


Mapping the Brain

Team questions the gold standard, advocates for noninvasive functional imaging

- ▶ Researchers look for innate immunity factors to guide urinary tract infection treatment
- ▶ Communication between families, care team boosts experience scores



NEJM publishes RSV antiviral breakthrough

An antiviral treatment has safely reduced the viral load and clinical illness of healthy adult volunteers intranasally infected with respiratory syncytial virus (RSV) in a clinical trial.

Results of the study were published in the Aug. 21 issue of the *New England Journal of Medicine*. The trial is part of Infectious Disease Specialist Dr. John DeVincenzo's RSV antiviral program.

In the journal, DeVincenzo describes a novel oral RSV antiviral medication, GS-5806, which inhibits RSV from entering human respiratory epithelial cells. Using this novel medication, DeVincenzo's team demonstrated for the first time that a small molecule antiviral could therapeutically reduce the quantity of virus after a human RSV infection had already started. For another medical first, as soon as the amount of virus was reduced, the symptoms and severity of the disease also were rapidly reduced. The trial used the RSV experimental challenge model, which was also developed in DeVincenzo's lab. DeVincenzo has since announced promising findings on a second antiviral in development — AL-8176. AL-8176 drug was developed to inhibit RSV from copying itself by causing chain termination of the virus.

RSV is the most common cause of lower respiratory tract infections in young children in the United States and worldwide. It hospitalizes 125,000 children in the United States each year and was the cause for 1.5 million annual outpatient visits, according to the Centers for Disease Control and Prevention (CDC).

DeVincenzo serves as medical director of the Molecular and Viral Diagnostics Laboratories at Le Bonheur and as professor of Pediatrics and professor of Microbiology, Immunology, and Biochemistry at the University of Tennessee College of Medicine.



Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Our medical staff of more than 700 physicians provide care in more than 40 subspecialties.

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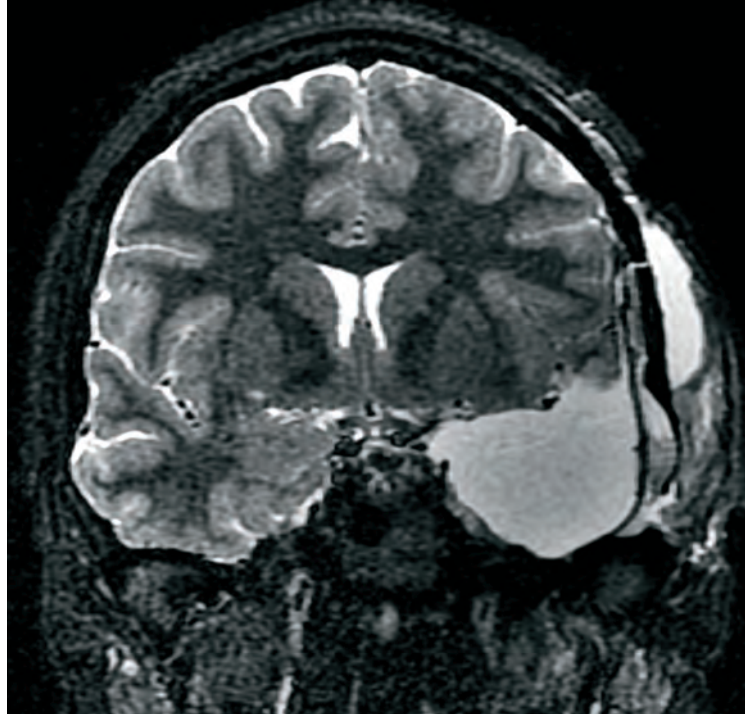
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MAPPING THE BRAIN



Team questions the gold standard, advocates for noninvasive functional imaging

They are questions of curiosity. Thoughts on the intricate ways the human brain works and how each part works together to help us speak, let us move, give us memories. What happens when seizures disrupt brain activity and brain tumors grow? How does the mind adjust?

Finding answers meant everything for 17-year-old Grace Hugueley. After six years of ongoing seizures, her parents were afraid to leave her home alone. As doctors tried to control Grace's generalized tonic-clonic seizures, her parents tracked her food consumption and activities. In all, they tried multiple seizure medications, cut caffeine from her diet and tried hormone regulation.

Grace was frustrated. "We couldn't figure out what the

common denominator was. At one point, I went three months without a seizure, and I was thinking, 'Gosh, we finally figured it out.' And then one hit me. That's what frustrated me the most, I thought we figured it out and then we didn't," she said.

Grace didn't want her parents to worry. One day, she wanted to

go to college.

That's what Andrew Papanicolaou, PhD, a pioneer in neuroimaging, wants for all children – for them to live at their highest potential. It's why he studies the brain, using noninvasive brain mapping to understand structure and function. As chief of Le Bonheur



Watch a video about Grace Hugueley's journey to control her seizures.
www.lebonheur.org/promise

Six years of seizures left 17-year-old Grace Hugueley frustrated. The Clinical Neurosciences team at Le Bonheur used noninvasive brain-mapping technology to pinpoint the location of seizures and guide surgery in Grace's left temporal lobe.



Information gathered from fMRI, MEG and TMS help guide neurologists and neurosurgeons in developing treatment plans for patients with brain tumors and epilepsy. The team meets weekly to collaborate on these cases.

and the University of Tennessee Health Science Center's (UTHSC) clinical neurosciences teams and co-director of Le Bonheur's Neuroscience Institute, he and his colleagues have changed how brain mapping is used to make surgical decisions for children with epilepsy and brain tumors.

He's finding hope for kids like Grace.

NO "TEXTBOOK CASE"

The goal is two-fold: find areas of the brain that are the cause of abnormal activity (seizures) and identify the areas nearby responsible for specific functions like speech and motor skills.

"We know no two children's brains are the same," said James Wheless, MD, director of the epilepsy program and co-director of

the Neuroscience Institute. "They may have similar-looking seizures. Imaging allows us to treat each child as an individual patient and have the best outcome for them. At the end of the day, that's really what we want to do."

Clinical neuroscientists tackle their search from both a structural and functional perspective. Modalities like MRI and CT take pictures of the brain structure while functional MRI (fMRI), magnetoencephalography (MEG) and transcranial magnetic stimulation (TMS) provide information about brain functions like language, memory and movement.

The clinical neurosciences team collaborates with neurologists, neurosurgeons, neuroradiologists and neuropsychologists to interpret



Andrew Papanicolaou, PhD

information and guide surgical decisions. Noninvasive brain mapping gives families a much better idea of what life will be like post-surgery – whether physical therapy will be needed or if a patient will experience a weakness.

