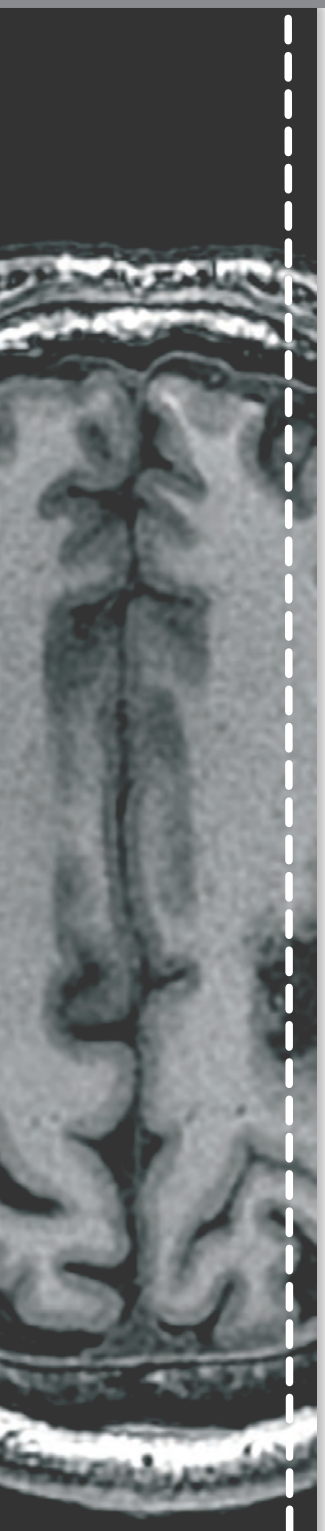
Le Bonheur Children's Hospital
Memphis, Tennessee

Brain Waves

Neuroscience Institute

Spring 2015



New device gives epilepsy patient hope

Le Bonheur first pediatric hospital to implant NeuroPace® RNS® system

After 10 years of seizures, 23-year-old Hannah Lawrence says she feels hopeful that she may finally be able to move forward with her life.

In January, Hannah, a Le Bonheur Children's Hospital patient, became the first U.S. patient to receive the NeuroPace® RNS® system at a pediatric hospital outside of the clinical trial. RNS is the first closed-loop responsive brain stimulation system approved by the U.S. Food and Drug Administration for reducing seizures in individuals 18 years of age and older with partial onset seizures.

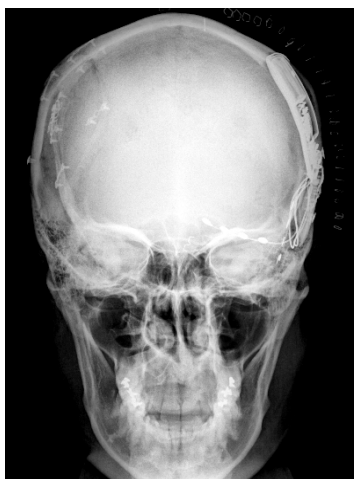
Ten years ago, Hannah developed what seemed like the flu. But after the flu test was negative and then a seizure left her on the floor, her parents thought something else might be going on. The local emergency room in Brandon, Miss., sent her to Blair E. Batson Children's Hospital in Jackson, Miss. where she was diagnosed with viral encephalitis. Inflammation of the brain left scar tissue on both sides of her brain, which caused the uncontrolled seizures.

"We didn't know 10 years ago what we were in for," said dad Kenny.

"Being new to epilepsy, we thought, well, you go to the doctor and get some medicine and everything will be ok," said mom Rhonda.

Now the Lawrence family knows that just isn't the case. Hannah came to Le Bonheur's Neuroscience Institute in 2007 after her pediatric neurologist in Mississippi encouraged the family to travel to Memphis. James Wheless, MD, co-director of the Neuroscience Institute, and his team have explored every option for Hannah.

Lateral and AP radiographs of the skull show the NeuroPace device overlying the left parietal bone, with electrodes extending intracranially.



