Vitals...
According to data compiled by the Organ Procurement and Transplant Network, 11.55% of all US liver transplants are in children under the age of 18. In a 2003 study on pediatric liver disease epidemiology and impact, the authors call for research efforts to focus on understanding the mechanisms of pediatric disease, developing and instituting definitive therapy for pediatric hepatobiliary disease, educating clinicians and the public, developing tools for early diagnosis, and initiating targeted preventative efforts.

USING MRE TO HELP CHANGE THE COURSE OF PEDIATRIC LIVER DISEASE

Imagine your three-year-old child is showing symptoms of jaundice, dark urine, pale stool, easy bleeding, itching, spider-like blood vessels visible in the skin, and chills. After a visit to the pediatrician, the diagnosis could potentially be life threatening liver disease.

Consider these facts: According to the Children’s Liver Disease Foundation, more children in the UK are currently diagnosed with liver disease than childhood leukemia. Additionally, at least two children are diagnosed with liver disease every day in the UK. There are more than 100 different liver diseases that can affect children—some are life threatening, but all require a lifetime of care.

Diffuse liver disease occurs in children for a variety of reasons. For example, childhood obesity is a leading cause of liver disease in pediatrics. Infections such as hepatitis A, B, and C and drug reactions may lead to the development of liver disease in young children.
The right diagnosis

Especially in children with liver disease, determining the right diagnosis quickly can have a profound effect on the outcome. An important diagnostic task in assessing patients with suspected liver disease is to detect the presence of hepatic fibrosis, which can be treated if diagnosed before it progresses to irreversible cirrhosis.

The current practice for evaluating liver fibrosis is needle biopsy. However, the risks of biopsy are well known as it is invasive and has the potential for side effects such as a collapsed lung, complications from anesthesia, injury to the gallbladder or kidney, and internal bleeding.

Richard Ehman, MD, and colleagues at Mayo Clinic (Rochester, MN) developed a technique for non-invasively measuring liver tissue stiffness—Magnetic Resonance Elastography (MRE). Although MRE is not completely without risk, it is a non-invasive way to measure tissue stiffness. This technology, licensed by Mayo Clinic, employs low frequency sound waves in combination with MR to probe tissue stiffness.

There are three steps to the process: generating acoustic waves within the tissue of interest; imaging the micron level displacements of the tissue that result from wave propagation using a special MR technique with oscillating motion-sensitizing gradients; and generating maps of the tissue stiffness, known as “elastograms,” using a mathematical algorithm developed by Mayo Clinic physicians and researchers.

MRE of the liver can be accomplished in an acquisition that lasts only 15 seconds and is easily added to a standard MR examination of the abdomen. A simple drumlike, acoustic driver is placed in contact with the body. A flexible tube is connected to a driver device outside the scan room that generates low-frequency sound waves in the range of 40 to 90 Hz. The vibration should not cause discomfort and has an amplitude that is typically less than 0.1 mm, which falls well within established safety limits for vibration exposure.

Some peer-reviewed literature indicates that MRE has a promising ability to help evaluate relative tissue stiffness. Different levels of liver tissue stiffness can be associated with severity of diffuse liver disease.

Changing pediatric management

Cincinnati Children’s Hospital Medical Center (Cincinnati, OH) ranks third in the nation among all Honor Roll hospitals in U.S. News and World Report’s 2011 Best Children’s Hospitals ranking and number one in gastroenterology. It is internationally recognized for improving child health and transforming delivery of care through fully integrated, globally recognized research, education, and innovation. It also has a huge pediatric liver disease population.

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According to Daniel Podberesky, MD, Associate Director, Clinical Services and Chief, Thoracoabdominal Imaging Division at Cincinnati Children’s, when he learned about MRE, he believed his hospital would find the technology beneficial when applied to pediatric liver disease. So he contacted Dr. Ehman at Mayo Clinic to put a collaborative research agreement in place. Between August, 2011 and March, 2012, the hospital performed over 40 pediatric MRE exams.

The department of radiology has three child life specialists. Before the MRE scan, they take the children to a special room with a mock-up of the MRE drum. It’s placed on their abdomens so they can feel the vibration and get comfortable with the “tickling” sensation before the exam. So far, the staff has not had any complaints or “freak outs.” The hospital gives any child over five or six the opportunity to be scanned without sedation.

