Breast screening tools step it up

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The current method of breast screening involves stair stepping from full-field digital mammography (FFDM) to ultrasound (US) to breast tomosynthesis (3-dimensional digital mammography) or breast MRI. Although, FFDM is a proven and cost-efficient method for breast cancer screening, it has its limitations, particularly in women with dense breast tissue.

Recently, improvements in cancer detection using ultrasound and tomosynthesis are prompting radiologists to rethink their protocol to deliver the most effective breast-cancer screening program.

The breast-density breakdown

Several states have adopted laws requiring referring physicians to notify patients when the interpreting radiologist determines that their pattern of fibroglandular tissue is considered dense. This notification may lead to an adjunct-imaging exam. Many sites are determining follow-up exams by categorizing patients by risk and breast density.

Radiologists at Magee Women's Hospital, the University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA, have categorized patients with dense breasts and recommend tests as follows:

- *Normal risk patients*: mammogram or mammogram and tomosynthesis for fatty and scattered fibroglandular tissue starting at 40.
- *Heterogeneously dense breasts*: mammogram and tomosynthesis.
- *Extremely dense tissue in normal risk women*: mammogram and screening ultrasound.
- *Intermediate risk women, women with <20% lifetime risk for developing breast cancer, for fatty and scattered fibroglandular tissue*: mammogram or mammogram plus tomosynthesis.
- *High risk, ie, women with >20% lifetime risk, regardless of the density category*: mammogram and tomosynthesis and MRI at least until the age of 70.

"There are several risk models, which calculate risk based on factors, such as family history, personal history of relatives, personal history of breast cancer, genetic testing, and prior high-risk histology identified from a prior breast biopsy. It also may be helpful in those extremely high-risk women, with heterogeneous and extremely dense breast tissue to consider ultrasound, although MRI is currently the gold standard for them," explained Jules Sumkin, MD, Professor and Chief of Radiology, Magee Women's Hospital UPMC, Pittsburgh, PA.

Lowering the dose on digital mammography

Although FFDM remains the gold standard in screening for breast cancer, helping reduce deaths from breast cancer among women ages 40 to 70, screening mammograms miss about 20% of breast cancers present at screening.[1] The main cause of these false-negative results in screening mammography is high breast density,[3] which is usually collectively referred to as fibroglandular tissue.[2] A phenomenon known as masking, in which the surrounding dense breast tissue obscures a cancer, may occur during mammography.

Recent advances in FFDM technology may help the technique keep its gold-standard status, and one of the biggest improvements in the technology is the reduction in radiation dose without reducing image quality.

In that vein, Siemens Healthcare (Malvern, PA) has released the MAMMOMAT Inspiration PRIME Edition (Figure 1), which uses 30% less dose. The new upgrade uses PRIME (Progressive Reconstruction Intelligently Minimizing Exposure) technology, a software-based antiscatter solution for mammography, allowing a significant reduction in radiation dose and without compromising image quality, according to the manufacturer.

The PINK Breast Center in Flemington and Paterson, NJ, both Breast Centers of Excellence, have worked with the Siemens Mammomat Inspiration for over a year, and on the Mammomat Inspiration PRIME Edition since December at the Paterson location. Lisa Sheppard, MD, is one of the head radiologists at PINK Breast Center in Paterson, where they conduct 12,000 mammograms annually. She has seen a significant difference in the patient radiation dose on the Inspiration and even lower dose on the PRIME Edition with superior image quality. "I am seeing sometimes up to 75% less radiation dose with a sharper, clearer image," said Dr. Sheppard. "It also uses less compression and faster exposure times, resulting in increased patient throughput."

She added, "There are less artifacts from breathing, there are less repeats,

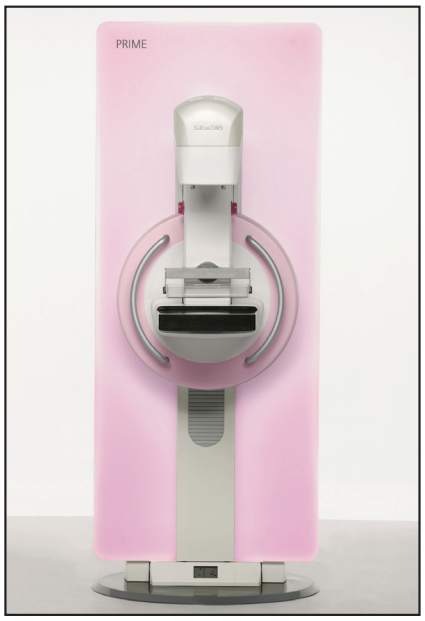

FIGURE 1. *The MAMMOMAT Inspiration PRIME Edition lowers patient radiation dose up to 30% without compromising image quality, replacing the standard scatter radiation grid with a new algorithm for progressive image reconstruction.*

and the turnaround time and patient throughput is faster. [Compared to the previous system that we were using] the images on the Siemens system look crisper, and from a cost standpoint, it is comparable. Plus, there is one-third lower dose."