"When I first saw Hannah, I knew controlling her seizures would be a challenge. She had already tried several good medical therapies without success. We evaluated her for all other treatment options available and began a plan of therapy. At a comprehensive epilepsy center

continued on page 2

About NeuroPace® RNS®

- A novel, implantable therapeutic device that delivers responsive neurostimulation and continuously monitors brain electrical activity, detects abnormal electrical activity and responds by delivering imperceptible levels of electrical stimulation to normalize that activity before an individual experiences seizures
- Approved by the U.S. Food and Drug Administration as an adjunctive therapy in reducing the frequency of seizures in patients 18 years of age or older with partial onset seizures who have undergone diagnostic testing that localized no more than two epileptogenic foci, are refractory to two or more antiepileptic medications, and currently have frequent and disabling seizures (motor partial seizures, complex partial seizures and/or secondarily generalized seizures)

Referrals: 866-870-5570
www.lebonheur.org/neuroscience

A pediatric partner with The University of Tennessee Health Science Center/College of Medicine and St. Jude Children's Research Hospital

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT NEUROLOGY & NEUROSURGERY 2014-15

New portable CT scanner eliminates need to move unstable patients

A portable CT scanner is the latest addition to technology available for patients with complex neurosurgical needs at Le Bonheur's Neuroscience Institute. Based in the Neurosurgical Intensive Care Unit, the CereTom® eight-slice small bore portable CT scanner provides the highest quality scans without moving a patient across the hospital to the stationary CT scanner.

"A portable CT scanner allows us to roll up to the bedside, in the operating room, intensive care units and emergency department, and perform scans on patients too unstable to move to the radiology department," said Frederick Boop, MD, co-director of the Neuroscience Institute and Semmes-Murphey neurosurgeon.

The CT scanner is a gift from the Herbert and Mary Shainberg Neuroscience Research Fund, which since 1996 has made significant investments in the Neuroscience Institute.

A new CereTom® eight-slice small bore portable CT scanner based in Le Bonheur's Neurosurgical Intensive Care Unit provides the highest quality scans without moving a patient across the hospital to the stationary CT scanner.

continued from page 1

like the one at Le Bonheur Children's Hospital, we are able to offer patients like Hannah every option available in the U.S., as we work to control her seizures," said Wheless.

Before January, Hannah took three different medications – 13 pills – each day. Surgeons implanted a Vagus Nerve Stimulator (VNS) in 2007, and it provided partial relief from her seizures. Hannah had a right temporal lobectomy in 2010 and further brain surgery in 2013. After each surgery, the seizures were reduced, but it wasn't enough for a teenager to have a normal life.

Before receiving the NeuroPace® RNS® system, Hannah and her parents learn how it works and how to download EEG (brain wave data) information to NeuroPace® Patient Data Management System (PDMS), an interactive web-based database used for storage and clinician remote access.

"Life was pretty tough. She'd have seizures at school. Seizures at restaurants. She couldn't take a bath alone. She couldn't lock a door. She has not been able to drive," Rhonda said.

Day-to-day life was hard – especially during high school. Her mom, Rhonda, eventually quit working because someone needed to pick Hannah up from school after she had a seizure. Hannah missed so much school that she fell behind. Her dreams of going to college were dashed. After high school, she decided to go to barber school to get her barber license and then join her dad in the family barber shop. The Lawrences wanted to give their teenager independence, but when they did, she'd have another seizure. One time she fell and broke her wrist while with a friend.

The family heard about NeuroPace® and started reading online. They called hospitals around the country to see if Hannah could enroll in a clinical trial, but all were full. Once the RNS® was approved by the FDA for those 18 and older, Wheless asked Hannah's family if they'd consider the device. The Lawrences didn't hesitate – yes, they wanted the RNS for Hannah.

On Thursday, Jan. 22, Le Bonheur Neurosurgeon Paul Klimo, MD, implanted the RNS Neurostimulator within Hannah's skull and beneath the scalp. The neurostimulator is connected to two leads placed directly on the area of the brain where the seizures are starting from.

"The partnership between the epilepsy team and the neurosurgery team at Le Bonheur has allowed our team to find innovative solutions for patients like Hannah," said Paul Klimo, MD, chief of Pediatric Neurosurgery for Le Bonheur and Semmes-Murphey neurosurgeon.

Nightly, Hannah pulls out a laptop and a remote monitor to "download her head," she says. The EEG (brain wave data) information is uploaded to NeuroPace® Patient Data Management System (PDMS), an interactive web-based database used for storage and clinician remote access. Wheless can review the EEG and any seizure activity to adjust Hannah's medication or the impulses the RNS provides.

