Digital mammography creates new opportunities in cancer detection

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Digital mammography has so much to offer that it might, almost, overcome the fact that it has yet to prove clinical superiority over screen-film mammography. Many users have, in fact, already decided that digital is worth its higher cost—about 40% of all mammography systems sold in the first half of 2004 were digital.

Digital mammography has so much to offer that it might, almost, overcome the fact that it has yet to prove clinical superiority over screen-film mammography. Many users have, in fact, already decided that digital is worth its higher cost—about 40% of all mammography systems sold in the first half of 2004 were digital.

Digital offers clear logistical advantages, such as the ability to integrate mammography images and reports with the rest of the digital radiology enterprise. And all major trials completed to date have concluded that clinically, digital is at least equivalent to, if not statistically better than, screen-film. With the high spatial resolution so critical for detecting masses and microcalcifications, film has long been the standard for breast cancer screening. But the current crop of FDA-approved digital mammography systems from Fischer Imaging, GE, Hologic, and now Siemens has improved markedly over the prototype devices prior studies were based on. New digital systems, for example, demonstrate improved depiction of low-contrast objects in contrast-detail studies and a wider dynamic range. Both attributes are expected to bolster the diagnostic quality of images acquired in dense breasts. Advances in soft-copy display features have honed the rough edges of early digital workstations that were less intuitive than those available today.

More intriguing than the digital versus film debate, however, is the opportunity that digital represents in terms of tomography and contrast subtraction applications. The advent of digital detectors has paved a new road for x-ray mammography that many considered beyond improvement.

From scientific papers to plenary sessions and update courses, the RSNA meeting in December offered a plethora of data on the clinical, socioeconomic, and practical aspects of digital mammography. Dr. Daniel Kopans, chief of breast imaging at Massachusetts General Hospital, offered a succinct summation of digital's status.

"Digital mammography is probably going to replace screen-film mammography, and for many of us it already has," he said. "Others are likely to stick to screen-film until studies show that digital is actually better—and that's fine."

CAPITAL ASSETS
When and if that determination will occur remains to be seen. Digital's clinical contribution to cancer detection is a topic researchers have tried to define since its introduction as a prototype technology in 1996.

Amid numerous smaller efforts, two major studies have been conducted to date: One took place in the U.S. in 2002, and another in Norway was recently completed. A third study, the Digital Mammography Imaging Screening Trial (DMIST), is in the final stages of data collection, with results expected to be published this spring. All have focused exclusively on comparing clinical attributes of digital mammography versus screen-film.

The 2002 study, sponsored by the U.S. Department of Defense, used a prototype system developed by GE. The paired study involved 6736 women. Final results were reported by Dr. John Lewin, an assistant professor of radiology at the University of Colorado Health Sciences Center (AJR 2002;179;[3]:671-677).

Screen-film and digital mammography scans were interpreted independently. No significant difference in cancer detection was found between the two techniques, although digital mammography resulted in fewer recalls, a trend that has been repeated in similar, smaller studies.
The group also found a statistically significant increase in biopsies for film over digital mammography, another trend that was echoed in a presentation at the RSNA meeting. Final results from the Norway trial were presented at the 2004 RSNA meeting. Like the Lewin study, it offered no statistical differences in cancer detection between digital and screen-film mammography. The study, conducted under the auspices of the Norwegian Breast Cancer Screening Program, was a randomized trial involving nearly 25,000 women.

The team, led by Dr. Per Skaane at Ullevaal University Hospital in Oslo, evaluated recall rates, positive predictive values, and cancer detection rates in women from two age groups-45 to 49, and 50 to 69-who were followed for two years. All digital mammograms were read in soft-copy format. Preliminary findings were reported in July (Radiology 2004;232:197-204).

Full-field digital mammography did detect more cancers than screen-film, but the difference was not statistically significant, in part due to higher recall rates tied to the technique. Positive predictive values for both technologies were comparable, Skaane said.

In the older group, for example, there was only borderline significance to FFDM's higher cancer detection rate of 0.93% versus 0.63% for screen-film. In the younger age group, the cancer detection rate was 0.33% and 0.24% for digital and screen-film, respectively, which was not a statistically significant difference.

Overall cancer detection rates for FFDM were significantly higher than SFM (p = 0.040), and in the 50 to 69 age group, the p value was close to statistical significance (p = 0.058).