Addressing the challenges of dose and improved detection in women with dense breast tissue, Philips Healthcare (Amsterdam, The Netherlands) recently released its FDA 510(k)-cleared MicroDose SI, a FFDM system engineered with digital photon-counting technology, called Single-Shot Spectral Imaging. With photon counting technology, the individual x-ray photon is counted by a 50-micrometer detector element, the smallest in the industry (as much as 4 times smaller). "The 50-micron resolution provides incredible diagnostic-quality images," said Raymond Tu, MD, Chairman, Department of Radiology, United Medical Center, Washington, DC; Partner at Progressive Radiology, Falls Church, VA; and Clinical Associate Professor of Radiology, The George Washington University School of Medicine and Health Sciences, Washington, DC.[3]

The single-layer detector counts individual photons, creating very low noise during the digital-to-digital data collection, and eliminating the analog-to-digital conversion used by other systems. During the image acquisition, by using a multi-slit pre-collimator and a matching multi-slit post-collimator, only those x-rays perfectly aligned with the detector are allowed to pass through the breast. All other x-rays are blocked, as that radiation would only increase patient dose without contributing to image quality; therefore, scatter radiation, which adds to patient dose and degrades image quality, is minimized.[3] Ultimately, the system uses low-radiation dose without compromising image quality. Although the actual result of the average dose reduction will vary based on variations in digital mammography systems, the average dose reduction is 40%, according to the company. Exam times can reportedly run under 5 minutes, including image acquisition. In addition, the system is ready for future single-shot spectral imaging applications, such as Spectral Breast Density Measurement, which measures the amount of fibroglandular tissue over the whole breast to objectively determine a volumetric density measurement.

Another new tool designed to assist the digital mammography screening process, particularly in the detection of dense breast tissue, is VolparaDensity breast imaging software by Matakina Technology (Wellington, New Zealand). This tool also supports radiologists in assessing breast density more objectively so that they can determine who might benefit from additional screening. VolparaDensity generates an objective, automatic measurement of volumetric breast density and an FDA cleared BI-RADS breast density category. The software is displayed on digital mammography and PACS workstations. "This automated, volumetric density measurement tool helps ensure that the proper women are being evaluated in a proper, consistent manner," said Jean Weigert, MD, FACR, director of Breast Imaging at The Hospital of Central Connecticut (HOCC), where VolparaDensity is integrated into HOCC's Fuji Synapse PACS.

At ProMedica Toledo Hospital, Toledo, OH, Robin B. Shermis, MD, Diagnostic Radiologist, and his staff use VolaparaDensity on every patient to obtain an objective assessment of breast density in addition to the subjective view from the radiologist. Together, he says, it's a pretty powerful package.

"There is some evidence to show that for breast tissue density you have a greater risk of having breast cancer, but the real problem is that the dense breast tissue masks underlying cancers. On a woman with a very dense mammogram, her tissue obscures findings we would like to see on a mammogram, but can't. For women with dense breast tissue, we are using VolparaDensity to measure that, and we also measure density subjectively and together — it's a pretty powerful package in terms of isolating women who may benefit from additional screenings," said Dr. Shermis. "The Volpara gives us a quantifiable measure of the breast tissue density. If a woman is very dense, we will formulate additional adjunct screening tests."

The measurement provides greater predictability for screening, although it is often confirming what the radiologists already sees subjectively, indicates Dr. Shermis. "It confirms our own objective view, and gives us scientific justification for going beyond a mammogram," he noted.

