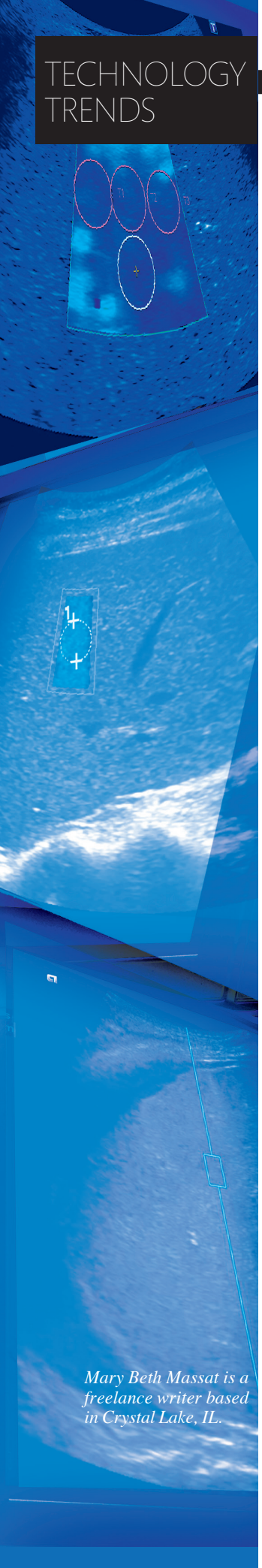


Ultrasound elastography gaining clinical use

Mary Beth Massat

Palpation has been used by doctors for centuries to aid in the diagnosis of disease or illness. Today, ultrasound elastography is extending palpation to organs located beyond the reach of physical touch, providing new opportunities for diagnosis and the noninvasive assessment of disease.

There are two commercially available techniques for ultrasound elastography: strain and shear wave. Although ultrasound systems providing strain elastography have been available longer than shear wave, the latter is quickly gaining traction as the preferred technique.

Richard G. Barr, MD, PhD, has been using ultrasound strain elastography for the last 15 years, and ultrasound shear wave elastography for the past five years as an early adopter of the Aixplorer featuring ShearWave Elastography (Supersonic Imagine). Dr. Barr also has experience using other ultrasound elastography systems from various manufacturers. While he uses both ultrasound elastography technologies in his Youngstown, Ohio, practice he finds that shear wave is often the more useful technique, particularly for liver, prostate and MSK imaging.

Evaluating liver fibrosis

"What is really taking off is the evaluation of liver stiffness," Dr. Barr says, adding that shear wave elastography has been used to replace a large number of biopsies for liver fibrosis. "It's the shear wave speed that tells us the stiffness of the liver," he adds. "The technology is here to stay—as the technology improves and becomes more established, it will become part of a regular ultrasound exam."

Technologically, shear wave elastography is more easily reproducible than strain or compression elastography, says Sara M. O'Hara, MD, FAIUM, FAAP, Chief, Section of Ultrasound at Cincinnati Children's Hospital Medical Center.

Dr. O'Hara uses the Aplio 500 (Toshiba America Medical Systems) to evaluate liver stiffness in pediatrics at liver disease diagnosis and to follow its progression. This includes children with liver transplants, metabolic disorders, cystic fibrosis and those on prolonged intravenous feeding (TPN).

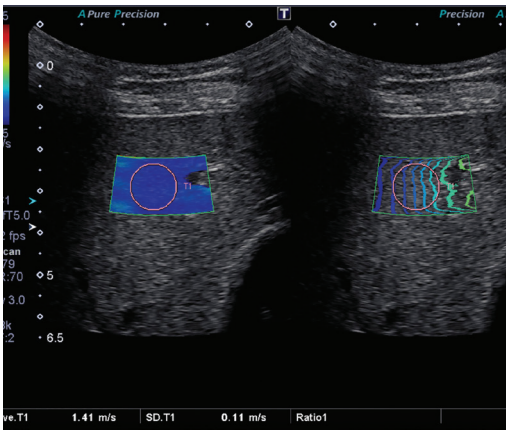
Dr. O'Hara is not yet tracking a reduction in liver biopsy, although she does think shear wave elastography in guiding biopsy is useful, since hepatic fibrosis is not uniform throughout the liver. Her department is also gathering data to try to find normal stiffness values in pediatrics. "All of the published data is based on adults, with few clinical papers in children," she says.