Just 48 hours after surgery, Hannah returned home. She returned to work the next Friday. She has been seizure free since surgery.

Hannah and her parents hope the RNS gives her freedom to move forward with life. Hannah has dreams of going to college to become a special education teacher. She wants to drive and be independent.

"I wanted to go to Mississippi State, but that didn't happen. In high school, I wished I could be a teacher. Now, I'd like to be a special education teacher, because I think I can relate to those kids," Hannah said.

Two more patients are expected to receive the RNS device this spring.

After 10 years of seizures, 23-year-old Hannah Lawrence became the first U.S. patient to receive the NeuroPace® RNS® system at a pediatric hospital outside of the clinical trial.

Nine pediatric neurology programs study cognitive outcomes in partial seizures

Le Bonheur Children's Hospital has joined eight other pediatric neurology programs in studying the cognitive outcomes in children treated for partial seizures. The hospital has enrolled 14 children in the COPE (Cognitive Outcomes in Partial Seizures) study since June. The study currently has 35 children enrolled and 129 screened.

Children presenting to the Emergency Department with new onset partial seizures are referred to New Onset Seizure Clinic for neurological evaluation within one to three days. Children that have had two or more partial seizures are then eligible for enrollment into the COPE study. Baseline neuropsychology testing is preformed within one to three days and at that time the child is randomized onto one of three antiepileptic medications. Neuropsychological testing is then repeated at three months and again at six months to assess cognitive functioning.

"By partnering with the Emergency Department, we're able to see new onset seizure patients quickly to begin treatment. This collaboration has resulted in not only the enrollment of 14 patients, but will contribute to our understanding of how these medications affect the cognitive functions of patients with partial seizures on a larger scale," said Nurse Practitioner Lauren Siebrase, who staffs the New Onset Seizure Clinic.

COPE study participants:

- Le Bonheur Children's Hospital
- Children's Hospital of Philadelphia
- University of California at San Diego
- Children's Healthcare of Atlanta
- Children's National Medical Center
- Cincinnati Children's Hospital Medical Center
- University of Rochester
- Johns Hopkins University
- Washington University

NEUROLOGY UPDATE SET FOR APRIL 24-25

Le Bonheur Children's Hospital and the University of Tennessee Health Science Center faculty will host the ninth annual Greater Mid-South Pediatric Neurology Update April 24-25 at The Westin Memphis, Beale Street.

The seminar has been designed to encompass state-of-the-art practices and trends in treating pediatric neurology patients. Faculty who are both clinically and academically oriented will address relevant issues and provide valuable information and insight into situations commonly presented to subspecialists in pediatric neurology. This will be performed using case-based learning and didactic lectures with time for questions and answers.

The event will include the annual Kayden R. Vinson Distinguished Scholar Lecture by Shlomo Shinnar, MD, PhD, professor of Neurology, Pediatrics and Epidemiology and Population Health at Montefiore Medical Center and Albert Einstein College of Medicine in Bronx, N.Y. Gagan Joshi, MD, director of the Autism Spectrum Disorders Program in the Pediatric Psychopharmacology Clinical and Research Program and medical director of the Bressler Program at Massachusetts General Hospital, will also serve as a guest lecturer.

Topics include:

- Consequences and treatment options of prolonged febrile seizures
- Utility of advanced MRI techniques
- Psychopathology in high-functioning autism spectrum disorder
- Current standards in evaluation and treatment of neuromuscular disorders
- Common sleep disorders in pediatric neurology patients
- Case review of neurology cases with neuro-radiologic findings
- New seizure medications and formulations in epilepsy treatment

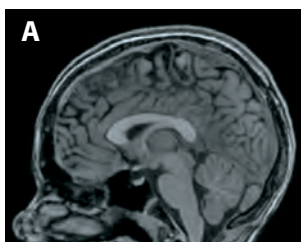
For more information or to register, visit www.methodistmd.org or call 901-516-8933.

