

New Insight Into Breast Disease

Study uses information from ultrasound signals to differentiate cancerous from noncancerous breast lesions.

By Amy Cook

When it comes to fighting breast cancer, most women realize the importance of early detection. Whether women are in a high-risk category and have a strong family history of the disease, or little to no risk of developing the disease, awareness is uncommonly high throughout the United States, Europe, Australia, and Asia. This is primarily due to the enormous amount of research and published studies that have appeared since the early 1980s. Celebrities with breast cancer have helped to create awareness as well, and global outreach organizations can be thanked for the ever-increasing education about this disease.

Scientists and researchers are continuously trying to find better ways to identify and cure breast cancer. The established annual screening mammogram can help detect breast cancers early, when they are most treatable, and recent research confirms that regular screening mammograms help save lives. But for women younger than 40 and for those who have a higher risk of breast cancer, such as a known genetic abnormality (a mutation in the BRCA1 or BRCA2 gene), mammograms are not as effective in detecting the disease. This is because cancers are harder to see on mammograms of younger women than on those of older ones. Younger

women also have thicker breast tissue, which may look as dense as cancer tissue on a mammogram. As a result, doctors will recommend ultrasound for women at high risk, starting at age 30.

Density of Breasts Determines Imaging Method

Dense breasts contain more glandular tissue, and breast cancer is also made up of dense tissue. Oftentimes both cancer and normal breast glandular tissue appear dense on a mammogram, making it difficult to find a cancer in the midst of normal glandular tissue. Researchers are studying other screening methods, such as magnetic resonance imaging (MRI) and ultrasound, to see if they offer better screening results for women at high risk for breast cancer with dense breasts.

Researchers are also looking for advanced techniques that more specifically identify breast cancer or tumor development in its earliest stages. Techniques using ultrasound are of great interest because they are safe and inexpensive. Unfortunately, images are not sufficient to develop many new techniques and investigators require radio frequency (RF) signals that are normally buried deep in the instrument and are generally inaccessible without help from the manufacturer. To make

these signals more routinely available to researchers, the National Cancer Institute (NCI) developed a special grant program to encourage the industrial and academic communities to work together. Siemens Medical Solutions applied for funding and was awarded a two-year contract to build an interface that would facilitate research development on commercial ultrasound systems and, as a result, speed translation of the most promising approaches to clinical trials.

The result is a new, innovative research technology available on the SONOLINE Antares™ ultrasound system, which provides great potential for breakthroughs in cancer research. Using the Axis™ direct ultrasound research interface (URI), biomedical engineers and physicists can now develop new research protocols and explore ultrasound characterization of specific diseases in collaboration with a broader clinical research community. Michael F. Insana, Ph.D., professor of bio-engineering at the University of Illinois at Urbana-Champaign and an investigator on the NCI project, has been working with Siemens for the past five years in cancer and vascular imaging research. He is currently using the Axis URI to improve breast cancer detection.

Ultrasound Elasticity Imaging of the Breast

“Our research objective is to develop new forms of diagnostic imaging such as ultrasonic elastography for the detection of breast disease,” says Insana. “Now, with the URI and the SONOLINE Antares system, we can accelerate development and testing of new ideas on patient populations in a safe manner. Hopefully these new tools will speed up the translation of laboratory research into clinical practice.”

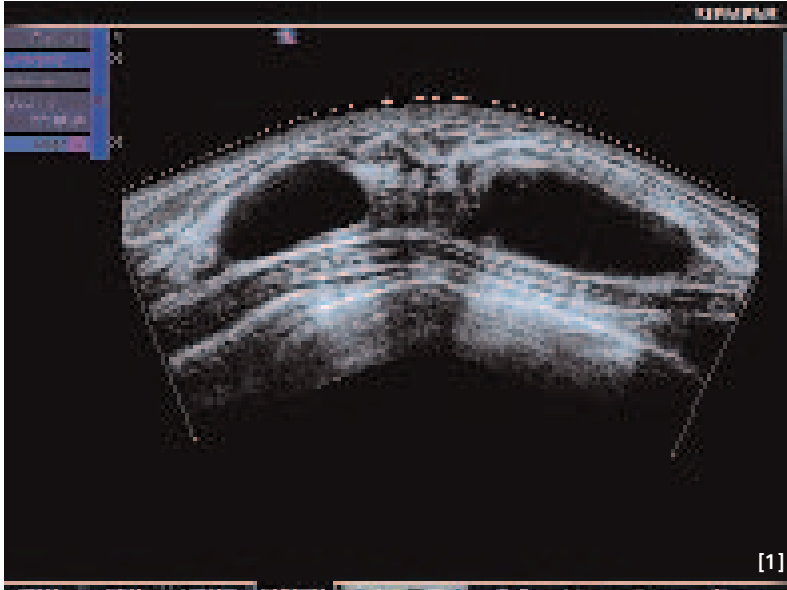
Manual palpation (breast self-exam) has long been the first line of defense in the fight against breast cancer. To improve the ability to detect small, early tumors in the breast and to increase sensitivity in deep tissues, especially near the chest wall in the breast, it is necessary to use ultrasound signals to image deformation, specifically strain, in a