"In children with known liver disease, shear wave elastography is a useful tool to determine how rapidly their fibrosis is progressing—how much of the liver is damaged and how much is functional. We can evaluate this noninvasively without biopsy using ultrasound elastography," Dr. O'Hara explains.

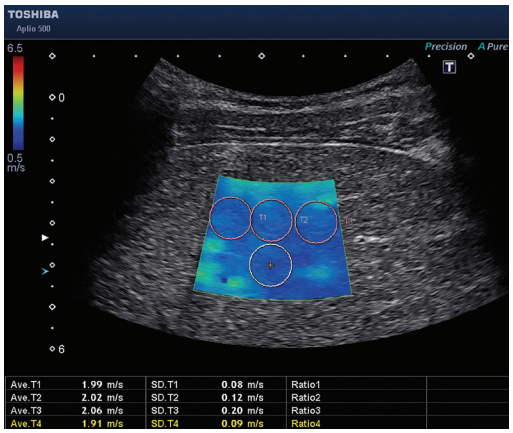
With the Aplio 500, Dr. O'Hara can also see the shear wave propagating, similar to ripples of water, as it spreads out across the tissue. "That pattern reassures me that the pulse was applied properly and there are no artifacts from surgical staples or vessels that would give me an erroneous result," she says.

Different systems also vary in the depth that they measure the shear wave. At a 5 cm depth, it may be difficult to scan the liver in a large or obese patient, Dr. O'Hara says. Her system can achieve depths of 6 cm and up to 8 cm; however,

Mary Beth Massat is a freelance writer based in Crystal Lake, IL.



Twin view of transverse image of the liver with color map and region of interest (ROI) on the left and propagation map on the right. Notice the lack of color on the right side of the color map due to artifact and how the propagation map also shows altered, irregular wave fronts. This would be a poor site to sample with ROI. Image courtesy of Dr. Sara O'Hara, Cincinnati Children's Hospital.



Transverse image of the liver during shear wave elastography shows the color map which is well centered about 4 cm deep to the skin surface and 1 cm deep to the liver capsule. Four different ROI's have been placed in the color box with average shear wave speeds tabled below the image. The color map is homogenous and the shear wave speeds also show little variability. This is a reliable sample volume. Image courtesy of Toshiba America Medical Systems

results are not reproducible at 8 cm across all currently available ultrasound elastography vendors.

To collect data on shear wave elastography in pediatrics, Dr. O'Hara and her team are performing it on different types of patients at Cincinnati Children's, including newborns with jaundice or cholestasis. She captures 10 measurements, which adds 4 to 5 minutes to the ultrasound exam and does not require any adjustments in the day's schedule.

"We're adding another layer of confidence to help diagnose conditions such as biliary atresia," she says, citing a rare, life-threatening condition in infants where the bile ducts in the liver lack normal openings. The bile becomes trapped, builds up and damages the liver. In one small study, Dr. O'Hara says that these babies had stiffer livers than with other causes of jaundice.

Shear wave elastography is not yet well understood, in Dr. O'Hara's experience, for evaluating children with NASH and fatty liver disease, as it gives variable results that are less reproducible.

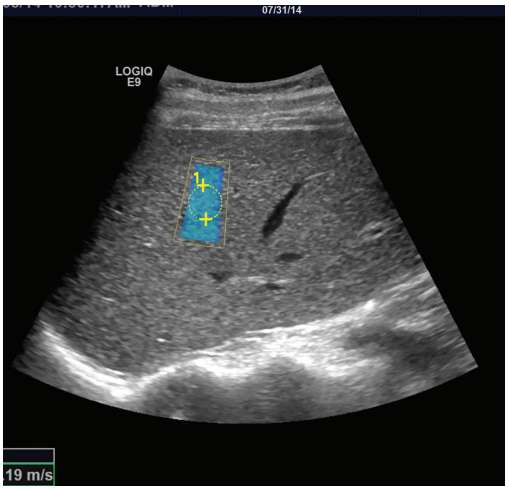
Hisham Tchelepi, MD, a radiologist with the Keck Hospital of USC and the USC Norris Comprehensive Cancer Center and Hospital, also utilizes shear wave elastography for evaluating liver fibrosis in patients with Hepatitis C, fatty liver, and alcoholic liver diseases to quantify the degree of fibrosis. He's also using the LOGIQ E9 Shear Wave Elastography (GE Healthcare) to guide liver biopsies and in some cases avoid or postpone biopsy .

