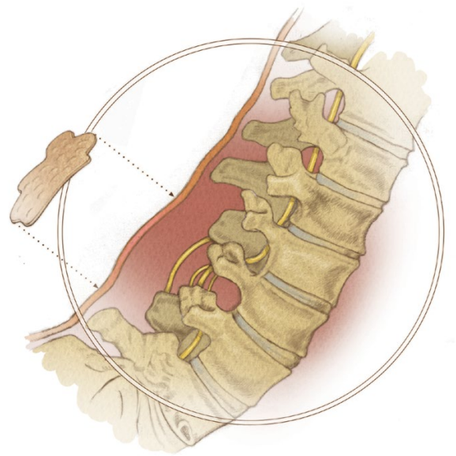
"HUC could be a game changer for spina bifida repair," Papanna says. "Our ultimate goal is to ensure that babies born with the disorder can walk and lead normal lives. We also think HUC will lead to new paradigms in fetal wound healing for other spinal defects and repairs."

Fetoscopic Spina Bifida Repair for Small Defects Using a Human Umbilical Cord Patch

Researchers at McGovern Medical School at UTHealth and Children's Memorial Hermann Hospital are now enrolling patients in a study to determine the feasibility of fetoscopic surgery to repair spina bifida and facilitate vaginal delivery. The single-center study is led by Ramesha Papanna, MD, MPH, 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 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 will repair the spina bifida defect in two layers through three small incisions in the uterus using fetoscopes and tiny surgical tools. The first layer will be closed using a 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 will undergo vaginal delivery, unless there is an obstetrical indication for delivery by C-section."

Developed by Amniox, the NEOX CORD 1K patch is made of cryopreserved umbilical cord and amniotic membrane. Extensive laboratory and clinical research on an ocular wound surface has shown that placental tissues help manage inflammation in wounds, facilitate cell proliferation and create an environment for tissue regeneration. NEOX CORD 1K has demonstrated consistently high closure rates in real-world experiences.



A patch is made from the donated outer layer of the umbilical cord of healthy newborns. When applied to the neural tube defect, the patch allows local tissue to grow at the repair site, which may help improve spinal cord function by reducing the effects of scar tissue.

The study, the first to use a meningeal patch to cover the spina bifida defect, will enroll 15 patients age 18 and older with a singleton pregnancy, a spina bifida 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 will be captured immediately after the repair, and efficacy of the fetoscopic repair will be assessed after birth by three blinded reviewers. 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 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.

"We have published promising preclinical data and have 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 NEOX CORD 1K patch optimizes long-term outcomes for these kids."

Innovation in Surgery for Unicoronal Craniosynostosis: Presurgical Preparation on a 3D Model Ensures Success in Two Cases

Raelynn Guidry in May 2020 after distraction surgery for unicoronal craniosynostosis. Inset: September 2019, two weeks before the procedure.

During the last two decades, treatment for craniosynostosis has evolved from procedures that produced relatively poor results to tailored cranial vault reconstruction and cranioplasty.

But unicoronal craniosynostosis remains challenging to treat because it affects the skull base, the middle cranial fossa, and the intrafacial fossa, the structure that houses the eyes.

"The classic presentation of unicoronal craniosynostosis is harlequin eye – one eye that is larger than the other," says Manish N. Shah, MD, FAANS, assistant professor in the Division of Pediatric Neurosurgery and director of pediatric spasticity and epilepsy surgery at McGovern Medical School at UTHealth. "The standard surgery is fronto-orbital advancement, an open cranial vault procedure that involves cutting the bones of the skull into pieces and putting them together with plates and screws to push the affected side of the skull forward. Across all centers in the U.S., this is the most common procedure, and it is appropriate for older children from 8 to 12 months of age. The surgery works to a variable degree, but when you look at these kids a year later, the result is not as good as it could be."