Scans were evaluated on a five-point scale, and any finding that ranked between two and five was discussed in a consensus meeting, Skaane said. That policy may be the reason the Oslo study, unlike the Lewin trial and other, smaller studies, reported a higher recall rate with digital mammography than with film.

"I thought in our first study that the higher recall rate for digital was due to unfamiliarity with equipment and soft-copy reading," Skaane said. "But this higher rate is also confirmed in our final assessment."

As a result, the higher cancer detection rate of digital is at least partially explained by the higher recall rate, Skaane said.

"Ultimately, our goal was to determine whether full-field digital mammography with soft-copy reading is suitable for breast cancer screening," he said. "This study confirms the findings of our initial study that it is."

WAITING FOR DMIST

The final word on digital versus screen-film may come this spring, when results of DMIST are published. The trial, conducted under the auspices of the American College of Radiology's Imaging Network, began in 2001.

Updated information on the highly anticipated trial results was presented at the RSNA meeting by principal investigator Dr. Etta Pisano, chief of breast imaging at the University of North Carolina, Chapel Hill. She warned at the outset that not even preliminary results are available yet. The study involves 49,500 women, digital mammography systems from four manufacturers, and 35 medical centers across the U.S. It is in its final phase of data collection, she said.

In addition to measuring the cancer detection performance of FFDM and screen-film mammography, the trial is assessing other aspects of digital mammography, from image quality to radiology interpretation of soft-copy exams. The image quality portion of DMIST is an attempt to evaluate the types of tests necessary to ensure digital mammography exam quality. Not all tests now required by the Mammography Quality Standards Act for screen-film mammography may be appropriate for digital, Pisano said. That information will be useful when Congress revamps the MQSA later this year as part of the bill's reauthorization.

"We've learned a huge amount about what digital needs for quality control," Pisano said. "We've found out a lot of tests that are not needed, which will hopefully make our lives easier and feed into the recommendations from both the ACR and the FDA on the types of tests that are needed."

A cost-effectiveness assessment is another component of DMIST.

"We are looking at the difference in predictions of false positives, and perhaps digital will be worth (the cost) based on that alone," she said. "We're also looking at downstream costs generated by both screen-film and digital in terms of long-term cost-effectiveness."

Finally, DMIST investigators will evaluate quality of life issues associated with patient callbacks that are based on false-positive results.

TOTAL RECALL

The trend toward lower recall rates with digital mammography reported in other studies was confirmed at the RSNA meeting by radiologists at Sarasota Memorial Hospital in Florida. Researchers
there found a significantly decreased recall rate for digital compared with screen-film. In 91.2% of digital mammography patients, recommendations for biopsy of suspicious microcalcifications were made without recall.

"Breast centers everywhere are juggling increasing demand for breast imaging amid inadequate reimbursement, malpractice pressures, and the need for well-trained mammography specialists," said lead investigator Dr. Nancy Wilson, a staff radiologist at Sarasota Memorial. "Increasing breast center efficiency with digital mammography is one way to meet these challenges."

Mammography services at the hospital include a diagnostic center and a busy screening center, both of which received two new FFDM units. Two additional screening sites continue to use screen-film mammography. Data on recalls for additional mammography and ultrasound views were tracked from all sites, totaling 7196 screen-film mammograms and 3862 full-field digital mammograms. A total of 2.4% of FFDM patients were recalled for either additional views or ultrasound, Wilson said. Screen-film mammography demonstrated a higher recall rate of 4.1%. As a result, 41.5% fewer recall exams were performed on FFDM patients as compared with screen-film. An additional review was performed in all cases recommended for biopsy. Imaging and pathology reports were retrospectively reviewed to determine whether callbacks were needed or if the final imaging assessment was based on the initial four-view mammogram. The research team found 78 screen-film and 55 FFDM patients with an assessment of BI-RADS 4 or 5, based on the screening exam. In 23 of the 78 screen-film patients, the suspicious finding was microcalcification, as was the case in 34 of the 55 FFDM patients. A total of 56.5% of screen-film patients were recalled for magnification views prior to final imaging assessment, compared with 8.8% of FFDM patients, Wilson said. "The difference is highly significant," she said. "In other words, in 91.2% of digital mammography patients, a decision was based on screening views."