"When you biopsy the liver, there can be erroneous and inadequate samples, or the sample size may not be good enough for interpretation," Dr. Tchelepi explains. By taking multiple elastography samples across the liver and then generating a mean value, it is possible to minimize the number of unnecessary biopsies, which can help to further minimize the cost of medical care as well as the associated morbidity of liver biopsy.

Dr. Tchelepi believes that shear wave elastography can assist with earlier detection of liver fibrosis resulting from conditions such as Hepatitis C. He also sees promise in patients with both fatty liver and alcoholic liver disease.

"This is a great tool to use in conjunction with the patient's lab work to follow the course of treatment and see if the liver will normalize," he says. "If we catch the disease before it reaches Metavir Stage 4 cirrhosis, then there is a good chance for reversibility."

At Radiology Associates of South Florida and Baptist Health South Florida, Ann Podrasky, MD, FSRU, Section Chief, Ultrasonography, utilizes ARFI (acoustic radiation force impulse) shear wave elastography on the ACUSON S2000 and ACUSON S3000 ultrasound systems, Helx Evolution with Touch Control (Siemens Healthcare) to provide hepatologists with the information they need for determining which Hepatitis C patients should receive viral therapy. In the past year since implementing the



In this ultrasound shear wave elastography image, the colored region displays a qualitative assessment of how soft or hard the tissue is. The circle inside the blue box is a quantitative measurement of the shear waves' velocity, which can help physicians in diagnosis, staging, and management of liver disease associated with changes in tissue elasticity. The measured value in this patient is typical of a normal liver. Image courtesy of GE Healthcare

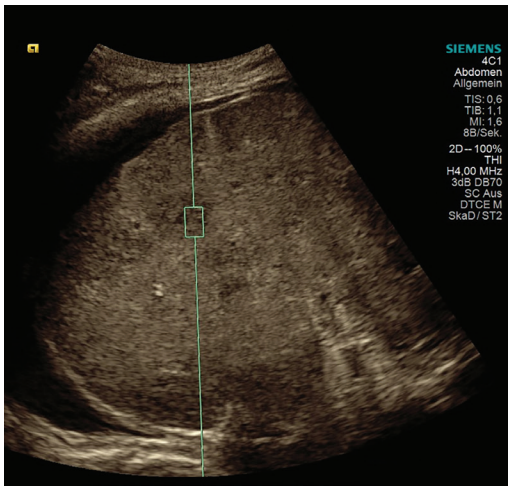
technology, the practice has imaged close to 500 patients with ultrasound elastography.

"We see cases that we would not suspect that the patient had severe fibrosis or even cirrhosis based on the gray scale imaging," Dr. Podrasky explains. "We may see subtle things like slight contour abnormality of the liver, but there is no surface nodularity or other signs of cirrhosis evident. But with elastography, we can diagnose severe fibrosis of the liver in that same patient."

While Dr. Podrasky has used ultrasound elastography in patients with fatty liver disease, she cautions that the reliability of the test results is lower in these cases.

In order to obtain good reproducible results that match serological tests in patients, it is important to perform the procedure correctly with very precise technique, Dr. Podrasky explains. First, patient positioning is very important, with the patient in a left posterior oblique position with their arm raised up. The patient should be instructed to breathe slowly, and then suspend respiration, as any movement of the liver can lead to a less accurate measurement. Samples are taken in segment 8, at least 2 cm from the capsule at a depth between 4.5 and 6 cm, Dr. Podrasky adds.

This protocol mirrors the Society of Radiologists in Ultrasound Consensus Conference Statement, with Dr. Barr as lead author, as published in the September 2015 issue of *Radiology*.[1]



VTq quantifies stiffness in this cirrhotic liver for assistance in disease staging and patient management. Image courtesy of Siemens Healthcare.

Breast lesions

Both strain and shear wave ultrasound elastography have been utilized for evaluating breast lesions. A 2012 literature review published in the *Journal of Ultrasound* reported that the two techniques "complete each other" and therefore they should be combined to overcome the limitations of both.[2]

Specifically, strain imaging is a qualitative method that can be influenced by histotype and lesion size. The use of semi-quantitative indices was not found to improve performance or reduce interoperator variability. Shear wave, on the other hand, is a quantitative method that can provide a more accurate assessment of the spatial distribution of tissue stiffness; however, there are limitations in measuring shear wave velocity in very stiff breast lesions.[2]

Dr. Barr prefers to use both strain and shear wave ultrasound elastography for breast studies, as he is more confident in his diagnosis if they provide the same result. "If both are negative, I am confident to cancel the biopsy," he says. In fact, his practice has eliminated 70% of unnecessary breast biopsies based on the results of the two ultrasound elastography tests.