The advent of the endoscope allowed surgeons to use smaller incisions to access the cranial sutures. "Endoscopic-assisted surgery has been used for more than 20 years in the craniofacial skeleton with some degree of success in children who are 3 to 6 months of age," says Phuong Nguyen, MD, assistant professor of surgery and director of craniofacial surgery in the Division of Pediatric Plastic Surgery at McGovern Medical School. "The bones are much softer at that age and the brain is growing exponentially. We can take advantage of that time of life by removing the abnormal or fused suture and fitting the infant with a cranial modeling helmet for two months to a year, depending on the patient. But our ultimate goal is a better result than what cranial vault remodeling provides and a much better patient experience."

In 2019, the two physicians were approached by mothers of two girls born with unicoronal craniosynostosis; both families were looking for alternatives to the cranial vault procedure and the prospect of wearing a helmet 23 hours a day. Nguyen and Shah offered them a newer, innovative option.

Raelynn Guidry

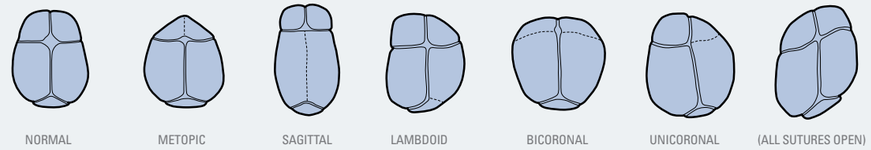
When Raelynn was 10 days old, her mother, Danielle Guidry, BS, RN, NCM, looked down at her daughter from above and noticed a ridge on the right side of her head. A case management nurse in Louisiana, Guidry suspected craniosynostosis.

"My pediatrician confirmed it, but I had no idea where to go," she says. "That evening my sister told me her best friend's son had a rhizotomy for cerebral palsy in Houston, and they were happy with the result and the experience they had."

The friend's surgeon was Shah, the leading neurosurgeon in the region for selective dorsal rhizotomy and an expert in pediatric epilepsy, craniofacial surgery, and craniocervical spine surgery. Guidry texted Shah's office and the following day, July 3, 2019, she, Raelynn, and her husband, Andy Guidry, made the four-hour drive to Houston. They saw Shah and his team, followed by Nguyen and his team. The two surgeons ordered a CT scan and asked the family to give them time to consult.

"After we saw Raelynn, I talked with Dr. Shah about a relatively new minimally invasive procedure for unicoronal craniosynostosis," Nguyen says. "We were upfront with the family and told them that we'd done parts of the surgery

What Is Craniosynostosis and When Is Surgery Necessary?



One in 2,500 infants per year is born with craniosynostosis, a relatively rare birth defect of the skull marked by premature closure of one or more of the cranial sutures, the fibrous joints between the bones of the skull. The most common manifestation of the defect is the closure of a single suture.

The sutures allow the baby to exit the birth canal, and continue to mold after birth. The infant's brain grows exponentially in the first year of life, and normally the skull expands uniformly to accommodate the growth. Premature closure of a single suture restricts the growth in that part of the skull, allowing for growth in other parts of the skull where the sutures remain open. While the brain may continue to develop normally, closure of one suture results in a misshapen skull. If many sutures are fused, the skull cannot expand to accommodate the infant's growing brain.

The most apparent sign of craniosynostosis is an abnormally shaped skull. Other signs may include increased intracranial pressure, developmental delays, or impaired cognitive development caused by restriction of brain growth.

More than half of all cases of craniosynostosis involve the sagittal suture, which runs from a spot in the front of the head to the back of the skull. Fusion of the suture results in a long, narrow skull with or without bulging of both the front and the back of the head. Metopic craniosynostosis results in a narrow, triangular forehead with lateral pinching of the temples. There are two coronal sutures that begin at the ear and continue to the top of the skull, where they join the sagittal suture. When one is fused, there is compensatory growth on the other side of the skull. Coronal craniosynostosis may involve one or both coronal sutures.

Unicoronal craniosynostosis – one fused coronal suture – results in a flattened forehead on the affected side, with the classic presentation of harlequin eye – one larger eye. When both coronal sutures are affected, the presentation is a short, wide head with bulging of the eyes. Brain growth may be restricted.

