RADIOLOGISTS ARE WORKING TO INCREASE ACCESS TO LIFE-SAVING BREAST IMAGING IN NATIONS THROUGHOUT THE WORLD.

By Lyndsee Cordes
When it comes to breast cancer, the difference between access to screening and treatment resources from one nation to another can be striking. The Bulletin caught up with three radiologists working in countries across the globe to explore efforts to increase imaging, understand cultural barriers, and cut breast cancer rates.

Uganda

**Background.** The only available mammography in Uganda is located in the capital city, Kampala. For most of the population, if there is any breast cancer screening, it is done only by physical exam. In addition, recent data shows Ugandan women are developing breast cancer at a younger age than women in the United States. And because of the lack of screening, women generally present at more advanced stages, greatly reducing survival rates.

Cultural attitudes toward breast cancer and breast exams present additional challenges. “Breast cancer is difficult for women to talk about because there is a strong sense of modesty in the country,” says Ginger Merry, MD, MPH, who works with Imaging the World, a nonprofit dedicated to improving global health through imaging. “And due to a variety of cultural and economic barriers, women don’t necessarily seek care early on for a breast mass.” In Uganda, community education stressing early detection is key to boosting survival rates.

**Efforts.** While mammography is the gold standard for breast cancer screening, most agree that it’s not currently a realistic option for most of Uganda. “Mammography is an expensive modality that requires equipment and technical expertise that is currently not practical for the rural setting of Uganda,” says Merry. “Ultrasound is a much more practical option due to its lower cost, smaller size, fewer requirements for supporting infrastructure, and lower power demands compared to mammography.”

So while screening continues to center around the physical exam, imaging is playing a valuable role in diagnostic evaluation through the use of ultrasound. If something suspicious is discovered during the physical exam, an ultrasound study can provide valuable clues about the nature of the mass and the next steps for treatment. “It’s portable, it’s more cost efficient, and it can be used for multiple different types of studies,” says Merry, explaining the rationale behind the selection of ultrasound.

**Outlook.** While bringing mammography to rural Uganda will most likely be a long-term objective, Merry reports that ultrasound has been received positively and is adding valuable options in diagnosing not only breast cancer but also a variety of other clinical conditions. And ultrasound may well be a stepping stone on the path to mammography. “The first step to getting there is creating a diagnostic and treatment pathway for these women,” says Merry. From there, the goal is to expand to more proactive measures in combating breast cancer.

Guatemala

**Background.** Income distribution is highly unequal in Guatemala and greatly affects access to health care. With more than half of the population living below the poverty line and mammography affordable only for members of the relatively small upper- and middle-classes, the average woman has little or no access to this vital screening exam. In addition to the logistical obstacles, preventive medical treatment is not yet ingrained in the culture. Since women often wait to seek medical treatment until they notice a problem, demonstrating the value of screening becomes just as important as making such screening available.

**Efforts.** A variety of nonprofit organizations operate in Guatemala, taking on a range of health issues. Radiology Mammography International (RMI), founded by Richard N. Hirsh, MD, FACR, focuses on increasing Guatemalan women’s access to mammography. “Are there more deadly diseases than breast cancer? Perhaps there are,” says Hirsh, “but mammography is a service that we feel women are entitled to, especially as breast cancer has become the most common cancer affecting women in the entire world.”

RMI works to increase screening rates by boosting access and increasing awareness about the importance of mammography. In August, Hirsh headed to Guatemala with a team of three radiologists, six technologists, one equipment engineer, and two women’s health educators. Each member of the team played a valuable role.

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— Richard N. Hirsh, MD, FACR
in installing the two donated machines, training the local medical staff, reading the resulting exams, and reaching out to the community.

**Outlook.** In terms of general health care and access to more modern imaging technologies, such as mammography, Guatemala remains among the most underserved countries in the region, with one of the lowest life expectancies at birth. In recent years, public health attention has increased the focus on preventive care across the health-care spectrum, including breast cancer screening. While a variety of NGOs work to increase breast cancer awareness and access to screening, much work remains to be done.