"The motivation of any researcher is to find out things. In this case, the intricate ways in which the brain works, sustains and mediates all the variety of functions that humans are capable of performing including memory, emotion, attention and so forth," Papanicolaou said.



The intricate ways of the brain can get even more complicated for individuals with epilepsy or tumors, as normal pathways are disrupted. A brain will reorganize itself, and the area that controls a specific function will move. It can be unpredictable.

“If everything would stay put, you could read in the textbook where everything is, and the surgeon would not need this advanced information in order to maximize his surgical approach,” said Papanicolaou.

QUESTIONING THE GOLD STANDARD

Direct cortical stimulation (done outside the operating room or in the operating room with an awake craniotomy) and Wada testing have been gold standards in evaluating function prior to tumor and lesion resection for decades.

With direct cortical stimulation, a neurosurgeon opens a patient’s skull, sedation is reduced and the patient is asked

questions or to perform simple tasks. Responses help the surgeon know how to proceed. Still widely used across the country, the process is not ideal for children. With the Wada test, half of the brain is put to sleep using a medication (a barbiturate) while a patient’s ability to speak and respond is evaluated. Adolescent compliance is challenging and nearly impossible for younger

children.

Le Bonheur’s clinical neurosciences



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TMS studies
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team, after many documented cases, is advocating for an eventual replacement of the awake craniotomy and Wada test with noninvasive methods for most cases.¹ MEG, TMS and fMRI together provide equally trustworthy results, the team believes.

A complete movement to only noninvasive brain mapping is still some years off, as very few centers have all of the technology and expertise to interpret results all under one roof.

“Tri-modality mapping and looking for concordance of the data between these three different techniques gives us belt and suspenders that we’re in the right location,” said Frederick Boop, MD, chairman of the Department of Neurosurgery for UTHSC and co-director of the Neuroscience Institute.

The adage “measure twice, cut once” applies. Measuring with noninvasive testing twice, and in some cases three or four times, gives the team complete confidence in anatomical and functional location of the abnormalities.

While invasive methods, including

Mapping the brain noninvasively

Functional brain imaging is used to record sensory, motor and cognitive functions happening in a patient’s brain. The goal is to identify areas of abnormal activity and the areas responsible for specific normal functions. When functional imaging is combined with the structural images from MRI and CT, neurologists and neurosurgeons have a map to guide treatment plans.



Magnetoencephalography (MEG)

What: Records neuronal responses based on the magnetic fields that are produced when groups of brain cells become active

Insight: Used to localize the origin of magnetic fields and identify areas of the brain that are active during movement, sensation and the production and perception of speech



Functional MRI (fMRI)

What: Identifies areas of brain activity by detecting blood flow alterations related to increased oxygen extraction from functioning cortex

Insight: Shows areas of the brain that control complex language functions (verb generation, sentence completion and picture naming) or motor tasks (hand, foot or facial movement). In conjunction with DTI, it is possible to map the nerve bundles that send information throughout the body.



Transcranial Magnetic Stimulation (TMS)

What: Imparts magnetic fields that penetrate the skull painlessly to stimulate areas of the brain, using a coil that is placed near the scalp in a form of noninvasive cortical stimulation. Navigated TMS uses an MRI of the patient’s brain to move about the skull – much like a GPS system helps a person navigate a car.

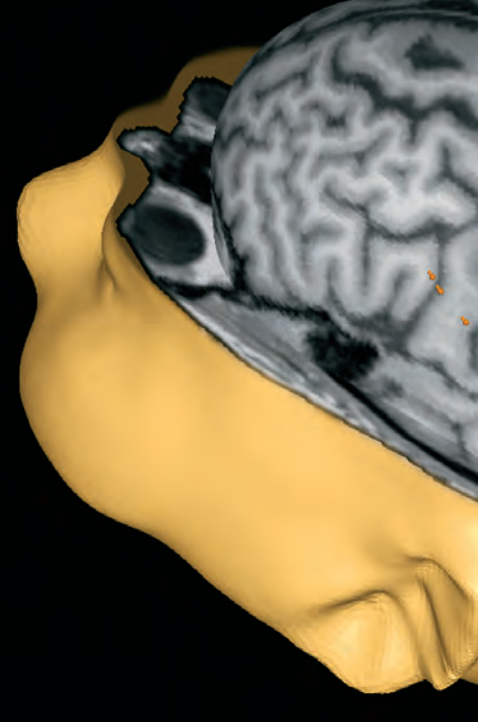
Insight: Allows clinical neuroscientists to connect brain activation and the responses that follow for motor and language areas



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MEG studies
2013



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grid placement, haven't been eliminated at Le Bonheur, the team feels more and more confident in relying on noninvasive mapping when necessary. This is especially important for patients who have had previous surgeries or patients with significant developmental delay that would prohibit the use of grids.

PhD, runs the TMS lab and hopes one day, the complications from invasive mapping will no longer be barriers for patients.

"As you can imagine, there is no going back. Direct cortical stimulation is a one-time test. There are a lot of disadvantages to that – sedation, patient compliance,

The four-member clinical neurosciences team was recruited to Memphis to complement and support the growing neurology and neurosurgery program. Le Bonheur is home of one of the nation's largest pediatric surgical brain tumor program² in conjunction with St. Jude Children's Research Hospital and a robust epilepsy program. The new members joined the hospital and the University of Tennessee Health Science Center in the last two and a half years – bringing with them clinical and research expertise in each of the modalities.

