The Fetal Center

FIVE-YEAR REPORT

UTHealth
McGovern Medical School
The University of Texas Health Science Center at Houston

Children's Memorial Hermann Hospital

UT Physicians
A Part of UTHealth

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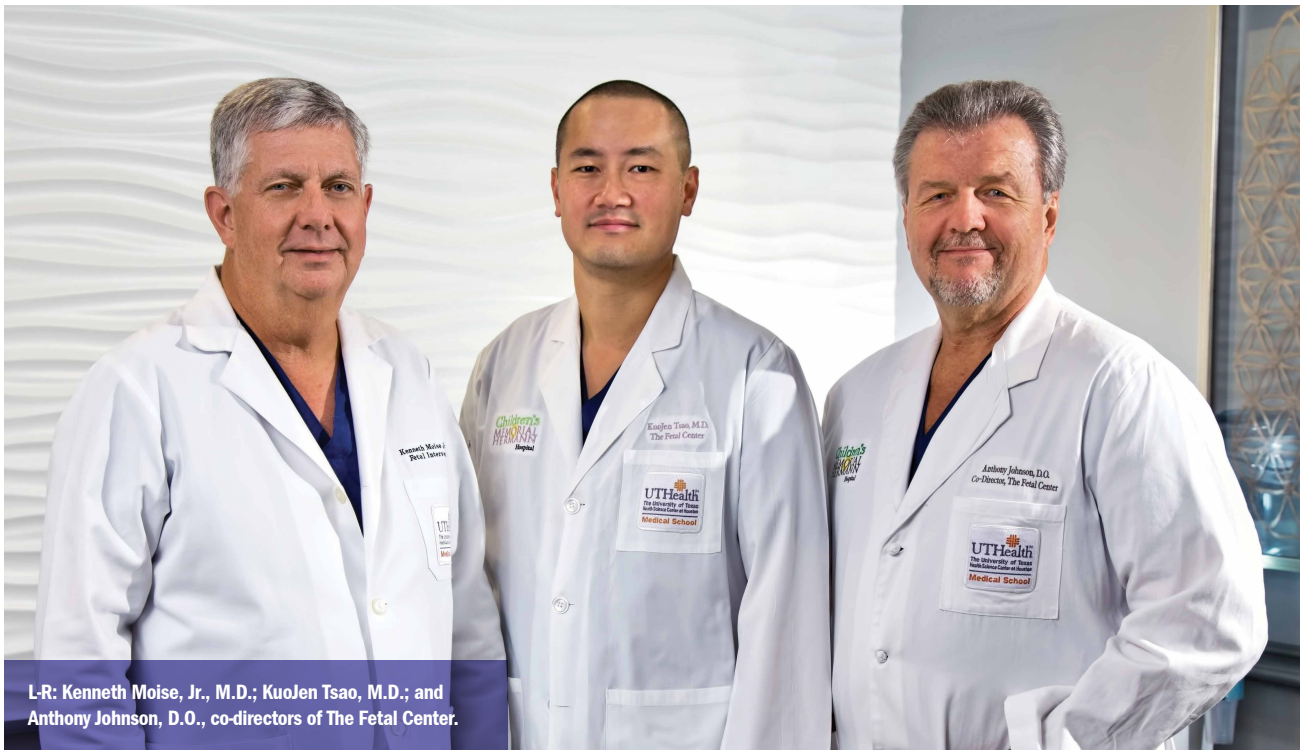
Introduction

Dear Colleagues and Friends,

September 2016 marked the fifth anniversary of The Fetal Center at Children's Memorial Hermann Hospital, affiliated with the physicians at McGovern Medical School at UTHealth. In 2011, we began the initiative to develop an outstanding multispecialty group to serve the maternal-fetal needs of mothers, their families and their referring physicians, building on strong clinical and research programs in neonatology, maternal-fetal medicine, pediatric surgery, neurosurgery, fetal and pediatric cardiology, orthopedics, plastic surgery, radiology, nephrology, urology and anesthesiology.

Since that time, The Fetal Center has evolved into a national and international leader in fetal diagnosis, fetal intervention and comprehensive fetal care for infants with congenital anomalies or genetic abnormalities. The Fetal Center's affiliated physicians are faculty members at McGovern Medical School and specialists in the field, actively pursuing and participating in research to develop new therapeutic prenatal interventions aimed at improving our patient outcomes, which are well above the national expected benchmark as shown in this report.

A leader in research, The Fetal Center is one of only three U.S. centers to hold membership in all three key maternal-fetal research networks: the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network, NICHD's Maternal-Fetal Units (MFMU) Network and the North American Fetal Therapy Network (NAFTNet).



L-R: Kenneth Moise, Jr., M.D.; KuoJen Tsao, M.D.; and Anthony Johnson, D.O., co-directors of The Fetal Center.

We are pleased to share with you The Fetal Center five-year report, which highlights our ongoing efforts in clinical quality, patient safety and outcomes, patient education and research. In addition, our focus on innovation, quality outcomes and physician education continues to attract outstanding physician faculty members to The Fetal Center and McGovern Medical School. At the same time, we have expanded our capability to treat fetal disease through the addition of new technology, leading-edge procedures and clinical trials of therapies that otherwise would be unavailable to our patients. A strong basic science research program aims to bring innovative therapies from the bench to the bedside quickly.

We are especially grateful to our donors for providing philanthropic support, which allows us to continue to lead clinical care and research and make a difference in the lives of our families through patient-assistance programs. **If you would like more information about our programs, visit childrens.memorialhermann.org/thefetalcenter or contact us directly at 832.325.7288.**

With best wishes,

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Professor, Department of Pediatric Surgery
Director, Fetal Intervention Fellowship Program
McGovern Medical School at UTHealth

KuoJen Tsao, M.D.
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Chief, Division of General & Thoracic Pediatric Surgery
Associate Professor, Department of Pediatric Surgery
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Anthony Johnson, D.O.
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About Children's Memorial Hermann Hospital

For more than three decades, Children's Memorial Hermann Hospital has provided superior health care to infants, children, adolescents and women, serving patients and their families in the Greater Houston area and beyond.

310 TOTAL
CHILDREN'S AND WOMEN'S BEDS

5,500+
BABIES DELIVERED ANNUALLY

118
NICU beds (Level II & IV)

116
Pediatric Intensive Care & Intermediate Care beds

76
Women's Center beds

5,800
PEDIATRIC SURGERIES PERFORMED ANNUALLY
(Texas Medical Center campus)

Children's Memorial Hermann Hospital serves the global community as the primary teaching hospital for the Department of Pediatrics and the Department of Obstetrics, Gynecology and Reproductive Sciences at McGovern Medical School at UTHealth. Through this unique collaboration, the specialized physicians at McGovern Medical School conduct and participate in research programs to advance medicine as well as care for patients at our facility and affiliated clinics. Our academic partnership with McGovern Medical School is essential in our mission to provide comprehensive patient care, offering patients access to state-of-the-art technology and clinical trials, and the most advanced treatment therapies, including highly specialized, technically challenging surgeries.

40+ SPECIALTY PROGRAMS

Located in the Texas Medical Center, Children's Memorial Hermann Hospital is a 310-bed quaternary care hospital for women and children.

As part of the Memorial Hermann Health System, Children's Memorial Hermann Hospital has access to clinical resources, perspective and knowledge that differentiate it from other hospitals in the region. Affiliated physicians practice evidence-based medicine with a relentless focus on quality, patient safety and exceptional end-to-end care experiences, efforts that continue to lead to national awards and recognition.

19,000

EMERGENCY DEPARTMENT VISITS PER YEAR

Busiest **Level I Trauma Center** – designated for both children and adults – capable of caring for **entire family** in the same facility.

230+

ACTIVE RESEARCH PROJECTS

Over 230 active research projects and more than **$40 million** invested in research trials, aimed to deliver innovative solutions that create the best hope for a healthier future for children and women.

Nearly **50** YEARS

ACADEMIC AFFILIATION WITH UTHEALTH

A unique clinical collaborative with UT Physicians and McGovern Medical School at UTHealth, the most comprehensive academic health center in the U.S. Gulf Coast region.

To learn more about Children's Memorial Hermann Hospital, visit us online at childrens.memorialhermann.org.

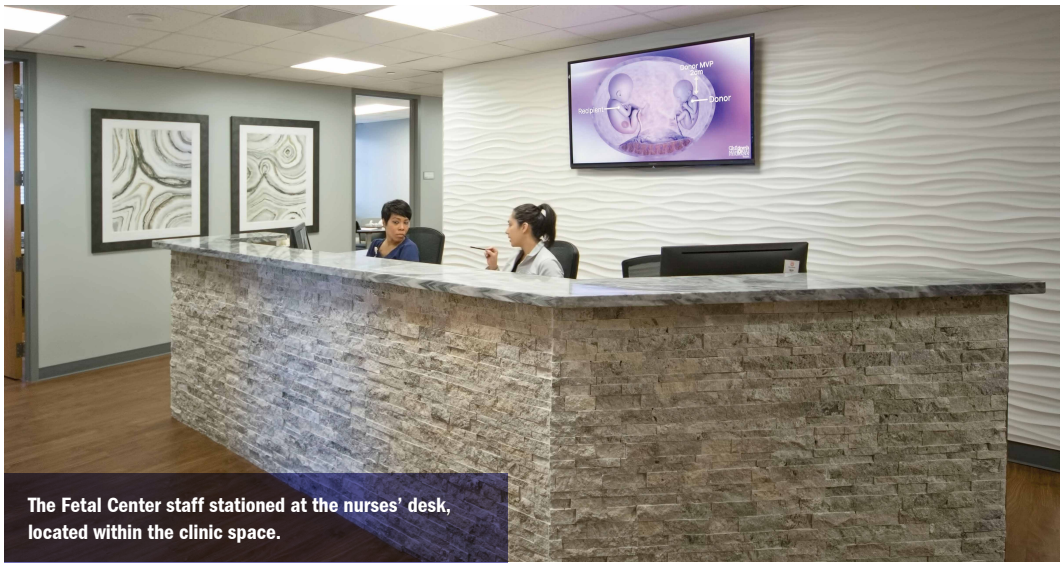
Children's Memorial Hermann Hospital is located within Memorial Hermann-Texas Medical Center.

About The Fetal Center

The Fetal Center at Children's Memorial Hermann Hospital is a national referral center and an international leader in comprehensive fetal care.

Located within the UT Physicians Professional Building in the Texas Medical Center, The Fetal Center is affiliated with Children's Memorial Hermann Hospital and the physicians at McGovern Medical School at UTHealth. The Fetal Center's affiliated physicians offer patients the full array of prenatal testing and fetal interventions through a coordinated program for mother and baby before, during and after birth. From the initial prenatal consultation through pediatric follow-up visits, specialists at The Fetal Center work closely with mothers, families and their referring physicians to provide evidence-based care and treatment, as well as provide support, counseling and education.

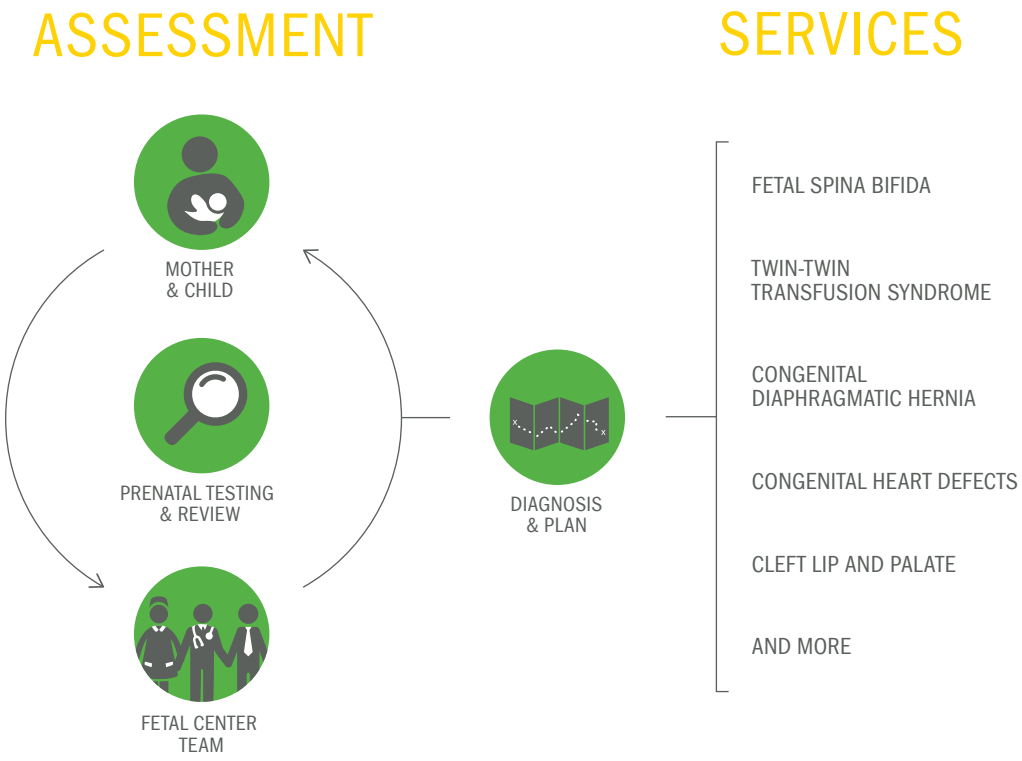
The Fetal Center clinic, located within the UT Physicians Professional Building, is accessible from Children's Memorial Hermann Hospital by a skywalk connecting the two buildings in the Texas Medical Center.



The Fetal Center staff stationed at the nurses' desk, located within the clinic space.

The Fetal Center's affiliated physicians excel in the treatment of a wide range of complex fetal conditions, some of which are highlighted in this report. Through the academic partnership between McGovern Medical School and Children's Memorial Hermann Hospital, the affiliated physician researchers at The Fetal Center are actively engaged in research programs focused on the mechanisms, treatment and cure of fetal disorders. Clinical trials currently in progress cover the scope of prenatal conditions and treatments, including spina bifida, regenerative stem cell therapies, laser surgery for Stage I twin-twin transfusion syndrome, and the fetoscopic endoluminal tracheal occlusion (FETO) trial for congenital diaphragmatic hernia.

A comprehensive, personalized plan of care is developed for each patient, and the team of affiliated specialists identifies potential risk factors and early complications for both mother and baby. After initial prenatal testing, patient families meet with a maternal-fetal medicine specialist to review results and learn more about their particular diagnosis. A dedicated nurse coordinator ensures that all care remains centered around the patient.



To learn more about The Fetal Center and the clinical services provided, visit childrens.memorialhermann.org/thefetalcenter.

Meet The Fetal Center Team

The Fetal Center team is an interdisciplinary group of medical experts and care coordinators brought together to provide the most comprehensive care for mothers and their babies.

They work in tandem to create the best treatment plan and provide excellent medical care for mothers and infants before, during and after delivery.

The Fetal Center is comprised of neonatal and pediatric specialists in the fields of maternal-fetal medicine, fetal cardiology, heart surgery, pediatric cardiology, pediatric surgery, neonatology, neurosurgery, nephrology, orthopedic surgery, plastic surgery, urology, radiology, anesthesiology, chronic and palliative care, certified genetic counseling and sonography as well as spina bifida specialists, dedicated nurse coordinators and follow-up care coordinators.

L-R: Saul Snowise, M.D.; Roopali Donepudi, M.D.; Ramesha Papanna, M.D.; Helena Gardiner, M.D., Ph.D.; Kenneth Moise, Jr., M.D.; Gurur Biliciler-Denktas, M.D.; KuoJen Tsao, M.D.; Anthony Johnson, D.O.

The Fetal Center Physician Team

The Fetal Center Co-Directors

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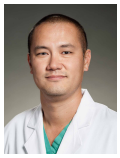

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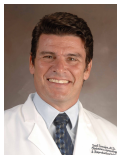

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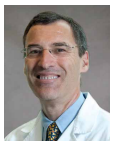

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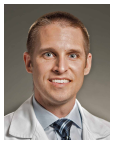

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Pediatric Neurology

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Pediatric Radiology

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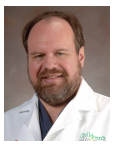
McGovern Medical School at UTHealth

Jennifer H. Johnston, M.D.
Clinical Assistant Professor, Diagnostic and Interventional Imaging
McGovern Medical School at UTHealth

Pediatric Urology



Lawrence J. Cisek, Jr., M.D., Ph.D.
Professor and Chief, Division of Pediatric Urology
McGovern Medical School at UTHealth

Five Years of Accolades & Advancing Fetal Health

The Fetal Center Spearheads a Bill to Establish Guidelines for Fetal Programs in Texas

In Texas, the emergence of new fetal procedures has led to a proliferation of programs using the designation "fetal center" without clarification of what referring physicians and patients should expect in terms of quality, patient safety and outcomes. In response, physicians affiliated with The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth forged a relationship with Texas Representative Sarah Davis to determine criteria that define Centers of Excellence for Fetal Diagnosis and Therapy.

The result was House Bill 2131, which was signed into law by Texas Governor Greg Abbott in June 2015. The bill created a subcommittee to advise the Perinatal Advisory Council and the Texas Department of State Health Services on the designation of one or more health care facilities or programs in the state – including institutions of higher education – as fetal centers of excellence. The bill also establishes the rules necessary for achieving the designation.

In a process that took more than a year, maternal-fetal medicine specialists Anthony Johnson, D.O.; Kenneth J. Moise, Jr., M.D.; and pediatric surgeon KuoJen Tsao, M.D., co-directors of The Fetal Center at Children's Memorial Hermann Hospital, provided testimony that led to the creation of the bill. Dr. Moise and Dr. Tsao have been named members of the subcommittee on Centers of Excellence for Fetal Diagnosis and Therapy, which is now working to establish the criteria a program must meet for designation.

The bill also established priority considerations for center of excellence designation. They include a health care entity or program that:

- Offers fetal diagnosis and therapy through an extensive multispecialty clinical program that is affiliated and collaborates extensively with a medical school in Texas and an associated hospital facility that provides advanced maternal and neonatal care in accordance with its level of care designation
- Demonstrates a significant commitment to research and advancing the field of fetal diagnosis and therapy
- Offers advanced training programs in fetal diagnosis and therapy
- Integrates an advanced fetal care program with a program that provides appropriate long-term monitoring and follow-up care for patients.

"One of the key elements of House Bill 2131 is transparency, which will allow us to compare outcomes among fetal centers in Texas," Dr. Moise says. "As part of our own commitment to improving maternal and fetal care, The Fetal Center is one of the first in the country to post outcomes on our website."

For more information and to view The Fetal Center's outcomes, visit **childrens.memorialhermann.org/thefetalcenter/outcomes**.

Dr. KuoJen Tsao Named Physician of the Year

Pediatric surgeon KuoJen Tsao, M.D., was named 2016 Physician of the Year at Children's Memorial Hermann Hospital. The award recognizes his commitment to patient-centered practices; to health care based on dignity, respect, and participation; to information sharing and collaboration; and to teamwork in creating a safe environment for patients.

Dr. Tsao is co-director of The Fetal Center and is the Children's Fund, Inc. Distinguished Professor in Pediatric Surgery and chief of the division of General and Thoracic Pediatric Surgery at McGovern Medical School at UTHealth. He is board certified in general and pediatric surgery with a special interest in clinical trials, fetal surgery and minimally invasive pediatric surgery. As vice-chair of quality for the department of Pediatric Surgery, he leads the Pediatric Surgical Safety Initiative at Children's Memorial Hermann Hospital. He is currently in the second year of a three-year term as secretary/treasurer of the North American Fetal Therapy Network (NAFTNet).

Dr. Kenneth Moise Named Among Houston's Top Doctors

Maternal-fetal medicine specialist Kenneth Moise, Jr., M.D. has been named to *Houstonia* magazine's 2016 listing of Top Doctors in Houston. Physicians named to the list were selected based on nominations from more than 16,000 medical professionals practicing in eight counties in the Greater Houston area.

The Fetal Center Friends and Family Reunion

In April 2015, families, friends, physicians and staff members at The Fetal Center gathered for The Fetal Center Friends and Family Reunion, held at the Houston Downtown Aquarium. The inaugural event included more than 200 guests, who enjoyed a morning full of activities, and were reunited with members of The Fetal Center care team. The second biennial event will take place in Spring 2017.