Treatment for craniosynostosis consists of surgery performed by a pediatric plastic/craniofacial surgeon and pediatric neurosurgeon to improve the symmetry and appearance of the head and to relieve pressure on the brain and cranial nerves. The neurosurgeon opens the skull and exposes the area where the plastic surgeon will remove the bones, reshape them and put them back into place. The combined expertise of the two surgical specialties produces optimal results.

For decades, the only surgery was open, with an incision from ear to ear, called cranial vault remodeling or cranial vault reconstruction. It involves removal of bone by a neurosurgeon to free the area that has been restricted in growth, and is still the most common procedure for older children from 8 to 12 months of age in most centers across the U.S. When craniosynostosis is diagnosed early, between 3 and 6 months of age, treatment options include minimally invasive procedures that mean less scarring, less blood loss, less patient discomfort, and shorter hospital stays than the traditional corrective cranial vault surgery.

Manish N. Shah, MD, FAANS

Director of Pediatric Spasticity and Epilepsy Surgery

Director of Texas Comprehensive Spasticity Center

Assistant Professor, Department of Pediatric Surgery Division of Pediatric Neurosurgery

McGovern Medical School at UTHealth

Phuong Nguyen, MD, FACS, FAAP

Assistant Professor and Director of Craniofacial Surgery, Division of Pediatric Plastic Surgery

McGovern Medical School at UTHealth

before, but had never used it for this particular application. They said they were willing to take the journey with us."

The surgery they proposed involved the use of a distractor, a controlled instrument that very slowly pulls apart the bone to create space. As new bone grows in, it remodels the skull. "We've used the procedure often for children with bicoronal craniosynostosis and based on the limited experience of physicians at two other centers, we wanted to apply it to unicoronal craniosynostosis for better skull shape and cosmetic results," Shah says. "Because we're moving the bones slowly, the resulting symmetry is better. Later we remove the distractor in a small surgery. The skull correction is done at a much earlier age than with the open cranial vault surgery, it's much less invasive, and the children won't need a later surgery."

Manish N. Shah, MD, left, and Phuong Nguyen, MD, prepare for distractor surgery using a 3D model they designed and had printed at UTHealth.

Precision Through 3D Modeling

Using the CT scans of Raelynn's skull, the two surgeons designed a 3D model and had it printed at UTHealth. They performed the surgery on the model skull the day before they took Raelynn to the OR, which allowed them to plan and fine tune the incisions they would make.

"We operate and wait two to three days to begin turning the distractor, which slowly ratchets the bones out," Shah says. "After a period of about a month, on average, the distractor has done its work."

Raelynn was discharged on the third day following surgery, after her parents made the first turn of the distractor at 7 a.m. on the day she was released. The Guidrys made two turns twice a day for a total of 100 turns of the distractor over 25 days, resulting in 33 millimeters of movement.

"We're very happy with the results. We didn't want a second surgery or a helmet," says Danielle Guidry, who posted the family's experience on a closed craniosynostosis Facebook page, thanking her friends for their support. Among those who commented was Marisa Medlin, who asked for the names of her surgeons. She was excited to learn that Raelynn's surgeons were the same doctors she and her family had met with the day before.

Kate Medlin

Marisa Medlin noticed that her daughter Kate's nose was crooked while she was nursing during her first month of life. When she was one month old, Kate was referred to a pediatric ENT, who saw no reason for concern. At her 4-month visit, it was apparent that the facial asymmetry had not corrected itself, and her pediatrician referred the family to Nguyen at UTHealth.

"As soon as he saw her, he recognized the signs of craniosynostosis, and a CT scan confirmed it," says Medlin, who lives in Magnolia, Texas, about an hour north of the Texas Medical Center, where Nguyen and Shah practice. "I had never heard of craniosynostosis and was trying to learn as much as I could about Kate's diagnosis. One source of information was a craniosynostosis Facebook group, which I joined. I happened to see Danielle's post that her daughter was about to have surgery for right unicoronal craniosynostosis with Shah and Nguyen. I was so excited to connect with her because her daughter had the same diagnosis as Kate and was having the same procedure with the same doctors we were considering. I messaged her immediately and we have been in constant communication since then."