**Chile**

**Background.** Mammography is routinely available in Chile, particularly in the capital, Santiago. In rural areas, however, access is somewhat more limited.

Prior to 2005, the national program for breast cancer prevention centered around breast self exams. Nevertheless, in the eight years since then Chilean women have been encouraged to seek imaging, and mammography has made great strides, though barriers still exist. Mary F. Wood, MD, a radiology resident at Eastern Virginia Medical School, conducted a survey of Santiago women and found that 35 percent perceive cost as a barrier to getting screening, followed by lack of time and “self neglect” (translated from the Spanish term *flocera*, which refers to a lack of energy for things not considered essential). The study also found that women who reported higher incomes and those who were privately insured were more likely to get screening than those with lower incomes and other forms of insurance.

**Efforts.** A nationwide public-awareness campaign seeks to educate women about the benefits of mammography. October is Breast Cancer Awareness Month, and campaigns are very similar to those found in the United States. The National Breast

**ENDNOTES**


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— Mary F. Wood, MD

Four years after the release of controversial 2009 mammography guidelines, a study published in the journal *Cancer* shows the effect (or lack thereof) on mammography rates in the United States.¹
Cancer Screening Program offers free mammograms to women between the ages of 50 and 54, in hopes of encouraging women to form the habit of seeking mammograms.

In Santiago, where most of the available data originates, a 2008 study found screening rates around 12 percent. Wood’s study, done at the end of 2012, showed the rate at 55 percent. “A lot of improvement has been seen over a short period of time with the initiation of national health campaigns and public awareness,” says Wood.

**Outlook.** “The future of mammography in Chile is very promising,” says Wood. “From my experience, there is a great interest in public health in Chile. And there are a lot of proactive people in multiple fields working towards increasing screening and improving national health.”

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As it turns out, speaking with patients from cultures different from your own is a lot like speaking with … any other patients. Physicians working around the world share their tips for connecting with patients and conveying vital information, whether the patient hails from down the street or half a world away.

**Communicate respectfully.** The word “respect” comes up a lot when you ask about patient interactions. “If you treat everyone with the utmost respect,” says Mary F. Wood, MD, “I think patients are very appreciative of your interest in their health.” Richard N. Hirsh, MD, FACR, also emphasizes the importance of a patient-centered approach, regardless of the setting. “I make every effort to communicate with the patients abroad the same way that I do with my patients here in Ohio,” he says.

**Set the tone.** Ginger Merry, MD, MPH, believes it is the physician’s responsibility to help patients feel comfortable and confident that they have all of the information they need. “We need to listen to the patient, provide comfort, and take that extra time to talk things through,” she says. Good advice for interacting with patients from any background.

**Don’t expect the patient to ask all the right questions.** Levels of comfort with sharing personal information, even in a medical setting, vary by culture (and by individual). “Patients from some cultures often will not ask questions,” says Merry. “But it’s our role to provide them with the information they need.” Wood agrees, cautioning against making assumptions either way about a patient’s knowledge about her health. “It’s important not to assume anything about people’s awareness of whatever issue you’re speaking to them about,” she says.

**Don’t overthink it.** Hirsh encourages physicians not to tiptoe around patients. “Just be yourself, but always be respectful of your patients’ cultural backgrounds,” he says.

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The U.S. Preventive Services Task Force (USPSTF) releases guidelines that suggest delaying screening mammography until age 50, against the recommendations of every major medical organization with demonstrated expertise in breast cancer care.

Medical societies in opposition to the USPSTF guidelines:
- American College of Radiology
- American Medical Association
- American Congress of Obstetricians and Gynecologists
- American Cancer Society
- American Society of Breast Surgeons
- American Society of Breast Disease
- Society of Breast Imaging

Women 40+ who report receiving a mammogram

2011 (most recent year for which data is available)

<table>
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<tr>
<th>Year</th>
<th>Percent</th>
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<td>2011</td>
<td>53.6%</td>
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Whether through their impact on patients, providers, or both, it seems that the vigorous policy debates and coverage in the media and medical literature have limited adoption of these recommendations.