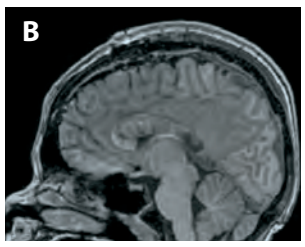
CORPOUS CALLOSTOMY BRINGS SEIZURE RELIEF FOR 14-YEAR-OLD BOY

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 Vagus Nerve Stimulation hadn't made a big enough difference, so Caesar, 14, and mom Dana Martinez traveled to Memphis – from their Oklahoma home – to see if there was anything left to do.

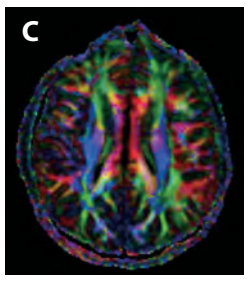
"We've been trying for 10 years to figure this out. Our doctor told us if anyone could give us answers, Dr. Wheless could," Martinez said.

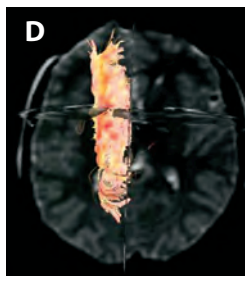
After four days in Le Bonheur's Epilepsy Monitoring Unit, and Magnetoencephalography (MEG) and Transcranial Magnetic Stimulation (TMS) testing, the option was clear as the neurologists, neurosurgeon, neuroradiologist, neuropsychologist and clinical neuroscientists discussed Caesar's case in their weekly meeting. Just a week after he arrived in Memphis, he underwent a corpous callostomy – a surgery that separates the two hemispheres of the brain in order to limit the severity of seizures. Semmes Murphey Neurosurgeon Stephanie Einhaus, MD, performed the surgery.





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 last spring.





Sagittal T1W image (A) shows a normal appearance of midline structures, including the corpus callosum. Sagittal T1W image after surgery (B) shows transection of the corpus callosum. Axial directionally encoded FA map from DTI (C) shows absence of midline continuity of the fibers of the corpus callosum; red normally indicates fibers that travel from side to side, and they are disrupted. Tractography image obtained from DTI processing (D) confirms no fiber bundles cross the midline.

A team from Le Bonheur Neuroscience Institute published its preliminary experience using an intraoperative MRI-compatible infant head holder in the Journal of Neurosurgery.

Team documents experience with new iMRI-compatible infant headrest

Until recently, intraoperative MRI (iMRI) has been unavailable to infants and patients with calvarium defects due to the need to pin the calvarium during surgical procedures. The surgical team at Le Bonheur recently published its findings using a new MRI-compatible horseshoe headrest by IMRIS in the *Journal of Neurosurgery Pediatrics*. The team found the Visius horseshoe headrest offered a technical advance in iMRI technology for infants, patients with cranial defects or prior craniotomies in whom pin fixation may not be safe or in whom the need to move the head during surgery is required.

The article provides two case studies – a 4-month-old infant for resection of a supratentorial tumor and a 2-year-old with a thin and pliable skull.

"The IMRIS horseshoe headrest worked well for providing the ideal prone positioning during this procedure," said Frederick Boop, MD, chairman of the Department of Neurosurgery at the University of Tennessee Health Science Center, co-director of Le Bonheur's Neuroscience Institute and Semmes-Murphey neurosurgeon. "In the past we would not have had an iMRI option for this child, and now the tumor is completely gone. We have now advanced our treatment to a group of kids for whom it will really make a difference. Even our youngest and most fragile patients can benefit from intraoperative MR, which would not have been possible otherwise."

The device provides non-pinned (or non-rigid) head support in prone, lateral and supine positions during head, neck and cervical spine surgeries where use of a head fixation device (HFD) – a clamp-like device – is not desirable because the skull is too fragile for pinning. These patients may be babies whose skulls are still soft or older patients with weakened skull bones. This headrest may also be useful for other applications not requiring rigid fixation, such as those that access the skull through the nose.

Boop FA, Bate B, Choudhri AF, Burkholder B, Klimo P. Preliminary Experience with an Intra-operative MRI Compatible Infant Headholder: Technical Note. Journal of Neurosurgery Pediatrics published online Feb.13, 2015. DOI: 10.3171/2014.10.PEDS14447

Le Bonheur Children's Hospital

Brain Waves is a quarterly publication of the Neuroscience Institute at Le Bonheur Children's Hospital. The institute is a nationally recognized center for evaluation and treatment of nervous system disorders in children and adolescents, ranging from birth defects and learning and behavioral disorders to brain tumors, epilepsy and traumatic injuries.