Medlin had done enough research to know that undergoing cranial vault remodeling was not the ideal solution for Kate. "It's a very invasive procedure, an eight- to nine-hour surgery requiring a blood transfusion and a five-night stay in the hospital," she says. "The thought of this major surgery being performed on our 5 month-old baby was very scary for us. Dr. Nguyen told us there was a newer, less invasive procedure that had shown good long-term results. He talked with me about the distraction technique and told me that he and Dr. Shah were performing their first distraction surgery for unicoronal craniosynostosis the following Friday. That was Danielle's baby."

Kate's right coronal suture was fused. "The right side of her head was not growing and the left side was," she says. "The bridge of her nose was being pulled to the right, and her right eyebrow was raised. She had a perpetual surprised look on her face. We had to make the decision about whether to do the standard but invasive procedure or decide if we were willing to take a chance on a new surgery they had done only one time before us. When Dr. Nguyen told me they would use her CT results to create a 3D printed version of the skull and perform the surgery beforehand, we felt better about it. In the end, we felt it was the right choice for Kate and our family."

After the surgery to place a distractor, the Medlins turned the device twice a day for 25 days, moving the right front portion of Kate's skull forward. They stopped turning the distractor on Nov. 2, and left it in place for two more months to allow new bone growth to fill the gap. It grew faster than expected, and Nguyen removed the distractor two weeks early on Jan. 6, 2020.

Friendship Forged Through Shared Experience

Parents of children with craniosynostosis go to great lengths to find the best possible center for treatment. They do their research, and they're willing to travel.

"After Danielle and I found each other, we texted or spoke every day about what our daughters were going through," Medlin says. "It was so comforting for me to talk with another mom who was going through the exact same process that we were going through. I am so incredibly grateful to have met her and to have had her to lean on through this experience."

The two families met in person in late December 2019 at Santa's Wonderland in College Station, Texas, where both had planned family holiday outings.

"Marisa and I still text at least every other day," Guidry says. "In my eyes, our meeting was divine intervention. Everything aligned perfectly. We couldn't have gotten to where we are without God sending us where we needed to go. Giving us a friend was putting the cherry on top. People who haven't gone through craniosynostosis can never really understand."

Guidry has been a nurse for a decade. "I've been all over Louisiana, and I have never met physicians like Dr. Nguyen and Dr. Shah," she says. "Not many doctors will give you their cell phone numbers and email addresses. They saw us on their off days and came to the hospital when they knew we were in Houston for a checkup or a procedure. When we were in the hospital, they rounded two or three times a day. They don't disregard anything you say. No matter what emotions you're experiencing, they understand and empathize."

Marisa and Shawn Medlin with their daughter Kate, who benefited from a new minimally invasive procedure for unicoronal craniosynostosis.

Medlin is happy that things turned out the way they did. "We're so thankful that Dr. Nguyen and Dr. Shah were willing to challenge the status quo and perform an innovative procedure that we feel was the best choice for our daughter," she says. "Kate looks amazing! We're so happy with her result and so incredibly grateful to Dr. Nguyen and Dr. Shah. In our eyes, they're rock stars. They went above and beyond through this entire process to make sure all of our questions were answered and that we felt as comfortable as possible. We hope to help spread awareness of this treatment option to other families who find themselves in the same situation we were in."

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

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

Professor, Departments of Pediatric Surgery and Neurosurgery

Dr. Marnie Rose Professor in Pediatric Neurosurgery

McGovern Medical School at UTHealth

Director of Pediatric Neurosurgery

Children's Memorial Hermann Hospital and Mischer Neuroscience Institute

The outlook for children with recurrent malignant brain tumors originating from the posterior fossa is extremely poor. Most clinical trials offer systemic chemotherapy or re-irradiation, both of which can have serious side effects and most often fail in children with recurrent tumors. In three single-center studies under way at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth, researchers are investigating novel therapies with the potential to improve outcomes for children with fourth ventricular brain tumors, while avoiding systemic toxicity.

