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Molecular Breast Imaging: Potential New Tool for Detecting Cancers

By Charlie Schmidt

Mammography may be a “gold standard” for breast cancer screening, but for some women, its interpretation amounts to little more than a coin flip. In women with dense breasts, which contain more stromal and epithelial tissues than fat, interpretation of mammograms is difficult. Among these women, tumor detection rates with mammography barely exceed 60%. Both tumors and breast tissues appear white on a mammogram, but fat looks black. Clinicians can easily detect cancerous lesions against the darker fat backdrop, whereas dense tissues obscure tumors that could be life threatening.

Now researchers at the Mayo Clinic in Rochester, Minn., say that a different screening method—molecular breast imaging (MBI)—may offer a promising alternative for women with dense breasts, who make up much of the female population. Deborah Rhodes, M.D., an assistant professor at the Mayo Clinic, said roughly a quarter of all women older than 40 years have breast tissue that is more than 50% mammographically dense.

Compared with mammography, she said, MBI detected three times as many cancers among a population of 940 dense-breasted women who also had at least one additional breast cancer risk factor, such as a family history of the disease. These preliminary findings, announced in September at the American Society of Clinical Oncology’s 2008 Breast Cancer Symposium in Washington, D.C., came from an ongoing, comparative study of MBI and mammography that was launched at the Mayo Clinic in 2005. “We’re talking about a supplement to mammography that could be readily adopted by communities, instead of just major academic institutions,” said Rhodes, who is also the study’s principal investigator. “While [mammography is] terrific for some women, it doesn’t work well for others. For them, we need a better test, and that’s what MBI could provide.”

Improving Scintimammography

MBI uses a screening method in nuclear medicine that was first developed in the early 1990s for diagnosing heart disease. Using this method, clinicians gave cardiac patients intravenous injections of a solution known as sestamibi, which contains a radioactive tracer called technetium-99m ($^{99m}$Tc). Sestamibi also contains a molecular substance that guides $^{99m}$Tc toward mitochondria, the cytoplasmic organelles that generate energy for cells. Because they consume more energy than sick cells, healthy cells concentrate proportionately more of the solution, which emits gamma rays as $^{99m}$Tc decays toward a ground state. Early medical cameras captured those rays by using a scintillator, which is a substance that absorbs radiation and responds by releasing photons of light. By collecting and measuring that light, clinicians could locate sick cardiac tissues, which emit fewer gamma rays than healthy tissues.

Unexpectedly, cardiac screens with the technique also revealed evidence of breast cancer in some patients: Cancer cells, which need a great deal of energy to proliferate, have hyperactive mitochondria that absorb sestamibi at high levels. Therefore, cancer cells emit more gamma rays than healthy cells, causing them to essentially glow.

Despite that finding, scintimammography—as the technique was called when applied to breast cancer screening—was never widely adopted. Designed for whole-body imaging, scintillating medical cameras couldn’t be brought close enough to the breast to resolve small cancerous lesions, explained Martin Tornai, Ph.D., an associate professor at Duke University Medical Center. “The cameras could...
locate very large and aggressive stage 4–5 tumors,” he said. “But for smaller cancers, particularly those less than 1 cm, their sensitivity and specificity dropped significantly.”

Because of that, Rhodes and her colleagues faced some resistance to their study when it was first proposed. But nuclear medical cameras have evolved since the 1990s, making them more appropriate for breast cancer screening today, said Mayo researcher Carrie Hruska, Ph.D., a member of the research team. An important advance, Hruska explained, was the development of smaller, solid-state cameras that could be placed directly on the breast. Solid-state cameras use semiconductor materials that convert gamma rays directly to measurable signals. “The main advantage of the solid-state detector is that it offers superior energy resolution,” said Hruska, a biomedical engineer. “That is, it is better able to distinguish gamma rays of different energies. This is important because we can then filter out gamma rays of lower energies, giving better contrast in the image.”

Mayo Clinic researchers designed a dual-head detector system that produces opposing views of the breast simultaneously. The device compresses the breast slightly, both to prevent movements that might generate artifactual measurements and to minimize the distance that gamma rays must travel from the cancer cell to the detector. According to Hruska, the dual-head system yields sensitivity improvements of greater than 90% for tumors smaller than 10 mm. Hruska and her colleagues call the technique MBI not because it offers molecular resolution of a tumor but because the molecules in sestamibi each have one 99mTc tag.