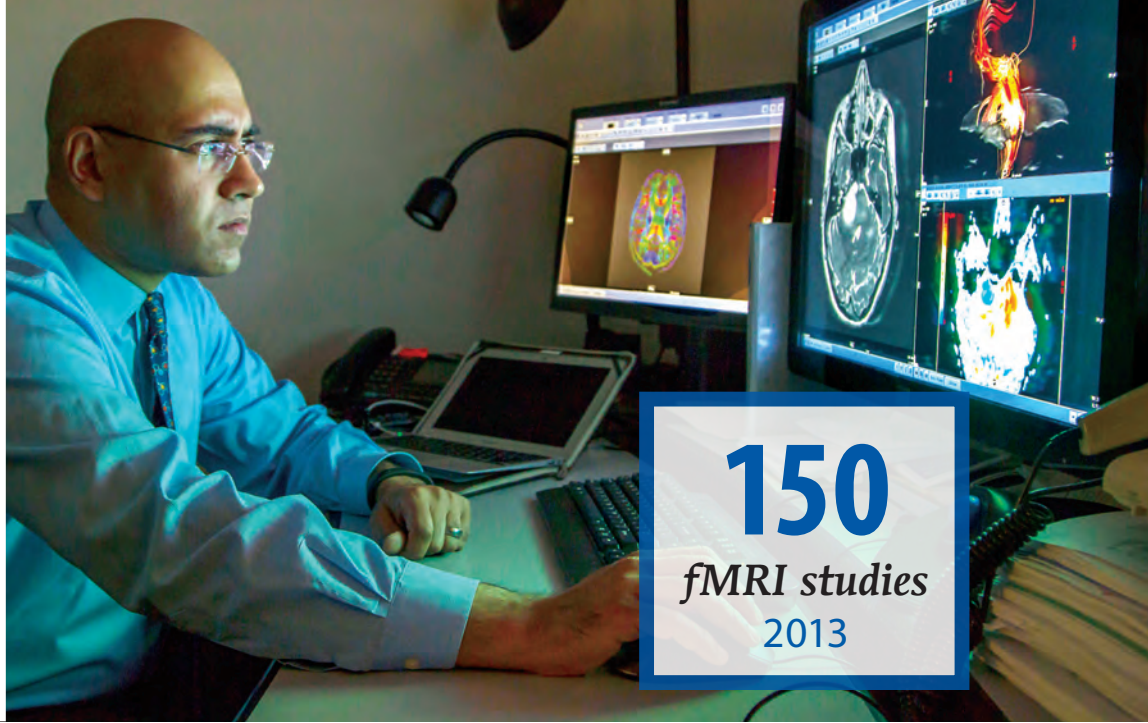
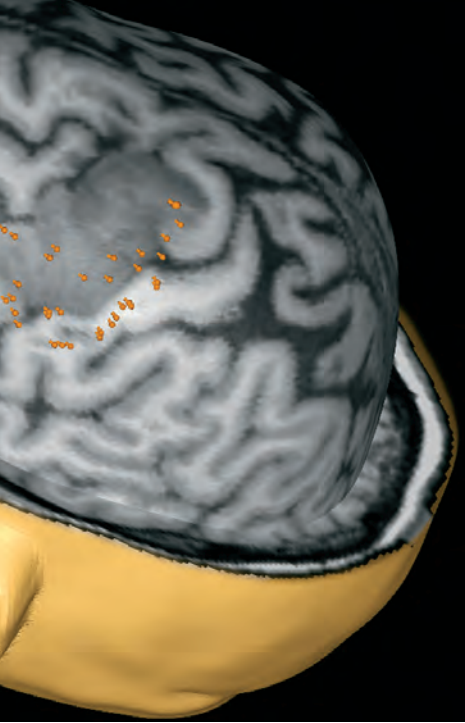
Measuring with noninvasive testing twice, and in some cases three or four times, gives the team complete confidence in anatomic and function location of the abnormalities.

"The more concordance we see between the invasive procedures that are considered the gold standards and the noninvasive approaches we emphasize here, the closer we may be in replacing the former with the latter," said Roozbeh Rezaie, PhD, MEG lab director.

Shalini Narayana, MS, MBBS,

longer duration, more morbidity for the patient. When surgeons are armed with the information gathered from noninvasive mapping, they can actually tailor surgery to be more focal and less invasive. This can reduce the morbidity and lead to better outcomes," she said.

Papanicolaou has dedicated his career to the development of MEG, or magnetoencephalography. He wrote the very first textbook on the clinical applications of MEG and organized the International



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fMRI studies
2013

Society for the Advancement of Clinical Magnetoencephalography. He's published dozens of papers on clinical MEG applications primarily about the localization of language networks in the brain.

In Memphis, he says he saw the opportunity to incorporate new developments in neuroimaging applications to pediatric neurosurgery and to collaborate with world-class clinical

neuroscientists.

And the team he's recruited says that the technology, patient population and access to high-quality data open the door for discoveries.

Rezaie says the unique clinical cases and opportunities for research using all these modalities attracted him to the program.

"The success we have using these approaches is very rewarding and keeps you motivated to continue down this avenue, but also to try and develop new ideas from a research perspective. At some point in time, this research has the potential to make an impact clinically, with an emphasis on rapid turnarounds and improved outcomes for patients," he said.

And it's not just about the technology, it's the team of experts

working together who collaborate on every case.

"All of us work together," said Asim Choudhri, MD, director of Neuroradiology. "We eat lunch together every day. We're not different groups in different buildings that occasionally email each other. We work together every day because each patient is different. Each disease process is different. By not treating it in a cookie cutter manner, we can help patients and families understand, in their specific case, what they might expect after surgery."

EFFICIENTLY MAPPING THE BRAIN

Because it works so closely, the clinical neurosciences team has also perfected efficiency in gathering functional information.



“Here, we can do all these tests in an afternoon, and the next morning, the surgeon has the information for the surgery. We’ve proven this and published case studies³ that show how efficient it can be when all the modalities are in close proximity and the people who operate them belong to the same group and collaborate,” said Papanicolaou.

Jennifer Barnes, 42, learned she had a rare brain tumor – an oligodendroglioma – after experiencing a seizure while driving in 2007. At that time, her medical team felt the tumor wasn’t safe to resect because of its location, so her

seizures were treated with medication. In 2013, the seizures couldn’t be controlled any longer.

Surgery was the best option.

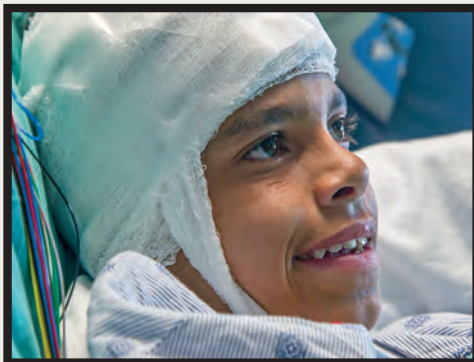
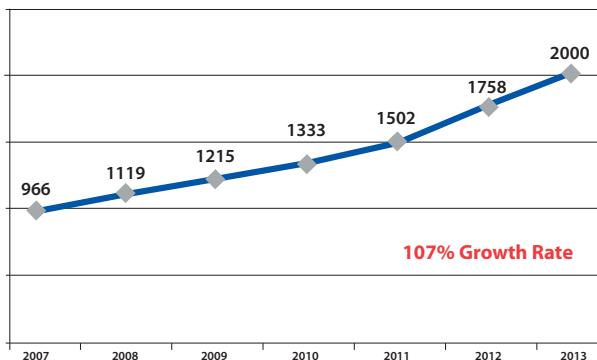
Neurosurgeon Boop wanted to perform pre-surgical mapping and surgery to remove the tumor at Le Bonheur.