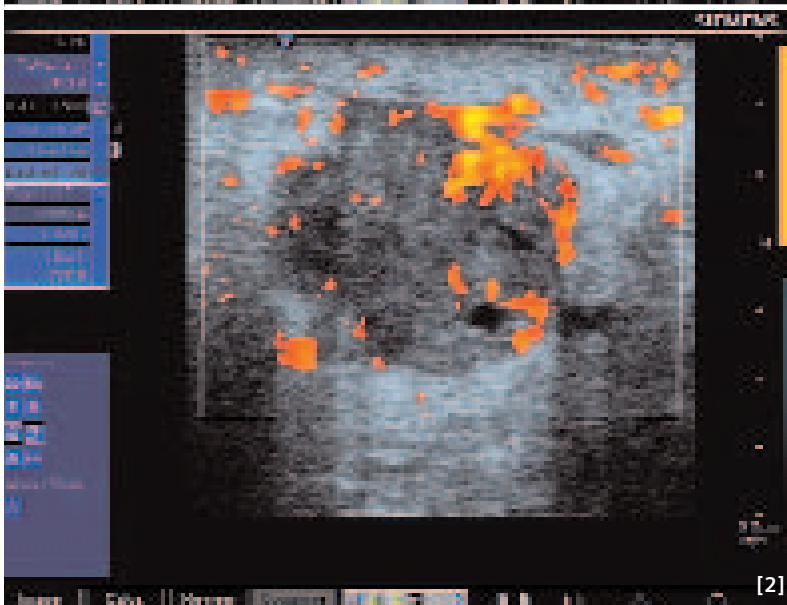
MICHAEL F. INSANA, PH.D., has been working with Siemens for the past five years and is currently using the Axis URI on the SONOLINE Antares system.

manner that describes stiffness variations. Although the scanning procedures are very similar, the information provided by strain images is different from that of routine breast ultrasound imaging.

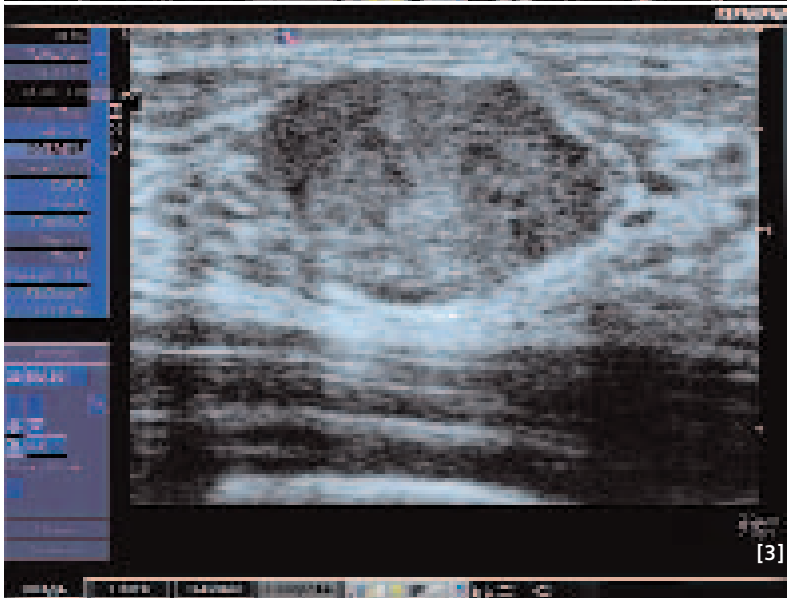
This is how it works: a breast is scanned with ultrasound and the RF echo signals are recorded. The tissue is slightly compressed and the breast is scanned a second time. Signal processing techniques are then applied to image the deformation patterns in the breast as a result of compression. Stiff regions, that indicate cancer, strain very little, so they appear as dark regions in the elastogram. Ultrasonic elastography enables physicians to view the internal structure and tissue stiffness, and thereby detect abnormalities



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[2]



[3]

SONOLINE ANTARES IMAGES:

- [1] SieScape™ panoramic imaging of large breast cysts.
- [2] Large solid breast mass with use of Power Doppler.
- [3] Large breast cyst.

by providing new diagnostic information not available with other diagnostic tests. At the same time, it retains the advantages of conventional ultrasound because it is safe, inexpensive, and noninvasive.

