

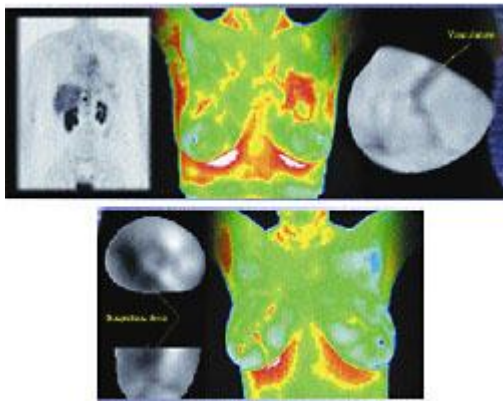
Issue Stories

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Technology Trends: The Booming Breast Imaging Market

by Lisa Fratt

Radiologists maintain that mammography is the gold standard for breast cancer detection. At the same time, they also say that the technology can be riddled with holes and does not serve young women or women with dense breasts very well.



Clinical Images from left: Coronal PET FDG image from Princeton Radiology, positive thermogram from Clinical Thermography, CT laser mammography image from Imaging Diagnostic Systems, Coronal PET FDG image from Princeton Radiology, CT laser mammography image from Imaging Diagnostic Systems, normal negative thermogram from Clinical Thermography.

Despite all the criticism and controversy surrounding mammography, most radiologists maintain that it is the gold standard for breast cancer detection. At the same time, most radiologists acknowledge that this gold standard is so riddled with holes that it looks more like Swiss cheese than a gold standard. The statistics are as familiar as they are alarming.



Systems from left: University of California Davis is working on a breast CT system, Aurora Imaging Technology's Aurora MRI system

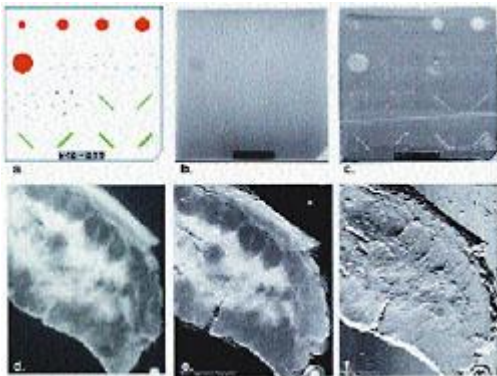
For starters, mammography does not serve young women or women with dense breasts very well. Eric Milne, M.D., professor of radiology at the University of California Irvine and chief radiologist for Imaging Diagnostic Systems Inc. (Plantation, Fla.; the maker of the CT Laser Mammography System), points out, "Thirty to 40 percent of women have very dense breasts, and the sensitivity of mammography for dense breasts is around 40 percent." That's not exactly a rate to write home about.

Another problem is mammography's design. It is designed to see minute flecks of calcium, and a large percentage of positive mammograms are actually microcalcifications. Still many of these patients must proceed to biopsy. Yet only 20 out of every 100 biopsies performed because of a suspicious mammogram are discovered to be cancerous.

Then there are the cancers missed by mammography — 10 to 15 percent of breast cancers occur in spite of a normal mammogram. Other issues include concerns about radiation exposure and the pain associated with breast compression.

Add the demographic realities of an aging population and the corollary increase in breast disease to the picture, and the need for supplemental early-stage detection technologies and post-diagnosis imaging improvements becomes even more apparent. In fact, Medtech Insight's (Newport Beach, Calif.) "U.S. Markets for Breast Disease Detection and Diagnostic Technologies" report projects that the market for early-stage breast disease detection technologies will reach nearly \$130 million over the next decade.

A host of companies have responded to the call and are developing new early detection and breast imaging technologies. The intent with each device is similar: plug one or more of the holes associated with mammography. Some technologies aim for earlier detection of breast cancer; others are designed to better differentiate benign and malignant lesions; and some may better identify the extent of breast cancer, which helps physicians better devise a treatment plan. Many of the new technologies also are more patient-friendly than mammography.



Examples of DEI applied to mammography. Figure a: schematic layout of the American College of Radiology (ACR) quality assurance test object for mammography with embedded tumor, calcification and spicule simulations of various size and thickness. Figure b: a radiograph of the ACR test object. Figure c: a DEI image both taken at 18keV. Figures d, e, and f are of a mastectomy tissue sample. (Courtesy of Illinois Institute of Technology.)

Kinder, gentler breast MRI

Like many of his colleagues, Mark Novick, M.D., radiologist and medical director for Manhattan East Breast Imaging (New York City), is sold on breast MRI. "MRI is very, very important to the breast imaging spectrum. It fills in many of the blanks and gaps left by mammography and mammography and ultrasound." Yet, breast MRI does pose a few issues. Most scanners are designed for general use, and breast patients are forced to accommodate the imaging requirements for body MR scanners. Many breast MR patients are repeat customers, and often, even those without claustrophobia develop symptoms because of the tunnel effect encountered during an MRI scan.