While he has privileges at adult hospitals in the area, none was equipped to give him the precise information he needed to ensure Barnes that he could operate and minimize her risk for any deficits to her hand and facial motor and language functions.

“We entertained the idea of traveling to another city for treatment. My mother is an oncology nurse, and she’s done



EMU Growth (Monitored Days): 2007-2013



Seizures have been part of CAESAR WILSON’S life for 10 years. His mom has lost count of how many different drugs they have tried to control his epilepsy. The ketogenic diet didn’t work, and the VNS hadn’t made a big enough difference, so Caesar and mom Dana Martinez traveled to Memphis – from their Oklahoma home – to see if there was anything left to do.

“We’ve been trying for 10 years to figure this out. Our doctor told us if anyone could give us answers, Dr. Wheless could,” Martinez said.

After four days in Le Bonheur’s Epilepsy Monitoring Unit, and MEG and TMS testing, the option was clear as the neurologists, neurosurgeon, neuroradiologist, neuropsychologist and clinical neuroscientists discussed Caesar’s case in their weekly meeting. Just a week after he arrived in Memphis, he underwent a corpus callostomy – a surgery that separates the two hemispheres of the brain in order to limit the severity of seizures.

Caesar left Le Bonheur five days after surgery, took a trip to the Memphis Zoo the next day, and then returned home. He has been seizure-free since surgery.



Neurologist James Wheless, MD, discusses treatment options with Jason and Jessica Vinson, parents of 4-year-old Kayden, in the Epilepsy Monitoring Unit.

tremendous research on my condition. She discovered that Le Bonheur is on the cutting edge and has technology no one else has,” Barnes said.

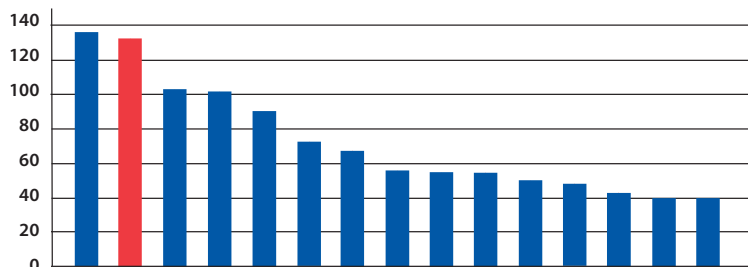
So in one afternoon last July, Barnes underwent fMRI, MEG and TMS testing. The clinical neurosciences team, neuroradiologist, neurologist and neurosurgeon interpreted the results together and developed a plan to safely remove as much

tumor as possible while minimizing the loss of function. Because of the complexity of the tumor, Jennifer had two surgeries – the first for subdural grid placement and the second for grid and tumor removal.

Using structural and functional images along with the results from grid placement, a three-dimensional model of Jennifer’s brain and the tumor was used to guide the surgery. Before leaving the operating room, Boop used scans

Brain Tumor Volumes

Pediatric Research in Inpatient Settings (PHIS) Peer Hospitals*
January- December 2013



* designated by U.S. News & World Report as Best Children's Hospitals for Neurology and Neurosurgery
Data Source: Pediatric Health Information Systems (PHIS), 2013

MEET THE TEAM



Andrew Papanicolaou, PhD
chair, division of clinical neurosciences, The University of Tennessee Health Science Center and co-director, Le Bonheur Neuroscience Institute



Roozbeh Rezaie, PhD
magnetoencephalography (MEG) lab director, performs and interprets clinical MEG studies, is involved in translational research activities



Shalini Narayana, MBBS, PhD
transcranial magnetic stimulation (TMS) lab director, performs and interprets TMS studies, oversees clinical and research activities



Abbas Babajani-Feremi, PhD
performs and interprets MEG clinical studies; medical image and signal processing; brain connectivity analysis using MEG, EEG, electrocorticography (ECoG) and fMRI



Marina Kilintari, PhD
post-doctoral fellow, works with faculty on developing and optimizing clinical and research studies within in the clinical neurosciences division



Liliya Birg
patient education, MEG data quality control and acquisition and processing of MEG/EEG studies



Katherine Schiller
patient education, TMS data quality control and acquisition and processing of TMS studies



Holly Smith, BSN, RN, CPN
patient education, coordinates clinical and research studies within the division of clinical neurosciences and patient care during sedation



Asim Choudhri, MD
director of neuroradiology, interprets CT and MRI scans of the brain, performs and interprets functional MRI



Adeel Siddiqui, MD
neuroradiologist, interprets CT and MRI scans of the brain, performs and interprets functional MRI

by the intraoperative MRI (iMRI)⁴ to confirm that the maximum amount of tumor was resected while preserving eloquent cortex. See case study below.

DECISIONS MADE EASIER

In a perfect world, the clinical neurosciences team would hope to preserve all neurological function for its patients following surgery. But epilepsy and tumors can cause so much harm to a brain that it's not possible.

“The truth is these patients are going to surgery for a reason. They’re having intractable seizures that are impairing their daily lives, impairing them going to school, impairing them from interacting appropriately with their family. They have tumors that could potentially take their life. So these are difficult decisions,” said Choudhri.

But thanks to noninvasive brain mapping, the conversations families are having before surgery have changed considerably in the

last decade. Families have a better idea of what life could be like after surgery and what deficits may be possible. They can make a decision if life without seizures is worth those possible long-term deficits or short-term injuries.

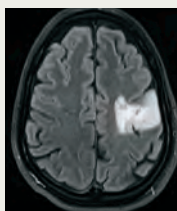
“We are able to get information that we can go over with the family in a very calm manner, have a matter of fact discussion about what the information is telling us, and what the next steps are. It gives the family a chance to think about



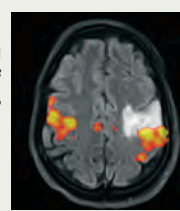
JENNIFER BARNES was in a car accident in 2007

as a result of a seizure. An MRI revealed a tumor in her posterior frontal lobe. She had a biopsy at the time, but surgeons felt the tumor was not safe to resect. Seizures were controlled by medication until 2013. The tumor was touching areas of the brain responsible for movement in her right hand and right side of the face. Barnes had two surgeries at Le Bonheur – the first to place the subdural grids for direct cortical stimulation and mapping. This supported information gathered noninvasively. She then returned for surgery to remove the grid and tumor. Barnes was asleep for both surgeries. Barnes experienced motor skill delays in her right hand following surgery and completed physical therapy. She also has some difficulties with word and sentence generation. Following surgery, Barnes completed six weeks of radiation and chemotherapy and continues chemotherapy today. She is unable to work as an executive assistant as she did before diagnosed, but she finds joy in spending time with her daughter and dogs and working in her yard. Her seizures are resolved.