Scan to learn more about our Neuroscience Institute.

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Transcranial magnetic stimulation: Safe and effective tool in pediatric brain mapping

Researchers at Le Bonheur recently published an overview of the clinical applications of transcranial magnetic stimulation (TMS) in the *Journal of Child Neurology*. The team discusses the basic principles and safety of the noninvasive brain stimulation method that is used as a diagnostic aid and in the treatment of neuropsychiatric disorders in adults and increasingly in children.

TMS 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 non-invasive cortical stimulation. Navigated TMS uses an MRI of the patient's brain to move across the skull – much like a GPS system helps a person navigate a car. The data gathered from TMS allows clinical neuroscientists to connect brain activation and the responses that follow for motor and language.

Le Bonheur Clinical Neurosciences team published a review of clinical applications of transcranial magnetic stimulation (TMS) in a recent issue of the *Journal of Child Neurology*.

"We've found that TMS is a safe and non-invasive means of localizing motor and language functions in the brain of pediatric patients. It's an important tool in presurgical planning in our practice," said TMS Lab Director Shalini Narayana, MBBS, PhD.

In the article, the team demonstrates the clinical utility of functional mapping in pediatric neurology practices in four cases including presurgical evaluation, cortical dysplasia and cortical reorganization. In addition, the merits of TMS functional mapping are compared with Magnetoencephalography and Functional Magnetic Resonance Imaging.

Narayana S, Papanicolaou AC, McGregor A, Boop FA, Wheless JW. Clinical Applications of Transcranial Magnetic Stimulation in Pediatric Neurology. J Child Neurol published online 23 October 2014

National Dup15q registry begins in Memphis

A new national registry for chromosome 15q Duplication Syndrome (Dup 15q) launched recently at Le Bonheur Children's Hospital. The national registry constructed and maintained here in Memphis with the assistance of Children's Foundation Research Institute Technical Director Tee Viangteeravat, PhD, is designed to capture data from consortium clinics associated with the Dup15q Alliance (www.dup15q.org) across the United States.

The database will be used to gather clinical data, including behavior and seizure history data collected through surveys from family members. One eventual goal is for researchers to conduct multi-site studies to develop better treatments for the 15q Duplication syndrome and facilitate clinical trials.

Dup15q syndrome is caused by various duplications of chromosome 15q. Duplications that are maternal in origin often result in developmental problems including autism. Large duplications on 15q, including individuals with the isodicentric 15q duplications, involves a wide range of developmental disabilities including autism spectrum disorders; motor, cognitive and speech/language delays; digestive issues and seizure disorder. Information gathered from the clinics will inform and further refine already available treatments and therapies for 15q Duplication syndrome.

Lawrence T. Reiter, PhD, serves as the principle investigator of the database and director of the Memphis clinic site. Reiter says he has hopes for the discoveries and improved treatment protocols that will be made with information from the database.

"The No. 1 priority for this particular group of kids is better seizure management. By working across multiple sites, we hope to have a better handle on what medications work best for these kids," Reiter said.

Le Bonheur is home to one of a handful of Duplication 15q11 clinics across the country.

"Our comprehensive multidisciplinary team collaborates on finding the best care for every child. By collecting information in a systematic manner, we'll be better able to develop targeted treatments," said Kathryn McVicar, MD, Dup 15q clinic medical director.

Dup15q clinics contributing to this national registry

- Massachusetts General Hospital – Boston, Mass.
- NYU Langone Medical Center – New York, N.Y.
- Geisinger Health System – Lewisburg, Pa.
- Miami Children's Hospital and Miami Children's Hospital Dan Marino Center – Miami, Fla.
- Minnesota Epilepsy Group – St. Paul, Minn.
- University of Tennessee Health Science Center and Le Bonheur Children's Hospital – Memphis, Tenn.
- Pediatric Neuroscience Center at Swedish Neuroscience Institute – Seattle, Wash.
- University of California San Francisco – San Francisco, Calif.
- University of California Los Angeles – Los Angeles, Calif.