Less Worry:

New Imaging Approach May Significantly Decrease **Mammography False-Positive Results**

by Mary Jo Blackwood, RN, MPH

For the woman who has a suspicious mammogram, dilemmas abound. When the mammogram identifies a suspicious abnormality but turns out to be benign, it's called a false positive. Of course, she's relieved. She doesn't have cancer. Getting to that diagnosis, however, may have required additional tests and procedures—all of which cost money and time and produce a great deal of anxiety.

Almost 50 percent of women have dense breast tissue; on a mammogram the dense glandular tissue may mask an underlying tumor, making it more difficult for the radiologist to interpret. Undetected abnormalities, although occurring at a low rate, can falsely reassure a paitent.

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According to one study published in the *New England Journal of Medicine*, approximately one in four women will have a false-positive screening mammogram over a 10-year period. An abnormal screening mammogram then requires a diagnostic imaging workup, which may include additional tailored mammographic views and/or ultrasound. Some women may also undergo breast biopsy. Researchers want to reduce the number of false-positive screening mammograms while maintaining high sensitivity for detecting a malignancy.

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A pilot study currently underway at Mallinckrodt Institute of Radiology (MIR) at Washington University School of Medicine is looking at the use of three-dimensional synthesized digital mammography—called tomosynthesis—to reduce the number of false-positive results and to point clinicians in the right direction for identifying cardinal features of malignant masses.

Dione Farria, MD, MPH, associate professor of radiology, is a specialist in breast imaging and the principal investigator in this study. "Our objective is to compare the results from conventional digital mammography to the results from three-dimensional tomosynthesis in reducing the numbers for patient recall for diagnostic workup of breast masses.

"Although conventional mammography can reduce breast cancer mortality by detecting the cancer in its earliest, most treatable stage, the technology has limitations, such as trying to acquire two-dimensional data from a three-dimensional object—the breast. As a result, there is superimposition of normal breast structures in the path of the X-ray beam, leading to a false-positive result. If a cancer is obscured, the superimposition of normal structures over an abnormality can lead to a false-negative result," says Farria.

Most breast masses recalled from a screening mammogram are classified as benign after a diagnostic workup. By providing additional data to the radiologist regarding the features of the mass, tomosynthesis may be helpful in classifying more of these masses as benign at the time of the screening mammogram.

Dr. Dione Farria, with a full-field digital mammography unit housed in the Joanne Knight Breast Health Center in the Center for Advanced Medicine

How 3-D tomosynthesis works

In conventional 2-D digital mammography, two screening images of the breast are acquired: one from above (craniocaudal view), one from the side (mediolateral oblique view). Tomosynthesis provides multiple images. Therefore, rather than two images, a series of 15 images are taken as the X-ray source moves in an arc above the patient's breast. Each image uses about one-fifteenth of the radiation dose of a conventional mammogram.

The imaging data is fed into a computer fitted with software that synthesizes it into 15 slices, allowing a more complete view of certain areas.

The tomosynthesis images are reconstructed using mathematical algorithms (similar to computed tomography reconstructions) to generate a set of 3-D, thinly-sliced images, which can be viewed individually as multiple images from the same breast or sequentially in a movie format that scrolls through the different planes of the breast, allowing for greater visibility of objects and lesion margins. Relative to conventional mammography, the tomosynthesis slices provide improved visibility within the cross section of breast tissue, while reducing the contrast and visibility of tissues in overlying planes.

MIR's pilot study

Phase I

This phase, which is already completed, included 12 healthy volunteers. By imaging healthy volunteers, the study investigators optimized image quality and reduced technical problems for Phase II of the study as well as for any future clinical studies.