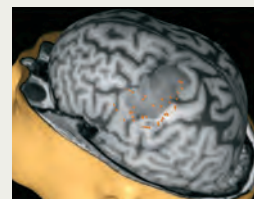
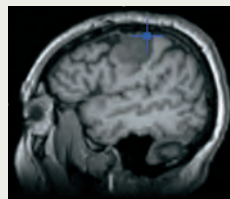
1. Before surgery MRI



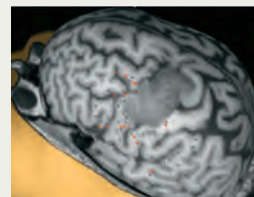
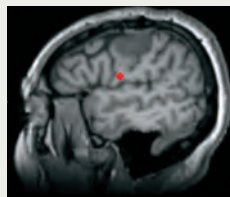
2. fMRI showing location of hand motor



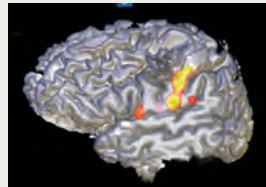
3. Sensory area mapped with MEG (left); motor areas mapped with TMS (right)



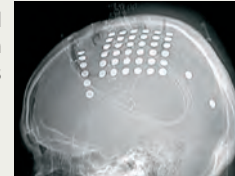
4. Language areas mapped with MEG (left) and TMS (right)



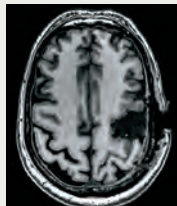
5. 3D rendering of MRI with fMRI overlay of language and motor for surgical planning



6. Subdural grid to confirm findings



7. After surgery MRI



For larger images and descriptions, visit lebonheur.org/promise.



it, to discuss it with the surgeon,” said Wheless. “We are not doing it like we used to with the invasive electrodes. When we put these electrodes in, we’ve got to make a decision quickly because we have electrodes sitting in your child’s head, on their brain. Noninvasive mapping allows us to have the risk benefit discussion in a more relaxed manner with the family.”

When Grace Hugueley and her parents sat down to talk about surgery with Wheless and Boop, the teen was ready, but she had some questions. Would she still be the girl who loves to curl up in her dad’s lap? Would she be able to play the piano again?

The seizures originated from Grace’s left temporal lobe, the area that controls language and memory. The MRI appeared normal, so SPECT (single photon emission computed tomography) perfusion studies were used and detected an abnormality in the left temporal lobe. From there the concordance of data from fMRI, TMS, MEG and eventually subdural grid placement gave her team confidence that, despite the normal MRI, they could perform a surgical resection of the area. *See case study at right.*

Since the surgery in July 2013, Grace hasn’t had one grand mal seizure, and medication minimizes the few brief focal seizures she’s experienced. Grace graduated from high school, got her learner’s permit to drive and will attend college this fall.

The sweetest part, her father Doug says, was hearing his daughter play “Clair de Lune” on the piano just days after the surgery.

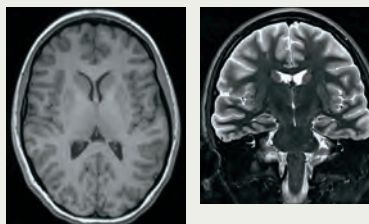
“She didn’t miss a note,” he said. □

GRACE HUGUELEY’S MRI showed no abnormalities, but there were the foot-prints of focal and generalized tonic-clonic seizures.

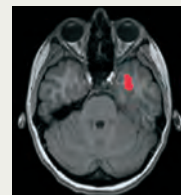
The video-EEG and other studies revealed the seizures were coming from the left temporal lobe – the area that controls language and memory. Because Grace was so high functioning and right-handed, the team wanted to be certain before removing a portion of the left temporal lobe. MEG, TMS and fMRI confirmed findings that Grace’s important language functions were above the lesion. Grids were placed on her brain to increase the team’s level of confidence. The neuroradiologist, neurologist and neurosurgeon discussed the best place to perform the surgical resection.



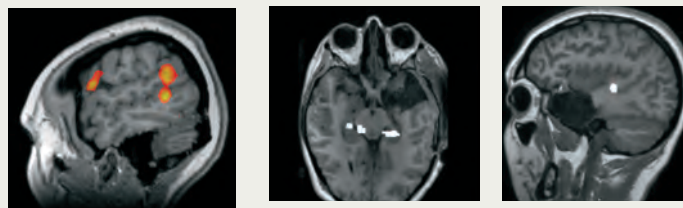
1. MRI shows normal brain



2. Subtraction Ictal-Interictal SPECT perfusion study overlaid upon MRI, showing seizure origin in the left temporal pole

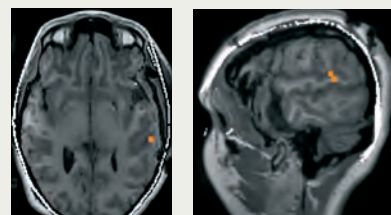


3. fMRI showing location of expressive and receptive language

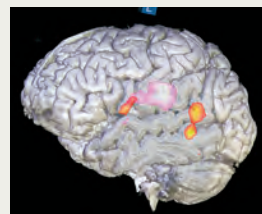


4. Language mapping with MEG showed that language areas were away from the seizure onset area. Axial (left) and sagittal (right) views

5. Language mapping with TMS confirmed that the language areas were behind the brain area that was later removed. Axial (left) and sagittal (right) views



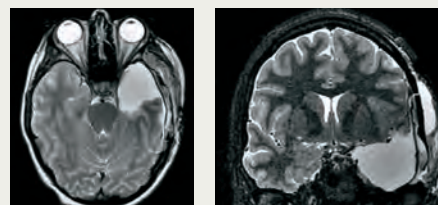
6. 3D surgical planning rendering of MRI with overlay for language and motor



7. Subdural grid to confirm findings



8. MRI after surgery



¹ Papanicolaou, A; Rezaie, R; Narayana, S; Choudhri, AF; Wheless, J; Castillo, E; Baumgartner, J; Boop, FA. Is it time to replace the Wada test and put awake craniotomy to sleep? *Epilepsia* 55 (5): 629-632, 2014.

² Data source: Pediatric Health Information Systems (PHIS) Peer Hospitals ranked by *U.S. News and World Report* as Best Children’s Hospitals for Neurology & Neurosurgery, 2013.

³ Choudhri, AF; Narayana S.; Rezaie, R.; Whitehead, M.; McAfee, S.; Wheless, J.; Boop, FA.; Papanicolaou, A. Same Day Tri-Modality Functional Brain Mapping Prior to resection of a lesion involving the eloquent cortex: Technical feasibility. *The Neuroradiology Journal* 26: 548-554, 2013.