“Having the ability to easily and non-invasively assess the child’s liver could help us identify the issue early and begin the right course of treatment in a timely and effective manner,” comments Dr. Podberesky. “This technique could give us the opportunity to help slow, stop, or even reverse the progression in some cases.”

He underscores the benefits of MRE, which Dr. Podberesky and his staff use on their Signa* HDxt 1.5T system from GE Healthcare, using three real-life scenarios. In the first scenario, MRE showed inconspicuous tissue stiffness.

Dr. Daniel Podberesky

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The care team decided to cancel a planned biopsy in a child with non-alcoholic fatty liver disease because, in this situation, the treatment might be diet and exercise—and monitoring with additional MRE scans.

In a second scenario, an ultrasound suggested only mild fatty liver infiltration, but MRE indicated a greater degree of tissue stiffness. A subsequent biopsy confirmed a diagnosis of inflammation and fibrosis. In the past, based solely on the ultrasound, it’s unlikely that a biopsy would have been performed and the disease could have been missed.

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A 15-year-old obese patient with elevated liver enzymes and fatty liver infiltration on ultrasound and MR. The MRE was performed to evaluate tissue stiffness. The MRE returned with evidence of mild steatohepatitis and mild fibrosis. Subsequent biopsy confirmed those findings.
Daniel J. Podberesky, MD, is Associate Director, Clinical Services, Chief of the Thoracoabdominal Imaging Division, and Assistant Professor, Division of Pediatric Radiology, Cincinnati Children’s Hospital Medical Center. Dr. Podberesky obtained his undergraduate and medical degrees at the University of Maryland, and completed a residency in diagnostic radiology at the San Antonio Uniformed Services Health Education Consortium as an active duty member of the U.S. Air Force. After completing a fellowship in pediatric radiology at Cincinnati Children’s Hospital Medical Center, Dr. Podberesky served as Chief of Pediatric Radiology at Wilford Hall Medical Center, the U.S. Air Force’s flagship tertiary care medical facility. Dr. Podberesky returned to Cincinnati Children’s Hospital as Chief of Body CT in July 2008. He helped create the Division of Thoracoabdominal Imaging, and became its Chief in 2009.

Cincinnati Children’s Hospital Medical Center ranks third in the nation among all Honor Roll hospitals in U.S. News and World Report’s 2011 Best Children’s Hospitals ranking. It is ranked #1 for gastroenterology and in the top 10 for all pediatric specialties—a distinction shared by only two other pediatric hospitals in the United States. Cincinnati Children’s is one of the top two recipients of pediatric research grants from the National Institutes of Health. It is internationally recognized for improving child health and transforming delivery of care through fully integrated, globally recognized research, education, and innovation. Additional information can be found at www.cincinnatichildrens.org.

Third, congenital heart disease patients who undergo a Fontan procedure often develop liver disease as a late complication—diagnosing it as early as possible is critical. With MRE, Dr. Podberesky and his team could see that the liver stiffness was more pronounced than expected. A biopsy confirmed this and mild to moderate fibrosis was diagnosed.

The liver MRE protocol at Cincinnati Children’s Hospital Medical Center includes a 3D FSPGR axial opposed phase imaging sequence, a coronal T1 sequence, an axial T2 frFSE sequence with fat-saturation and respiratory triggering, and the MRE sequence. The patients are scheduled in a 30 minute time slot and the imaging takes approximately 15 minutes.

MRE vs. ultrasound
Ultrasound is often used to assess liver disease. However, according to Dr. Podberesky, it has limitations, especially in obese patients. With ultrasound, each user is subjectively grading the degree of fatty infiltration, but no two clinicians/radiologists will always grade it the same. On the other hand, MRE is consistent, providing reproducible color-coded stiffness maps of the liver that help reduce the subjectivity and differences in reading interpretations. MRE takes advantage of MR’s strength in imaging obese patients or patients with ascites.

The future is bright
Dr. Podberesky is confident that MRE has a bright future. Once the hospital staff became familiar with MRE, the application became very intuitive and user friendly. “We push our limits and expand our horizons because our patients expect us to be on the cutting edge. Right now, with MRE, we have a chance to change the course of pediatric liver disease. It has provided us with a paradigm shift on how we approach our patients,” offers Dr. Podberesky. “And down the road, we’ll probably be able to use it with other diseases. It gives us hope for a better future for sick children.”

References:
1. www.childliverdisease.org/content.aspx?CategoryID=426