Enter Aurora Imaging Technology's (North Andover, Mass.) Aurora Breast MRI system, the only FDA-approved MR scanner designed for and devoted to breast imaging. With Aurora, the patient enters the scanner feet first on her belly with her shoulders, arms and head at the edge of the magnet. The technologist remains in the room during the scan. All of these features enhance patient comfort and reduce claustrophobia. Novick believes the result is a higher quality scan with fewer motion artifacts and less misregistration.

The primary breast MRI patient pool consists of women diagnosed with breast cancer. An Aurora MRI scan can better determine the extent of the cancer and help physicians devise the best treatment plan. The scan may detect additional unsuspected pathology and change treatment protocol. Preliminary unpublished data from the Faulkner-Sagoff Breast Imaging and Diagnostic Center (Boston) show that up to 30 percent of planned lumpectomies should actually be mastectomies based upon results from the Aurora scanner.

Other candidates for breast MRI include women with especially dense breast tissue, those with high risk factors including a family history or previous breast cancer and those with lumpectomy scarring. Breast MRI may be especially effective for these women; it may find smaller cancers at earlier stages. In a recent German study of 100 patients, breast MRI scans found nine 1 cm or smaller cancers not found by mammography or ultrasound.

Breast PET gains acceptance

In many instances, it is not the development of a new technology but rather changes in reimbursement that spur clinical acceptance and use. Breast PET seems to follow this paradigm. Since the Centers for Medicare and Medicaid Services (CMS of Washington D.C.) approved reimbursement for breast PET in 2002, radiologists have expanded its use. Medicare does not pay for global coverage for breast patients; however, PET scans are reimbursable when used to stage patients with distant metastasis, restage local/regional reoccurrences or metastasis and monitor tumor response to treatment with locally advanced and metastatic breast cancer.

The change has increased the breast PET patient load, but not significantly. Still, breast PET can have a dramatic impact on treatment for some patients. John Ghazi, M.D., staff radiologist at Princeton Radiology Associates and the Medical Center at Princeton (Princeton, N.J), explains, "Thankfully, because of mammography, most patients do not have advanced disease [and are not candidates for breast PET]. Only about 10 percent of breast cancer patients fall into these indicators. But in that group, close to 50 percent have a change in management after the PET scan."

Ghazi believes PET will play an increased role in breast disease diagnosis in the future. He opines, "It would not surprise me if the next indication CMS approves reimbursement for would be the evaluation of breast masses before biopsy." PET also is becoming more cost-effective, and is nearly as cost-effective as MRI, says Ghazi.

Thermography goes mainstream

Thermography may be the oldest kid on the block of mammography complements. The FDA first approved thermography in 1982, and several companies have new scanners in the FDA pipeline. Still, many surgeons and radiologists remain a bit skeptical about thermography in diagnosing breast cancer.

The basics of thermography are fairly simple. During the scan, an infrared camera records thermal images of the breast that can be used to detect the physiologic changes that characterize breast cancer — angiogenesis and neovascularity. During the process of tumor formation, the tumor creates its own blood supply; blood vessels dilate and additional capillaries develop. A lesion becomes clinically significant when it begins to recruit its own blood supply. Thermography can identify the abnormal thermal patterns associated with malignancies and other breast pathologies. Abnormal scans are referred to physicians for clinical correlation.

Thermography can be used as a screening adjunct to mammography. Lynn Marshall, R.N., B.S.N., and co-owner of Clinical Thermography of Colorado (Denver) reports, "By itself, thermography is 86 to 90 percent effective in screening for breast cancer. Studies show that the combination of thermography and mammography can raise the rate to 98 percent. It is believed that infrared cameras can detect lesions as small as 2 to 3 mms."

Clinical Thermography of Colorado opened its doors in July 2002 and uses Meditherm's (Lake Oswego, Ore.) Digital Infrared Thermal Imaging system. Scans are non-invasive and complete in 15 minutes; physicians trained to read thermograms read the scans offsite. Marshall notes, "Physician acceptance has been higher than I anticipated." In fact, some local physicians are referring patients for thermography. One surgeon recognized the value of thermography after a patient elected a double mastectomy based on her thermogram, which revealed abnormal patterns in both breasts. After the surgery, the surgeon found that the patient's thermogram matched the pathology report. A number of patients are women who have had mastectomies and need to monitor remaining breast tissue, but don't want to be compressed during a mammogram. Other patients have cancer and want to monitor their condition.

Insurers are slowly coming on board as well, and some are reimbursing women for their scans. Marshall concludes, "Thermography is not the 'be all' in breast imaging, but it should be in the arsenal."

Angiogenesis and CT

Thermography may be the first imaging technology to evaluate angiogenesis, but that club is growing. Imaging Diagnostic Systems hopes its CT Laser Mammography (CTLM) system will receive FDA approval within the next year or two. Milne explains, "Our technology looks only at blood in the breast. In fact, you could say it's molecular imaging because it measures molecules of hemoglobin." CTLM does not image lesions, it images the neovascularity associated with them. If the scanner does not pick up any neovascularity, the diagnosis is benign. When CTLM does image neovascularity, the diagnosis is malignant.