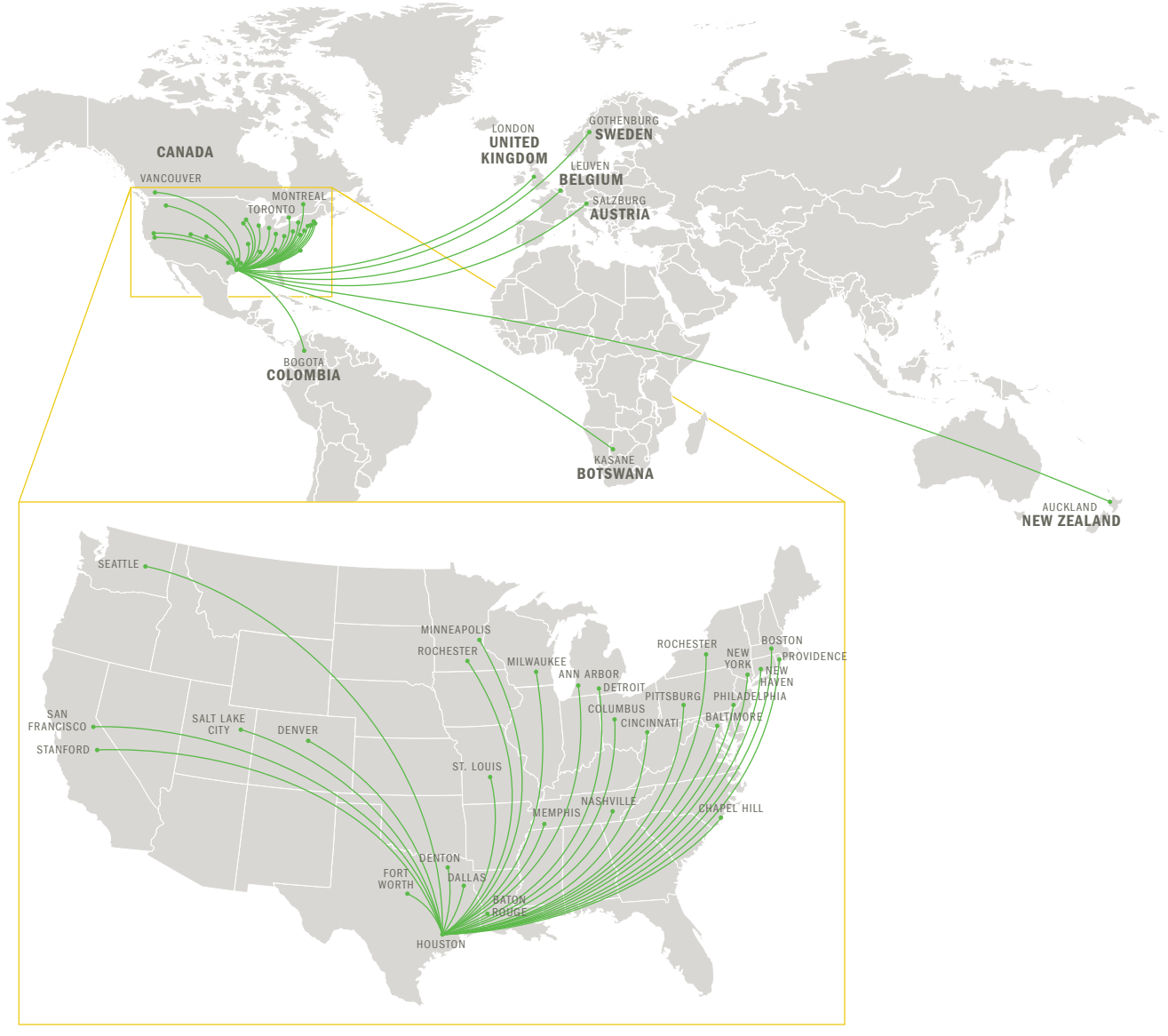
Patient families, friends, physicians and staff members at The Fetal Center Friends and Family Reunion in 2015.

Innovation and Collaboration

Advancing Fetal Medicine Through Shared Expertise

Knowledge is the single most important factor in global health. Physicians affiliated with The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth are grateful for the help they received from specialists at other centers over the years. Today, they are advancing fetal medicine by sharing their expertise with maternal-fetal medicine teams across the globe. Through these collaborations, they create highways to disseminate knowledge about innovative treatments developed or refined at The Fetal Center, serving as a major resource for physicians and their patients. The map below displays The Fetal Center's collaborations with other maternal-fetal medicine centers around the world.

WORLDWIDE COLLABORATION LOCATIONS

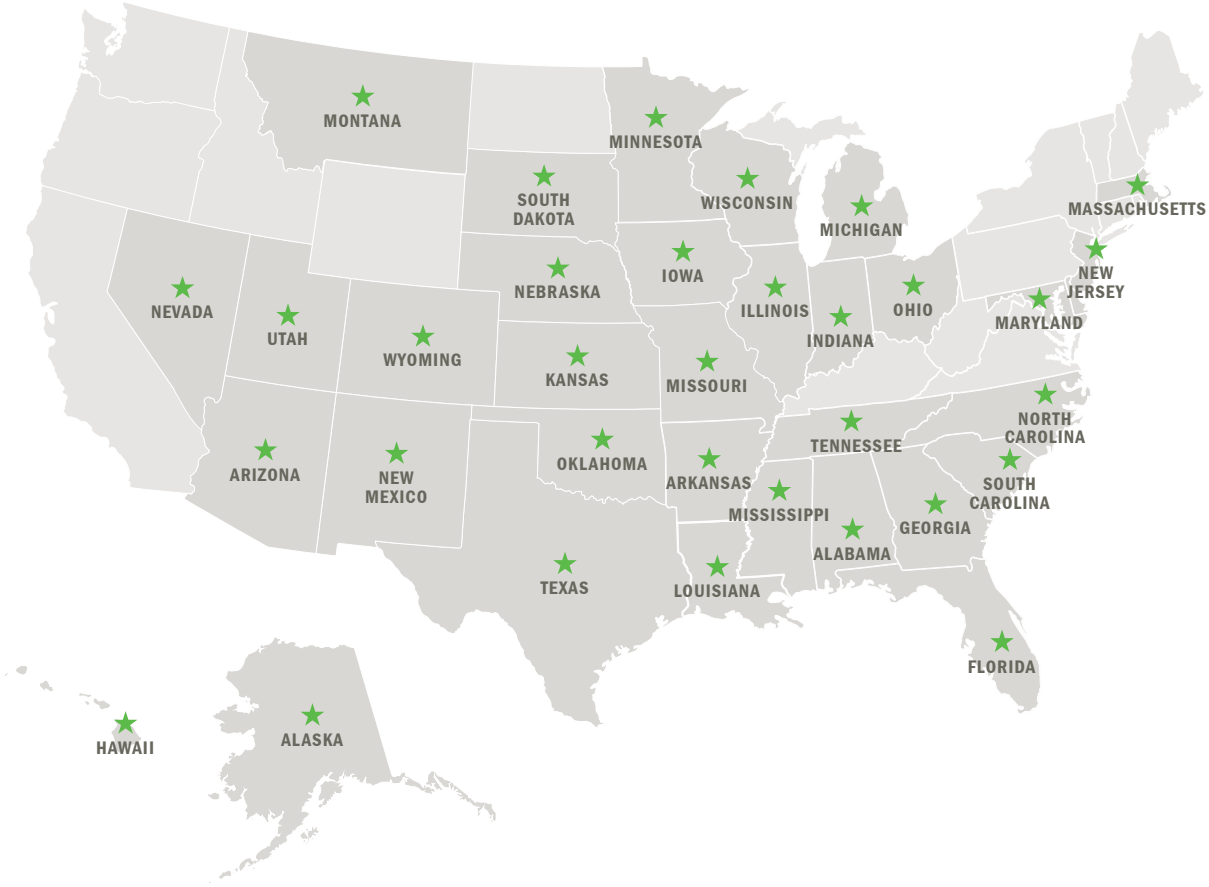


Referrals

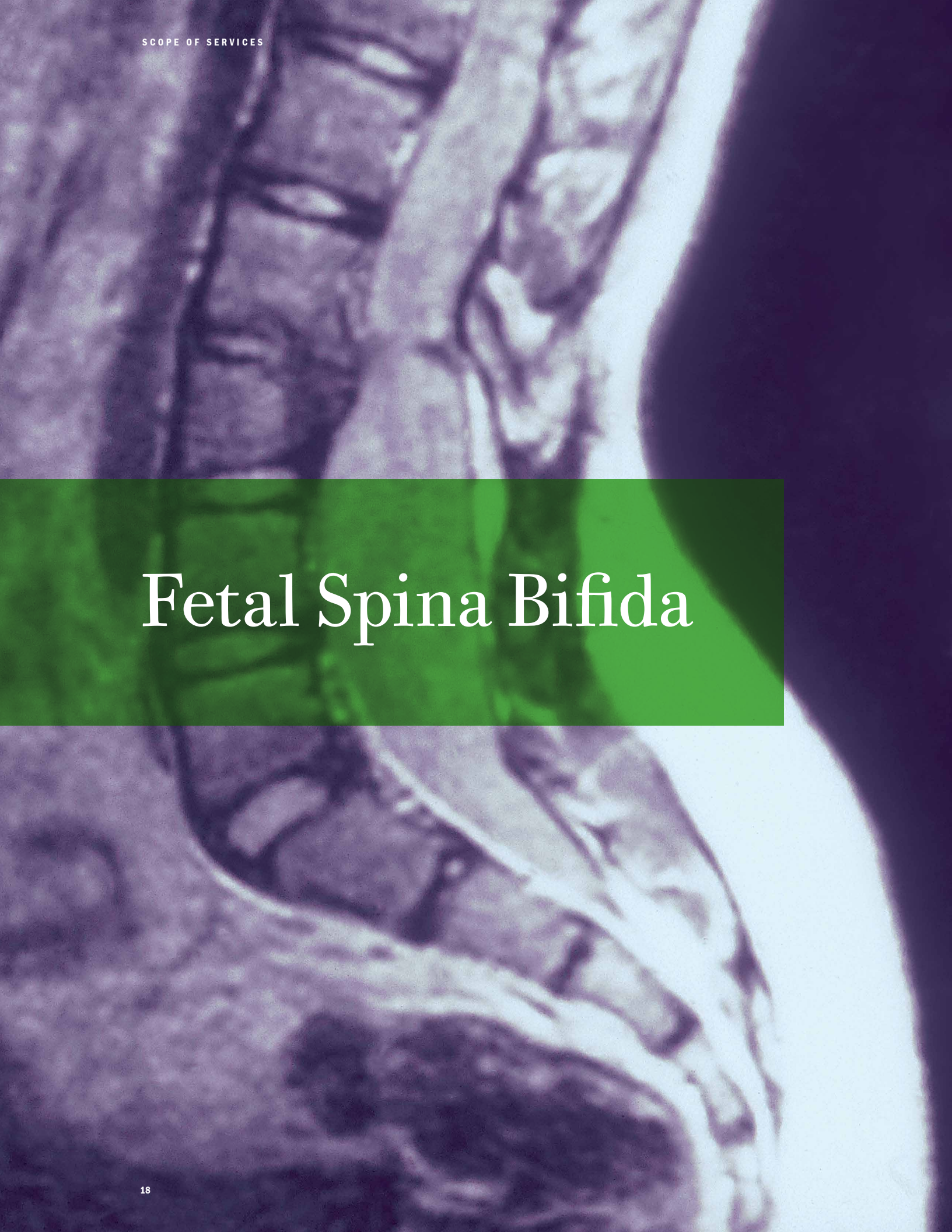
As a national referral center and an international leader in fetal diagnosis, fetal intervention and comprehensive fetal care for infants with congenital anomalies or genetic abnormalities, The Fetal Center has a reputation for innovation, high-quality clinical outcomes and the best possible healthcare experiences, which draws patients from around the country.

The map below highlights the extended reach of our skilled team, with starred referral locations indicating the sites across the United States. that patients have come from to visit The Fetal Center. Our patients travel great lengths for the exceptional care and advanced treatment options provided at The Fetal Center.

THE FETAL CENTER REFERRAL LOCATIONS



For more information or to refer a patient to The Fetal Center, call 832.325.7288 or complete an online referral form at **childrens.memorialhermann.org/thefetalcenter**.



Fetal Spina Bifida

The Fetal Spina Bifida Program

Spina bifida, also known as myelomeningocele, is characterized by the abnormal development of the spinal cord and/or meninges, the protective covering around the brain and spinal cord. It is the most common neural tube defect in the United States, affecting approximately 2,000 of the more than 4 million babies born in the country each year. An estimated 166,000 individuals with spina bifida live in the United States.

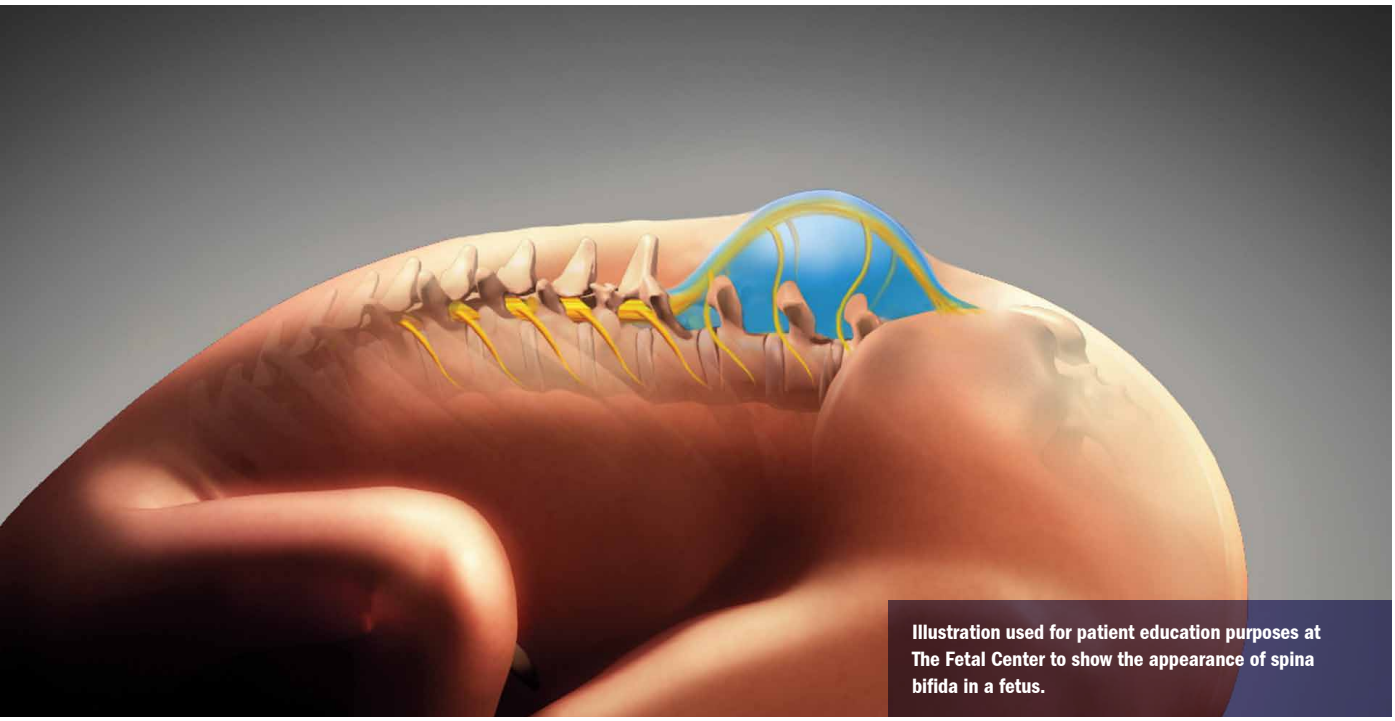


Illustration used for patient education purposes at The Fetal Center to show the appearance of spina bifida in a fetus.

Since the 1930s, the first step in the treatment of newborns with spina bifida has been to surgically close the incompletely developed portion of the spinal cord within a few days of birth. In 2011, the Management of Myelomeningocele Study (MOMS), sponsored by the National Institutes of Health, found that infants who undergo surgery in utero had a decreased need for ventriculoperitoneal (VP) shunting and improved motor function when compared to the standard-of-care procedure performed after birth. After publication of study results in March of that year, a team affiliated with The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth was among the first in the country to perform in utero repair – with excellent outcomes.

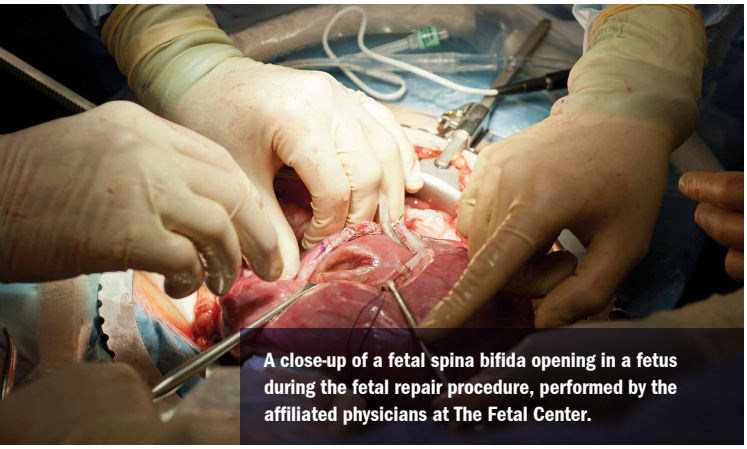
Based on the results of the MOMS trial, fetal surgery for spina bifida is now considered an alternative option for select fetuses prenatally diagnosed with spina bifida. Surgery is scheduled between 22 and 26 weeks of pregnancy, and candidates are accepted for open fetal spina bifida surgery based on criteria set forth by the MOMS trial. The risks and benefits to both mother and baby are considered in the process.

Early diagnosis of spina bifida is important. Due to the small window of opportunity for fetal repair, specialists prefer to see mothers at 22 or 23 weeks of gestation, which allows the family time to complete the consultation, return home and consider their decision.

Some children require intensive spina bifida treatment throughout their lives due to the range of complications associated with the defect, including hydrocephalus, neuromuscular issues, lack of bladder and bowel control, and learning disabilities. The level of the spinal defect can provide some prediction of the severity and extent of any neurological problems. However, the severity of problems can only be determined over time. The Fetal Center helps coordinate visits to specialists and services necessary to support parents as they care for their child.

The five-year-old program at The Fetal Center continues to produce good outcomes with patients chosen based on the selection criteria established in the MOMS trial. As a member of the North American Fetal Therapy Network (NAFTNet), the Center maintains its adherence to the best practices network members have established. The selection process for in utero repair is based on a strict prenatal algorithm that emphasizes education, preparing families to make an informed decision about treatment.

Surgical Outcomes



A close-up of a fetal spina bifida opening in a fetus during the fetal repair procedure, performed by the affiliated physicians at The Fetal Center.

In the last five years, physicians affiliated with The Fetal Center have evaluated more than 143 patients as potential candidates for fetal myelomeningocele repair. As of May 2016, 32 patients had undergone the in utero procedure at The Fetal Center. The data shown below and on the opposite page is based on 32 infants with spina bifida who were delivered prior to May 1, 2016.

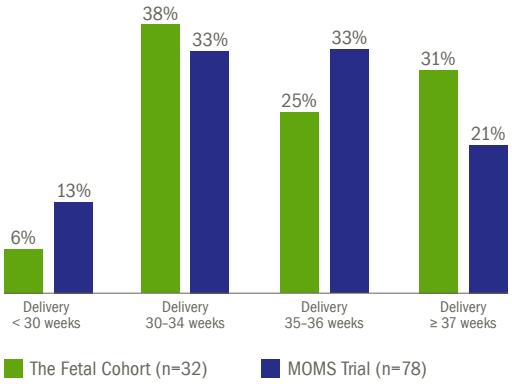
Fetal Surgery for Spina Bifida Repair – Summary

	Fetal Center Cohort (n=32)	MOMS Trial – Fetal Surgery (n=78)	MOMS Trial – Postnatal Surgery (n=80)
Gestational Age at Surgery	24.8 ± .7	23.6 ± 1.4	n/a
Gestational Age at Delivery	34.5 ± 3.2	34.1 ± 3.1	37.3 ± 1.1
Perinatal/Neonatal Demise	1 (3%)	2 (3%)	2 (2%)
VP Shunt at One Year	14 (44%)	31 (40%)	66 (82%)

(The Fetal Center) Date range: May 2011 – May 2016; N=32 patients

Gestational Age at Delivery

A C-section delivery is scheduled at 37 weeks for patients at The Fetal Center. Overall, 31 percent of our patients delivered past 37 weeks gestation as compared to 21 percent in the MOMS trial. At The Fetal Center, the mean gestational age at delivery is 34.5 weeks, the median is 35.3 weeks, and the range is 11.9 weeks.



(The Fetal Center) Date range: May 2011 – May 2016; N=32 patients

Neonatal Outcomes & VP Shunt Rate

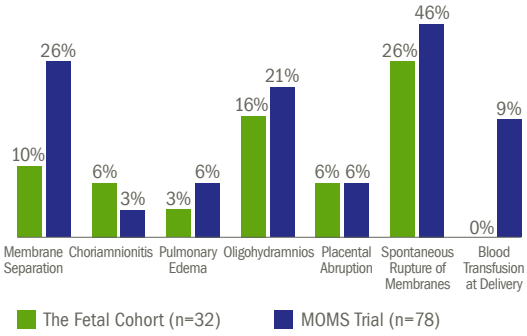
The MOMS trial showed increasing benefits to the baby including a significant reduction in hindbrain herniation and reduction in the need for shunts. Overall, The Fetal Center's cohort data closely mirrored or was better than the neonatal outcomes of the MOMS trial.

	Fetal Center Cohort	MOMS Trial
Repair Site Dehiscence	1/31 (3%)	10/77 (13%)
Any Hindbrain Herniation, Defined by Chiari	16/31 (52%)	45/70 (64%)
VP Shunt at One Year	14/32 (44%)	31/78 (40%)

(The Fetal Center) Date range: May 2011 – May 2016. One patient's data is not available.

Maternal Complications

The affiliated team makes significant efforts to eliminate or minimize potential maternal complications related to fetal surgery. For most of the conditions considered below, The Fetal Center had a lower complication rate as compared to the MOMS trial.

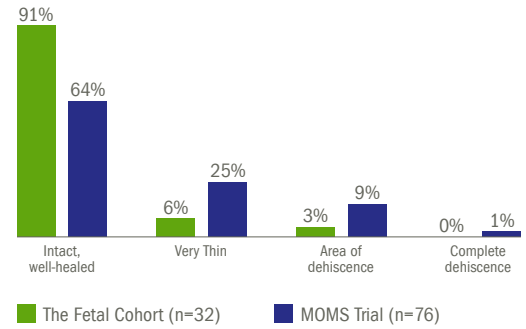


(The Fetal Center) Date range: May 2011 – May 2016; N=31 patients. Maternal complications data for one patient is pending.

Status of Hysterotomy Site

The graph below reflects the known outcomes for The Fetal Center specifically detailing the status of the mothers' hysterotomy site – an incision in the uterus required to perform open fetal surgery – at the time of delivery.

Overall, 91 percent of mothers, as compared to 64 percent in the MOMS trial, had a hysterotomy site that was intact and well-healed, similar to those of a classic cesarean section. The Fetal Center showed lower percentages of complications related to the hysterotomy than the MOMS trial cases.



(The Fetal Center) Date range: May 2011 – May 2016; N=32 patients

Outcomes

To view The Fetal Center's clinical outcomes data for the treatment of fetal spina bifida repair and other conditions, visit **childrens.memorialhermann.org/thefetalcenter/outcomes**.