When recall was based on a suspected mass or density, 92.7% of screen-film mammography patients were recalled prior to final assessment, compared with 90% of FFDM patients. The similarity reflects the equivalent use of spot compression and breast ultrasound to evaluate masses and asymmetric densities in both digital and screen-film mammography patients, Wilson said. In all cases, screening mammograms were compared with prior screen-film exams. Determining the significance of mammographic findings when comparing digital and film can be problematic, she said. Increased conspicuity of calcifications on digital mammography, for example, can raise concerns about apparent interval changes, prompting callbacks.

"Superior visualization of microcalcifications and soft-copy reading options of digital mammography often obviated the need for callback," Wilson said. "Despite our being new to digital mammography, when the finding was microcalcification, a decision was much more often based on the initial four-view digital mammogram than on the screen-film mammogram."

Most useful were soft-copy display options such as full resolution and zoom mode. FFDM has other advantages that are important as well, Wilson said. "Decreased recall rates for FFDM have benefited us in a number of ways," she said. "That includes more predictable scheduling in our busy diagnostic center, with fewer appointments held in reserve for callback patients. That means more available appointments for symptomatic and screening patients."

Payers also benefit from lower overall costs due to reduced diagnostic mammograms and breast ultrasounds and fewer unnecessary biopsies, she said. "Economic benefits to breast centers and third-party payers are obvious, but other benefits are more difficult to quantify," Wilson said. "The most important of these is lessening the anxiety produced simply by requesting a woman to return for additional workup."

CAD JUMPS IN

Computer-aided detection has become a valued ally in breast cancer screening, boosting overall detection rates as well as early cancer diagnoses. An estimated 25% to 30% of all screening exams performed in the U.S. are interpreted with the help of CAD. But in a screen-film environment, CAD can slow down workflow. Some sites have found it inefficient to implement CAD in a film-based environment, due to the additional time required to digitize each screening exam for computer analysis. Pairing CAD with FFDM facilitates time savings and may also bolster reader accuracy during the initial learning curve with digital mammography. In a study conducted as part of the Oslo trial, Skaane compared the cancer detection performance of CAD with independent double reading of screen-film mammography and FFDM soft-copy exams. The prospective, paired study involved 3683 women who underwent both screen-film mammography and FFDM.
CAD correctly marked 90% of cancers on the screen-film exams and 93.3% on the FFDM scans. Double readers correctly identified 93.3% of cancers on screen-film and 73.3% on FFDM. CAD sensitivity for calcifications on both modalities was 100%. CAD marked one of two cancers missed by double readers on screen-film mammography and all seven cancers missed by double readers on FFDM. Of the 26 cancers that were subsequently diagnosed, the initial double reading was positive in four cases on FFDM and in three other cases on screen-film mammography, Skaane reported.

In terms of overall performance, CAD picked up 9% of the cancers that were overlooked by double reading on screen-film mammography and 25% of the cancers that were overlooked by double readers on FFDM, Skaane said. "One problem with the study is that the learning curve for digital may overestimate the additional benefit of CAD," Skaane said. "The additional benefit of CAD in digital would be at the beginning of the curve."

ADVANCED APPLICATIONS

Many breast imagers expect that the clinical promise of digital lies in advanced applications such as contrast mammography and breast tomosynthesis. These and other techniques on the horizon can be performed only because of the digital nature of mammographic data. As such, these applications could contribute increased sensitivity to cancer detection and specificity in terms of characterizing lesions, and they could provide improved information about disease extent. Contrast mammography, for example, may be useful for diagnostic workup of abnormalities detected by screening. Variations on the technique, which involves image subtraction, are being explored in the U.S. as well as by researchers in Germany and France.

Use of contrast to detect breast cancers is new to x-ray mammography but not other breast imaging modalities. In studies focused on CT and MR imaging, breast cancers have been shown to enhance with iodinated contrast media and gadolinium-based agents, respectively. But problems arise in evaluating the effects of contrast paired with mammography. As noted by Lewin, breast compression creates external pressure that is greater than venous pressure, potentially decreasing delivery of contrast to tissues (Radiology 2003;229:261-268).