Patients receive a letter providing them with a level of their breast tissue density. "If they are high risk and have a dense mammogram, we recommend

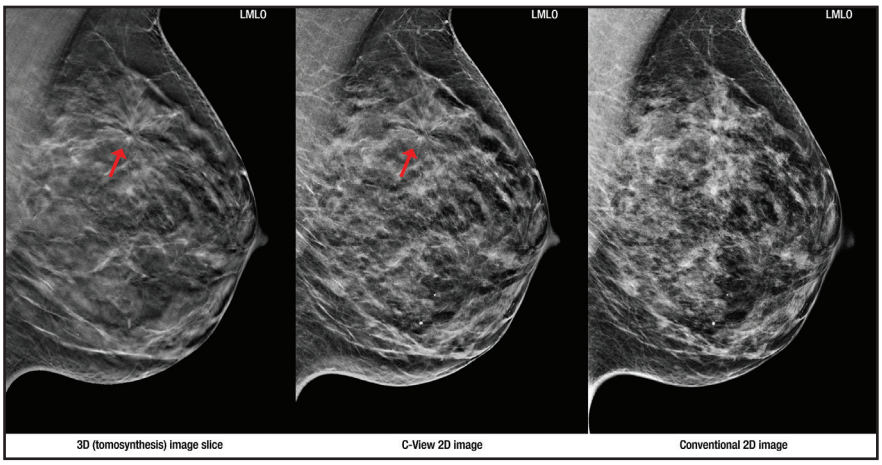

FIGURE 2. *C-View images by Hologic Inc. are generated from the 3D tomosynthesis data acquired during the mammography exam, eliminating the need for additional 2D exposures.*

a breast MRI, and if they are non-high risk patients with dense breast tissue, we recommend molecular breast imaging," said Dr. Shermis.

Taking it a step further, combining VolparaDensity with computer-aided detection (CAD) on the same digital mammography platform supports radiologists in screening with greater accuracy and triaging patients with dense breast tissue. Radiologists at Carolina Breast Imaging (CBI) Specialists, Greenville, NC, use the PowerLook Advanced Mammography Platform (AMP) by iCAD (Nashua, NH), the next generation digital mammography CAD platform that provides radiologists with the ability to customize their CAD solution to meet the needs of their individual work environment. The platform features SecondLook Digital CAD algorithms that analyze mammography images using methodologies that are complementary to the radiologist.

As Bruce F. Schroeder, MD, Diagnostic Radiologist at CBI Specialists explains, CAD today is much smarter and more effective than earlier versions. "With CAD, the algorithms got much smarter, so there are now fewer false positives. What CAD does well is it shows the areas where you should spend your extra analysis. CAD is fairly good at finding very small, bright calcifications," said Dr. Shroeder.

"Both CAD and the VolparaDensity tools are on the platform. Our Volpara output is integrated with our MRS. My report will change based on density assessments as do the breast-density notification letters to the patients. This process is now entirely automated, which is helpful since North Carolina is a recent state to enact the breast density notification bill," said Shroeder.

He added, "Volpara is an objective tool, and you could potentially take note of the breast-density reading and triage the patient immediately. That is a potentially a good workflow."

Digital breast tomosynthesis — growing adoption

Although US is frequently used as an adjunct test with mammography, radiologists today are considering whether breast tomosynthesis will be the primary screening tool, particularly with women with dense breast tissue.

Digital breast tomosynthesis has been found to be superior in performance to standard digital mammography in both screening and diagnostic settings for the early detection and improved diagnosis of breast cancer.[5]

"In dense breast tissue it's not as easy to pick up on 2D mammography because it is white. It is like it hiding a snowflake in the snow," said Harmindar Gill, MD, Medical Director, Premier Women's Radiology, Bonita Springs, FL, who uses Hologic's Selenia Dimensions tomosynthesis system as part of her center's screening protocol.

In the opinion of Margarita L. Zuley, MD, Magee Women's Hospital, Director of Breast Imaging at the University of Pittsburgh Medical Center, Pittsburgh, PA, the issue is that mammography is simply limited for screening dense breast tissue. "The literature shows that tomosynthesis and US both detect more invasive cancers than 2D alone. Facilities have to choose which additional modality will work for them for ancillary screening to mammography in these women. There currently is no head-to-head study showing that one finds more cancers than the other," said Dr. Zuley. "Tomosynthesis, however, does not have the false positive problems of US, and we definitely find cancers by tomosynthesis that you cannot see on mammography or ultrasound."

"Ultimately, if a large controlled multicenter comparison between tomosynthesis and ultrasound is performed, we will most likely find cancers, which are identified with tomosynthesis that are not identified by ultrasound, and there will likely be cancers that we find with ultrasound that are not identified by tomosynthesis. Also, do not forget that there will be false positives that result from both of these tests," said Dr. Sumkin.