Research

UMBILICAL CORD PATCH SHOWS PROMISE AS NOVEL METHOD FOR TREATING SPINA BIFIDA IN UTERO

A patch made from cryopreserved human umbilical cord may prove to be a novel method for treating spina bifida in utero, according to researchers at McGovern Medical School at UTHealth. The findings were published in July 2016 in *Obstetrics & Gynecology*,[1] the journal of the American College of Obstetricians and Gynecologists.

A patch comprised of the donated outer layer of the umbilical cord from healthy newborns was used for the repairs, which were performed at Children's Memorial Hermann Hospital. "The umbilical cord contains specific natural material called heavy chain hyaluronic acid/pentraxin 3, which has regenerative properties," says lead author Ramesha Papanna, M.D., maternal-fetal medicine specialist at The Fetal Center at Children's Memorial Hermann Hospital. "It allows the local tissue to grow in at the repair site instead of healing by scar formation that occurs with traditional

"For the first time, a bioscaffold has been successfully employed to allow the fetus to heal itself. The implications for the future of a minimally invasive approach to fetal spina bifida repair and even neonatal spina bifida repair are enormous."

Assisted by surgical staff, the co-directors of The Fetal Center, Kenneth Moise, Jr., M.D.; Anthony Johnson, D.O.; and KuoJen Tsao, M.D., perform open fetal surgery for spina bifida repair on a patient of The Fetal Center.

repair methods. This decrease in scar formation may help improve the spinal cord function further and reduce the need for future surgeries to remove the effects of the scar tissue on the spinal cord."

In 2011, the MOMS trial found that if a fetus underwent in utero surgery to close the defect, the serious complications associated with spina bifida could be reversed or lessened. In cases where the defect was too large to close with the fetus' existing skin, a patch was necessary. But in some cases, scar tissue may cause adherence of the patch to the underlying spinal cord. This could result in a loss of neurologic function as the child ages. Further surgery was often needed to remove this scar tissue.

"The use of this patch for fetal repair heralds a new era for fetal spina bifida repair," says Kenneth Moise, M.D., co-author, professor, and co-director of The Fetal Center. "For the first time, a bioscaffold has been successfully employed to allow the fetus to heal itself. The implications for the future of a minimally invasive approach to fetal spina bifida repair and even neonatal spina bifida repair are enormous."

To read the full abstract, visit ncbi.nlm.nih.gov/pubmed/26489897.

Patient Outcomes in Research Trial Participants

In the first case study, the skin lesion in the fetus measured five centimeters by six centimeters and there was evidence of Chiari II malformation, a complication of spina bifida in which the brain stem and the cerebellum protrude into the spinal canal or neck area, which can lead to problems with feeding, swallowing or breathing control.

At 24 weeks gestation, the patient underwent fetal surgery by KuoJen Tsao, M.D., co-director of The Fetal Center, and Stephen Fletcher, D.O., co-author, associate professor in McGovern Medical School's Department of Pediatric Surgery, and pediatric neurosurgeon affiliated with Children's Memorial Hermann Hospital. Dr. Moise and Dr. Papanna participated in the surgery.

The lesion was closed with skin edges sutured to the human umbilical cord patch in a watertight fashion. The mother was discharged on postoperative day five. The baby was born at 37.5 weeks and the patch was intact with no leakage of fluid. The patch at the site of the lesion appeared semi-translucent with incomplete regeneration of the skin. Within two weeks, the skin had healed over the patch spontaneously. The child had normal movements of the lower extremities and bladder control function, and there was a complete reversal of the Chiari II malformation.

In the second case, performed by the same team, the patient's fetus had a lesion of four centimeters by five centimeters and Chiari II malformation. The expectant mother underwent surgery at 25 weeks gestation, and the procedure and application of the patch were similar to the first case. The baby was delivered at 37.5 weeks and there was complete covering of the lesion with the patch but without skin grown into the patch. As with the first case, the skin grew over the patch, and by day 30 was completely healed. There was normal motor and urinary function, and the Chiari II malformation was completely reversed.

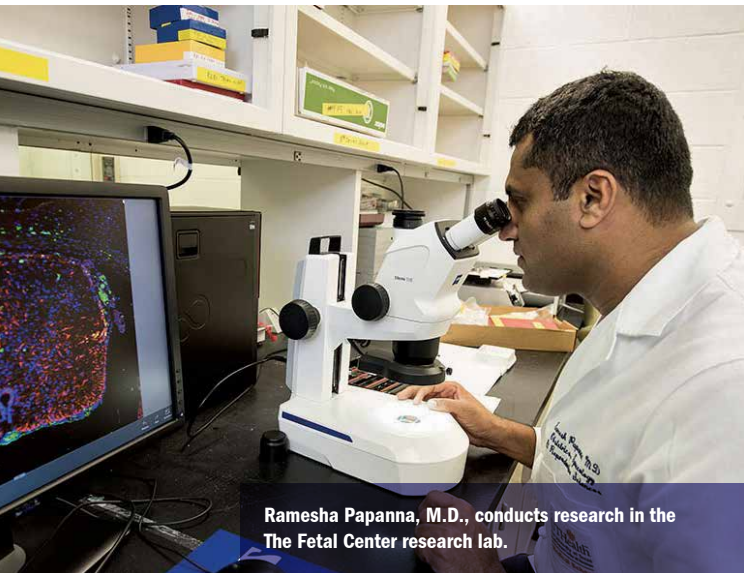
Both cases were approved by the Food and Drug Administration under Expanded Access use, the Fetal Therapy Board of The Fetal Center at Children's Memorial Hermann Hospital, and UTHealth Institutional Review Board prior to the surgery.

Transforming Fetal Surgical Care

The clinical cases were the culmination of seven years of research after Dr. Papanna, and co-author Lovepreet K. Mann, M.B.B.S., instructor in McGovern Medical School's Department of Obstetrics, Gynecology and Reproductive Sciences, began brainstorming ideas about possible patch materials. This led them to co-author Scheffer C.G. Tseng, M.D., Ph.D., of Ocular Surface Center and TissueTech™, Inc., in Miami, Fla., who was using human amniotic membrane and umbilical cord – donated by mothers of healthy infants – to repair corneas. The patch is approved by the FDA for corneal repair.

"This patch acts as a scaffold, which is watertight and allows native tissue to regenerate in an organized manner, and has anti-scarring, anti-inflammatory properties. Preventing the scarring could prevent tethering, which can prevent further damage to the cord," Mann said. The patch was first tested in animal models by a team of researchers that included Mann, Dr. Papanna, Dr. Moise, Dr. Fletcher and Saul Snowise, M.D., assistant professor in the Department of Obstetrics, Gynecology and Reproductive Sciences.

The team has since completed a third patient surgery, and Dr. Fletcher has used the new patch in surgeries to untether the spinal cord of children who had previous spina bifida surgery. They are waiting to see if the umbilical cord patch will help prevent tethering in the long run. "If we can make a small change and improve the quality of life for the child, that will mean we really accomplished something spectacular," Mann says.



Ramesha Papanna, M.D., conducts research in the The Fetal Center research lab.

Currently, the team members are working on finding ways to make the skin 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," Dr. Papanna says. "Taking an idea from the lab to human use typically takes about a decade. We've been able to reduce that time to two and a half years. We have a good system in place with strong collaborators."

Research collaborators from other institutions and disciplines across the country include Sanjay Prabhu, M.B.B.S., assistant professor of pediatric neuroradiology at Harvard Medical School; Raymond Grill, Ph.D., associate professor of neurobiology and anatomical sciences at the University of Mississippi; and Russell Stewart, Ph.D., professor of biomedical engineering at the University of Utah.

"There's still plenty of work to do," Dr. Papanna says. "What we've done to date in showing real benefit to children is just the tip of the iceberg. We want all babies who undergo the fetal surgery to be able to walk at age 3. Right now, the percentage is less than half. Our goal is to take it to 100 percent."

1. 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.

TOWARD MINIMALLY INVASIVE FETOSCOPIC REPAIR

Data from the MOMS trial, completed in 2011, showed that approximately 80 percent of pregnancies are delivered preterm, 25 percent develop membrane separation, and 30 percent suffer from thin or dehisced uterine incision. In response to these complications, many fetal surgeons have advocated for a minimally invasive approach to the repair of fetal myelomeningocele. Investigators at The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth are conducting laboratory studies aimed at developing an approach to minimally invasive spina bifida repair that is safe for both mother and child.

Current clinical applications of fetoscopic repair utilize carbon dioxide in the in utero operative environment, multiple trocars and bulk closure of the spina bifida defect, but this approach remains controversial. "A major concern about this procedure is that the effect of carbon dioxide on the fetus remains unknown," says Kenneth J. Moise, Jr., M.D., co-director of The Fetal Center. "We know that the fetus lacks an enzyme that allows it to process carbon dioxide. In a sheep model, fetuses subjected to CO_2 became acidotic. We also haven't adequately studied the effects of the gas on fetal membranes. Will it damage their integrity? We simply don't know."

"Our goal is to develop techniques that minimize the morbidity to mothers associated with the open operations, without jeopardizing the optimal operation for the fetus and compromising the fetal outcome."

Surgeons and researchers at The Fetal Center and McGovern Medical School are investigating the optimal approach to minimally invasive repair for spina bifida. "Our goal is to develop techniques that minimize the morbidity to mothers associated with the open operations, without jeopardizing the optimal operation for the fetus and compromising the fetal outcome," says KuoJen Tsao, M.D., co-director of The Fetal Center. "We need to be doing the same operation for the baby. Otherwise, the risk/reward balance as demonstrated through the MOMS trial would no longer apply to fetal spina bifida surgery."

"We're using regenerative matrix, underwater adhesive and biomimetic suturing devices that could be delivered through a tiny port in an underwater environment to create a watertight seal and heal the defect with minimal damage to the spinal cord," says Ramesha Papanna, M.D., lead physician scientist on the project. "We're performing extensive bench side testing of these methods, including preclinical studies, to explore the optimal closure techniques before bringing it to the bedside."

The researchers' long-term goal is to reduce the risks associated with open spina bifida repair. "We know open repair presents all the risks to a mother involved with a uterine incision, including preterm delivery," Dr. Moise says. "Although no data equivalent to the MOMS trial outcomes has been presented showing that the minimally invasive approach produces equivalent results, in my heart I believe it will. The challenge lies in how to get there. We're pushing the envelope but doing it in a scientific fashion. I'm as cautious as I was when we first started doing myelomeningocele repair. We're still working on the next chapter in the story."

Extended Criteria for Fetal Myelomeningocele Repair: A New Clinical Trial

Researchers at The Fetal Center are engaged in a single-center study that offers prenatal myelomeningocele repair surgery to mothers with a body mass index (BMI) of 35 to 40 kg/m2. The trial extends the BMI criteria beyond that used for the 2011 MOMS trial, for which the cutoff was 35 kg/m2.

"The new study will allow us to evaluate the efficacy and safety of the extension by capturing clinical and outcome information," says KuoJen Tsao, M.D., principal investigator of the trial. "This operation is about balancing the risks and benefits for two patients: mother and fetus. We want to be sure that we rigorously study any broadening of the eligibility criteria and understand the impact on both patients."

Eligibility criteria for inclusion in the MOMS trial include:

- Mother between ages of 16 and 45
- Prenatal diagnosis of myelomeningocele
- Prepregnancy BMI of 35 to 40 kg/m2
- Meet the inclusion criteria for the original MOMS trial:
    - Myelomeningocele lesion that starts no higher than the first thoracic vertebra and no lower than the first sacral vertebra with hindbrain herniation present
    - Gestational age of 19 weeks 0 days to 25 weeks 6 days
    - Normal karyotype (a test that identifies and evaluates the size, shape and number of chromosomes in a sample of body cells)
    - A singleton pregnancy
- A United States resident and able to travel to The Fetal Center at Children's Memorial Hermann Hospital for study evaluation, procedures and visits. Mothers who are chosen to undergo prenatal surgery must be able to stay near the Center until delivery and have a support person to travel and stay with them.

For more information on the trial, contact Yisel Morales, research coordinator, at 713.486.6560 or yisel.morales@uth.tmc.edu.

Management of Myelomeningocele Study 2 (MOMS2)

In 2011, affiliated pediatric researcher Jenifer Juranek, Ph.D., Associate Professor, Department of Pediatrics at McGovern Medical School at UTHealth, was awarded a subcontract as the neuroimaging expert for the multicenter follow-up clinical trial known as the MOMS2 study, sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development. In this study, prenatal versus postnatal spina bifida repair is being investigated with respect to the child's behavior and development, physician and cognitive function and clinical outcomes. Dr. Juranek developed the neuroimaging protocol used across all three national centers (The University of California San Francisco Medical Center, Children's Hospital of Philadelphia and Vanderbilt University) to acquire structural brain MRIs from this cohort of children, who are now 6 to 10 years old, and is responsible for analyzing these MRIs.

Educating Families About Spina Bifida

Education plays a key role in the delivery of patient-centered care. Each mother referred to The Fetal Center with a diagnosis of fetal spina bifida undergoes extensive counseling with specialists in maternal-fetal medicine, fetal surgery and spina bifida regardless of whether she and her baby qualify for fetal repair. Over the span of two days, the family also meets with a pediatric surgeon, a pediatric neurosurgeon, a genetic counselor, an expert in long-term spina bifida outcomes, a neonatologist, an anesthesiologist, all affiliated with McGovern Medical School at UTHealth, as well as a social worker and a representative of Child Life services at Children's Memorial Hermann Hospital.

Each mother referred to The Fetal Center with a diagnosis of fetal spina bifida undergoes extensive counseling with specialists in maternal-fetal medicine, fetal surgery and spina bifida regardless of whether she and her baby qualify for fetal repair.

Parents are encouraged to view The Fetal Center's online patient education video on fetal surgery for spina bifida before the two-day consultation. A guide to help families explore their treatment options, the animated feature describes the decision-making process, providing information on the etiology and natural history of spina bifida, and the pathophysiology leading to the many complications associated with the condition.

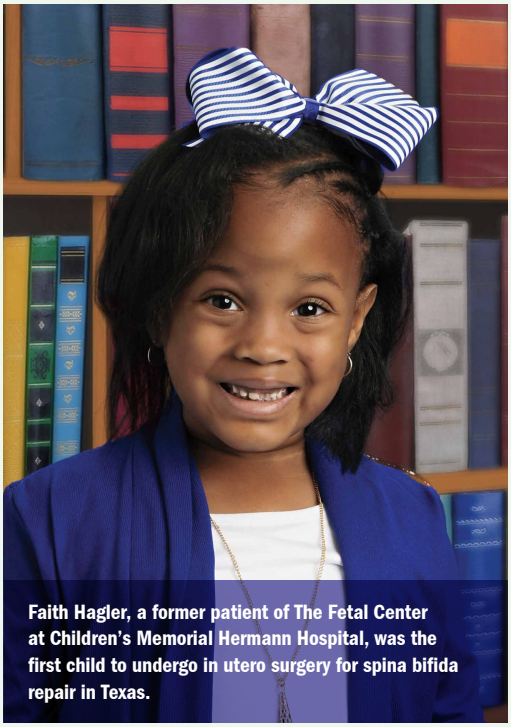
Part of a series of innovative patient education videos, the fetal spina bifida video serves as a comprehensive guide to the condition and treatment options for patients.

An extensive breakdown of the results of the Management of Myelomeningocele Study (MOMS) is also provided in a patient-friendly format to help parents understand the key principles and outcomes associated with the randomized clinical trial. The video also provides a step-by-step guide through the comprehensive multidisciplinary evaluation and consultation process, followed by a detailed look at the fetal surgery patient experience. By reducing information gaps and addressing any preconceived notions, the video helps patients begin with a better knowledge base, preparing them to ask more in-depth questions when they meet with the team at The Fetal Center.

To view the patient education video, in English or Spanish, visit childrens.memorialhermann.org/spina-bifida.

Faith Hagler Five Years Later: Celebrating Independence from Spina Bifida

Patient Story



Faith Hagler, a former patient of The Fetal Center at Children's Memorial Hermann Hospital, was the first child to undergo in utero surgery for spina bifida repair in Texas.

Picture the bounciest, bubbliest five-year-old you can imagine. Her songs and dance moves come straight from Beyoncé. She loves bright colors and runs to the mirror to check every outfit. Her goal is to be a superstar. And she is a child who was born with spina bifida, one whose immediate future appeared more filled with shunts, catheters and leg braces than mirrors and dancing.

First in Texas

Faith's medical team would become the first in Texas to perform in utero surgery for spina bifida repair. A complex and sometimes permanently disabling birth defect that affects about 1 in every 1,500 pregnancies, spina bifida involves incomplete development of a portion of the spinal cord and associated nerves, as well as the surrounding spinal bones and overlying muscle. Infants born with spina bifida are at risk for a range of disorders, including hydrocephalus, which may require a shunt to relieve pressure inside the skull. They are prone to life-threatening infections and may suffer loss of sensation or paralysis, difficulty walking and other problems that lead to lifelong disability.

In 2011, fetal surgeon KuoJen Tsao, M.D., and pediatric neurosurgeon Stephen Fletcher, D.O., were following the results of a landmark trial, the Management of Myelomeningocele Study (MOMS), which found that if a fetus undergoes surgery in utero to repair the 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 shunting for the infants, and nearly half were able to walk without crutches by the age of 30 months.

Faith's parents, Ivan and Colette Hagler of Dallas, were referred to The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth, and based on the MOMS trial protocols, Dr. Tsao determined that Colette was an ideal candidate for the procedure.

After Fetal Surgery

After the fetal surgery, she remained at Children's Memorial Hermann Hospital and delivered Faith eight weeks later on the Fourth of July, a date that Colette describes as "so symbolic" of the independence her daughter has achieved since her birth.

Since Faith was the first patient to undergo this surgery in Texas, her parents faced challenges finding a team to provide care in Dallas at that time. Her first year was difficult, her mother says, with several bouts of a respiratory virus common among preemies, but when the medical team determined that no shunt or catheterization was necessary, "we began to see the benefits that the clinical trials indicated, even though there were no guarantees," Colette says.

Dr. Tsao no longer treats Faith, but sees the family when he's in Dallas or when they come to Houston. "He helped us in so many ways," her husband says. "He's an uncommon and special person. I'm so grateful he watched over my family during the time she was in Houston."

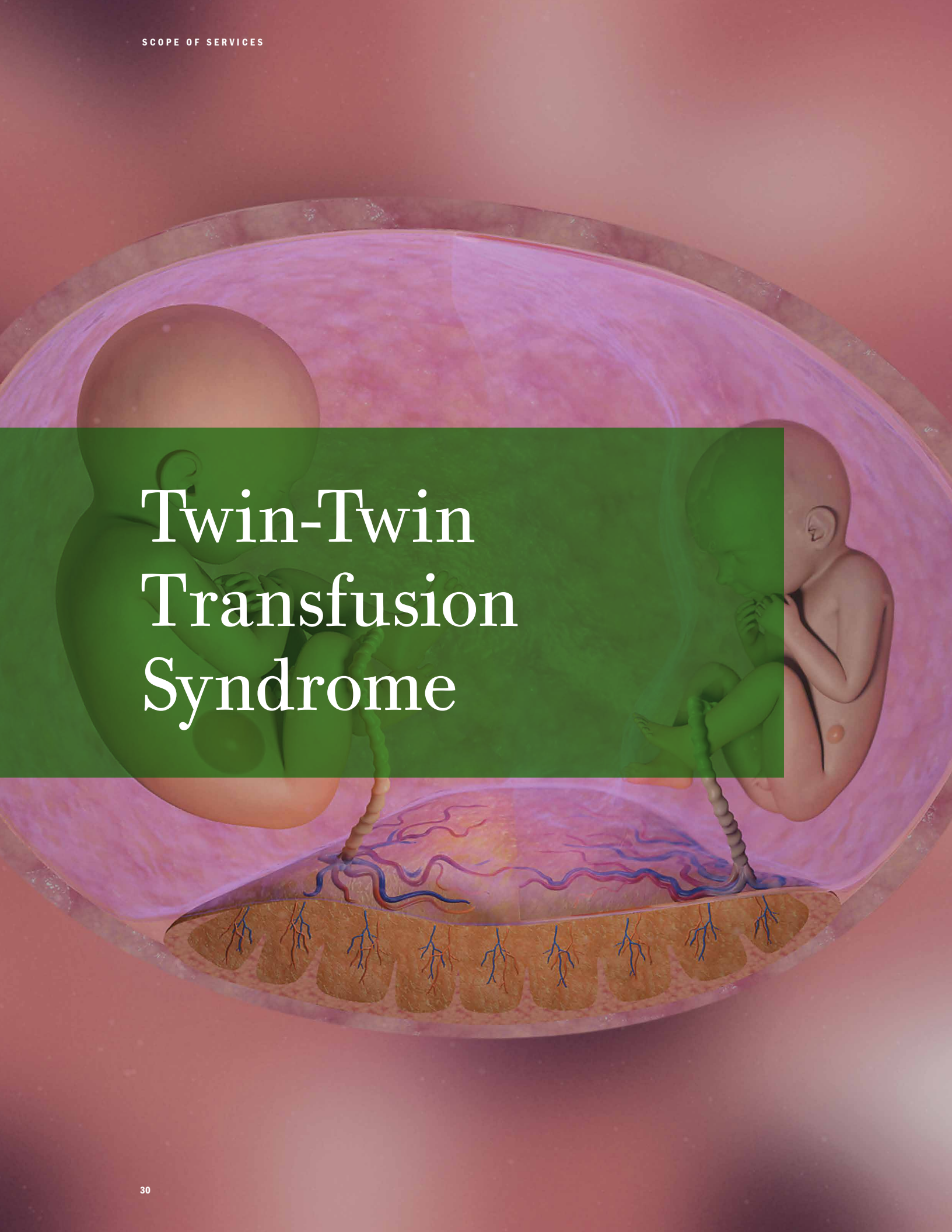
Meeting Milestones

At 11 months, Faith began crawling, and at 21 months, she was taking her first steps. It was a memorable moment. Ivan Hagler confesses that while shooting videos of his daughter, he was trying hard not to cry. His immediate thought was to "thank God who blessed us by letting our little girl walk." Today, he's still making videos. "You never know when she'll break out dancing. She is not shy," he says. "We prayed for her to be a vibrant child, and we got what we asked for."