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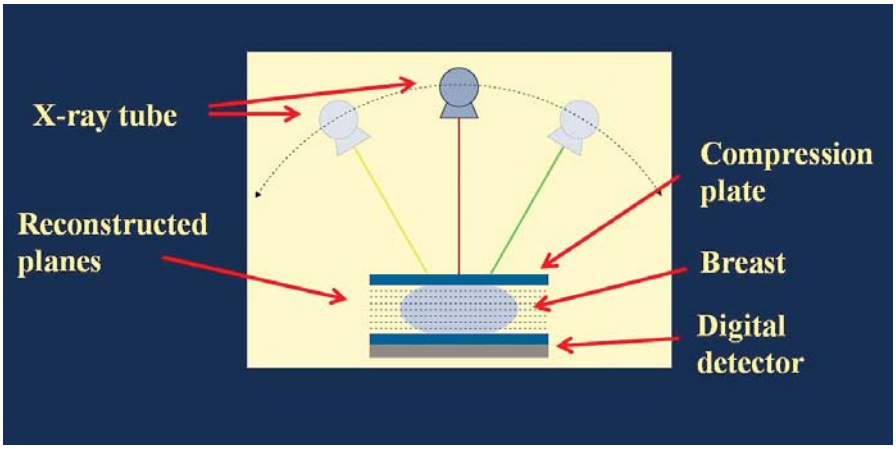
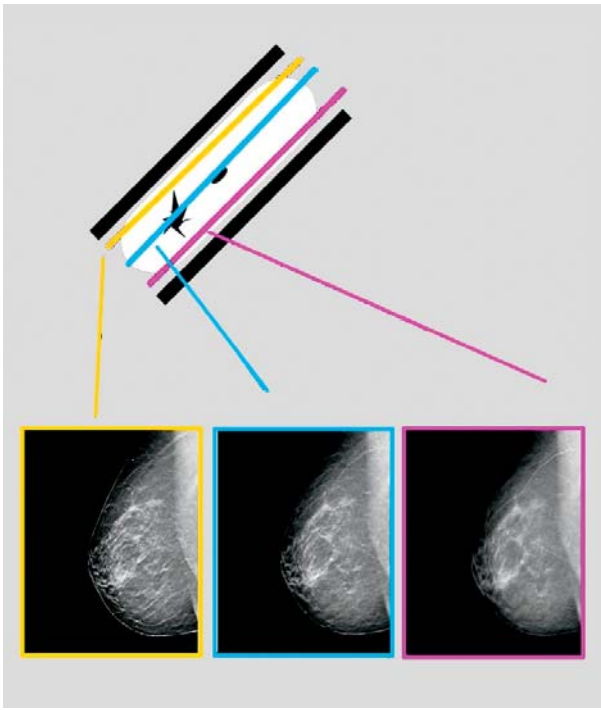
Although tomosynthesis is similar to current 2-D digital imaging, none of the technologists involved in the pilot study had previously used tomosynthesis technology. They had to be knowledgeable about patient positioning and about the new software prior to imaging patients with abnormalities. Three dedicated breast-imaging technologists each imaged a minimum of four volunteers. During this training phase, system manufacturer personnel were on-site for troubleshooting and to provide additional training.





Acquisition geometry for a mediolateral oblique view (MLO)

During imaging, 15 projection images are acquired as the X-ray tube moves from -7.5 to +7.5. Each projection image is a low dose mammogram, which images the breast from different angles. Fifteen projections are obtained, regardless of the breast size.

Image reconstruction

Based on the imaging data, reconstructed slices are obtained at different levels in the breast. The reconstructed slices are obtained at 1mm intervals. The number of reconstructed slices will vary with the breast thickness during compression. The interpreting radiologist views the reconstructed images in a cine or movie format.

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Inclusion criteria for this phase of the study included females of any race or ethnicity, 35 to 80 years of age, prior screening done at Barnes-Jewish Breast Health Center. Exclusion criteria included men, prior history of breast conservation therapy, breast implants, pregnancy, current lactation, intolerance to breast compression.

Barbara Monsees, MD, chief of Breast Imaging, and (right) Kimberly Wiele, MD

Phase II

This is a reader study of 100 cases, with 17 patients already participating. Each case includes a mass that was detected on screening or diagnostic mammography, is noncalcified, has never been biopsied or aspirated, and warrants further evaluation.

Cases will be read by four radiologists who are dedicated breast imagers with at least two years experience in digital breast imaging and with additional formal training in tomosynthesis interpretation. To reduce bias, these four readers do not participate in the standard clinical workup—which is conducted by two dedicated breast imagers with Mammography Quality Standards Act certification. This workup typically includes 2-D digital mammography tailored views and/or targeted ultrasound. Based on this workup, radiologists will determine the appropriate clinical management for the patient, who will undergo 2-D mammography and a tomosynthesis study of the breast that will be interpreted separately.

Study implications

Says Farria: "Tomosynthesis helps with false negatives by increasing the number of cancers that breast imagers can detect, especially in women with dense breasts. Its biggest impact, however, should be in reducing recalls (false positives) by as much as thirty percent, according to preliminary research studies. Three-D tomosynthesis has great promise in differentiating overlapping normal breast tissue from underlying lesions, but we need to collect more data on all types of breast lesions."

Farria also wants to get a sense of whether certain cancer features better seen with tomosynthesis, such as margins, contours, and

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size, may increase the breast imager's ability to identify malignancies. That, in turn, may help to develop criteria for what makes a mass more likely to be malignant. Depending on the results, this pilot study of only 100 participants could spawn a larger study that may influence the number of women who have to endure the stress caused by false-positive mammograms.

Editor's note: On behalf of the Joanne Knight Breast Health Center, Dr. Farria received an $8,000 award from the St. Louis Men's Group Against Cancer to support testing of digital breast tomosynthesis. MIR