⁴ Choudhri, AF; Klimo, P.; Auschwitz, TS; Whitehead, M.; Boop, FA. 3 Tesla intraoperative MRI for management of pediatric CNS neoplasms. *American Journal of Neuroradiology* 2014 (DOI: 10.3174/ajnr.A4040)



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GENETIC FACTORS

Researchers look for innate immunity factors to guide urinary tract infections treatment

Nephrologist David Hains, MD, is studying how genetic factors affect children with vesicoureteral reflux who contract recurrent urinary tract infections. Above, Hains (standing, back) discusses results with Research Associate Dong Liang, PhD, (left, standing) and Research Assistant Keith Pierce (sitting).

Lizzie Work was 6 weeks old when she contracted her first urinary tract infection (UTI). Then came another, and another – every six to eight weeks.

“She would not eat and had a super high fever,” said her mom, Wendi. “It’s constant worry. We don’t sleep through the night. It’s really hard to watch.”

Lizzie’s diagnosis: vesicoureteral reflux, a condition where urine backflows from the bladder to the upper urinary tract, allowing bacteria to enter the bladder and kidney. Testing later showed scarring and hydronephrosis

in her left kidney.

Vesicoureteral reflux is present in a third of children who have had a urinary tract infection. Of those children, one in 15 will have recurrent UTIs, which can lead to kidney scarring, permanent damage and even the need for dialysis.

Le Bonheur Nephrologist David Hains, MD, is trying to learn why kids like Lizzie get repeat infections while other kids with reflux can go through childhood without infection. His theory: genetic factors, especially those in the urinary tract, are game changers for some patients. By understanding genetic makeup, treatment can be



Lizzie Work



tailored for each child.

To find answers, Hains has established the first genetic ancillary study to the national RIVUR (Randomized Intervention for Children with Vesicoureteral Reflux) trial. The RIVUR trial includes 600 children with reflux who have had at least one urinary tract infection. Half have been given prophylactic antibiotics; half have not.

“We are studying the entire genetic code of children with reflux to determine the genetic causes of developing multiple infections,” Hains said. “We are looking for genes that are clearly important in our innate immune system for kids with reflux. We hope it will help us better understand what makes some children with reflux more or less susceptible to infection.”

In the newly formed Innate Immunity Translational Research Center at Le Bonheur’s Children’s Foundation Research Institute, Hains and his lab

members study antimicrobial peptides within the urinary tract, specifically those that occur in multiple copies. These peptides are natural antibiotics, so if someone has a genetic predisposition to making fewer of these peptides, perhaps bacteria gain an advantage and cause urinary tract infections, he believes. Children with higher copies, he suspects, have higher immunity to infection.

With access to the RIVUR study’s clinical data, he is now using results from RIVUR to validate potential genetic candidates that may play a role in providing immunity from UTIs.

Eventually, Hains hopes discoveries in his lab will help scientists better understand the role genes play in disease, and help physicians cater treatment for children with reflux. Knowing if a child is prone to UTIs – based on his or her genetic makeup – can ensure treatment is specific to his or her needs and antibiotics aren’t overused.

Today, Lizzie, now 7, continues to take prophylactic antibiotics to avoid additional UTIs. She hasn’t had an infection in more than 15 months and is relatively healthy. Both kidneys are working, though one has lost a “good deal of function,” Wendi said.

“If we had known prenatally that Lizzie would develop the number of UTIs that she did, I think we might have gone ahead and pushed for earlier intervention,” said Wendi. “The recurring infections are so miserable, especially when they are so tiny.”



Russell Chesney, MD

RIVUR study: Antibiotics reduce UTIs for kids with reflux

Le Bonheur’s Chesney co-authors NEJM study

In May, the RIVUR study published its primary outcome paper in the *New England Journal of Medicine*, showing that long-term antimicrobial prophylaxis can significantly reduce the risk of recurrent urinary tract infections in children with vesicoureteral reflux. The two-year, 19-site study enrolled more than 600 children with vesicoureteral reflux.

Le Bonheur Children’s Nephrologist Russell Chesney, MD, serves as chairman of the RIVUR study steering committee and was a co-author of the recent article. The study was funded by the National Institutes of Health.

“We hope these findings will help inform physicians – and parents – on the best ways to treat children with reflux who develop urinary tract infections, depending their grade of reflux,” said Chesney. “We also think this may lead to more debate about the need for imaging studies in children with reflux.”

Improved Communication Boosts Experience Scores



Hospitalist Cynthia Cross, MD, asks 2-year-old patient Kaden Moore how he's feeling. After looking at the things that drive patient satisfaction, Le Bonheur focused on communication between families and their child's physicians and nurses.

When 8-year-old Sutherland Smith was diagnosed with Kawasaki disease in April, his doctors spoke to him directly about his diagnosis and made sure he was part of the treatment plan.

His mom, Betsy, was impressed.

“The doctors made a point to include Sutherland in the dialogue and always took the time to ask him, specifically, if he had any questions,” said Betsy. “Our family had what felt like a million questions, and the team made sure we understood everything regarding Sutherland’s treatment. We are beyond grateful for our excellent experience.”

The Smiths’ experience wasn’t always the norm for families at Le Bonheur. The hospital assembled a multi-disciplinary taskforce of hospital executives, physicians, nurses, family members and other care providers to address recurring concerns about overall patient experience and a lack of coordination of care.

“We knew we wanted patients to have a safe experience here, to receive excellent medical care and to have good outcomes,” said Chief Medical Officer Bill May, MD. “In partnership with several Le Bonheur families, we determined that patient experience hinges on three things: how we connect with patients, how we listen to

their needs and expectations and how well we honor our commitments.”

May and his team knew the hospital needed to create better ways for families and caregivers to share information. The plan paid off.

Since the taskforce’s formation, Le Bonheur has seen a significant increase in its inpatient experience scores, landing in the 90th percentile among children’s hospitals. This score is measured by National Resource Corporation (NRC) in response to the question, “Using any number from 0 to 10, where 0 is the worst hospital possible and 10 is the best hospital possible, what number would you use to rate this hospital during your child’s stay?”

PHYSICIAN COMMUNICATION IS KEY

Hospital administrators attribute the spike in patient satisfaction to initiatives focused on three of Le Bonheur’s key drivers for measuring patient experience:

- communication with physicians
- communication with nurses
- pain management

Survey results shows that communication with physicians is currently Le Bonheur’s most influential driver. NRC measures physician communication as showing courtesy and respect to families and the child; listening carefully to the parent; and explaining things in a way that’s easy for everyone – including the child –

to understand.