"When I see her," her mother says, "I see faith – the substance of things hoped for. She's definitely the evidence of things not seen in the amazing things she has been able to do in the past five years."

According to Dr. Tsao, Faith has demonstrated exactly what the MOMS trial showed the in utero surgery was designed to do. Now in kindergarten, Faith has met all the milestones for her age: She speaks in full sentences. She can write her first name. She can identify shapes and knows her numbers from 1 to 20. "Cognitively and linguistically, she's right on track," he says. "Much of her follow-up medical care now focuses on keeping an eye on things through her growth and development."

In early June 2016, Faith asked her parents whether she could be baptized. The rite was held the day before her fifth birthday, a significant milestone for the family. Like the independence implicit in her birth date, there's providence in Faith's name as well. "When I see her," her mother says, "I see faith – the substance of things hoped for. She's definitely the evidence of things not seen in the amazing things she has been able to do in the past five years."



Twin-Twin Transfusion Syndrome

The Twin-Twin Transfusion Syndrome Program

Identical twins that share a common placenta (monochorionic twins) usually have blood vessel connections between the two fetuses. In about 10 percent to 15 percent of these pregnancies, twin-twin transfusion syndrome (TTTS) occurs when these blood vessels produce an imbalance or uneven sharing of the blood. As a result, blood from one twin, the *donor* twin, is pumped to the other twin, the *recipient* twin.

Anthony Johnson, D.O., performs an ultrasound scan for a patient of The Fetal Center.

In cases of TTTS, the heart of the donor twin must do extra work to support the recipient twin. The recipient twin gets too much blood and the donor twin does not get enough. This unequal sharing of blood causes problems for both babies, and if left untreated, TTTS can lead to preterm delivery, fetal and neonatal death, and long-term developmental delay in the survivors.

Diagnosis and Monitoring

Once a diagnosis of monochorionic twins is determined, the current standard of care is to perform ultrasounds every two weeks beginning at 16 weeks' gestation, to look for signs of TTTS, which is usually described in five stages:

- Stage I – Significant difference in the amniotic fluid volume in each twin's sac
- Stage II – Discordant amniotic fluid volume and the inability to see the donor twin's bladder in ultrasound
- Stage III – Abnormal blood flow through the umbilical cord or fetal vessels leading to the heart of one or both babies
- Stage IV – Development of hydrops or cardiac failure in either fetus (occurs more frequently in the recipient twin)
- Stage V – The death of one or both fetuses

Once TTTS is diagnosed, a detailed fetal ultrasound is typically performed at The Fetal Center to detect the presence of any additional fetal anomalies. Amniocentesis may be recommended to evaluate for genetic conditions, particularly if structural abnormalities are seen. A fetal echocardiogram, an ultrasound of the fetal heart, is recommended in all monochorionic twins, with or without TTTS, between 18 and 22 weeks of pregnancy, due to the increased risk of cardiac anomalies in identical twins.

Progression to higher stages of TTTS can occur slowly or very rapidly, which is why active surveillance is key to managing monochorionic twin pregnancies. The role of imaging – ultrasounds, including echocardiograms – in early detection and ongoing monitoring of patients with TTTS cannot be overstated. The Fetal Center's team of highly trained affiliated ultrasonographers are at the forefront of fetal imaging.

Treatment Options

Laser ablation therapy of the communicating placental blood vessels between the twins is the optimal therapy for TTTS. A fetoscope (a small telescope) is inserted into the pregnancy sac of the recipient twin, and the placental surface is evaluated to find the connecting vessels. When a connection is identified, laser energy is used to ablate it, stopping the further blood exchange between the fetuses.

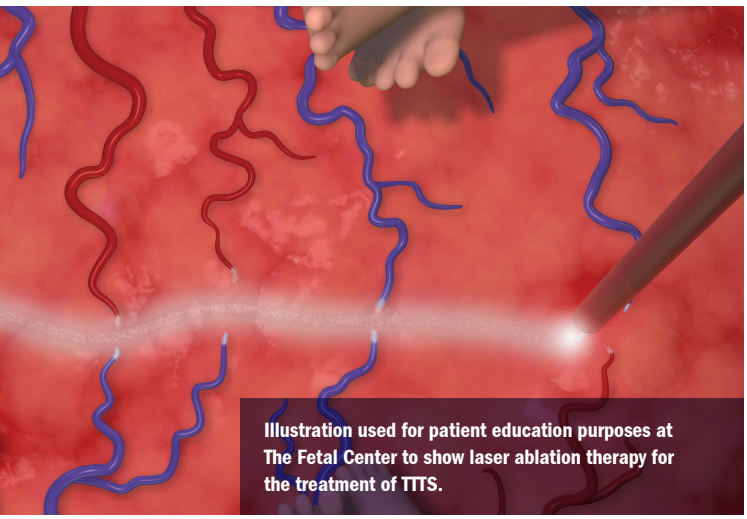


Illustration used for patient education purposes at The Fetal Center to show laser ablation therapy for the treatment of TTTS.

In cases of TTTS with severe discordance in fetal growth between the twins or when fetal malformations are present as well, a selective pregnancy reduction can be considered as an alternative therapy. The goal with this treatment is to decrease risk to the unaffected, normally growing fetus. If there is a spontaneous demise of one of the twins, the presence of connecting blood vessels in the placenta and additional shunting of blood places the surviving co-twin at a 15 percent risk of death or 26 percent risk of neurological compromise.

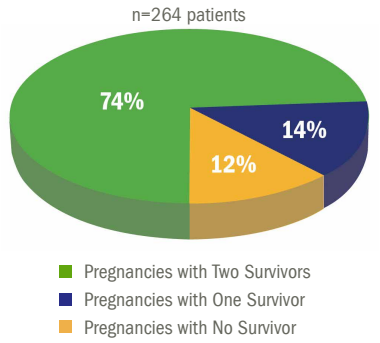
Surgical Outcomes

Since 2011, The Fetal Center has performed 315 cases of laser photocoagulation for the treatment of TTTS at Children's Memorial Hermann Hospital. The data below reflects surgical volume from September 2011 – June 2016 and represents 264 patients with known outcomes at 30 days post-delivery. **Overall, survival of both babies is seen in 74 percent of cases, with survival of one twin in 14 percent of cases.**

Total Number of Laser Case Procedures	315
Number of Laser Repeat Cases	2
Number of Twin Pregnancies	299
Number of Deliveries	268
Number of Deliveries with 30-Day Known Outcome	264

TTTS 30-Day Post-Delivery Survival Outcome by Gestational Age at Time of Fetal Intervention

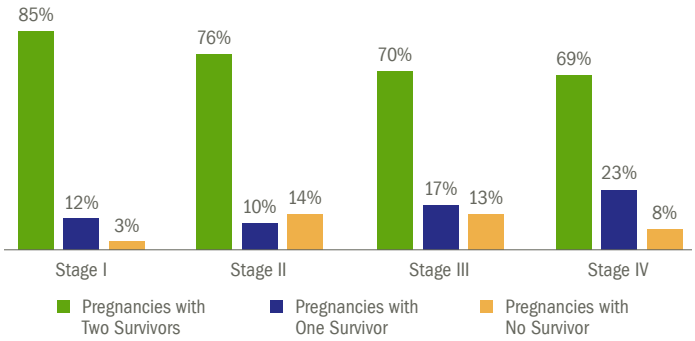
Gestational Age at Time of Procedure	Total	Pregnancies with Two Survivors	Pregnancies with One Survivor	Pregnancies with No Survivor
16–18 weeks	72	49 (68%)	13 (18%)	10 (14%)
19–21 weeks	113	87 (77%)	10 (9%)	16 (14%)
22–24 weeks	60	44 (73%)	10 (17%)	6 (10%)
25–27 weeks	19	15 (79%)	4 (21%)	0 –
Summary	**264**	**195 (74%)**	**37 (14%)**	**32 (12%)**



30-Day Post-Delivery Survival Outcome by TTTS Stage

The table below represents total number of cases (n=264) aggregated by stage of TTTS. The affiliated graph reflects the 30-day survival outcome as represented by TTTS stage. (Date range: September 2011 – September 2016)

TTTS Stage	Cases (percent of total cases)
Stage I	34 (13%)
Stage II	84 (32%)
Stage III	133 (50%)
Stage IV	13 (5%)



Taking on the Toughest Cases

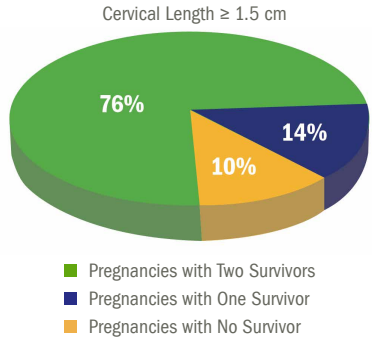
In order to give patients the best chance for a positive outcome relevant to the severity of their condition, The Fetal Center is committed to a highly aggressive approach to the overall survival of all twin pregnancies. The Fetal Center takes on all TTTS cases – even the most severe or complex, such as cases in which the mother has a cervical length of less than 1.5 cm, which increases a mother's risk of spontaneous preterm birth by almost 50 percent, according to the *American Journal of Obstetrics & Gynecology*, or cases in which there has been past failure. Despite taking on these higher-risk cases, The Fetal Center's TTTS outcomes are as favorable as any in the country.

In order to give patients the best chance for a positive outcome relevant to the severity of their condition, The Fetal Center is committed to a highly aggressive approach to the overall survival of all twin pregnancies.

The below data reflects surgical volume from September 2011 – June 2016. The data represents 264 patients with known outcomes at 30 days post-delivery, specifically highlighting outcomes based on mothers' cervical length. As noted below, a cervical length of ≥ 1.5 cm was found in 97 percent of all cases at The Fetal Center.

TTTS 30-Day Post-Delivery Survival Outcome by Cervical Length

	Number of Cases	Pregnancies with Two Survivors	Pregnancies with One Survivor	Pregnancies with No Survivor
Number of cases with Cervical Length ≥ 1.5 cm	250	190 (76%)	35 (14%)	25 (10%)
Number of cases with Cervical Length < 1.5 cm	14	5 (36%)	2 (14%)	7 (50%)
Total	264	195 (74%)	37 (14%)	32 (12%)



Note – Those with a cervical length of less than 1.5 cm are at increased risk and should be seen by a physician as soon as possible. Please call The Fetal Center at 832.325.7288.

We encourage you to reach out to other healthcare centers to request and review their outcomes data in order to utilize the information available when choosing your healthcare options. **For more information, visit childrens.memorialhermann.org/thefetalcenter or call 832.325.7288.**

Research

The Fetal Center conducts ongoing research to improve pregnancy outcomes, with a focus on reducing the incidence of preterm labor to increase babies' survival rates. Ongoing studies at The Fetal Center for the treatment of TTTS include:

Prolonging Pregnancy After Laser Ablation in Patients With Short Cervixes

The Fetal Center is one of three fetal centers in Texas affiliated with the North American Fetal Therapy Network, or NAFTNet, a voluntary association of medical centers in the United States and Canada that perform advanced in utero fetal therapeutic procedures. Through its affiliation with NAFTNet, The Fetal Center has published over 20 papers on the use of laser ablation in TTTS pregnancies and the outcomes, led by maternal-fetal medicine specialist Ramesha Papanna, M.D.

The researchers have identified short cervix as one of the risk factors associated with preterm birth after surgery. As a result, a study was recently approved by the NAFTNet panel for a clinical trial in women with a short cervix with a diagnosis of TTTS. The trial will test two different treatments to prolong pregnancy after laser ablation in these patients. The hope is that patients may participate in the clinical trial starting October 2017.

L-R: Loverpreet Mann, M.B.B.S.; Ramesha Papanna, M.D.; and Jong Hak Won, Ph.D., collaborate on research in The Fetal Center research lab.

Fetal Cardiac Research to Predict the Development of TTTS

Affiliated fetal cardiologist Helena Gardiner, M.D., Ph.D., led an important piece of fetal cardiac research on "The use of aortic displacement as a surrogate for intertwin pulse pressure differences in monochorionic pregnancies with and without TTTS." Dr. Gardiner's team employed new ultrasound techniques (speckle tracking) to measure heart wall strain in monochorionic twin pregnancies to predict the development of TTTS. A novel application of this technique is the measurement of the strain of

the aorta to deduce recipient twin hypertension, which cannot be measured directly. This won best oral presentation at the 2015 International Society for Ultrasound in Obstetrics and Gynecology (ISUOG) conference in Montreal, Canada.

Fetal Membrane Repair to Prevent Preterm Birth Following Fetoscopic Surgery

The hole in the fetal membranes does not heal after fetoscopic surgeries, contributing to the very high risk for preterm premature rupture of membranes and preterm birth. The collaborative team consisting of Lovepreet K. Mann, M.B.B.S., Research Instructor, Department of Obstetrics and Gynecology, McGovern Medical School, and Dr. Papanna have been conducting research to design a fetal membrane patch consisting of cryopreserved human amniotic membranes and underwater adhesive coacervate to seal the fetal membrane hole after fetoscopic surgery to prevent preterm premature rupture of membranes. The research has been funded by an R01 Grant from the National Institutes of Health, and the principal investigator is Russell J Stewart, Ph.D., Professor, Bioengineering, University of Utah, Salt Lake City, Utah. The researchers are refining the adhesive and delivery system and testing it in preclinical studies before applying it in humans.

Impact of Twin-Twin Transfusion Syndrome on Long-term Heart Health

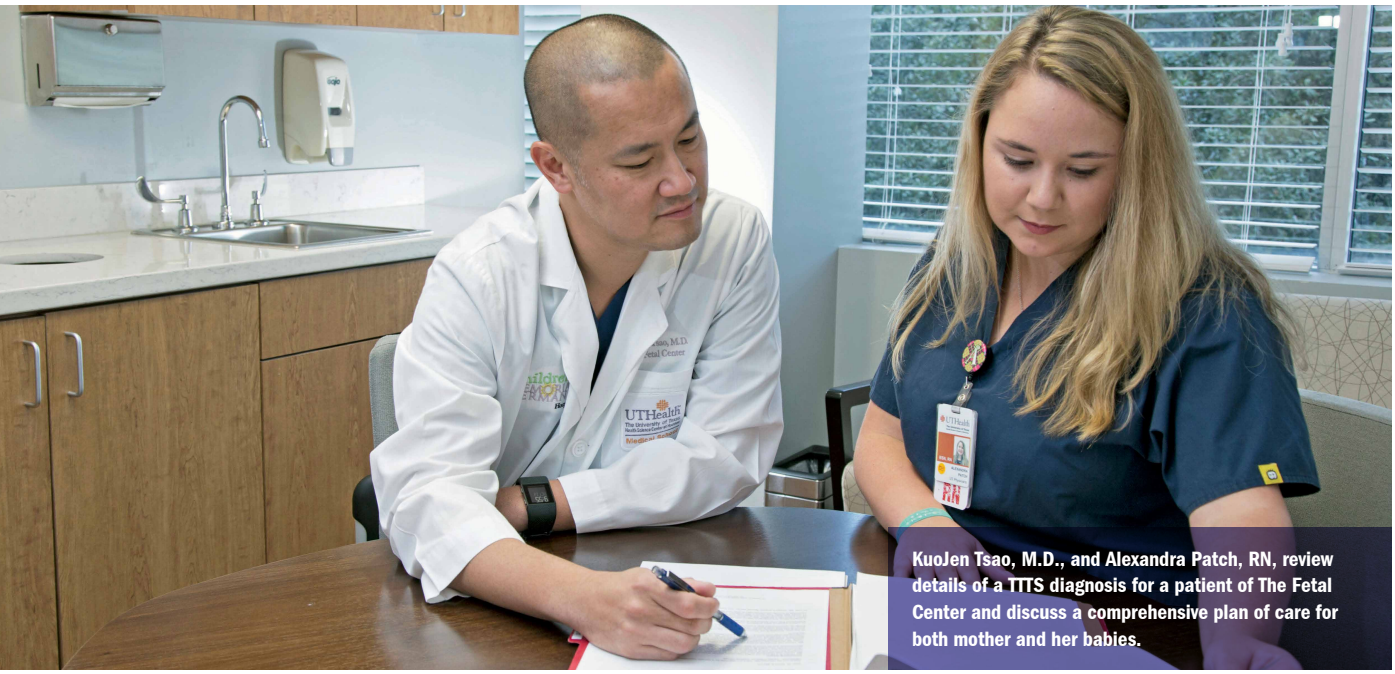
A team led by Dr. Papanna and Roopali Donepudi, M.D., both assistant professors, Division of Maternal-Fetal Medicine at the McGovern Medical School at UTHealth, are conducting a study to predict the impact of umbilical artery lengthening associated with twin-twin transfusion syndrome (TTTS) on long-term heart health. The recipient fetus in TTTS has elevated blood pressures and this condition for a prolonged duration can affect the health of the growing blood vessels. The preliminary findings seen in their research show that the recipient umbilical artery in the umbilical cord is elongated in comparison to the corresponding vein in more than 50 percent of the fetuses. The effects of these findings on the long-term cardiovascular health outcomes need to be determined.

Outreach and Collaboration

Another characteristic that sets The Fetal Center apart is the team's dedication to collaborating with the healthcare community to advance TTTS diagnosis and treatments.

In 2016, The Fetal Center collaborated on a "Think Tank" event to discuss three major topics impacting fetal medicine – fetal center designations, new instruments for fetal surgery, and clinical trials. A group of 30 individuals, including private maternal-fetal medicine specialists, fetal surgeons, fetal radiologists, fetal cardiologists, pediatric surgeons, pediatric cardiologists, architects, administrators and an entrepreneur, convened to discuss and provide input into the three topics. Among the outcomes, the group developed a recommendation for a national, voluntary three-tier system for designating fetal centers.

As it pertains to TTTS, under the proposed system, Tier 1 centers would have diagnostic capabilities; Tier II centers would provide laser therapy for TTTS; and Tier III centers would provide complete diagnostic, treatment and surgical care for TTTS patients. Tier III fetal centers would need to be affiliated with a Level IV neonatal



KuoJen Tsao, M.D., and Alexandra Patch, RN, review details of a TTTS diagnosis for a patient of The Fetal Center and discuss a comprehensive plan of care for both mother and her babies.

intensive care unit (NICU) and Level IV maternal center, based on guidelines from the American Academy of Pediatrics and the American Congress of Obstetricians and Gynecologists (ACOG). The Fetal Center at Children's Memorial Hermann Hospital, affiliated with the physicians at McGovern Medical School at UTHealth, would be among a small group of Tier III facilities in the United States.

Educating Families About TTTS

The Fetal Center is also committed to providing patients and their families with accurate, current information about TTTS. Several resources are available to patients on the Children's Memorial Hermann Hospital website, including a fact sheet, patient stories and the latest outcomes statistics.

The TTTS patient education video serves as a comprehensive, objective guide to the condition and treatment options for patients and their families.

In addition, The Fetal Center has created an online patient education video series dedicated to informing patients and their families about prenatal and postnatal care for specific fetal conditions, among them TTTS. The TTTS video provides families with objective clinical information about the potential risks associated with monochorionic twins as well as detailed information about available treatment options, including laser photocoagulation for severe TTTS. An animated guide depicts the five stages of TTTS, along with information about other common conditions that may affect multifetal gestations.

To view the TTTS video in English or Spanish, visit childrens.memorialhermann.org/ttts.

Johnson Twins Survive TTTS – and Thrive

Patient Story

The Johnson twins, Amelia and Ainsley, were prenatally diagnosed with TTTS and underwent fetal surgical treatment, performed by affiliated physicians of The Fetal Center at Children's Memorial Hermann Hospital.

When Stacy and Jason Johnson learned they were pregnant with twins, they were surprised and delighted. Two weeks later, an ultrasound revealed an even greater surprise – identical twins, a rarity, occurring in fewer than four of 1,000 pregnancies.

Even without complications, a twin pregnancy is considered a high-risk pregnancy, so early in her pregnancy, Stacy began seeing high-risk pregnancy physician Sean Blackwell, M.D., Chief-of-Service at Children's Memorial Hermann Hospital and chair of the Department of Obstetrics, Gynecology and Reproductive Sciences at McGovern Medical School at UTHealth. As part of her prenatal care, Stacy was examined every two weeks, and routine ultrasounds were performed, to make sure the fetuses were growing and developing properly.

When Stacy was 21 weeks pregnant, an ultrasound revealed a potential problem, and Dr. Blackwell referred the Johnsons to The Fetal Center at Children's Memorial Hermann Hospital for further evaluation. There, a fetal echocardiogram ruled out heart problems, but additional ultrasounds revealed an imbalance of amniotic fluid in the twins' sacs. Anthony Johnson, D.O., co-director of The Fetal Center, explained that the fluid imbalance is characteristic of a complication of monochorionic twins (identical twins where the fetuses share one placental mass) called twin-twin transfusion syndrome, or TTTS.

In monochorionic twins, vascular connections within the shared placenta allow the exchange of blood, hormones and biochemical products between the fetuses. Normally, this exchange is balanced, but in 10 percent to 15 percent of cases, an imbalance develops, with one twin, the donor, becoming hypotensive (low blood pressure) with reduced amniotic fluid volume, and the other twin, the recipient,

developing hypertension (high blood pressure) with hydrops (increased amniotic fluid volume). If left untreated, the condition can lead to preterm delivery, fetal and neonatal death, and long-term developmental delay in the survivors.

Stacy recalls, "On the day of our initial diagnosis, a Monday, Dr. Johnson told me I was in Stage I, and if I progressed I would feel more pain, which I did for the next 48 hours. It became almost unbearable. On Wednesday morning at my follow-up, we were told I had progressed to Stage III, and I would need surgery the next day."