These studies are led by David Sandberg, MD, FAANS, FACP, FAAP, professor of pediatric neurosurgery at McGovern Medical School and UTHealth Neurosciences, and director of pediatric neurosurgery at Children's Memorial Hermann Hospital. "Despite the advances that have been made in pediatric neuro-oncology, we are still seeing too many children die of malignant brain tumors," says Sandberg, who holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery at UTHealth. "The treatments currently available are not satisfactory for children. We believe we can do better."

Clinical Trial of High-Dose MTX110 (Soluble Panobinostat) Begins After Safe Administration into the Fourth Ventricle in a Non-Human Model

A novel clinical trial of MTX110, a new formulation of soluble panobinostat from Midatech Pharma, is now enrolling patients. 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 are often associated with considerable toxicity, and when tumors recur despite these treatments, survival rates are low.

"The current treatments for children and adults with medulloblastoma are inadequate," says Sandberg. "Children have low survival rates despite salvage therapy, and novel approaches are needed. This is a new trial of a novel drug, and we are very hopeful that we can help patients overcome this devastating disease."

The clinical trial follows a successful study led by Sandberg 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 study team at Children's Memorial Hermann Hospital and McGovern Medical School found no neurological deficits after fourth-ventricle infusions.

"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, the most common malignant brain tumor in children," 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 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.

The study is listed at clinicaltrials.gov at https://clinicaltrials.gov/ct2/show/NCT04315064. For more information, please contact Bangning Yu, MD, PhD, at bangning.yu@uth.tmc.edu or 713-500-7363.

[1]*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 non-human primate model. J Neurosurg: Pediatr. 2020 May 1:1-9. [Epub ahead of print]*

David Sandberg, MD, is now enrolling patients in three clinical trials of novel therapies with the potential to improve outcomes for children with fourth ventricular brain tumors.

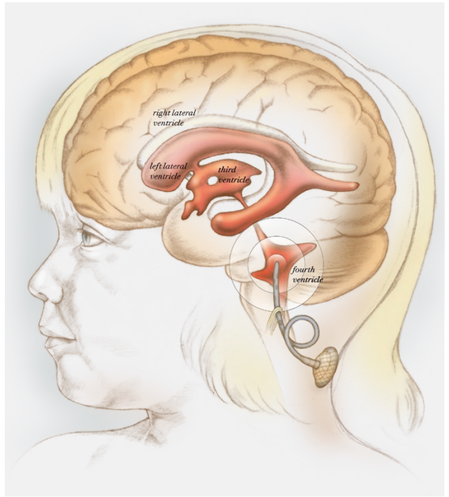
Combination Intraventricular Chemotherapy Pilot Study and Infusion of 5-Azacytidine

Two additional clinical trials of infusions into the fourth ventricle or resection cavity of children with brain tumors are currently enrolling at McGovern Medical School at UTHealth and Children's Memorial Hermann Hospital. Both build on translational models of direct infusion of chemotherapy into the fourth ventricle of the brain in animal models, developed by Sandberg. Neither involves 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."

The other trial involves infusion of 5-Azacyti-



Sandberg's research focuses on infusions of chemotherapeutic agents directly into the fourth ventricle or resection cavity of children with malignant brain tumors to avoid systemic toxicity.

dine (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.

"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. Moreover, 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 study is open to patients age 1 to 21 years old with recurrent ependymoma that originated in the posterior fossa of the brain.

If you have questions about the clinical trials or would like more information about enrollment, contact Bangning Yu, MD, PhD, at bangning.yu@uth.tmc.edu or call 713-500-7363.

[1]*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 Non-human Primate Model. J Neurosurery: Pediatrics. [In press]*

Nanotechnology for Drug Delivery: The Science of Moving Chemotherapeutic Drugs Directly to 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. Most clinical trials offer systemic chemotherapy or radiation therapy, both of which have side effects and often fail in children with recurrent tumors. Bioengineer and research scientist Rachael Sirianni, PhD, aims to change that by bringing novel nanomedicine approaches to the clinic to improve outcomes.

"There are many drugs available to treat brain tumors, but most don't go directly to the site where they provide the most benefit," says Sirianni, an assistant professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth and faculty member of MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences. "My science is the science of drug delivery and understanding ways to circumvent these barriers."