CTLM addresses many concerns associated with mammography. The methodology is virtually identical to x-ray CT except the x-ray tube is replaced with a laser, so there is no radiation exposure. The patient's breasts don't need to be compressed, and breast density has no effect on the quality of a scan because the laser shoots through dense tissue like light through a goldfish bowl. Early results are promising. Milne reports, "In 500 cases, we've improved the specificity of mammography from approximately 40 percent to 75 percent."

Pipeline technologies

Although a number of new breast imaging systems are poised for FDA approval, researchers continue to explore a variety of new breast imaging techniques. John M. Boone, Ph.D., professor of radiology and biomedical engineering at the University of California Davis, and Thomas R. Nelson, Ph.D., professor of radiology at the University of California San Diego, have built a breast CT prototype. Boone opines, "Dedicated breast CT may be more than a mammography adjunct. We think it has the potential to work in a screening role itself."

The benefit of CT is its superior soft tissue contrast. Breast CT essentially eliminates the overlying and underlying anatomy of the breast, which could more clearly indicate the presence of a lesion. Instead of looking for a needle in a haystack, the radiologist would examine the haystack one strand at a time. While the approximately 150 breast CT images are obviously more than two x-ray mammograms, breast CT easily lends itself to soft-copy reading and reading in a stack mode. And although radiologists would need to be retrained, the potential benefits outweigh the costs.

Boone says, "According to theoretical calculations, breast CT may be able to detect 3 to 5 mm lesions. If this is the case, computer models show a 15-year survival rate on the order of 95 to 97 percent versus the current 15-year survival rate of 86 percent."

Boone and Nelson have secured funding to build two breast CT prototypes and complete a phase 2 trial. Clinical testing is slated to begin in the spring of 2004, and breast CT could earn FDA approval in three to five years.

Another potential replacement for mammography is diffraction enhanced x-ray imaging (DEI). DEI could detect malignancies earlier than mammography with significantly less radiation. How does it work? The method relies on new sources of x-ray contrast and generates two to four new images. One of these, the refraction image evaluates the density variation, which would allow radiologists to see the edges of breast cancer as cancer is denser than normal tissue. Contrast of the fibrils associated with cancer also is improved with DEI based on the scattering of these fibrous tissues observed in a scatter image, also an new image.

The technology also alleviates some of the common concerns associated with mammography-namely radiation dosage and breast compression. Because DEI does not rely solely on absorption images, radiation exposure can be decreased by a factor of 20 at higher x-ray energies where tissue becomes more transparent. At these energies, the compression to minimize the x-ray thickness is reduced as well.

Dean Chapman, Ph.D, associate professor of physics at Illinois Institute of Technology (Chicago), said DEI is "very, very good for soft tissue imaging. While there are very small absorption differences in [cancerous tissue], these differences occur, because cancer is a denser tissue which DEI measures directly with higher sensitivity than absorption imaging."

Researchers predict that DEI could be three to five years from clinical use, depending on the levels of funding.

Improving on ultrasound

Ultrasound's ability to image breast cancer is well documented. In fact, a new study indicates that sonography is more accurate than mammography for detecting breast cancer in symptomatic women 45 years old and younger. Australian researchers found that ultrasound correctly identified 85 percent of breast cancers in symptomatic women 45 years old and younger, whereas mammography correctly identified 72 percent of breast cancers in this group. Still, there are pitfalls associated with breast ultrasound. Robert Bell, M.D., director of women's diagnostics at St. Mark's Hospital in Salt Lake City, says, "There are all kinds of possibilities that could go wrong with breast ultrasound. For example, what if you look at the wrong spot?" And an ultrasound is only as good as the technologist holding the transducer.

Current handheld ultrasound systems are designed to look for a particular abnormality. Yet, TechniScan Inc. (Salt Lake City) has developed a new computerized ultrasound system that scans the entire breast and evaluates the speed and absorption of sound, transmission and reflectivity. Bell explains, "Research indicates that you can look at the absorption and speed of sound to determine malignancy".



Right now, very early research with the TechniScan system is confirming this hypothesis. Of the less than 20 patients examined with the system, cancers fall into the high speed of sound and high absorption range of the graph, and benign lesions have had lower speed of sound and absorption values and wind up in a different part of the graph. This could potentially allow women with suspicious lesions who fall into the low probability portion of the graph to avoid biopsy. Bell admits, "It's far too early to tell if these results will be universal."

In younger women and women with dense breasts, given mammography's shortfalls for this group. And for women with a family history of breast cancer, the scan is harmless and inexpensive. TechniScan is working on a second prototype system, and the technology is probably three to six years from clinical use.

Evaluating new technology

The FDA does have ultimate approval for new breast imaging options, but even FDA approved technologies may not be appropriate for every practice. Novick says, "One question to ask with each of these emerging technologies is how well does it lend itself to breast localization and biopsy."

Another issue to consider, include reimbursement. Is the technique reimbursable? Novick recommends the fee-for-service route. The practice is essentially out of the reimbursement loop. And while payors may stiff physicians time and time again, they are unlikely to maintain a solid, satisfied customer base if they gain a reputation for putting off patients.