On Thursday, Dr. Johnson and The Fetal Center surgical team performed surgery that included two procedures. First, they performed laser ablation of the placental blood vessels between the twins, to stop blood exchange between the fetuses. Then, the excess amniotic fluid from the sac of the recipient twin was removed as part of the procedure.

The surgery went smoothly, and 10 weeks later, two teams, led by Dr. Blackwell, delivered the Johnsons' healthy twin daughters. Amelia, the recipient twin, was born at 7:55 a.m., weighing 3 pounds, 5 ounces, and Ainsley, the donor twin, was born four minutes later, weighing 3 pounds, 2 ounces. To Stacy's delight, both of the girls have her family's trademark dimpled chins. Because of their low birth weights, they were admitted to Children's Memorial Hermann Hospital's neonatal intensive care unit (NICU) for continuous monitoring.

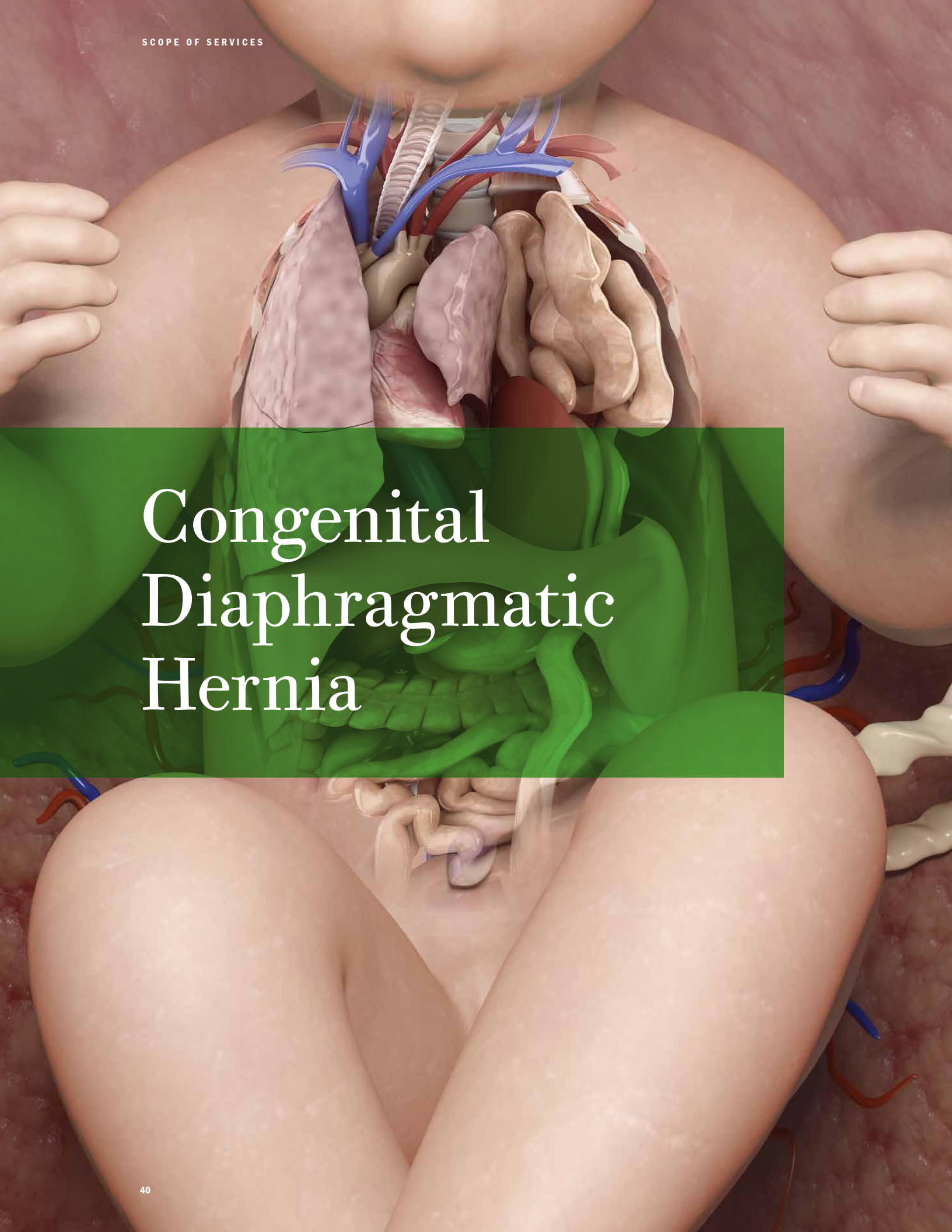
"Fortunately, through regular screening ultrasounds, the Johnsons' situation was diagnosed early, and we were able to successfully ablate the vessels between the two fetuses. The delivery went off without complication, and the Johnson twins are beautiful, healthy babies."

The Johnsons credit the team at Children's Memorial Hermann Hospital and The Fetal Center, especially Drs. Blackwell and Johnson, with their successful outcome. Says Jason, "They were great communicators, both between the two of them, and with us. They explained what was going on the whole time, then gave us time to think and to make decisions. There was so much synergy between the maternal-fetal medicine specialists and the rest of The Fetal Center team."

Says Dr. Johnson, "Fortunately, through regular screening ultrasounds, the Johnsons' situation was diagnosed early, and we were able to successfully ablate the vessels between the two fetuses. The delivery went off without complication, and the Johnson twins are beautiful, healthy babies."

After four days, the twins were transferred to the NICU at Memorial Hermann Memorial City Medical Center, closer to the Johnsons' home. Stacy and Jason enjoyed the convenience of having their daughters close by and appreciated having a private room there where they could spend time with the babies.

When the twins finally came home four weeks later, Amelia had grown to 4 pounds, 11 ounces, and Ainsley weighed in at 4 pounds, 8 ounces. They're now six months old, and Stacy says they have continued to thrive. "On all of our pediatrician and neurology appointments, the girls' doctors have said they are very healthy and happy babies, meeting all the developmental milestones for term babies. It's been such a team effort!"



Congenital Diaphragmatic Hernia

The Congenital Diaphragmatic Hernia Program

Congenital diaphragmatic hernia (CDH) results from the abnormal development of the fetal diaphragm, causing a hole in the muscle that can lead to underdevelopment of the lungs and potentially life-threatening breathing difficulties after birth. One in every 2,500 infants is born with CDH. Its cause remains unknown, and because each case is different, there is wide variation in recovery time and postnatal care that varies based on the severity of disease.

L-R: Srikanth Sridhar M.D.; KuoJen Tsao, M.D.; Kevin Lally, M.D., M.S., FACS; Suzanne Lopez, M.D.; Kenneth Moise, Jr., M.D.; Jan Deprest, M.D., Ph.D.; Anthony Johnson, D.O.

Experienced Team

Surgeons and other physicians affiliated with Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth have a long history of dedication in caring for newborns with CDH. In addition to establishing the first extracorporeal membrane oxygenation (ECMO) program in Texas, and an ECMO Center of Excellence since 2006, Children's Memorial Hermann Hospital is home to an integrated CDH team that includes affiliated pediatric surgeons, neonatologists, pediatric anesthesiologists and maternal-fetal medicine specialists, who provide optimal and seamless care from prenatal diagnosis to delivery to postnatal care. This treatment approach has translated to higher-than-expected risk-stratified survival, as well as one of the highest rates of surgical repair in the world.

Prenatal Intervention

Congenital diaphragmatic hernia (CDH) remains an unsolved problem and a challenging clinical disease for physicians, surgeons and scientists, despite decades of research. Although the hole in the diaphragm is a surgically correctable defect, the arrest in development of the lungs prenatally results in unacceptably high rates of neonatal mortality and long-term morbidity for the surviving child.

In an ongoing effort to provide optimal patient care, The Fetal Center at Children's Memorial Hermann Hospital and the affiliated physicians at McGovern Medical School at UTHealth have been granted FDA and institutional approval to offer fetoscopic endoluminal tracheal occlusion (FETO) for the prenatal treatment of severe CDH, aimed to demonstrate the Center's ability to safely insert and remove the FETO device in severe CDH fetuses. This minimally invasive fetoscopic procedure is typically performed between 27 and 29 weeks* gestation and is removed at 34 weeks. **The Fetal Center is now accepting patients for evaluation as study participants, see criteria on page 42.**

*Amendment to FETO trial inclusion criteria is pending IRB approval at time of print. Contact The Fetal Center with related inquiries.

L-R: Co-directors of The Fetal Center, Kenneth Moise, Jr., M.D.; KuoJen Tsao, M.D.; and Anthony Johnson, D.O., work with visiting professor Jan Deprest, M.D., Ph.D., to perform the FETO procedure for the prenatal treatment of CDH for a patient of The Fetal Center.

Approaching Every CDH Patient as a Potential Survivor

While awaiting results of the trial, the CDH team at The Fetal Center continues to make progress in the management of diaphragmatic hernia with optimized mechanical ventilation strategies, pharmacotherapy and other therapeutic modalities, including extracorporeal membrane oxygenation. Physicians at The Fetal Center take a very aggressive approach to the management of the condition, and are one of a handful of teams in the country that operate on 93 percent of all patients, repairing the hole in the diaphragm surgically to give each child a chance of survival.

Thanks to more accurate prenatal diagnosis and the work of the International CDH Study Group Registry, which resides at Children's Memorial Hermann Hospital and McGovern Medical School, the global survival rate of infants born with CDH is

steadily rising. Based on risk-adjusted data, The Fetal Center's outcomes are in the top 10 percent or higher.

Investigators at The Fetal Center are also engaged in promising research using extracellular vesicles, small membrane particles released from mesenchymal stem cells, to help manage pulmonary hypertension and reduce the mortality rate for CDH. While their research remains in the early stages, their aim is to translate innovative therapies to the clinical setting as quickly as possible.

Extracorporeal Membrane Oxygenation

Children's Memorial Hermann Hospital was the first hospital in Houston to offer an organized program for pediatric extracorporeal membrane oxygenation (ECMO), a treatment used for newborns and children who are critically ill with respiratory failure, functioning like a heart-lung bypass machine allowing time for the heart and lungs to rest and recover. The program was the first in the Greater Houston area to be named a Designated Center of Excellence by the Extracorporeal Life Support Organization (ELSO), which has recognized the program continually since the inception of the award. The ELSO award recognizes ECMO programs worldwide that distinguish themselves by having processes, procedures and systems in place that promote excellence and exceptional care in extracorporeal membrane oxygenation.

Affiliated specialists and nurses at Children's Memorial Hermann Hospital perform ECMO treatment to deliver cardiac and respiratory support to a Neonatal Intensive Care Unit (NICU) patient.

Research

Fetoscopic Endoluminal Tracheal Occlusion (FETO) Trial

In 2015, The Fetal Center was granted FDA and institutional approval to offer fetoscopic endoluminal tracheal occlusion (FETO) for the prenatal treatment of CDH. FDA approval for the utilization of the fetoscopic balloon device for FETO intervention in the United States was spearheaded by Anthony Johnson, D.O., through North American Fetal Therapy Network (NAFTNet).

Patients undergoing FETO intervention at Children's Memorial Hermann Hospital will participate in The Fetal Center's feasibility study, aimed to demonstrate The Fetal Center's ability to safely insert and remove the FETO device in severe CDH fetuses. Upon completion of the feasibility study, The Fetal Center, along with other centers of the NAFTNet FETO group, will move to join the Tracheal Occlusion to Accelerate Lung Growth (TOTAL) Trial, led by Jan Deprest, M.D., Ph.D., Professor of Obstetrics and Gynaecology at the University Hospitals Leuven in Belgium. The international, multicenter randomized controlled trial is evaluating survival and morbidity in fetuses with severe CDH detected prior to 29 weeks gestation. The fetal surgeons affiliated with Children's Memorial Hermann Hospital and McGovern Medical School, with

extensive experience in fetoscopic intervention (> 500 fetoscopic cases), have worked with Professor Deprest in Belgium and in Houston to bring the FETO technique to The Fetal Center. **The Fetal Center is currently accepting patients for evaluation as FETO trial study participants.**

Criteria for potential inclusion in the FETO trial include the following:

- Isolated left CDH
- Normal fetal karyotype
- Gestational age of less than 30 weeks (the procedure is performed between 27 and 29 weeks)*
- Severe CDH as defined by an observed-to-expected lung-to-head ratio of less than 25 percent on fetal ultrasound*
- Liver herniation into the fetal chest

Exclusion criteria are:

- Additional life-threatening anatomic or genetic anomalies
- Multi-fetal pregnancy
- History of latex allergy
- Shortened cervix (less than 15 millimeters)
- Preterm labor or uterine anomaly strongly predisposing to preterm labor

Mothers must be between the ages of 18 and 50 with a singleton pregnancy and be willing to live within 30 minutes of Children's Memorial Hermann Hospital while participating in the study. The trial examines this group to determine whether tracheal occlusion will improve the overall outcome.

For more information about the FETO trial and CDH care at Children's Memorial Hermann Hospital, visit childrens.memorialhermann.org/FETO-trial. To refer a patient or speak to a clinical consultant, please call 832.325.7288.

*Amendment to FETO trial inclusion criteria is pending IRB approval at time of print.
Contact The Fetal Center with related inquiries.

International CDH Study Group and Registry

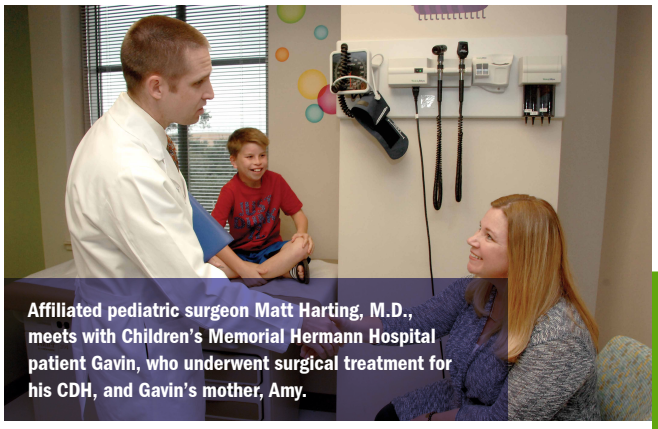
Overall worldwide survival of infants born with diaphragmatic hernia has increased from about 55 percent to close to 70 percent in the last 20 years. Unfortunately, CDH remains a challenge for physicians, surgeons and scientists. Although the defect can be corrected with surgery, the arrest in prenatal development of the lungs results in unacceptably high rates of neonatal mortality and long-term complications for children born with CDH.

Affiliated physicians at Children's Memorial Hermann Hospital and the division of General and Thoracic Pediatric Surgery at McGovern Medical School are internationally recognized leaders in providing state-of-the-art fetal care, neonatal critical care and minimally invasive surgical repair of CDH. The care they provide is based on data collected and new insights gained through the international Congenital Diaphragmatic Hernia Study Group and the CDH Registry, which reside at the hospital and medical school.

In the 20 years that have passed since the CDH Study Group was founded, the voluntary collaborative has gathered data on more than 9,500 babies with diaphragmatic hernia. The registry now represents centers in 14 countries. Information from this

registry has been used in more than 40 CDH Study Group reports. These projects evaluated diagnostic and prognostic variables such as preductal oxygen saturation, defect size/anomaly association and pulmonary hypertension.

Comprehensive Long-term Care

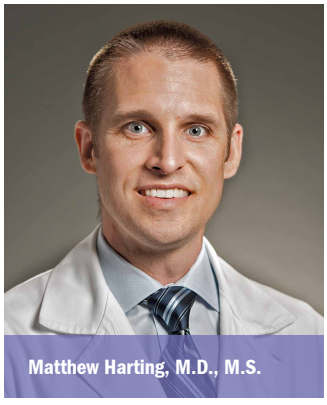


Affiliated pediatric surgeon Matt Harting, M.D., meets with Children's Memorial Hermann Hospital patient Gavin, who underwent surgical treatment for his CDH, and Gavin's mother, Amy.

Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth together operate the only long-term multidisciplinary follow-up clinic for CDH in the southwestern United States. Led by pediatric surgeon Matt Harting, M.D., the long-term clinic is staffed by a team of specialists from all associated medical disciplines. The clinic allows patients to conveniently see all physicians relevant to their case, in a single visit under one roof. In addition to offering patients and families convenience, the clinic allows physicians to optimize patient care, collect data and understand the challenges faced by families of children with CDH in ways that were previously impossible.

CDH is an embryonic defect with many facets. Along with underdevelopment of the lung tissue, the lung vasculature is compromised. Most children who survive severe CDH have long-term pulmonary problems. While the specialists at The Fetal Center can assess how much pulmonary hypoplasia infants are likely to have at birth, there are critical aspects of patient survival related to the lung vasculature that are difficult to measure and predict. The International Congenital Diaphragmatic Hernia Registry provides excellent information, but The Fetal Center also relies on the physicians who see patients over the long term to conduct research on outcomes and publish it.

To that end, specialists at the High-risk Multidisciplinary Clinic for Congenital Diaphragmatic Hernia track a range of outcomes across various subsets of its patient population, creating a rich source of long-term data that enables them to identify the best interventions for each case. Data collected can be tied to decisions about future research, enabling the physician researchers to positively impact patient outcomes throughout the timeline of patient care.



Matthew Harting, M.D., M.S.

Ashley Harmon, M.S.N., FNP-C, APRN, RN

Cheryl Samuels, RN, CPNP

Baby Luke's Battle

Patient Story

Megan Webb and her twins, Jayden (L) and Luke (R), who was diagnosed prenatally with CDH and treated by the multidisciplinary team at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth.

The Twin Medical Miracles

Jayden and Luke. Two-year-old identical twin boys. They run and wrestle, giggle and converse in their own shared lingo – jibber-jabber only they understand. But Jayden is taller, more robust. Luke wears the same size clothes as the boys' younger brother, Cooper. Each of the twins in his own way is a medical miracle. Luke was born with a congenital diaphragmatic hernia (CDH). In spite of being Luke's identical twin, Jayden was not affected.

CDH occurs when a hole develops in the fetus' diaphragm, allowing abdominal organs to intrude into the chest cavity. This results in compression and underdevelopment of the lungs and abnormalities in the pulmonary blood vessels. The exact cause of CDH is unknown.

Jayden and Luke's dad and mom, Ryan and Megan Webb of San Angelo, Texas, learned at 19 weeks that a sonogram had revealed an anomaly in one of the twins. Dr. Jorge Blanco, their maternal-fetal medicine specialist, suspected possible CDH and referred them to The Fetal Center at Children's Memorial Hermann Hospital.

Ryan Webb recalls, "On the Tuesday before Thanksgiving, the sonogram showed a part of Luke's stomach reaching into his chest cavity. On the Monday after Thanksgiving, we were in Houston."

Visiting The Fetal Center

The Webbs' initial meeting with The Fetal Center's co-director KuoJen Tsao, M.D., pediatric surgeon at McGovern Medical School, was followed by a sonogram, an

echocardiogram and a MRI. Then consultations with a geneticist and a cardiologist and a wrap-up with Dr. Tsao, who counseled them about what to expect and explained that the severity of the problem, which would become more apparent as the pregnancy proceeded, would determine how their baby's CDH would be treated. The MRI confirmed CDH in one baby, but showed no other malformations.

Megan's prenatal team – Dr. Blanco in San Angelo and the affiliated physicians at The Fetal Center – recommended that she return to Houston a month before her due date in case of a possible early delivery, so in January 2014, the Webbs temporarily relocated to Houston.

On February 8, the babies were delivered by C-section at Children's Memorial Hermann Hospital with two full medical teams in attendance: one for Luke, the other for Jayden. Ryan remembers a room packed with specialists all focused on bringing two special boys into the world.

The Webbs were prepared for the fact that Luke would have complete respiratory failure when he emerged. A nurse was standing by with a portable apparatus that would "breathe" for him until he got onto a ventilator. Megan kissed him on the forehead and he headed for the Neonatal Intensive Care Unit (NICU), where he would stay for the next 40 days.

Ryan describes Children's Memorial Hermann's NICU as "absolutely amazing." "They took care of Luke like he was their own child," Megan adds. "We couldn't hold him ourselves because it would overstimulate him, but the nurses knew exactly what he needed."