Currently, it is required to use tomosynthesis in combination with FFDM, known as the 'combo' method. This is due to the concerns that some abnormalities—in particular, microcalcification clusters—may not be as readily detected or interpreted correctly on the tomosynthesis images as on conventional mammograms[5] and the two-dimensional (2D) portion is important for accurate comparison with prior studies.

There are several benefits to the 'combo method' over the FFDM alone,

including a substantial increase in invasive cancer detection rates in the screening environment and improved accuracy over conventional diagnostic 2D additional views for soft-tissue density lesions in the diagnostic setting.[5] Despite the improvements in accuracy found in using combined tomosynthesis and FFDM, there are drawbacks to tomosynthesis. These are the increased volume of image data, resulting in longer interpretation times, the increased radiation exposure to the patient from the combined 2D and 3D exams, and the lack of reimbursement by many insurance companies.

In a recent study, researchers looked at the interpretation performance and radiation dose when 2D synthesized mammography images versus standard FFDM images are used alone or in combination with digital breast tomosynthesis images. They found that synthesized mammography alone or in combination with tomosynthesis is comparable in performance to FFDM alone or in combination with tomosynthesis and may eliminate the need for FFDM as part of a routine clinical study.[5]

What is certain is that with the increased volumes of data from tomosynthesis studies, radiologists will need tools to streamline their workflow. Recognizing the importance of 3D tomosynthesis to the diagnosis of breast cancer, iCAD is working closely with several of its OEM partners to design and develop a robust CAD solution specifically for tomosynthesis that will optimize workflow for the radiologists by making it easier to detect regions of interest.

Another new tomosynthesis solution is designed to lower radiation dose. A recently FDA-approved solution is Hologic's new C-View 2D imaging software (Figure 2). C-View 2D images may now be used in place of the conventional 2D exposure previously required as part of a Hologic 3D mammography (breast tomosynthesis) screening exam. C-View images are generated from the 3D tomosynthesis data acquired during the mammography exam, eliminating the need for additional 2D exposures. The combination of Hologic's 3D and C-View 2D images results in less time under compression and a lower radiation dose, while still providing the 2D images required as part of Hologic's FDA approved 3D mammography screening exam. Clinical studies have shown that screening with Hologic's 3D mammography technology using C-View imaging results in clinical performance superior to that of a conventional 2D mammogram.

"The whole purpose for C-view is to reduce the radiation dose. Most are doing the combo mode, where you get the radiation from the real 2D exam plus the 3D exposure. With the C-view, you are getting 40% less dose. If you can get the better 3D exam without really increasing does, that's fantastic," said Linda Greer, MD, Medical Director, John C. Lincoln Breast Health and Research Center, Phoenix, AZ.

Radiologists' cancer detection rates have improved significantly with C-View used with tomosynthesis. "My cancer detection rate went up from 5 per thousand to 8 per thousand once I started using tomosynthesis. My colleague's cancer detection rate also went up 100% to about 8 per thousand," said Dr. Greer.

According to Dr. Greer, tomosynthesis should be the primary screening tool. "Many facilities are deciding if they should use tomosynthesis on screening or diagnostic patients. With tomosynthesis we've reduced our recall rate significantly. If you separate out the number of times we call back people for additional mammogram views, my recall rate went down 93%. If I have a real finding on a screening tomosynthesis, then I don't need to do additional spot views, it goes straight to ultrasound, and then we go straight to biopsy. It really expedites things. With tomosynthesis screening, you eliminate the extra mammogram view. If you think there is a something suspicious on a mammogram, but with tomosynthesis you can see clearly that it is normal tissue, you have eliminated that call back altogether. That is the strength with tomosynthesis because if you're only using it for a palpable mass, you already know you're going to do an ultrasound, and you're going to work it up. The strength is screening because you can decrease your callbacks and increase your cancer detection."

But there is not yet a reimbursement code, and, as Dr. Greer explains, insurance companies are not routinely paying for tomosynthesis. "We are billing as a standard digital mammogram, which is unfortunate because the equipment is expensive and storing the data is expensive. That's why tomosynthesis hasn't replaced everything across the board even though it has been shown to be better," she said. "When there is a code for reimbursing tomosynthesis, I think there will more adoption."

The next step

The next step is to conduct head-to-head studies comparing US and breast tomosynthesis for screening accuracy. At that point, Dr. Sumkin pointed out, "The question is how to refine the subset of patients that benefits better from one test over the other — because it's very unlikely we could afford to do both."

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