— Lydia E. Pace, MD, MPH, Yulei He, PhD, and Nancy L. Keating, MD, MPH, authors of the 2013 study
ew technology always causes a splash in its particular community. In breast imaging, tomosynthesis (tomo) is creating ripples. Since its FDA approval in 2011, studies have examined everything from detection to preference among radiologists. Early results suggest that digital breast tomosynthesis may improve cancer detection over conventional full-field digital mammography, as well as reduce screening recall rates.1,2 Some radiologists believe we’re entering a whole new world in breast imaging. Others think that although tomo will help some women, it will not help every woman. Although tomo reduces recalls, opponents argue, its benefit is felt only by the relatively small number of women who would have been recalled without it.

Margarita L. Zuley, MD, director of breast imaging at the University of Pittsburgh Medical Center, has begun to implement tomo in her practice. Her recent study, “Digital Breast Tomosynthesis versus Supplemental Diagnostic Views for Evaluation of Non-Calcified Lesions,” found that the use of tomo improves accuracy and reduces false-positive rates when compared against standard mammography. In fact, the high false-positive rate is perhaps one of the greatest criticisms of conventional mammography.

For Zuley, the positives of tomo are important to note, particularly with respect to patient care. “It’s reducing recall rates, which is mitigating the potential harm of recalling normal patients,” she says. “It’s increasing cancer detection, which is mitigating the harm of a missed cancer. It’s decreasing the number of biopsies because it’s clearer when lesions are benign. So it’s beginning to directly address some of the criticisms of mammography.”

Despite its promise, however, the role of digital breast tomo is not entirely clear. Currently, the radiation dose for a combined examination of conventional mammography and tomo is slightly more than twice the dose of mammography alone. While this is still below the FDA-allowed dose, it is something to contemplate very carefully when considering a modality for possibly tens of millions of women each year. To help resolve the issue, one vendor has used innovative techniques to utilize the tomosynthesis data set to generate a synthetic planar mammogram, thereby eliminating the need to do a mammogram and reducing the dose.

Studies are underway to answer important questions about tomosynthesis. A trial conducted in Oslo by Per Skaane, MD, PhD, and colleagues released preliminary data that seems promising.1 As this trial comes to fruition, radiologists hope to learn more about the target population and whether the benefits accrued in the first screening round hold up in subsequent rounds. Another concern being addressed is the length of time needed to interpret tomo exams compared with standard mammography. Early experience shows that it takes 50 to 100 percent longer to read tomo exams, taking up more of a radiologist’s valuable time.

Some radiologists also have concerns about reimbursement. Currently, there is no separate billing code for reimbursement. It has taken years for data to be published about the use of tomo, hindering the process of creating new billing codes. Some facilities use an unspecified code in conjunction with the mammogram code, but this has mixed success with providers — and if patients have to make up the cost, they are likely to opt out of the procedure.3

New technology is expensive, so radiologists have to ascertain if the technology is going to be both helpful to the patient and affordable for the system.

Another consideration about tomo, or any new technology, is the learning curve. Not only will radiologists have to become comfortable and proficient in its interpretation, but patients and their referring providers will need to be educated about its utility. To educate patients and referring physicians, Zuley believes it is important to be proactive and to have a plan. Distributing flyers, speaking directly with referring physicians, contacting the local media, and having a list of commonly asked questions on hand are all good ways to keep individuals informed. Direct communication can help answer questions and reduce patient anxiety. Zuley, for instance, encourages patients and referring physicians to email her directly with questions about tomo.

The concerns expressed have so far been fairly basic — cost, time, and radiation dose are all common topics.

The future of tomo is uncertain, and the College continues to pay attention to studies that are designed to yield definitive data. It continues to encourage breast imagers to educate their patients about getting regular mammography screenings starting at age 40. For more information, visit www.mammographysaveslives.com.
A CR’s clinical research efforts bring together physicians throughout the medical community in search of new tools in the fight against breast cancer. In recognition of National Breast Cancer Awareness Month, the Bulletin spoke with ACRIN and Radiation Therapy Oncology Group (RTOG®) breast cancer research leadership about trials, results, and the future of breast cancer research.