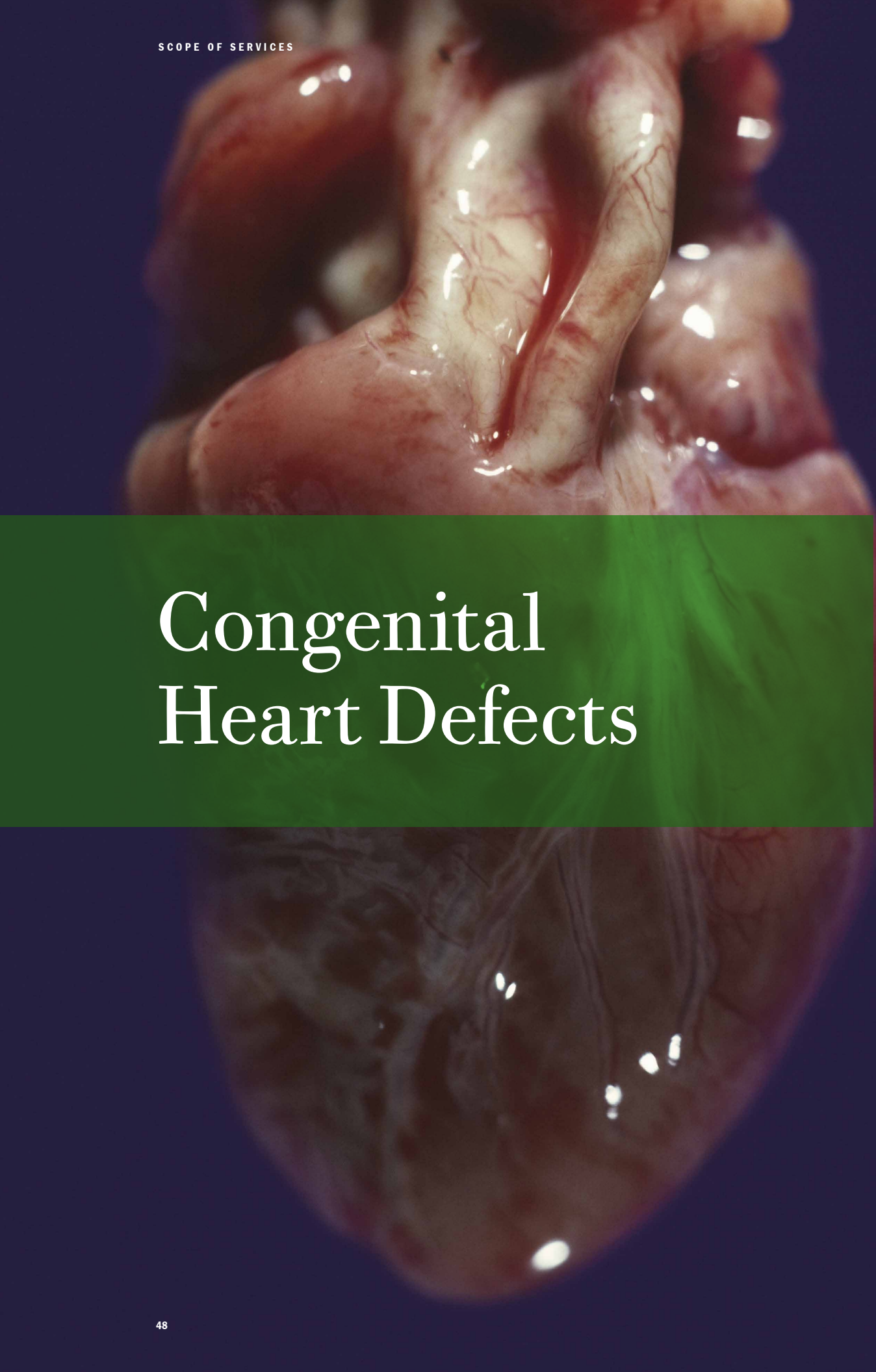
Luke's Medical Journey

Luke's condition had to stabilize and his blood oxygen levels improve before the hernia could be repaired. Mary Austin, M.D., a pediatric surgeon at McGovern Medical School and member of The Fetal Center team, monitored Luke's progress carefully to determine when conditions were optimal, which occurred when Luke was 11 days old. During the repair surgery, Dr. Austin performed a laparotomy, using Luke's existing tissue rather than mesh, to patch the hole in his diaphragm. The tissue allowed the repair to grow with him and minimized the need for subsequent surgery to replace an "outgrown" patch.

After the repair, Luke's lungs began to expand, paving the way for him to breathe without a ventilator. The next challenge was to deal with coarctation – narrowing – of the aorta. On March 1, a heart catheterization expanded Luke's narrowed aorta, allowing him some extra healing time before undergoing another major procedure. He started gaining weight and breathing on his own, and on March 18 he left the NICU for a long-awaited reunion with his twin brother at the Webbs' home away from home.

Today, Megan describes Luke as a "walking, talking, running machine." Both toddlers have crossed the developmental milestones that you'd expect at their age, but "Luke gets so excited when he does something before Jayden."

A half a state away from Houston, the Webbs speak glowingly of Children's Memorial Hermann and the love and care their family received at The Fetal Center and NICU. "There's nothing we can do to repay them for that."



Congenital Heart Defects

The Fetal Cardiology Program

Congenital heart defects are heart conditions that develop in pregnancy and are present at birth. They are the most common type of birth defect, affecting nearly 1 percent – or about 40,000 – of births per year in the United States. Some heart defects are critical, requiring specialized treatment immediately after birth.

L-R: Gurur Biliciler-Denktas, M.D., and Helena Gardiner, M.D., Ph.D., co-directors of The Fetal Cardiology Program at The Fetal Center.

The Fetal Cardiology Program at The Fetal Center at Children's Memorial Hermann Hospital, led by McGovern Medical School at UTHealth's physicians, Helena Gardiner, M.D., Ph.D., and Gurur Biliciler-Denktas, M.D., specializes in the early detection and diagnosis of critical congenital heart defects to reduce morbidity and mortality in babies.

Patients referred to the Fetal Cardiology Program are cared for by a multidisciplinary team of specialists, in collaboration with pediatric cardiologists and pediatric cardiothoracic surgeons affiliated with the Children's Heart Center at Children's Memorial Hermann Hospital and McGovern Medical School. The Fetal Cardiology Program's team of fetal and perinatal cardiologists has firsthand experience and a deep understanding of the needs of the baby with critical congenital heart disease, before, during and following birth. The Fetal Center evaluates approximately 125 cases of major congenital heart defects each year.

The vision of the Fetal Cardiology Program is to provide patients and physicians with:

- A collaborative patient care approach with referring OB/GYN and/or maternal-fetal medicine specialists to ensure proper co-management of all patients

- Timely and accurate diagnosis of a complex range of fetal heart defects, circulatory problems and the associated malformations seen in one-third of babies during pregnancy, as early diagnosis is critical to the patient's surgical care and long-term treatment plan
- Optimal management during pregnancy, delivery and into neonatal care, providing patients with immediate access to a multidisciplinary team that includes maternal-fetal medicine specialists, fetal cardiologists, genetic counselors, neonatologists, pediatric cardiologists, pediatric anesthesiologists, pediatric cardiothoracic surgeons, pediatric surgeons (for babies with multiple problems) and social workers
- Training and education of obstetricians and sonographers, to improve early detection and increase timely and accurate prenatal referral for critical congenital heart defects
- Research to increase knowledge of the early signs and progression of critical congenital heart defects and cardiac failure in babies with complex circulations, for example, in twins and babies with vascular tumors

William I. Douglas, M.D. – affiliated with the Children's Heart Center – performs cardiovascular surgery on a patient at Children's Memorial Hermann Hospital. Early and accurate recognition of these congenital cardiac conditions is required for appropriate and timely treatment.

Advanced Fetal Heart Screening and Diagnosis

Early diagnosis of fetal heart conditions is often critical to the long-term treatment plan and outcome of the baby, as it allows physicians to accurately plan for the baby's delivery, ensuring physician teams critical to the baby's care are on standby as needed. Each year, the Fetal Cardiology Program performs about 650 fetal echo scans, based on referrals for suspected heart defects or for complex pregnancies.

The Fetal Center's multidisciplinary approach enables the care of some of the most complex fetal cardiac cases, including:

- Complex structural congenital heart defects in singletons and multiple pregnancies.
- Twin-twin transfusion syndrome (TTTS) – a rare, serious condition that can occur in pregnancies in which identical twins share a placenta. Abnormal blood vessel connections form in the placenta, allowing blood to flow unevenly between the babies, often causing one of the babies to become anemic.

- Twin anemia-polycythemia syndrome (TAPS) – a form of TTTS in which one baby has a fetal cardiovascular problem that complicates usual management and laser therapy.
- Twin reversed arterial perfusion (TRAP) – twin pregnancy where one baby has not formed properly, creating a blood imbalance that adversely affects the other twin.
- Sacrococcygeal teratoma (SCT) – a tumor that can cause heart failure, requiring accurate assessment to plan the timing of fetal intervention or early delivery.
- Congenital diaphragmatic hernia (CDH) – a condition that may impact heart function and growth, resulting in a smaller left side of the heart. This may indicate structural heart disease and impact surgical planning.
- Arrhythmias – slow or fast heart rates, requiring complex assessment of the mechanism causing the arrhythmia and knowledge of the effect and timing of arrhythmia drugs to select the correct drug therapy.
- Hydrops – a condition in the fetus characterized by an accumulation of fluid, or edema, in at least two fetal compartments, potentially indicating cardiac hemodynamic failure.

Gurur Biliciler-Denktas, M.D., details the four chambers of the fetal heart (shown visually on the monitor) while performing an ultrasound scan for a patient of The Fetal Center.

Research

The Fetal Center is a leader in research to advance fetal cardiology and detection of congenital heart defects. The team's collaborations and contributions to research of fetal cardiology and fetal cardiovascular medicine include:

Measuring Fetal Cardiac Function

Dr. Gardiner has used new ultrasound techniques (speckle tracking) to measure heart and aortic wall strain in normal fetuses and those affected by congenital heart defects to compare different methods to measure heart function. This assessment of cardiovascular function has been adapted for use in complex twin pregnancies (including TTTS and TRAP) to provide insights into the pathophysiology and development of TTTS. This builds on her work investigating the programming effects seen in childhood of the differing uterine environments on genetically identical twins developing TTTS and undergoing different treatment strategies before birth.

In addition, Dr. Gardiner has collaborated internationally to develop automated systems to improve the reliability of measurements of fetal cardiac function in different centers (Myocardial Performance Index, MPI).

And in collaboration with a team in the Netherlands, Dr. Gardiner is clinically testing how well a new mathematical model predicts outcomes in high cardiac output pregnancies, including TRAP and fetuses with tumors such as chorangioma and sacrococcygeal teratomas (SCT).

Evaluation and Management of Fetal Aortic Stenosis

Dr. Gardiner led a multicenter study of 214 fetuses in Europe with aortic stenosis to document the natural history and whether a new treatment, fetal aortic valvuloplasty, alters outcomes. The team also investigated the role of postnatal management in determining success of the fetal procedure and published on institutional bias in multicenter contributions to such studies. This work was presented at the American Heart Association Scientific Sessions 2014 and won the Council of Cardiovascular Disease in the Young's Outstanding Research Award in Pediatric Cardiology. A subsequent presentation by the team was a finalist in the Young Investigator Award at the European Paediatric Cardiac Association's 49th Annual Meeting, Prague, Czech Republic, May 2015.

Application of Novel Imaging Techniques

The team's research includes using novel imaging methods, such as high-resolution episcopic microscopy (HREM), and ultrasound improvements, such as biplane technology, to improve the diagnostic ability and knowledge of the developing fetal heart and aid prediction of babies who will require specialized services at the time of delivery because of airway obstruction (the EXIT procedure).

Dr. Gardiner is also working with maternal-fetal medicine specialists at UTHealth to develop a novel method of preterm labor management using targeted drugs, using her knowledge and experience of novel HREM technology imaging methods – *"Uterus-targeted liposomes for preterm labor management."*

Brain Growth and Adverse Neurodevelopmental Outcomes in Fetuses With TTTS and Congenital Heart Disease

Dr. Gardiner and her research collaborators have used 3D MRI volume reconstruction of the fetal brain in TTTS to show that the brain volumes are similar following successful laser in ex-recipients and ex-donors (Best Poster Fetal Medicine, The British Maternal and Fetal Medicine Society, 2012) but that reduced brain volume in ex-donors predicts adverse outcomes (Best Oral presentation, International Society of Ultrasound in Obstetrics and Gynecology, 2012, Copenhagen).

The team has also described impaired brain growth in fetuses with congenital diaphragmatic hernia (Proceedings European Paediatric Cardiac Association 47th Annual Meeting, London, England. May 2013).

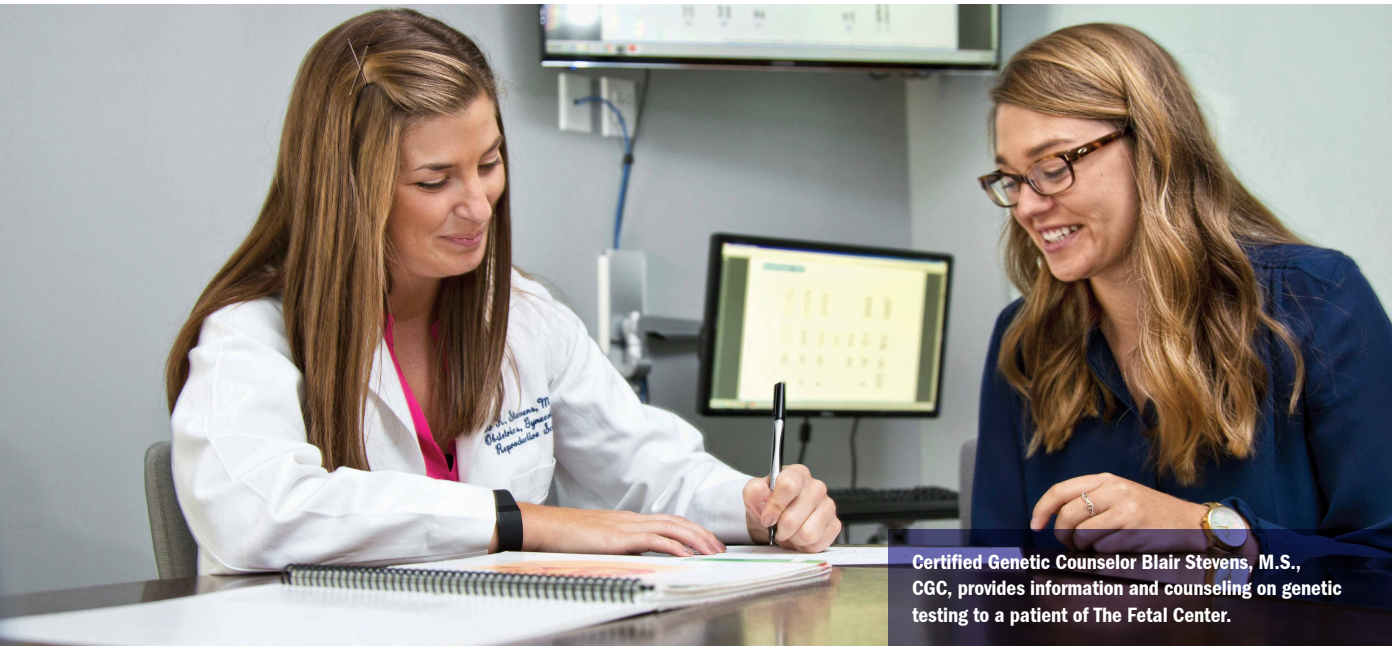
Prenatal Diagnosis of Congenital Heart Disease

Dr. Gardiner has participated in research to assess how well the clinical community screens for congenital heart disease, the role of adjunctive technology (telemedicine screening) and how clinicians can use public records to link mothers and babies and explore the regional variation in the prevalence, prenatal diagnosis rate and cost of critical congenital heart defects in infants in Texas (Ph.D. committee member – UTHealth, School of Public Health at Houston, Texas).

Dr. Biliciler-Denktas' research aims to estimate the sensitivity of prenatal ultrasound in diagnosing critical congenital heart disease in Texas. By using the data from the Texas Birth Defects Registry Database, she is working to identify factors that affect the sensitivity of diagnosis, especially related to the population of Texas.

Counseling Families Following a Diagnosis of Congenital Heart Disease

Counseling families is an important part of management following a diagnosis of congenital heart disease. Dr. Gardiner is a senior author in an ISUOG initiative in a worldwide survey of experts' attitudes to prenatal counseling for neurodevelopmental delay in congenital heart disease.



Certified Genetic Counselor Blair Stevens, M.S., CGC, provides information and counseling on genetic testing to a patient of The Fetal Center.

The presence of a heart defect increases the chances a baby may have an underlying genetic condition, such as Down Syndrome. Dr. Gardiner's and Dr. Biliciler-Denktas' diagnostic expertise is essential in determining the nature of the heart defect, so an accurate genetics assessment can be made. The genetic counselors at The Fetal Center work closely with the cardiologists to provide families with information about these risks, genetic testing options, emotional support and resources.

Outreach and Training

Prenatal screening of critical fetal cardiac anomalies is essential to improving patient outcomes and is an important part of an integrated, managed screening program to ensure healthcare professionals are properly trained and experienced in the latest techniques, and equipment is up to date and correctly set up.

The Fetal Cardiology Program training is based on an international standard – the Five Transverse Views – a systematic examination of the fetal heart based on a series of five views across the fetal body, using ultrasound technology. This is considered a practical and proven method of imaging the fetal heart. The optimal time for a fetal cardiac anomaly scan is around 20 weeks' gestation and consists of a sweep of the heart that takes in these five key views as it traces the connections and relationships of the heart structures. The Five Transverse Views protocol is designed to detect, but not diagnose, almost all forms of structural heart disease in a systematic, practical and timely way.

Helena Gardiner, M.D., Ph.D., provides training to Perinatal Sonographer Kelly Roberston, B.S., RDMS, at The Fetal Center.

Dr. Gardiner heads the Fetal Cardiovascular Fellowship and provides ongoing training to sonographers, affiliated obstetricians, maternal-fetal medicine specialists and pediatric cardiologists at McGovern Medical School at UTHealth via monthly fetal echo lectures and the in-house fetal echo American Registry for Diagnostic Medical Sonography (ARDMS) accreditation program. Her team also conducts training courses to obstetricians and sonographers across Houston.

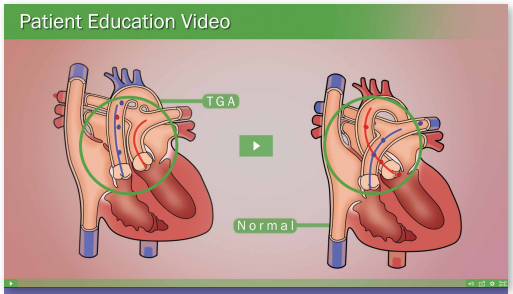
The Fetal Cardiology Program training is based on an international standard – the Five Transverse Views – a systematic examination of the fetal heart based on a series of five views across the fetal body, using ultrasound technology.

Dr. Biliciler-Denktas is the Program Director of Advanced Pediatric Non-Invasive Cardiac Imaging, a fellowship program for pediatric cardiologists interested in spending an additional year of training in advanced imaging, including fetal echocardiography. By training future fetal cardiologists, Dr. Biliciler-Denktas hopes to increase the number of U.S. centers with qualified fetal cardiac specialists who can diagnose and treat congenital heart disease patients from early gestations. She has helped organize hands-on fetal training courses internationally and has taught many pediatric cardiologists how to perform fetal cardiac scanning and to diagnose.

Dr. Biliciler-Denktas currently serves on the organizing committee of the World Pediatric Cardiology and Cardiovascular Surgery Congress 2017 and co-chairs the pre-Congress Fetal Cardiology meeting.

Educating Families About Fetal Cardiology

Children's Memorial Hermann Hospital offers educational resources intended to provide families with comprehensive, objective information on fetal complications that may require intervention. An online patient education video series helps patients and their families learn more about specific conditions and available treatment options and also serves as a helpful resource to physicians who strive to best communicate clinical details, so that families can make informed decisions for their loved ones.

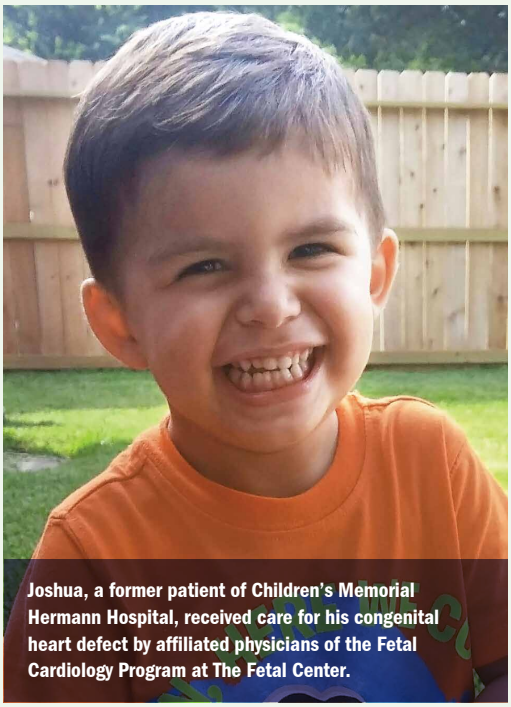


Part of a series of online patient education videos, the animated heart videos serve as a helpful resource for patients diagnosed with a heart condition.

The patient education video series covers four fetal heart conditions, including transposition of the great arteries (TGA), hypoplastic left heart syndrome, coarctation and tetrology of Fallot. **To view patient education videos on fetal conditions, visit childrens.memorialhermann.org/thefetalcenter/patient-education.**

Despite a Congenital Heart Defect, Joshua Doesn't Miss a Beat

Patient Story



Joshua, a former patient of Children's Memorial Hermann Hospital, received care for his congenital heart defect by affiliated physicians of the Fetal Cardiology Program at The Fetal Center.

Brandi recalls the mixed emotions she felt during her routine 20-week ultrasound. "They first said, 'It's a boy,' then seconds later, 'He has a heart defect.' It was unreal." Her OB/GYN referred her to the fetal cardiology team at The Fetal Center at Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth, where her unborn son was diagnosed with a rare congenital heart disease (CHD) known as truncus arteriosus, which comprises about 1 percent of congenital heart defects and is slightly more common in boys than girls.

Helena Gardiner, M.D., Ph.D., co-director of the Fetal Cardiology Program at The Fetal Center, met with the family and explained that her baby born with truncus arteriosus, often simply referred to as "truncus," has only one blood vessel coming out of the heart, instead of the two vessels (pulmonary artery and aorta) that exist in a normal heart. In addition, a baby with this condition will often be born with a hole between the two pumping chambers (ventricles) of the heart. To correct the condition, physicians must perform open heart surgery, typically within weeks of the baby's birth.

Dr. Gardiner went on to explain that in a baby without a CHD, the right side of the heart pumps oxygen-poor blood through the pulmonary artery to the lungs, and the left side of the heart pumps oxygen-rich blood through the aorta to the rest of the body. In a baby with truncus, the single, large blood vessel supplies blood to the body and gives off branches (called pulmonary arteries) to supply blood to the lungs. During surgery, the baby's blood vessels connected to the lungs are removed from the big vessel and connected to the right side of the heart with an artificial tube, and the hole between the pumping chambers is closed, so the left ventricle can pump blood to the body.