The mechanical properties of breast tissues have shown that benign lesions are measurably softer than many cancers. Elasticity images formed with the new algorithms show that significant contrast can be obtained for early detection of lesions as small as five millimeters. Benefits of this new protocol for breast disease studies could be a reduction in the number of patients with false-positive mammograms that are sent to biopsy and surgery. As a result, this could significantly reduce overall costs of disease management and reduce unnecessary anxiety suffered by patients.

Difference Between Disease and Healthy Tissues

“The most significant feature of the system and the research interface is the high quality of echo data available for analysis,” says Insana. The object contrast for mammography, MRI, and ultrasound is typically between one and 100 percent, yet the contrast for elasticity imaging is often 1 000 to 5 000 percent. With Axis URI, the high contrast is fully exploited without sacrificing sensitivity or spatial resolution while imaging; therefore, the difference between malignant and benign tumors can be more easily recognized.

“The fact that we know the molecular pathways for tumor development, and how those changes affect tissue stiffness, means we can now exploit these new diagnostic opportunities because we have the high-quality echo data for research,” says Insana.

As a result, he and his colleagues recently published a study in *J Mammary Gland Biology and Neoplasia*, reporting on their initial studies in breast patients. Insana and his team developed freehand scanning methods that were effective for human imaging, which allowed them to find the best scanning geometry. For example, the same examination position as the one used for a standard breast exam was found to give optimal access to most breast

locations and was more comfortable for women in general.

The study is continuing at the University of California at Davis Medical Center, where Insana and colleagues are collaborating with Dr. Karen Lindfors, chief of the breast clinic, to examine patients with suspicious breast lesions. They hope to verify the ability of elastography to detect stiff lesions and differentiate between benign and malignant tumors. The target population is patients with focal breast lesions that are mammographically visible and are suspicious enough to warrant core biopsy. Each woman must already have a core biopsy scheduled with her radiologist, and there are no ethnic criteria for participation.

Siemens' SONOLINE Antares systems are being used in the study. The systems contain the additional software that allows researchers to record echo signals unavailable to other users. The output power and gain settings are identical to those of clinical breast exams, which are at or below the FDA guidelines for breast imaging. Once the exam is under way, the entire process for research only takes a few minutes, so very little time is added to the patient's regularly scheduled exam.

Less Pressure for the Breast

Women participating in the study come in for their exam and a technologist or radiologist scans them to locate the breast lesion. At this point, students in Insana's lab record the RF signals from the immediate area being scanned. The ultrasound technician then manually applies a small compressive force to the breast, which can be released instantly if the patient experiences pain, and the region is rescanned. However, the total applied force on the breast is much less than that used during a typical X-ray mammogram.

Comparisons of the mammogram, sonogram, elastogram, and the biopsy findings allow researchers to verify the ability of their technique to detect stiff lesions and differentiate between cancer and noncancer.

The benefit, says Insana, is a reduction in the number of patients with false-positive mammograms who are sent to biopsy and surgery.

Because the mechanical properties of breast tissues have shown that benign lesions are considerably softer than many cancers, this new look at breast tissue could prove to be one more way of identifying this disease even earlier in the process – possibly before it develops at all.

And the fact that this new ultrasound research interface allows scientists to obtain the information they need during regularly scheduled exams means there is a very positive impact on workflow and efficiency. "In the past we would have had to rearrange the ultrasound system or take it apart completely to acquire the appropriate research data," says Insana. "Now that laborious step is removed from the research timetable."

Insana and his research team contributed to the Axius ultrasound research interface development by writing software that helps researchers read the radio frequency data acquired from the system and form simple images. This software is freely available to the worldwide medical community through the URI users' group website:

<http://www.bme.ucdavis.edu/URI/>.

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Michael F. Insana, Ph.D.,
Department of Bioengineering,
University of Illinois, IL

Official Recommendations

For all women 40 and over, an annual mammogram has become a standard recommendation in the United States, and is highly recommended in many countries worldwide. For women under 40 and considered at high risk, an ultrasound may be recommended for women in their late 20s to early 30s. The earlier breast cancer is found and diagnosed, the better the chances of treating the disease effectively.

Author: Amy Cook is a freelance writer and frequent contributor to *Medical Solutions*.