Hospitalist Cynthia Cross, MD, says she believes that, as team leaders, physicians set the tone.



“Many problems boil down to a simple rift in communication,” said Cross. “If we establish that communication is a priority for us – that we want our families to know what’s going on, to receive consistent messages and to hear information that they can understand and apply – then I believe everyone else will follow, and satisfaction will improve.”

To improve two-way communication among team members, staff remodeled white boards in patient rooms and changed the resident physician rounding process.

The new boards, developed from family input, are designed to encourage two-way communication

“If we establish that communication is a priority for us – that we want our families to know what’s going on, to receive consistent messages and to hear information that they can understand and apply – then I believe everyone else will follow and satisfaction will improve.”

Cynthia Cross, MD

WHITE BOARDS

Updated white boards in each patient room have improved communication between families and hospital staff. Families are encouraged to write questions and rate their child's pain. If family members aren't present during rounds, physicians can respond to their questions on the board.

Designed based on input from families, the new boards – printed in **English and Spanish** – have space for more information, including names of **multiple care team members**.

Family members are encouraged to list their names and **cell phone numbers**, so they can be reached quickly in the event of a change in condition.

Parents can rate their child's pain at any time using the Wong-Baker **FACES® Pain Rating Scale**, and a child's pain control plan is routinely updated.

Families write questions and comments for their child's care team members. If a family is out during rounds, physicians can leave responses on the board.

between the family and all members of the care team. Space is available to list the child's care team, family names and phone numbers, the day's plan of care, the child's pain level and questions from the family. When family members or nurses aren't present during physician rounds, the boards are used to help facilitate communication.

The new resident rounding process gives families a more consistent care team. Residents are divided into teams and assigned to specific inpatient units each month. Residents – led by an attending – participate in a formal hand-off and teaching rounds every morning between 7 and 8 a.m. with the patient's family and other

care team members.

The new model helps ensure everyone is on the same page and actively discussing the plan of care with families and with one another.

"Residents and nurses have a chance to build relationships with one another, and nurses are encouraged to participate in rounds, to share information and to offer suggestions for the plan of care," said Infant/Toddler Unit Clinical Director Jessica Fleener, MSN, RN-BC, CNML. "Resident rounding also helps bridge the gap between all consulted subspecialties and the pediatric team leading the plan of care, which has made a huge difference."



PRIORITIZING PAIN MANAGEMENT

In another effort to improve patient experience, Le Bonheur leaders and families looked at ways to reduce the pain and anxiety associated with needle sticks. In two years, Le Bonheur's pain management scores rose from the 21st to the 87th percentile among children's hospitals, according to the National Research Corporation.

"Parents don't want their children to be afraid, and they don't want them to suffer pain," said May. "Every time we stick a child – whether conducting a spinal tap or a routine blood draw – we want to minimize or eliminate that child's pain."

Le Bonheur implemented a program to educate clinicians, patients and families about ways to decrease pain and distract children during procedures. Techniques include topical anesthetic products and vapocoolant sprays, as well as non-pharmacologic interventions like oral sucrose, shot blockers, comfort kits, distraction therapy techniques and Buzzy® – a toy bee that uses both vibration and cold to help minimize pain.

Le Bonheur also implemented use of a "poke plan" – a written tool to help understand each child's needs when faced with pain – with inpatients and

patients in the hospital's outpatient clinics.

"We ask family members if the child has a fear of needles; if a parent would like to be present for all needle sticks and blood draws; if the child has favorite coping mechanisms and other questions to help us tailor a specific pain management plan. We then use the poke plan as a roadmap moving forward for all potentially painful encounters," said Neuroscience Clinical Director Ann Reed, MSN, RN, CNML.

The program has been so successful that Le Bonheur nurses are now partnering with community pediatricians to make interventions more widely available.

With pay-for-performance on the rise and family-centered care at the forefront of the hospital's goals, the taskforce will continue to explore ways to improve overall experience.

"Measuring patient experience matters because it gives us an idea of how well we're taking care of our patients," said Donna Vickery, administrative director of Quality Improvement. "If they don't tell us that something is broken, we won't know what we need to fix. These questions tell us how well we're communicating with families and if we're giving them what they need to help us care for their children."



Partnering for healthy babies

Nurses supporting families through pregnancy, first two years improves outcomes

Chasidy Harris was 18 when she learned she was pregnant. Too embarrassed to go to the doctor, Harris went looking for resources that could help her navigate the world of teenage pregnancy. That's when she connected with the Nurse-Family Partnership (NFP) program – a national early intervention program run locally by Le Bonheur Children's Hospital.

The program offered Harris, and hundreds of other first-time, low-income mothers like her, home visits with a registered nurse throughout her pregnancy and the first two years of her child's life. Le Bonheur has served more than 400 families through the program, which focuses on improving

pregnancy outcomes, child health and development and families' economic self-sufficiency.

This summer, the national office of Nurse-Family Partnership announced the results of a two-decade study looking at the program's impact on maternal and child health.

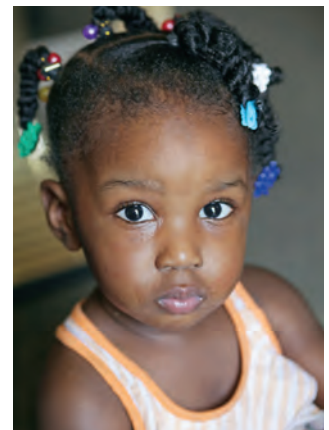


By the numbers

- **8** specially trained home-visitation nurses
- **99** mothers enrolled (as of July 2014)
- **71** percent of NFP mothers initiate breast-feeding, compared to a rate of 60 percent in Shelby County*
- **97** percent of NFP babies are current on immunizations at 18 months

*Urban Child Institute, 2010

able child death from birth to age 20. The Memphis follow-up is the most recent report from a series of trials conducted over a 37-year period to determine Nurse-Family Partnership's long-term effects.



Janiah Harris

“Nurse-Family Partnership is saving lives, and these nurses change the future for families and children,” said Marilyn Smith, RN, BSN-CLC, supervisor of Le Bonheur’s NFP program. Smith participated in the Memphis trial, which began in 1990.

For mothers like Harris, NFP nurses offer valuable education on everything from prenatal vitamins and diet to smoking cessation and child development – all in the privacy of their own home. Harris was 25 weeks along in her pregnancy when she enrolled in NFP and was paired with Elizabeth Pletz, RN, BSN.