Fetal Heart Screening

Brandi's story underscores the importance of fetal heart screening for prenatal diagnoses, to ensure babies with CHDs get the care they need, from initial diagnosis through delivery, and also for continued monitoring after birth. According to Dr. Gardiner, "Fetal diagnosis allows the family to learn about the condition and become familiar with what's to come. This familiarity leads to a level of comfort for the family when the actual treatment is provided. For the physicians, fetal diagnosis allows for better management planning."

On November 12, 2013, Brandi's son, Michael Joshua, was born, full-term and weighing in at a healthy 8 pounds, 11 ounces. "It was hard to imagine Joshua needing surgery," Brandi says, "He was the biggest baby in the neonatal intensive care unit. We got to hold and feed him. The only telltale sign of his condition was his rapid breathing."

Three weeks later, affiliated pediatric cardiovascular surgeon William Douglas, M.D., performed the four-hour open heart surgery at Children's Memorial Hermann Hospital. For Brandi and her family, the day of Joshua's surgery was difficult. "It was tough to let him go," she says, "but we had faith in Dr. Douglas and his team. And thankfully, everything went well."

"Fetal diagnosis allows the family to learn about the condition and become familiar with what's to come. This familiarity leads to a level of comfort for the family when the actual treatment is provided. For the physicians, fetal diagnosis allows for better management planning."

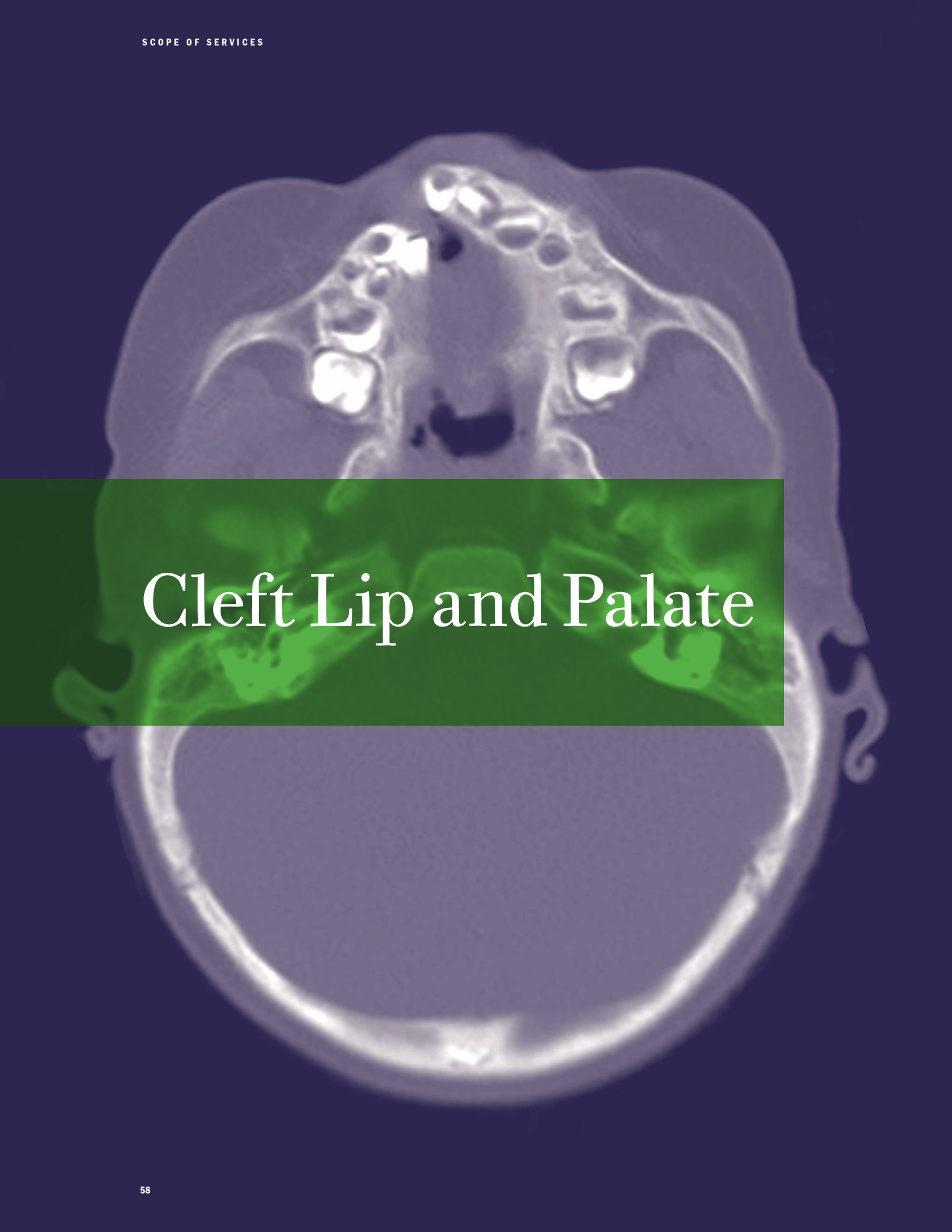
After five days in the pediatric intensive care unit, Joshua was home, breathing easier and well on his way to becoming a vibrant little boy. The family nicknamed his scar "The Zipper," citing it as tangible evidence that his heart defect couldn't beat him. As he was growing and thriving, he received routine tests every three months, to make sure everything was okay.

In February 2015, when Joshua was 15 months old, doctors detected a narrowing of his right pulmonary artery, and affiliated pediatric interventional cardiologist Duraisamy Balaguru, M.D., performed a heart catheterization with balloon angioplasty to stretch open the narrowed area of the artery. Then in July 2015, Joshua developed an aneurysm, and Dr. Douglas performed surgery to replace the right-ventricle-to-pulmonary-artery conduit in Joshua's heart.

Joshua's Recovery

Joshua made a full recovery and is outrunning, outpacing and outperforming the kids his age at day care. Brandi beams, "He knows no limits. He's a very bright kid. He's doing puzzles for 5-year-olds. He's already potty trained. It's amazing to see." At around age 10 – 12, the artificial tube Dr. Douglas used to connect the right side of Joshua's heart to his lungs will need to be replaced as he outgrows it.

Brandi and her family are extremely grateful for the care they have received at The Fetal Center and the Children's Heart Center, throughout their journey. "Everyone there has been absolutely amazing; they held our hands throughout the entire process, keeping us updated, answering our questions, encouraging us to call them anytime. We wouldn't be where we are today without them."



Cleft Lip and Palate

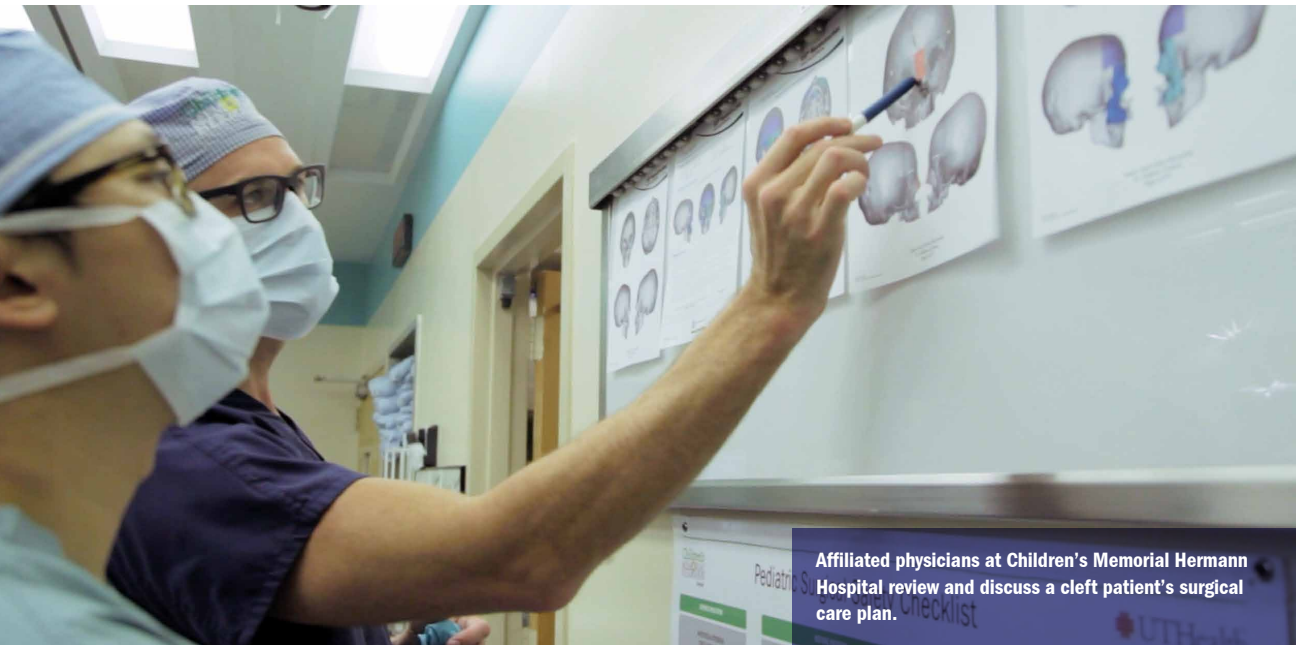
The Cleft Lip and Palate Program

A cleft lip, a cleft palate, or both occur in approximately one in 700 births, making cleft lip and/or palate one of the more common birth defects. Typically, the lip segments of a fetus join together during the seventh week of pregnancy, and the palate closes by the 11th week. When this process does not occur, for either genetic or environmental reasons, the result is a cleft lip and/or palate.

A patient diagnosed with cleft lip and palate.

Cleft cases can vary widely in severity, from small notches in the lip to more advanced cases involving large openings bilaterally of both the lip and the hard and soft palates.

Parents referred to The Fetal Center whose unborn child has been diagnosed with cleft lip and/or palate are referred to the Texas Cleft-Craniofacial Team at McGovern Medical School at UTHealth, which has one of the largest programs of its kind in the region. The multidisciplinary team is comprised of a number of specialists, including affiliated plastic and craniofacial surgeons, oral and maxillofacial surgeons, neurosurgeons, pediatric dentists, orthodontists, geneticists, speech pathologists, otolaryngologists and audiologists, nurses and a team coordinator, among others. Together they have successfully treated over a thousand patients across the spectrum of clefts, from simple to highly complex. This team approach ensures patients receive coordinated, evidence-based care and experience the best possible outcomes.



Affiliated physicians at Children's Memorial Hermann Hospital review and discuss a cleft patient's surgical care plan.

Diagnosis

An increasing number of cleft lip and palate cases are diagnosed in utero by maternal-fetal medicine specialists. In fact, over 70 percent of the cases that are seen in the Texas Cleft-Craniofacial Center are prenatally diagnosed in The Fetal Center or by the parent's primary obstetrician. The other 30 percent, including cases of isolated cleft palate that are rarely diagnosed prenatally, can still be a surprise for parents and physicians. Early detection in utero has become one of the most critical advances in helping parents cope with a cleft lip and/or palate diagnosis.

Volume

While not all patients were diagnosed in utero, the Cleft Lip and Palate Program specialists have seen over 1,850 new cleft patients since The Fetal Center's opening in 2011. This includes consultations and surgical procedures to treat cleft lip and/or palate.

Plan of Care

There are no fetal treatments for clefts; therefore, upon diagnosis, the focus is placed on developing a plan of care for the baby after birth. In most cases, management of pregnancy is routine, and The Fetal Center works closely with the obstetrician to determine the patient's delivery plan.

Babies undergo surgery during the first year of life, typically in two stages. The lip is repaired between 3 and 6 months of age and the palate between 10 months and 1 year. In later childhood, many will undergo upper jaw surgery with bone grafting and revision of both the lip and nose, usually somewhere between the ages of 7 and 10 years old. Finally, any surgery to correct the upper and lower jaw fitting together or a final rhinoplasty is completed around the age of 18.

Key Insights and What Sets Us Apart

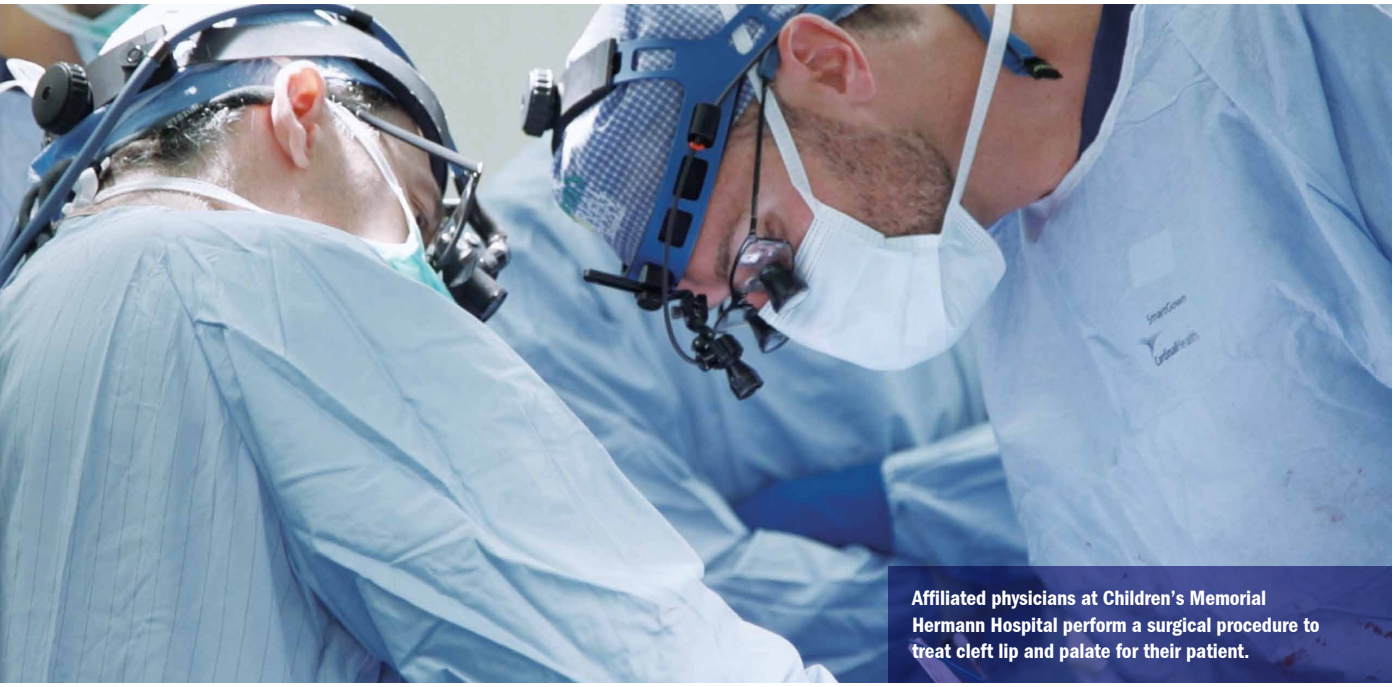
Members of the Texas Cleft-Craniofacial Program recently published an article, "Survey of Parent Experiences in Prenatal Visits for Infants With Cleft Lip and

Palate," in *The Cleft Palate–Craniofacial Journal*, a publication of the American Cleft Palate–Craniofacial Association. In the article, they report results of a survey conducted among parents of children who were born with cleft lip and/or palate, to determine the factors that influence a parent's choice of surgeon/cleft team.

The survey revealed that the surgeon/cleft team's experience level and overall personality were ranked as the most important, whereas the least important was distance traveled. Of the parents, 95 percent used the Internet or social media for research prior to their prenatal visit, 96 percent of the parents found the prenatal visit helpful, and the most useful topics discussed were treatments (surgical, nonsurgical) and feeding techniques.

The aforementioned survey highlights the importance of surgeon/team experience and parent information and support, two areas in which the Texas Cleft-Craniofacial program is unparalleled in Houston. The partnership between the Texas-Cleft Craniofacial Team and The Fetal Center allows parents to obtain information regarding their baby's cleft lip or palate prior to delivery. By coordinating their care, the team assists in the transition from pregnancy to infancy, providing all the information parents need regarding feeding, speech, genetics and a surgical plan for the child.

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



Affiliated physicians at Children's Memorial Hermann Hospital perform a surgical procedure to treat cleft lip and palate for their patient.

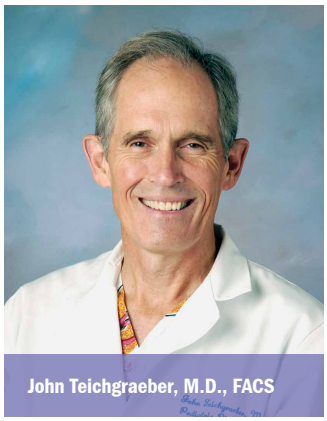
Integrated, Experienced Team

The Program is led by John Teichgraeber, M.D., FACS, professor and director, division of Pediatric Plastic and Craniofacial Surgery. Dr. Teichgraeber has been performing cleft lip and palate surgeries in Houston for over 30 years, during which time he has performed thousands of surgeries. He has also been active with Austin Smiles, a

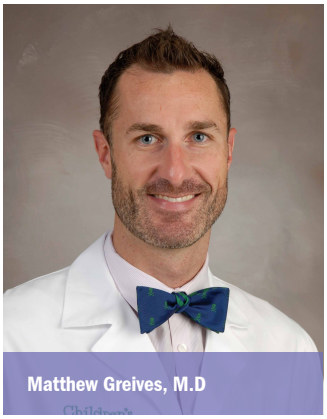
mission organization for cleft lip and palate in Mexico and Central America, for the past 20 years.

Working alongside Dr. Teichgraeber is Matthew Greives, M.D., assistant professor, division of Pediatric Plastic and Craniofacial Surgery. Dr. Greives joined the team in 2014 and has led the way in producing outcomes research to improve the care and experience of the patients and their families in the clinic.

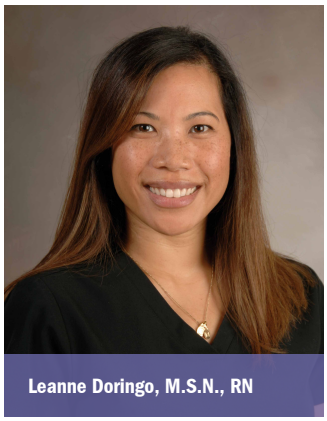
Another key contributor is Clinic Coordinator Irene "Leanne" Doringo, M.S.N., RN, who welcomes new families into the program and takes them under her wing to educate and support them throughout their journeys.



John Teichgraeber, M.D., FACS



Matthew Greives, M.D



Leanne Doringo, M.S.N., RN

A Community of Support and Educational Resources

The emotional effects surrounding a cleft diagnosis can be overwhelming, which is why education and access to appropriate resources are essential in ensuring the best outcomes for babies and their families. A key differentiator for the Program is the overwhelming support families receive.

3D models of a cleft patient's skull before and after surgical treatment, used for educational purposes.

By joining the Texas Cleft-Craniofacial Team's Facebook page as well as social media groups run and managed by the parents themselves, families connect with other cleft families and gain useful information. Connecting with other families is so important, especially to newly diagnosed families. Following a family's initial visit to The Fetal Center, Leanne Doringo has the ability to easily connect families (new or existing) in the Program for mentoring and support.

Parents and other family members can also listen to a prerecorded webinar with Dr. Greives, posted to Children's Memorial Hermann Hospital's website, to learn about advanced diagnostic tools for cleft lip and palate, as well as the latest management and surgical treatment options available at Children's Memorial Hermann Hospital. Dr. Greives also provides a timeline for cleft lip and palate care, and discusses feeding, dental and speech issues. **To view the webinar, visit childrens.memorialhermann.org/cleft.**

Once a baby is born, Leanne teaches new parents (and community hospital nurses and other healthcare providers) how to feed and care for their cleft babies. She frequently visits hospitals throughout the Memorial Hermann Health System to demonstrate techniques and offer treatment plans.

L-R: Leanne Doringo, M.S.N., RN; Matthew Greives, M.D.; Reanna Morales; and Vanessa Guerrero, M.A., members of the Texas Cleft-Craniofacial Team, helped host a day of beauty at a local salon for Program patients and their parents.

The team is also very active in the community. In 2016, they participated as sponsors for the second annual Cleft Smiles 5K Run/Walk in The Woodlands, Texas, which raises money for Operation Smile and generating awareness of the condition, and brings cleft families together. And in 2016, the team hosted a day of beauty at a local salon for Program patients and their parents.

Research

USING WHARTON'S JELLY TO BRIDGE THE BONY DEFECTS IN INFANTS WITH CLEFT LIP AND PALATE

Principal Investigators: Matthew R. Greives, M.D.; John F. Teichgraeber, M.D.; Fabio Triolo, Ph.D.; Charles S. Cox, Jr., M.D.

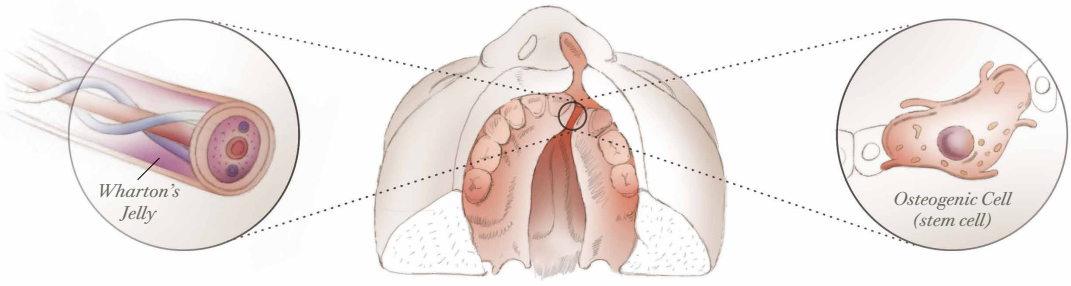
Major improvements in cleft surgical technique have lessened the physical stigmata associated with the diagnosis of a cleft lip and/or palate but have not reduced the number of procedures needed. Our team has initiated a clinical trial to reduce the total number of surgeries that these children undergo.