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 in between the spaces of the tumor's vasculature, such that they 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. However, there are some kinds of tumors and parts of tumors that do not receive a good blood supply. Delivery to these kinds of tumors remains a major challenge."

To address this challenge, Sirianni and her team are working on novel approaches. "Pediatric brain tumors have a tendency to metastasize along the surfaces of the brain and spinal cord. This is called leptomeningeal metastasis, and it remains very difficult to treat," she says. "Instead of delivering nanoparticles intravenously, we're working toward administering them directly to the cerebrospinal fluid that moves across these lesions to deliver more drug with less overall toxicity. Currently we're focused on 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.

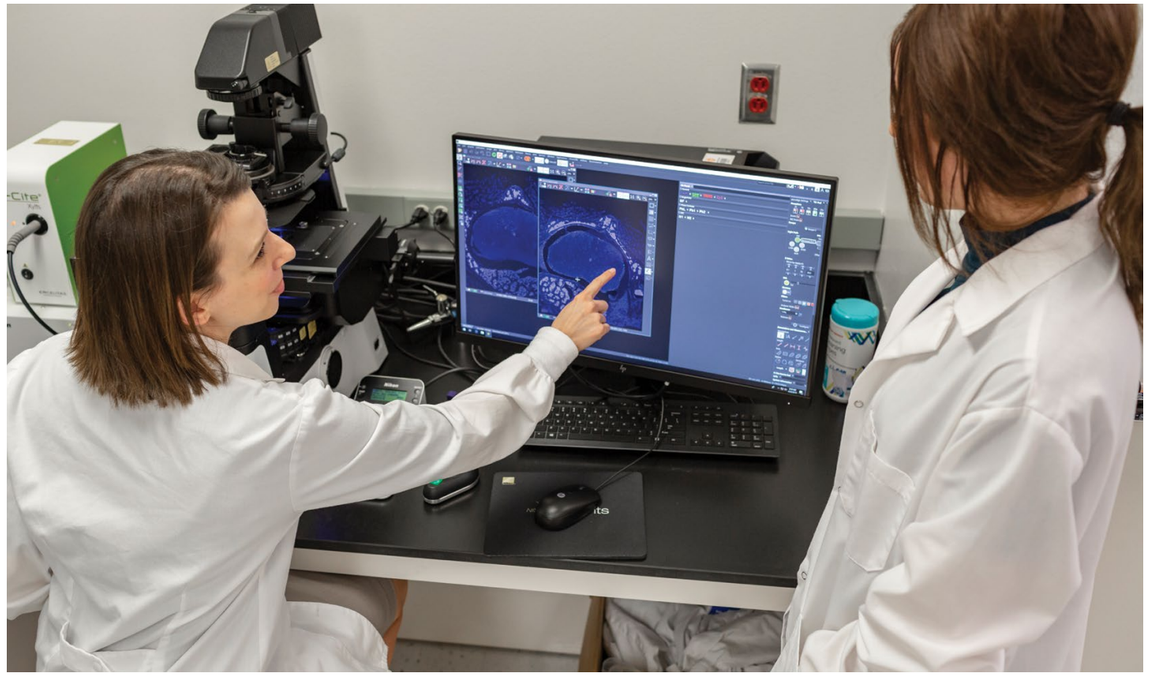
In May 2019 Sirianni was awarded a five-year, $2.7 million R01 grant by the National Institute of Neurological Disorders and Stroke to tackle exactly this problem: designing nanoparticles that can target drug delivery to leptomeningeal metastasis in pediatric medulloblastoma. Her laboratory will evaluate the safety and efficacy of these new approaches, as well as test whether delivery of drugs from nanoparticles can reduce the radiation dose needed to treat metastases.

In July 2019, Sirianni 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.

