3D Mammography Ups Detection, Lowers False Recall

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The addition of breast tomosynthesis, also known as 3-dimensional (3D) mammography, to standard digital mammography "offers the dual benefit of significantly increased diagnostic accuracy and significantly reduced recall rates for noncancer cases," researchers report in a study published online November 20 in *Radiology*.

As a result, patients can avoid unnecessary additional testing and decrease "attendant anxiety, inconvenience, and cost", write principal investigator Elizabeth Rafferty, MD, director of breast imaging at the Avon Comprehensive Breast Center, Massachusetts General Hospital, in Boston, and colleagues.

"It's actually pretty remarkable because with most technologies, any kind of gain in sensitivity will come at a cost in specificity," Dr. Rafferty told *Medscape Medical News*. "It's very, very rare to have improvements in both sensitivity and specificity," she added, calling breast tomosynthesis "the first major advance in breast imaging and breast cancer screening since the development of breast MRI."

Unlike conventional mammography, which involves 2 x-ray images of each breast, tomosynthesis captures multiple images from different angles, which are then used to make a 3D reconstruction of the breast, Dr. Rafferty explained. Radiologists still use standard 2-dimensional mammographic imaging for interpretation.

This combination of tomosynthesis and standard mammography can be integrated into the same piece of equipment. That approach was approved by the US Food and Drug Administration (FDA) in February 2011 (Selenia Dimensions, Hologic).

Dr. Rafferty explained that the strength of tomosynthesis is that it overcomes the source of standard mammography's limitations: overlapping tissue.

The limitations of mammogram sensitivity and specificity are related to overlapping tissue either "obscuring lesions or mimicking abnormalities and generating false-positive results. Because tomosynthesis minimizes the impact of overlapping structures, it's able to positively affect both sensitivity and specificity," she noted.

Study Results

The study, which was supported by Hologic, recruited 1192 women from 5 sites who presented for either screening mammography or prebiopsy breast imaging.

Participants underwent same-day digital mammography and tomosynthesis imaging of both breasts in the mediolateral oblique and craniocaudal positions.

The total radiation dose for the combined studies was less than 3 mGy, which is 2 times that of digital mammography alone but less than the limit for a single mammogram set by the FDA.

Two groups of radiologists who were experienced in mammogram interpretation but not tomosynthesis interpretation were trained by an experienced tomosynthesis reader to interpret the images.

Of the 997 women eligible for analysis (780 presenting for screening and 217 presenting for prebiopsy imaging), the images of 312 (including 48 cases of biopsy-proven cancer) were assigned to the first group of readers and 310 (including 51 cases of biopsy-proven cancer) were assigned to the second group of readers.

The readers first scored the digital mammograms alone and then scored the combined mammogram and tomosynthesis images. The accuracy of their interpretation was measured against the pathology results.

Training for the first group of 14 readers consisted of a review of approximately 150 cases. However, a few of those radiologists ignored "lesions that were what we call circumscribed or very well demarcated, but lobulated in shape," Dr. Rafferty explained. "It seemed clear from the types of lesions they were choosing to ignore that they were trying to translate some of their impressions from standard mammography over to tomosynthesis, despite having been trained not to do that."

Therefore, training for the second group of 15 readers was slightly different; it was reinforced with written material and included 3 additional examples. "Also, in the first [group], we did not ask the readers to actually mark the lesions they were recalling, so there was no way to confirm they had actually seen the cancer. In the second [group], we had the radiologists actually mark the lesions they were recalling rather than just describing them," she said.

For both sets of readers, diagnostic accuracy with the combined approach was significantly better than that with mammography alone ($P < .001$).

Combined imaging improved diagnostic sensitivity by 11% (from 65.5% to 76.2%) with the first group of readers and by 16% (from 62.7% to 78.7%) with the second group.

Specificity improved by 5.1% (from 84.1% to 89.2%) with the first group of readers but dropped by 1.7% (from 86.2% to 84.5%) with the second group of readers.

Positive and negative predictive values increased by 13% and 2%, respectively, with the first group of readers, and by 3% and 3%, respectively, with the second group of readers.

Almost all of the gains in diagnostic sensitivity with the combined approach were attributable to an improvement in the detection of invasive cancers — by 14.8% with the first group of readers and by 21.7% with the second group of readers.

There was also a statistically significant decrease in the mean false-positive recall rate with the combined imaging, compared with mammography alone, with the first group of readers (16.7% vs 55.1%; $P < .001$) and with the second group of readers (30.1% vs 48.8%; $P < .001$).