Published on *JAMA Pediatrics*’ website in July, the study followed 1,138 families in Memphis, Tenn., and found that NFP reduced preventable deaths among both children and their mothers. Mothers in the home-visitation program were less likely to die of external causes like suicide, drug overdose and homicide and unintentional injuries. Similarly, NFP reduced prevent-

Mothers in the home-visitation program were less likely to die of preventable causes like suicide, drug overdose, homicide and injuries.

“It was good to be able to have Nurse Beth come to my home where I could ask questions in

private,” said Harris. “She taught me a lot about the different phases [of pregnancy and a child’s life] and how to calm down if I’m upset.”

Nurses visit mothers regularly throughout their pregnancy and the first two years of their baby’s life. Visits increase during critical periods, including the six weeks after birth. Nurses also help connect mothers with an obstetrician/gynecologist and a pediatrician.

“One of my favorite things about NFP is the frequency

Current on immunizations		
Age	Le Bonheur NFP	Tennessee
6 months	87.0 %	81.2 % in 2008
12 months	94.6 %	
18 months	96.8 %	
24 months	91.2 %	

of the visits – getting to see my clients regularly and getting to know them,” said Pletz,

who has followed Harris for almost two years. Pletz joined NFP in June 2012.

Harris’ daughter, Janiah, was born on Dec. 22, 2012, her exact due date. Now 18 months, Janiah is a happy, healthy toddler. Mom Chasidy, too, is doing well. The now 20-year-old who has dreamed of becoming a chef since the sixth grade studies culinary arts full time at Memphis’ L’Ecole Culinaire and works five nights a week at the Madison Hotel, a boutique hotel.



Chasidy Harris works five nights a week at the Madison Hotel in Memphis. Since having Janiah, Chasidy has gone back to school to study culinary arts. Becoming a chef has been a longtime dream for the 20-year-old.

Briefs

Hospital recognized by U.S. News & World Report



U.S. News & World Report has again named Le Bonheur Children's one of the nation's best children's hospitals. The Memphis-based hospital was recognized in seven specialties – cardiology/

heart surgery, neonatology, neurology/neurosurgery, nephrology, orthopedics, pulmonology and urology.

Critical Care team receives ELSO award

Le Bonheur's Critical Care program recently received the Extracorporeal Life Support Organization Award for Excellence in Life Support. The three-year award from the International Extracorporeal Life Support Organization (ELSO) recognizes excellence in cardiopulmonary care.

Family-centered care efforts recognized

The Institute for Patient- and Family-Centered Care (IPFCC) recently recognized Le Bonheur Children's and Methodist Le Bonheur Healthcare as one of 12 exemplar hospitals leading the way in family-centered care. The 12 hospitals named in the Better Together campaign demonstrate success in changing the concept of families as visitors and working directly with families as care partners.

Bissler wins prestigious TS award



John Bissler, MD

The Tuberous Sclerosis Alliance (TSA) recently recognized Nephrology Chief John Bissler, MD, with the Manny Gomez Award. TSA gives the award annually to an individual who displays creative or pioneering efforts that improved

understanding of the tuberous sclerosis complex (TSC) or clinical care of individuals with the disease. Bissler is director of Le Bonheur's tuberous sclerosis program.

Langham named 2014 ACS/APSA Health Policy Scholar



Max Langham, MD

Max Langham, MD, vice chair of the General Surgery department at the University of Tennessee Health Science Center, was recently named the 2014 Health Policy Scholar for the American College of Surgeons (ACS)/American Pediatric Surgical Association (APSA). Langham will attend a week-long Executive Leadership Program in Health Policy and Management at Brandeis University before spending a year advising the APSA and ACS on health policy-related issues.

Sathanandam wins PICS-AICS Young Leadership Award



Shyam Sathanandam, MD

Pediatric Cardiologist Shyam Sathanandam, MD, received the 2014 Pediatric and Adult Interventional Cardiac Symposium (PICS-AICS) Young Leadership Award. The award recognizes early career interventionalists. He was also one of three selected as a finalist for the organization's Charles S. Kleinman Scientific Scholarship Award. Sathanandam is an assistant professor at the University of Tennessee Health Science Center.

Neuroradiologist named AJNR fellow



Asim Choudhri, MD

Asim Choudhri, MD, has been selected by the *American Journal of Neuroradiology* as an editorial fellow. During his editorial fellowship, he will participate in manuscript evaluation and selection, editorial-related research and conferences. Choudhri is an associate professor at the University of Tennessee Health Science Center.

Cancer risks increase with complex heart tests

Complex heart imaging can increase cancer risks for children throughout their lifetime, according to a new study in the American Heart Association's journal *Circulation*



Jason Johnson, MD, MHS

co-authored by Le Bonheur Cardiologist Jason Johnson, MD, MHS. In the study, Johnson and his fellow researchers found that radiation from standard X-rays doesn't significantly raise cancer risks for young children, in general, but children undergoing more complex procedures with higher radiation – like cardiac catheterizations and computed tomography (CT) scans – have higher risks. Johnson, an assistant professor at the University of Tennessee Health Science Center, participated in the research at Duke University Medical Center, where he completed his pediatric cardiology and advance imaging fellowships.

Individualized treatment for specific CF mutations becomes reality



Dennis Stokes, MD

A new multi-site clinical trial has shown significant improvements in lung function for people with two copies of the F508del mutation of cystic fibrosis. Le Bonheur is one of 200 sites in North America, Europe and Australia involved in the Vertex Pharmaceuticals Phase 3 trial of ivacaftor (KalydecoT) and lumacaftor (VX-809). Dennis Stokes, MD, has led the Le Bonheur trial with three patients participating in the Phase 3 trial and subsequent rollover to open label drug continuation. Based on favorable results, Vertex has submitted a new drug application to the U.S. Food and Drug Administration for approval of the combination therapy which will benefit a large group of CF patients. Another Le Bonheur patient with a rare CF mutation studied at Le Bonheur was recently started on ivacaftor (Kalydeco) after studies showed potential benefit in cell model systems and in a clinical trial. Recently this patient traveled to another children's hospital studying ivacaftor on CF-related diabetes for additional specialized testing. Studies at Le Bonheur have shown sweat chloride values have fallen from the prior elevated level of 80 to a normal level, and pulmonary function testing has shown significant improvements in lung function.

Partnering for healthy babies

Nurses supporting families through pregnancy, first two years improves outcomes

A national early intervention program pairing nurses with first-time, low-income mothers reduces preventable deaths among both children and their mothers, according to a study published in *JAMA Pediatrics*. Earlier follow-up studies of the Memphis trial showed better prenatal health, child health and development and economic self-sufficiency among families enrolled in the program.

The results were announced this summer at Le Bonheur Children's Hospital, which has served 410 families through the program.