In one study presented at the RSNA meeting, Dr. Christiane Marx of Fredrich Schiller University in Munich presented clinical experience of contrast media mammography in 55 patients. Images are acquired during and after bolus contrast administration, at 30-second and one-, three-, and five-minute intervals.

Of the 55 women, malignant lesions were found in 32 and benign abnormalities in 23. Use of breast fixation instead of traditional compression yielded a higher rate of true positives and true negatives, Marx said. The three-minute postcontrast interval led to the best images. In 37 patients, MR imaging was also performed to evaluate enhancement curves, and the information gleaned was important. "Dynamic curves in contrast mammography are often different from MRI curves," she said. "Motion correction and standardization of contrast mammography data are necessary. Once achieved, contrast mammography might become a useful method for differentiating benign from malignant lesions."

3D MAMMOGRAPHY

The standing-room-only crowd drawn to a plenary session at the RSNA meeting on digital breast tomosynthesis (DBT) showed the great interest and anticipation the topic is generating.

"Tomosynthesis is the beginning of what we are going to be able to do with digital mammography," said Kopans, who helped design a prototype digital tomosynthesis device using technology developed by GE. "X-ray imaging is a technology that we all thought was mature. Now we are able to take it to a higher level than it has been in the past."

Now undergoing tests at MGH, the DBT device acquires data from various points over a 50 degrees arc of the breast. Data obtained during a seven-second sweep are reconstructed to produce planar images 1-mm thick with a pixel resolution of 100 mm. The result is a 3D mammogram. Initial studies show that full-field DBT increases radiologists' ability to find cancers by digitally subtracting potential obstructions, enhancing lesion localization, and depicting a greater amount of morphological detail.

"The major benefit is that normal breast tissue is essentially eliminated from each image," Kopans said. "Studies conducted at MGH have shown an improved sensitivity to detect cancer using this technology, without decreasing specificity."

With structural noise removed, the margins of lesions become more apparent, he said. For example, cancers that appear ill defined on 2D imaging have spiculations on DBT.
That's important, according to Kopans, as interpretive problems tied to overlapping structures account for about 25% of patient callbacks. When superimposed tissues were removed with tomosynthesis, recall rates decreased by 87%. The current protocol practiced at MGH uses only the mediolateral oblique view for image acquisition. In a separate RSNA presentation, Dr. Elizabeth Rafferty, lead investigator for tomosynthesis studies at MGH, discussed the viability and rationale for this approach. "One view enables us to decrease the radiation exposure of digital breast tomosynthesis, keeping it under that of a conventional two-view mammogram," she said.

Rafferty conducted a retrospective study of breast cancer cases from MGH diagnosed between 1998 and 2003. The objective was to assess the frequency with which malignant lesions were included on the craniocaudal projection but not on the MLO projection on conventional mammography. The MGH team also assessed the adequacy of mammographic positioning in cases when lesions were not included in the MLO projection.

Of 380 cancers, 351 were visible on the MLO projection. Of the 29 cancers that were not seen, 26 were obscured by dense tissue due to poor positioning. The remaining three lesions, or 0.8% of the total, were seen only on the craniocaudal projection.

"In each case of lesion exclusion on the MLO, at least three basic positioning criteria, which can be assessed by the technologist, were not achieved," Rafferty said. "The most common location for a lesion to be excluded on the MLO projection was in the region of the intramammary fold."

DBT OR DIGITAL?
With DBT demonstrating easier visualization of abnormalities and lesion margins and the ability to precisely identify lesion location, the question arises whether would-be purchasers of digital mammography systems should wait for DBT. Commercial availability of DBT may be up to 18 months away. In addition to the GE unit undergoing tests at MGH and featured on the RSNA trade show floor, Hologic also showcased its work-in-progress digital tomosynthesis system. The company plans to begin marketing the device in mid-2006, pending FDA premarket approval.

"It's a judgment call," Kopans said. "If digital mammography makes sense to your practice for logistical reasons and to get rid of film, it may be a reason to move to it, which is why we did it at MGH."

A DBT study involving 3000 women will be conducted during 2005 that will provide a better idea about the comparative abilities of tomosynthesis versus screen-film mammography, he said. "We will be doing a blinded comparison to see if tomosynthesis is better at detecting cancers than 2D imaging," he said. "I suspect it will be."

Ms. Dakins is feature editor of Diagnostic Imaging.

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