"High-dose craniospinal radiation damages a child's developing nervous system, and few other treatment options are available once malignant cells have metastasized to the leptomeninges," she says. "Our preliminary data demonstrate that intrathecally administered histone deacetyle inhibitor quisiwnostat distributes readily across brain and spinal cord surfaces and localizes to slow the growth of leptomeningeal metastasis in medulloblastoma. We expect these studies to advance new nanotechnology toward the clinic for better treatment of pediatric brain tumors." ☼

Rachael Sirianni, PhD
Assistant Professor,
Vivian L. Smith Department of Neurosurgery
McGovern Medical School at UTHealth

With funding from the NIH, Rachael Sirianni, PhD, and her team are moving toward delivering nanoparticles directly to the CSF to deliver more drug to brain tumors with less toxicity.



News of Note

Dr. David Sandberg Receives the American Association of Neurological Surgeons Humanitarian Award

David I. Sandberg, MD, FAANS, FACS, FAAP, has received the American Association of Neurological Surgeons 2019 Humanitarian Award, one of the highest honors bestowed by the organization. The award recognizes his extraordinary work with children suffering from neurosurgical disorders throughout the world.

The award recognizes Sandberg's extraordinary work with children suffering from neurosurgical disorders throughout the world.

Sandberg is professor and director of pediatric neurosurgery at McGovern Medical School at UTHealth, where he holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery. He is also director of pediatric neurosurgery at Children's Memorial Hermann Hospital and Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center, as well as co-director of the Pediatric Brain Tumor Program at MD Anderson Cancer Center. Fellowship trained in pediatric neurosurgery with a special clinical and research interest in pediatric brain tumors, Sandberg specializes in minimally invasive endoscopic approaches to brain tumors, hydrocephalus, and arachnoid cysts, as well as surgical management of arteriovenous malformations of the brain, congenital spinal anomalies, Chiari malformations, and craniofacial anomalies. The recipient of numerous research grants, he is currently principal investigator of three single-center trials at Children's Memorial Hermann Hospital and McGovern Medical School investigating direct administration of chemotherapy into the fourth ventricle for treatment of malignant brain tumors that originate from that ventricle.

Sandberg is a magna cum laude graduate of Harvard University. He received his medical degree at the Johns Hopkins University School of Medicine and completed neurosurgery training at Weill Medical College of Cornell University/New York-Presbyterian Hospital. During residency, he was awarded the Resident Traveling Fellowship in Pediatric Neurosurgery by the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, which he completed at the Hospital for Sick Children in Toronto, Canada. He completed pediatric neurosurgery fellowship training at the Children's Hospital in Los Angeles. Before joining McGovern Medical School, Sandberg was an associate professor of clinical neurological surgery and pediatrics at the University of Miami Miller School of Medicine.

He began his medical mission work in high school and college, accompanying his father, Miami ophthalmologist Joel Sandberg, MD, on trips to Jamaica, Antigua, and the Dominican Republic. His father was his inspiration to practice medicine and also to contribute to the health of the world through international mission work.

As a junior neurosurgery resident, Sandberg made two trips to Guatemala with Neil Feldstein, MD, director of the Division of Pediatric Neurosurgery at Columbia University Medical Center/New York-Presbyterian Hospital, performing surgery on children with spina bifida. As a resident in neurosurgery, he used his vacation time to spend a month in Tegucigalpa, Honduras. There, with the help of Mark Souweidane, MD, director of pediatric neurosurgery at Weill Cornell Brain and Spine Center, he brought an 8-year-old girl with a brain tumor to the U.S. for treatment. She was the first of several patients he brought to the U.S.

Sandberg has been on the Board of Directors of the Foundation for International Education in Neurological Surgery (FIENS) since 2004 and served as secretary of FIENS from 2013 to 2018. Through FIENS, he made multiple neurosurgical humanitarian trips to Honduras, Peru, and Guatemala. In 2006, he traveled to Uganda with CURE International.

Since 2007 he has worked with Project Medishare, a Miami-based nonprofit organization with a 20-plus-year history of empowering Haitians to provide quality health care through community-based, Haitian-led programs. Through medical volunteers, the organization treats more than 180,000 people annually. Sandberg leads a team of pediatric neurosurgeons, pediatric anesthesiologists, nurses, and surgical scrub technologists from Children's Memorial Hermann Hospital and McGovern Medical School; they make the trip annually.