"Clinically, such a reduction in recall rate can be expected to translate to a substantial number of unnecessary diagnostic tests being avoided," write the authors.

Although the reduction in false-positive recalls "represents a clear advantage," the authors point out that the addition of tomosynthesis to standard mammography requires particular attention to the interpretation of the images.

"Care must be taken to avoid misclassification of malignant lesions," they write. With the first group of readers, "it was apparent that cancers manifesting as certain finding types, in particular circumscribed lobulated masses, were being inappropriately dismissed by some readers. In mammographic interpretation, radiologists often associate circumscribed masses with a benign or probably benign process. In tomosynthesis imaging, however, circumscribed margins, particularly when associated with lobulated lesions, may be an indication of malignancy. This is important to emphasize as clinical radiologists transition to interpreting tomosynthesis studies," the authors explain.

Radiation Dose Details

Although not reported in the study, Dr. Rafferty told *Medscape Medical News* that women with large breasts or implants or who had undergone breast surgery or biopsy were excluded from the study. Some have suggested that this might limit the generalizability of the results. However, she explained that such exclusions were necessary.

"Women with breasts too large to be imaged in 1 exposure were excluded because institutional review boards didn't want them exposed to too much radiation in the investigational phase, which is completely reasonable," she explained. "Women with implants were excluded for the same reason, because they routinely need twice the number of images." Women who had undergone previous surgery or biopsy were excluded because the readers were not provided with patient histories and scars can generate false-positive results, she said.

She emphasized that the findings do not suggest that tomosynthesis is inappropriate for such patients; in fact, the technique has been approved with no restrictions.

"Anywhere it is appropriate to perform a standard mammogram, it is acceptable to do this combination imaging. In the clinical setting, we haven't had any problem implementing the technology on women who have undergone previous surgery or who have a history of cancer," Dr. Rafferty said.

Adding tomosynthesis exposes patients to more radiation than standard mammography alone, although the dose is still within recommended limits, she said. "The whole mammography machine was redesigned to generate an x-ray beam that would allow this combined exposure to be below the limit for a single mammographic exposure."

This increased radiation concern might be short-lived because the FDA Medical Devices Advisory Committee recently endorsed a modification of the equipment that enables the generation of synthesized mammograms directly from the tomosynthesis data, as reported at the time by *Medscape Medical News*. "The key was to give the radiologist some 2-dimensional depiction of the breast while still getting the benefits of the 3-dimensional technology and cutting the radiation dose essentially in half," said Dr. Rafferty, who investigated and presented data on the modified Hologic technique to the FDA, but emphasized that she was not paid by the company for her time or expenses.

"I feel it is premature to describe [the study results] in such glowing terms. This may eventually be true and ethical to do, but not at this point, in my opinion," said Carl D'Orsi, MD, who was asked by *Medscape Medical News* to comment on the study.

Dr. D'Orsi, who is professor of radiology, oncology, and hematology and emeritus director of the division of breast imaging, director of breast imaging research at Emory University in Atlanta, Georgia, and a spokesperson for the Society of Breast Imaging, said the results show that tomosynthesis is

associated with a significant improvement in accuracy based on a difference in the mean area under the curve (AUC). However, this calculation might be misleading.

"The AUC takes into account both sensitivity and specificity. Thus, if one of these is significantly increased (say sensitivity) and the other is not significantly different (say specificity), there still could be an increase in the total accuracy, as measured by the AUC. Using the same logic, there may be nonsignificant increases in both, which, when plotted together...may demonstrate a significant increase in AUC," he wrote in an email to *Medscape Medical News*.

In fact, the study showed that "specificity did not significantly change for the better for the whole group and, actually, significantly decreased for 6 of the readers. This may be due to reader difference regarding skill training, etc. Additionally, only 10 of the readers increased their sensitivity significantly."

Dr. D'Orsi explained that his group recently published a study comparing stereoscopic with standard digital mammography. It showed findings that are similar to, but probably more cost-effective than, tomosynthesis.

Mammography review workstations, as well as a grant for image collection and equipment, were provided to each of the 5 participating sites by Hologic. Dr. Rafferty reports receiving research support from Hologic. Coauthor Loren T. Niklason, PhD, is an employee of Hologic. Coauthor Elkan F. Halpern, PhD, from the Department of Radiology at the Massachusetts General Hospital, reports being a consultant and statistician for Hologic. Dr. D'Orsi reports being a paid consultant to Fuji and Philips, receiving stock or stock options from Ho, and that his institution has received grants from Fuji.

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