Imaging Research
Christopher E. Comstock, MD

Comstock is an attending radiologist and director of breast imaging postgraduate training and education at Memorial Sloan-Kettering Cancer Center. He became chair of ACRIN’s Breast Committee in 2012 and now serves as diagnostic vice chair of the ECOG-ACRIN Cancer Research Group’s Breast Committee.

Q: What are some of the significant trends in breast cancer imaging research?
A: The question of how we can use imaging to improve breast cancer treatment underlies the recently opened Alliance A011104/ACRIN 6694 trial (which looks at the effect of preoperative breast MRI on surgical outcomes, costs, and quality of life of women with breast cancer). The trial includes 536 patients with stage I–II triple negative or HER2-amplified breast cancer who are eligible for breast-conserving therapy. Patients will be randomized to conventional imaging or conventional evaluation plus preoperative breast MRI, toward the goal of identifying patients with extended disease and reducing the rates of reoperation and breast cancer recurrence. Reflecting a “less is more” perspective, a developing trial of patients with ductal carcinoma in situ, or DCIS, will combine MRI with a genetic DCIS score to identify those at low risk of invasive disease who can forgo radiation treatment. Additional research focuses on identifying whether multiple lumpectomies can be completed when imaging indicates absence of bridging disease. Currently, all such instances are treated with mastectomy.

Q: What breast cancer imaging trial results are expected in the near future?
A: Soon to be published are the three-year results of the ACRIN 6657 trial that, at one year study participant follow up, found change in tumor volume measurement derived from dynamic contrast-enhanced, or DCE, MRI to be effective in predicting breast tumor response to neoadjuvant treatment. Positive three-year data regarding use of this imaging biomarker will provide radiologists with a valuable tool for multidisciplinary treatment planning.

Q: What are examples of breast cancer research in the pipeline?
A: A developing study evaluating the utility of MR diffusion-weighted imaging (DWI) for detection and diagnosis of breast cancer (ACRIN 6702). The trial will collect multicenter data to provide definitive answers about an imaging method that measures the mobility of water molecules in vivo. DWI is sensitive to such tissue characteristics as cell density, membrane permeability, and microstructure. Researchers hope that DWI and DCE techniques are shown to improve MRI specificity, which could influence clinical patient management by reducing the number of unnecessary biopsies of MRI-detected breast lesions.

Q: What are some of the research challenges of conducting multicenter trials in breast cancer?
A: Because funding is no longer readily available for the larger-type trials that evaluate new imaging technologies for breast cancer screening and diagnosis, it will be necessary to identify novel and more economical methods of conducting breast imaging research. A long-range challenge is to determine which imaging technology best meets the needs of women with average to moderate breast cancer risk associated with dense breasts. The need is exacerbated by the increase in states requiring breast screening facilities to notify such women of their need for additional screening, despite the lack of data establishing the most appropriate type of adjuvant imaging. This is a prime example of the type of mainstream clinical imaging questions that the ACRIN Breast Committee has tackled in the past.
Radiation Therapy Research
Julia R. White, MD, FACR

White is a professor in the Department of Radiation Oncology at the Ohio State Comprehensive Cancer Center. She has chaired the RTOG Breast Cancer Working Group since 2006 and is the co-chair of the NRG Oncology Breast Cancer Committee.

Q: What recent research results have emerged from the RTOG Breast Cancer Working Group?

A: A major accomplishment has been the reporting of results of RTOG 9804 (a phase III trial of observation versus radiotherapy for good risk DCIS of the female breast) at the American Society for Radiation Oncology 2012 Annual Meeting. Analysis of diligent seven-year study participant follow-up showed that standard clinical and pathological criteria could be used to identify women with DCIS who are at low risk for breast cancer recurrence. Of the group thus identified, those not receiving radiotherapy had a recurrence rate of 6.4 percent and those electing radiotherapy had a rate of 1 percent. This is important information for clinicians to consider when counseling patients diagnosed with DCIS about treatment options.