"Education is a major focus for all of our mission trips to Haiti," he says. "We work with a local neurosurgeon, Dr. Yudy Lafortune, to teach him modern neurosurgical care for pediatric patients. This is the 'teach-a-man-to-fish' concept. We're training Dr. Lafortune to be the pediatric neurosurgeon for the children of Haiti."

Sandberg grew up in a family with a strong commitment to public service. "I think how lucky I am to have been born into my family in the United States, and to be able to contribute in a small way to helping children in other countries," he says. "This award is a huge honor for me, and I'm humbled to receive it."

Dr. Rachael Sirianni Named UTHealth Women Faculty Forum Rising Star

Rachael Sirianni, PhD, was recognized with the 2019 Rising Star Award given by the Women Faculty Forum at McGovern Medical School at UTHealth. The excellence awards reception was held Oct. 7, 2019.

Trained as a biomedical engineer in the field of polymeric drug delivery, Dr. Sirianni earned her PhD from Yale University in 2008, and completed a postdoctoral fellowship in diagnostic radiology at the Yale School of Medicine.

Sirianni's research program, which has received funding from the Department of Defense and the National Institutes of Health, has designed creative approaches for treating central nervous system disease via encapsulation and tissue-specific delivery of drugs from polymeric nanoparticles. She also has developed biomaterial approaches for studying and manipulating the behavior of cells in engineered microenvironments mimicking the brain. These approaches have demonstrated preclinical success in applications ranging from neuro-oncology to neurodegeneration and neural engineering.

Sirianni's research methods are poised to make a significant impact in the field of pediatric neuro-oncology. Her goal at UTHealth is to develop nanoparticle systems that can effectively treat central nervous system infiltration and metastasis in children affected by recurrent malignant brain tumors.

Her professional accomplishments include invitations to speak at major research conferences, service on an NIH study section, book editorship, and extensive publications in the fields of biomaterials, drug delivery, and imaging.

The Women Faculty Forum at McGovern Medical School advocates on behalf of women faculty, provides opportunities for professional development, and offers an opportunity for networking among women faculty, as well as with leaders in academic science and medicine within and outside the institution.

Manish N. Shah, MD, and physical therapist Christy Hill see patients in the Texas Comprehensive Spasticity Center's multidisciplinary clinic.

Experts Discuss Innovative Treatment Options for Cerebral Palsy

About 50 parents, family members, and children with cerebral palsy, as well as occupational therapists and physical therapists, attended a seminar on innovation in cerebral palsy treatment at the John P. McGovern Museum of Health and Medical Science in Houston last October. Sponsored by UTHealth Neurosciences and Children's Memorial Hermann Hospital, the seminar featured informational talks by experts at the Texas Comprehensive Spasticity Center, who are faculty members at McGovern Medical School at UTHealth. Therapists received continuing education credits, and all attendees were invited to explore The Health Museum following the seminar and lunch.

Speakers were Manish N. Shah, MD, FAANS, director of pediatric spasticity and epilepsy surgery and an assistant professor in the Department of Pediatric Surgery, Division of Pediatric Neurosurgery; Stacey Hall, DO, an assistant professor in the Department of Physical Medicine and Rehabilitation; and Nivedita Thakur, MD, assistant professor in the Department of Pediatrics, Division of Neurology.

Children with spasticity, movement disorders, or cerebral palsy have complex care needs and typically see multiple providers for different opinions before parents make a treatment decision. In the process they lose valuable time and, in many cases, suffer irreversible damage. Experts at the Texas Comprehensive Spasticity Center aim to end the cycle of referral from specialist to specialist by providing carefully coordinated multidisciplinary care in a single location.

The Center is a collaboration of UTHealth Neurosciences, Children's Memorial Hermann Hospital, and McGovern Medical School. Shah is the leading neurosurgeon in the region for selective dorsal rhizotomy and also is an expert in pediatric epilepsy, craniofacial surgery, and craniocervical spine surgery. Thakur is fellowship trained in adult and pediatric movement disorders and pediatric neurology. Hall provides care for children with cerebral palsy, spasticity and dystonia, and myelomeningocele, as well those who have other activity and participation limitations. ☼

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