Breast elastography is unique compared to that of other tissues or organs, Dr. Barr adds. "Cancers in the breast tend to be larger on elastography than on (gray scale) ultrasound. On strain elastography, benign lesions appear smaller." With strain, he uses the ratio of how large it is in B mode and elastography to determine if the lesion is negative or positive. With shear wave, he is using the speed of the wave to determine if the lesion is negative or positive. If

the results are the same, then it increases his confidence in the results.

Additionally, many cancerous lesions in the breast are very hard, Dr. Barr explains. Instead of the shear wave propagating through the tumor, it tends to bounce back, resulting in a ring around the tumor. Even with these known limitations, Dr. Barr believes that with continued improvements in shear wave elastography, such as reducing the time needed for the exam and increasing the field of view, it may be possible in the near future to utilize it for breast cancer screening.

Other emerging uses

"There are many other opportunities for ultrasound elastography with other organs," Dr. Barr says, with the prostate being one key example.

In the prostate, Dr. Barr is comparing ultrasound elastography to MR elastography. He's also fusing the MR images with the shear wave ultrasound elastography to help guide biopsies. "In our early work, we are picking up significant prostate cancer in the peripheral zone where most cancers occur using ultrasound elastography. MR is still better in the transitional zone and anterior gland. We've also found that the stiffer areas correlate to a higher Gleason score. Shear wave elastography will have an important role in prostate cancer, and we're finding it's helpful when working with urologists," he explains.

As with breast lesions, Dr. Barr predicts shear wave ultrasound elastography may be able to help reduce unnecessary biopsies. "We are not there yet, but have found in our initial studies that if the elastogram shows normal stiffness then we may not need to biopsy." It could also be a tool for urologists to follow patients with low-grade prostate cancer and help them determine when to start treatment, as the stiffness value also correlates with the cancer aggressiveness, Dr. Barr adds.

Another area that gets Dr. Barr very excited about the potential for using shear wave elastography is in MSK imaging. Dr. Barr is imaging partial tears in tendons and monitoring the healing process. "It can be helpful working with physical therapists to help them tailor the treatment based on the elastography findings.

Kidney transplants would be another key area to utilize shear wave ultrasound elastography, adds Dr. Tchelepi. These patients also receive numerous biopsies, however, there are still technological limitations in the depth that shear waves can be captured and measured. Manufacturers will need to address this for effective use in kidney imaging.

In the neck, thyroid nodules or indeterminate lymph nodes are another area where early studies show ultrasound elastography can be helpful, says Dr. Podrasky. She also sees potential application for evaluating uterine fibroids. "The liver is a great springboard where it has done very well showing proof of concept, so over the next two years we'll be seeing other areas where elastography will become more useful."

Examining the spleen, particularly in children with portal hypertension, would be another excellent clinical use for shear wave elastography, says Dr. O'Hara, adding that its use in other organs and disease processes will only continue to grow, considering the technology is still in its early stages much like Doppler ultrasound was 30 years ago.

"Elastography provides one more characteristic of tissue—how stiff it is—that will help us further differentiate disease," Dr. O'Hara adds.

Lack of reimbursement

There is one key issue that needs to be addressed: the lack of reimbursement for shear wave and strain ultrasound elastography. In the US, hepatologists and gastrointestinal clinicians have a reimbursement code for transient elastography, yet thus far none exists for ultrasound elastography.

"Radiologists' confidence in image-based ultrasound elastography is increasing," says Dr. Podrasky. "We're getting good results on different patients and imaging in the right place as opposed to blind sampling with transient elastography."

Dr. Tchelepi adds that studies are showing a distinct clinical and economic benefit: avoiding unnecessary invasive biopsies reduces associated costs and complications. As more data is published, he's confident the evidence will drive future reimbursement.

References

1. Barr RG, Ferraioli G, Palmeri ML. Elastography Assessment of Liver Fibrosis: Society of Radiologists in Ultrasound Consensus Conference Statement. *Radiology*. 2015;276(3):845-861.
2. Goddi A, Bonardi M, Alessi S. Breast elastography: A literature review. *J Ultrasound*. 2012 Sep; 15(3): 192–198.