RTOG has also played an important role in developing accelerated partial breast irradiation (APBI) for breast-conservation treatment. Long-term outcomes at 12 years of RTOG 9517 (a phase I/II trial to evaluate brachytherapy as the sole method of radiation therapy for stage I and II breast carcinoma) were reported at the American Society of Clinical Oncology 2012 Breast Cancer Symposium. The trial showed an ipsilateral breast recurrence risk of 6 percent. At ASTRO this year, we reported an update at eight years of RTOG 0319, a phase I/II trial to evaluate 3-D conformal radiation therapy (3D-CRT) confined to the region of the lumpectomy cavity for stage I and II breast carcinoma. The results show good durable outcomes — a 5.9 percent ipsilateral breast recurrence rate — in terms of cancer control for APBI.

Q: What research results might the ACR Bulletin readership anticipate?

A: The encouraging results of the single-arm APBI trials provided key evidence that led to the conduct of the collaborative National Surgical Adjuvant Bowel and Breast Project (NASBP) B-39/RTOG 0413 trial, a randomized phase III study of conventional whole-breast irradiation versus partial-breast irradiation for women with stage 0, I, or II breast cancer. Although surveillance, epidemiology, and end results data indicate that partial-breast irradiation techniques are gaining momentum in clinical practice, we lack mature data comparing the strategy of irradiating only the highest-risk breast quadrant over an accelerated course of several days with irradiating the whole breast over several weeks. The NASBP B-39/RTOG 0413 trial results will provide crucial data about whether APBI yields equivalent local control for select low-risk patients. More than 2,000 of the accrued 4,200+ study participants were enrolled by RTOG.

Q: What about women who aren’t candidates for APBI?

A: More than half of the women who undergo lumpectomy would never have the opportunity to undergo APBI. That’s why I’m really excited about RTOG 1005, a phase III trial of accelerated whole-breast irradiation with hypofractionation plus concurrent boost versus standard whole-breast irradiation plus sequential boost for early-stage breast cancer. The rapidly accruing trial for women at higher-than-average risk for local recurrence is investigating whether using very modern technology, such as 3D-CRT and intensity modulated radiotherapy, enables physicians to treat the high-risk portion of the breast with a higher radiation dose and the remainder of the breast with a slightly lower dose, all within three weeks.

RTOG’s contribution to breast cancer care may result in an accelerated course of treatment lasting less than three weeks, which would help with sequencing chemotherapy, reduce fatigue, lessen the overall treatment burden, and potentially provide some biologic advantages.

Q: Are research efforts underway for women with later-stage cancer?

A: With the Alliance for Clinical Trials in Oncology, we are developing very exciting phase II and III protocols of stereotactic body radiotherapy (SBRT) for women with oligometastatic breast cancer. The trial will investigate whether ablation of discrete metastatic lesions in combination with systemic therapy improves both progression-free and overall survival. This is the first metastatic breast cancer trial investigating if survival is extended with the use of SBRT, a technology in which RTOG has played a key role. //

Nancy Fredericks, MBA (nfredericks@acr.org), is communications director, ACR Clinical Research Center.

Two suspicious DCE MRI-detected lesions (BIRADS 4) are present in two patients. Patient 1 presented with a 2.6-cm heterogeneously enhancing irregular mass with spiculated margins on DCE MRI (A), which exhibited relatively low apparent diffusion coefficient (ADC) (1.21 x10-3mm2/s) on DWI (B). Patient 2 presented with a 1.3-cm oval homogeneously enhancing mass on DCE MRI (C), which exhibited high ADC (2.42 x10-3mm2/s) on DWI (D). Ultrasound-guided biopsy revealed the lesion detected in patient 1 (A) to be invasive ductal carcinoma and the lesion in patient 2 (C) to be a benign fibroadenoma. ACRIN 6702 aims to investigate whether ADC may be useful in reducing unnecessary biopsy rates of breast MRI.

Courtesy ACRIN 6702 trial principal investigator Savannah C. Partridge, PhD, a research associate professor of breast imaging at the University of Washington.