Results So Far
To date, 1,000 women have been enrolled in the Mayo Clinic’s study (including the aforementioned 940), and among them, 13 tumors in 12 patients have been detected: eight by MBI alone, one by mammography only, two by both techniques, and one by neither. The strength of those findings led Rhodes and her team to forgo accruing more study subjects (the initial goal was 2,000 women) in favor of trying to replicate their results at lower radiation dose levels. The current results were obtained with levels seven to 10 times greater than those delivered by mammography, which is too high for routine screening, Rhodes said. “With the solid-state design, we can make technical changes to reduce the dose,” added Hruska. “We’ve been working on this for the last few months, and we’ve come up with some promising findings. I think we’ll be able to get our doses down to the level of screening mammograms within the year. The dual-head design permits us to reduce the dose... We can combine images from the two detector heads and use some special image processing tools to improve the low-dose images to the same quality we get with the current [higher] dose.”

Norman Boyd, M.D., D.Sc., a senior scientist at the Campbell Family Institute for Breast Cancer Research in Toronto, suggests that MBI might be beneficial for women with dense breasts who, according to his research, face uniquely elevated cancer risk. “What we see is that density is both a risk factor in and of itself, as well as a feature that impedes imaging [with mammography],” he said. “Every 1% increase in density raises the risk of breast cancer by 2%. And among women with 75% density, the overall cancer risk increases by four- to sixfold over that of women without extensive density.”

Just how density exacerbates cancer risk remains unclear and may relate to abnormally high levels of endogenous mutagens in such women that harm DNA, Boyd said. “We don’t know how to optimally screen or image women with dense breasts, and [we hope that] MBI will provide a solution,” he said.

Other Screening Options
Rhodes emphasized that MBI hasn’t emerged in a vacuum of other screening options. Magnetic resonance imaging
(MRI), for instance, is a sensitive screening test endorsed by the American Cancer Society for women whose lifetime breast cancer risk exceeds 20% (as determined by risk assessment modeling). But MRIs cost $1,000–$4,000 per treatment, Rhodes said, and they generate roughly 1,000 images per breast, which makes them time consuming to read.

Whole-breast ultrasound offers still another alternative, Rhodes added, but its added value for breast cancer detection is low, whereas its false-positive rate is high. Moreover, like MRI, whole-breast ultrasound is labor intensive, which adds to its cost. MBI, on the other hand, might be offered at an estimated $500 per treatment, Rhodes predicted.

“People ask me, ‘If MRI is so good, why build a better mousetrap?’ But we’re not trying to build a better mousetrap; we’re trying to build a cheaper one,” Rhodes said. “MRIs are costly to maintain, and they generate tremendous anatomical detail, most of which isn’t relevant. It’s a great diagnostic tool, but for screening it’s too expensive and it provides too much information.”

While the Mayo study proceeds, researchers elsewhere are developing alternative MBI designs. Tornai, for instance, is working on a three-dimensional system that requires no breast compression. Rather, patients lie flat on an examination table while the breast drops through an opening, making it accessible to cameras that move freely below. Unlike 2D systems, 3D imaging, such as that being developed at the Mayo Clinic, offers the ability to determine a tumor’s precise location in the breast, Tornai explained. “With 2D systems you can’t tell if a tumor is in front or behind some other tissue,” he said. “So, if you want to biopsy a suspicious region, you have to go back and get more images. 3D doesn’t have that limitation, and it also allows you to do cross-sectional slice imaging, which gives even more accuracy.”

With only limited clinical data, Tornai’s system is still in early developmental stages. Meanwhile, the Mayo researchers are following up on the patients screened thus far while they use MBI to study mechanistic questions, such as the relationship between chemotherapy-induced hormonal changes and breast cancer physiology. “We still don’t have enough data to know if this could replace mammography,” Hruska said. “MBI wasn’t able to pick up some small microcalcifications that could indicate early-stage ductal carcinoma in situ. We don’t know if we’ll be able to pick these up by refining our methods. It’s conceivable that many women could get this in addition to mammography, but we don’t know the appropriate interval and there are lots of unknowns still to answer. We’ve got some interesting data, and we’ll need to get more validation from other centers and follow-up with patients. Validation is what we need to do now.”

© Oxford University Press 2008 DOI: 10.1093/jnci/djn423