Stem cells have the ability to differentiate into any type of tissue, including bone. Previous work in the lab and others have demonstrated that Wharton's jelly (WJ), the substance normally found inside the umbilical cord, is a rich source of perinatal stem cells, a bridge between embryonic and adult stem cells without the limitations of either, in the newborn infant. Moreover, since WJ is typically discarded as post-delivery medical waste, its use, and/or the use of its cells, does not pose ethical concerns. Using a novel technique developed at McGovern Medical School at UTHealth, the umbilical cords are collected at the time of birth and the WJ, naturally seeded with the recipient's own stem cells, is isolated and stored for future use.

Initial preclinical studies have demonstrated that these stem cells generate bone quickly when exposed to the proper stimuli. Initial animal models have also demonstrated successful bone generation in the upper jaw following implantation of WJ. The Phase I clinical trial aims to utilize this potent naturally occurring "tissue engineering" construct to generate the bone that is absent in the upper jaw of infants with cleft lip and palate.

The current timetable for surgical correction of the cleft lip and palate deformity includes: repair of the lip at three to six months of age, palate repair at one year, bone graft to the upper jaw or alveolus (ABG) at age seven to nine, jaw surgery to correct the misalignment of the teeth at age 17, and finally a rhinoplasty to correct the nasal

shape and breathing issues at age 18. In this clinical trial, we will implant the WJ harvested from the patient's own umbilical cord into the upper jaw at the time of the cleft palate repair. The stem cells within the implanted tissue would then differentiate into bone cells and create bone to fill the defect in the upper jaw bone, sparing the child from needing to undergo the bone graft. While other clinical trials have used hormone or implanted substrates, this study is the first to utilize a child's own stem cells to effectively heal their own cleft lip and palate defect.



Umbilical Cord Section

In this clinical trial, we will implant the WJ harvested from the patient's own umbilical cord into the upper jaw at the time of the cleft palate repair at one year.

Cleft Palate Repair

The stem cells within the implanted tissue would then differentiate into bone cells and create bone to fill the defect in the upper jaw bone, sparing the child from needing to undergo the bone graft that is usually performed as a separate operation later in the child's life.

Evaluation and Study Process

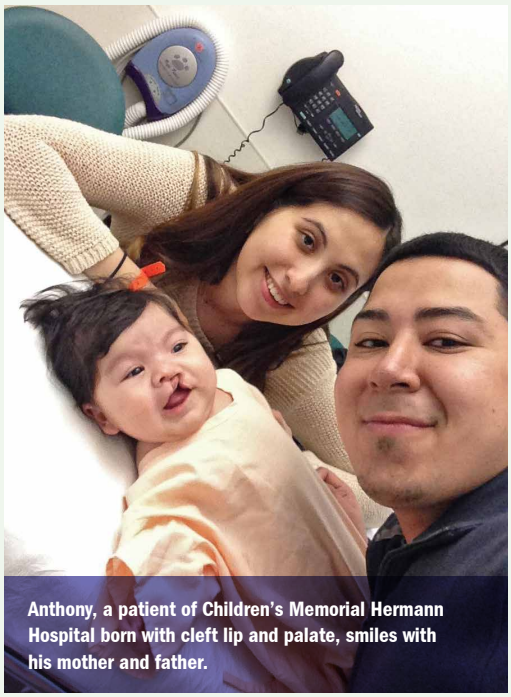
This project is a collaboration between the Texas Cleft-Craniofacial Center, under the direction of Dr. John Teichgraeber and Dr. Matthew Greives, and the Pediatric Program for Regenerative Medicine, under the direction of Dr. Charles Cox and Dr. Fabio Triolo. This prospective clinical trial would enroll patients when they present prenatally for evaluation at The Fetal Center for their infant's cleft lip and palate. At the time of the child's delivery at Children's Memorial Hermann Hosptial, the umbilical cord will be collected and processed to harvest the infant's own WJ. The stem cell-loaded tissue will then be processed and stored until the time of their palate repair, around one year of age. During the palate repair, the autologous WJ would then be implanted into the bony defect in the infant's upper jaw, and the palate closed around it. X-rays taken at 6 months and a year following surgery will be used to perform statistical analysis and quantitative measurements on the bone volume that is generated in the space.

We hope to show that the use of stem cells, through the implantation of autologous WJ, stimulates the formation of bone across the cleft and reduces the need for additional surgeries as the child ages.

To request more information about the prospective clinical trial, email contact.childrens@memorialhermann.org.

Anthony's New Smile

Patient Story

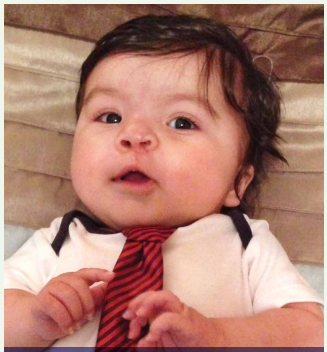


Anthony, a patient of Children's Memorial Hermann Hospital born with cleft lip and palate, smiles with his mother and father.

When Daniella Coca was five months pregnant, a 3-D ultrasound revealed that her unborn son, whom she would name Anthony, would be born with a cleft lip and palate. Learning of her son's condition during her pregnancy afforded Daniella and Anthony's father several months to meet John Teichgraeber, M.D., and his team, determine a plan of action, and prepare themselves emotionally for the journey ahead.

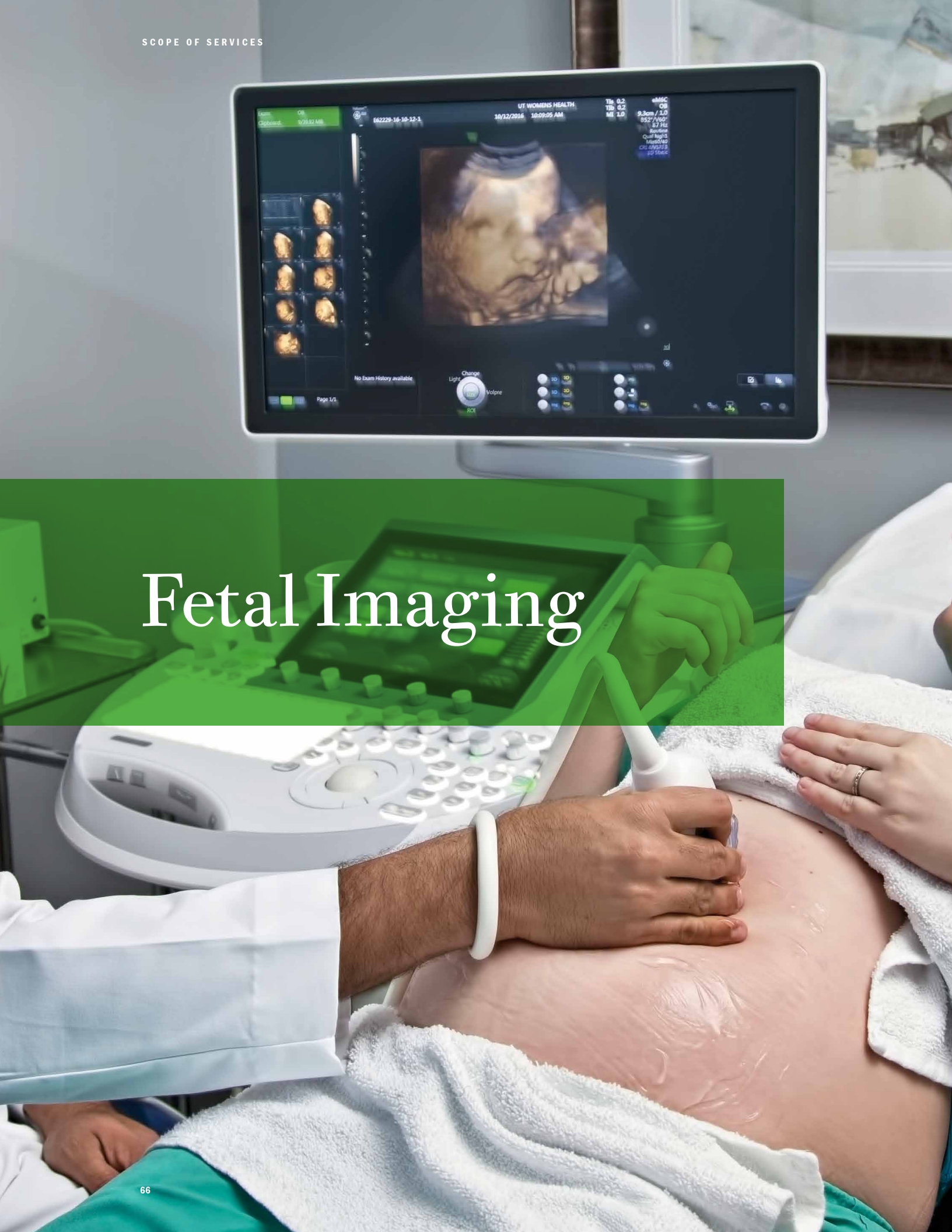
Anthony had surgery at Children's Memorial Hermann Hospital in 2014, undergoing a simultaneous lip and nose repair by Dr. Teichgraeber, ear tube placement by pediatric otolaryngologist Sancak Yuksel, M.D., and perineal anoplasty for a secondary medical condition unrelated to the clefts by Charles Cox, M.D., director of the department of Pediatric Surgery at McGovern Medical School at UTHealth. Prior to the lip repair surgery, Anthony received pre-nasal alveolar molding by pediatric dentist Bhavini Acharya, B.D.S., M.P.H., to help prepare his lip for the procedure. "I was overwhelmed when I first saw Anthony's face. My emotions were everywhere," said Daniella. "I was absolutely shocked at how different he looked and what a great job Dr. Teichgraeber did. Anthony looked like a different baby. If you didn't know he had a cleft lip and palate, you would not be able to tell."

According to Daniella, the team's clinical coordinators played an integral role in helping her cope. Following the surgery, Irene "Leanne" Doringo, M.S.N., RN, taught Daniella how to care for Anthony's palate, and Children's Memorial Hermann Hospital speech-language pathologist Kim-Loan Luu, M.A., CCC-SLP, evaluated Anthony's speech. "I still keep in close contact with both ladies. They were so understanding, responsive and supportive. They helped me better understand what to expect during the first year of Anthony's life and provided encouragement along the way. They were like my best friends and therapists all rolled into one."



Anthony poses for a picture after undergoing surgery at Children's Memorial Hermann Hospital to treat his cleft lip and palate.

Today, Anthony's prognosis is good, and his hearing has greatly improved. Daniella is confident in Anthony's ability to bounce back from his future surgeries. "He is such a strong child, and he recovers so quickly," said Daniella. "It has been really hard, but ultimately, I know that I am very blessed."



Fetal Imaging

Fetal Imaging

Unborn babies cannot be seen with the naked eye, so obstetricians, maternal-fetal medicine specialists and other healthcare providers depend on images to "see" babies before they are born, to help them make accurate diagnoses. An early and accurate diagnosis enables a physician and a family to create a plan for prenatal or neonatal treatment, potentially saving a life or greatly improving the chances of a child living a normal life.

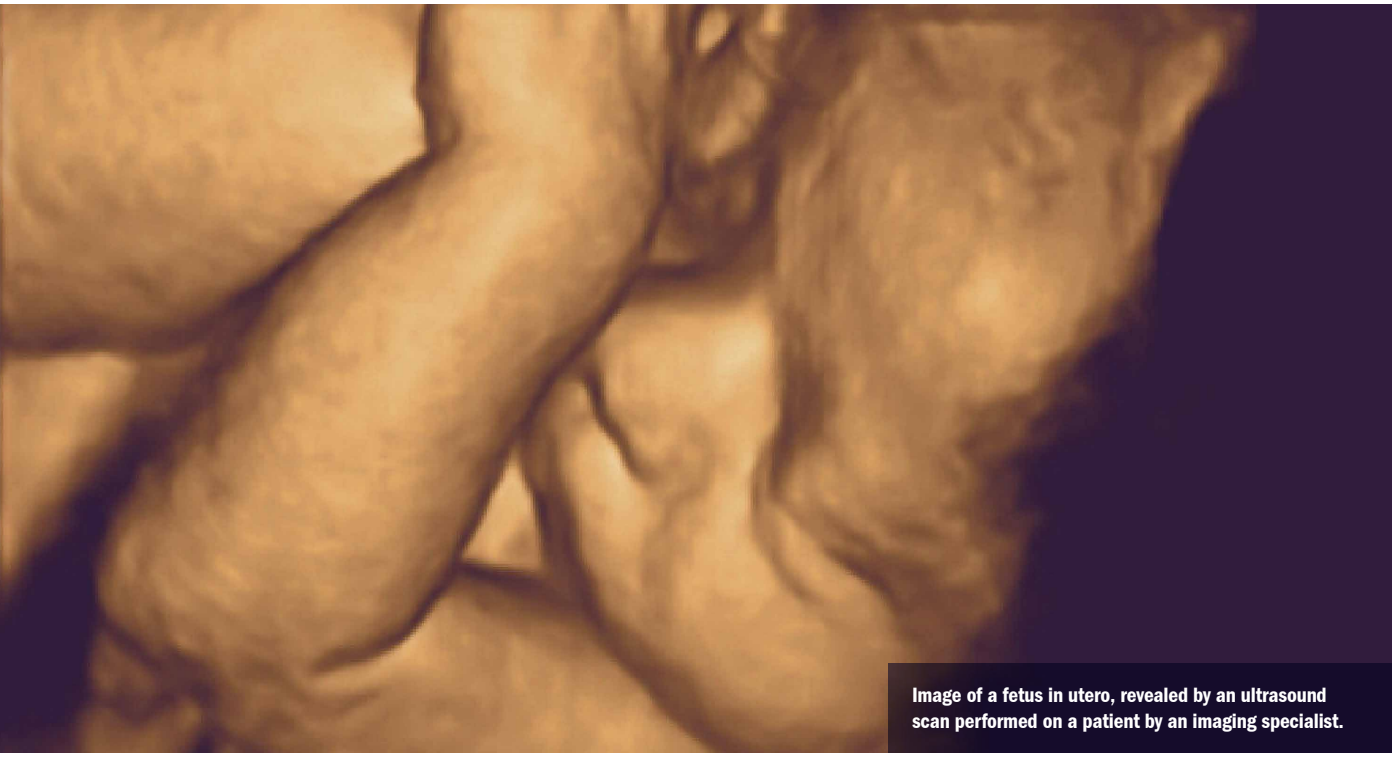


Image of a fetus in utero, revealed by an ultrasound scan performed on a patient by an imaging specialist.

One of The Fetal Center's key differentiators is its integrated, multidisciplinary team approach. The Fetal Center's affiliated maternal-fetal medicine specialists and fetal cardiologists work hand in hand with the team of sonographers, echocardiographers, genetic counselors, nurse coordinators and social workers to provide referring obstetricians and those who will be involved in postnatal care (neonatologists, pediatric cardiologists, pediatric and cardiovascular surgeons) with the most accurate diagnosis. Depending on the case, radiologists and other pediatric specialists, such as pediatric nephrologists and urologists, are involved.

To ensure continuity of patient care, the multidisciplinary team meets weekly to discuss new and ongoing cases. Members of the imaging team stay involved in patient cases, from initial screening and diagnosis to intervention, before and after birth.

The highly skilled sonographers and MRI radiologists affiliated with The Fetal Center are detectives, passionate about their mission: create and interpret clear images of the

structures of the fetus to help the team identify abnormalities. Their tools? Ultrasound, magnetic resonance imaging (MRI) and low-dose computed tomography (CT).

Fetal Ultrasound

Over the past five years, The Fetal Center has performed over 7,000 fetal ultrasounds, the most widely used technique in fetal imaging. Fetal ultrasound uses reflected sound waves to produce an image of the fetus, placenta and amniotic fluid (the liquid that surrounds the fetus), and is a safe way to check for problems and obtain information about a fetus.

Studies have shown that prenatal diagnosis of fetal cardiac disease improves the overall outcome for families and smooths the transition from birth to immediate cardiac care.

Ultrasound can be used to monitor fetal measurements to assess for normal growth and is important in all trimesters for the evaluation of fetal structural anomalies. It can also be used to assess fetal wellbeing. 3-D reconstruction of fetal anomalies is also used to evaluate complex fetal anomalies and allow for better planning of postnatal care. Finally, Doppler ultrasound allows for the evaluation of blood flow to and from the fetus and is especially important in fetal echocardiography, where advanced imaging techniques allow evaluation of heart function and rhythm.

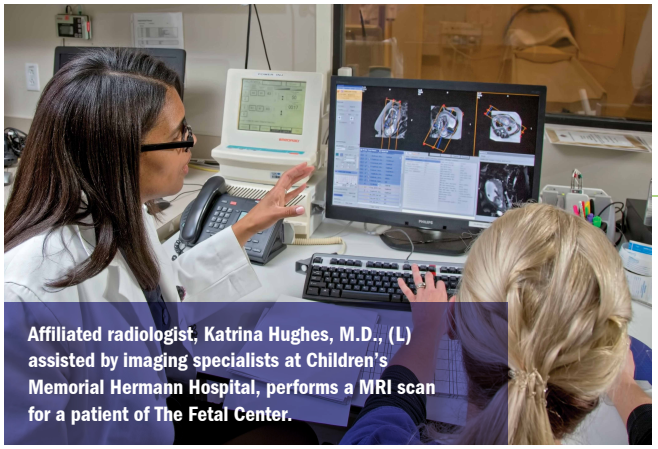
Studies have shown that prenatal diagnosis of fetal cardiac disease improves the overall outcome for families and smooths the transition from birth to immediate cardiac care. Each year, The Fetal Center performs about 650 fetal echo studies based on referrals for suspected heart defects or other complex pregnancies.

Affliated maternal-fetal medicine specialist, Ramesha Papanna, M.D., performs an ultrasound scan for a patient of The Fetal Center.

The Fetal Center supports population screening for fetal heart anomalies, using the international standard, the Five Transverse Views, a systematic examination of the fetal heart based on a series of five views across the fetal body at around 20 weeks gestation, to trace the connections and relationships of the heart structures. Approximately 125 cases of major congenital heart defects are evaluated annually at The Fetal Center.

Fetal MRI

The pediatric radiologists affiliated with The Fetal Center are specially trained in fetal MRI, a noninvasive method of evaluation. MRI uses a magnetic field to align the nuclear magnetization of hydrogen atoms of water in the body. This is safe for mother and baby and provides additional important information in the evaluation of the fetal brain, spine, neck, chest, abdomen and urinary tract. This information improves the accuracy of diagnosis and guides the prenatal and postnatal treatment of conditions such as intracranial or brain problems, lung masses, tumors and renal anomalies. Each year, The Fetal Center performs about 100 fetal MRIs to assess a variety of conditions.



Affiliated radiologist, Katrina Hughes, M.D., (L) assisted by imaging specialists at Children's Memorial Hermann Hospital, performs a MRI scan for a patient of The Fetal Center.

Advancing medical techniques through collaboration with the imaging community is important to the multidisciplinary team at The Fetal Center. Katrina Hughes, M.D., pediatric radiologist with primary area of expertise in fetal MRI and special interest in the placenta and placental invasion, serves on the Fetal Imaging Committee of the Society for Pediatric Radiology, allowing her to collaborate with other pioneers in the field to develop new protocols and techniques in fetal imaging. In addition, The Fetal Center imaging team is contributing to a growing body of knowledge on the use of 3 tesla magnetic resonance (3T MR) for fetal imaging. While the use of 1.5 tesla magnet strength has been the standard, there is growing interest in using 3 tesla to generate higher resolution images. One of the drawbacks, however, is that 3T MR generates artifacts that can distort the images. The imaging team at The Fetal Center is exploring ways to verify the diagnostic findings by optimizing the use of 3T MR, tweaking sequences to overcome this barrier, and is also expanding the use 3T MR for fetal diagnosis in obese patients.

Low-dose Computed Tomography (CT)

Low-dose CT is a valuable adjunct to fetal ultrasound, especially for use in diagnosing congenital skeletal abnormalities in fetuses. These abnormalities are relatively rare, as is the use of this technique. The Fetal Center is a referral center for these rare cases, seeing several affected families a year. The information provided is invaluable to maternal-fetal medicine specialists and certified genetic counselors to counsel families.

Conclusion

Publications

The affiliated physicians at The Fetal Center are dedicated to advancing the field of fetal medicine. Publication of clinical studies and innovative procedures are paramount to this mission. The list of peer-reviewed publications shown below are but a snapshot of the ongoing work at The Fetal Center.

2011

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2013

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To Our Donors

Philanthropy gives The Fetal Center at Children's Memorial Hermann Hospital a margin of excellence, helping our affiliated team stay on the cutting edge of clinical care and research. Those who give to The Fetal Center do so out of a desire to improve fetal diagnosis, fetal intervention and comprehensive fetal care for infants with congenital anomalies or genetic abnormalities.

Your generosity makes a difference in the lives of individual patients and helps us provide outstanding clinical programs and a richer patient experience. It funds educational videos that help patients make informed decisions, and important research that we quickly translate to bedside care.

Since March 2013, when The Fetal Center initiated its fundraising program, our generous donors have provided more than $1.3 million in philanthropic support. These funds allow us to say yes to one more mother, child and family in need of the services we provide and supports ongoing innovation through research and discovery to benefit mothers and their babies.

To make a contribution to The Fetal Center, visit childrens.memorialhermann.org/thefetalcenter/donate or call the Memorial Hermann Foundation at 713.242.4400.

The Fetal Center's Patient Resource Fund

Families with a prenatal diagnosis of a fetal anomaly or genetic abnormality are faced with tremendous physical and emotional challenges. At a time when they should focus on treatment and healing, some have financial limitations that leave them challenged by the need to travel to The Fetal Center. To ease the burden, The Fetal Center established the Patient Resource Fund, available to patients in need of assistance for travel and accommodations during their treatment.

For information about eligibility and assistance, call 832.325.7288. Part of The Fetal Center's mission is to provide every family with compassionate care and the best treatment options available to them.

To learn more about how to help a family in need, visit childrens.memorialhermann.org/thefetalcenter/donate or call the Memorial Hermann Foundation at 713.242.4400.

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