New Breast Imaging Modalities Show Promise for Cancer Screening and Staging

By Bryan Tutt

New technology to supplement digital mammography may improve breast cancer screening and diagnosis. Although some of these new imaging modalities are still under development, others are already in clinical use as adjuncts to mammography for breast cancer screening and staging.

The current standard of care for breast cancer screening is digital mammography, a time-tested modality that has helped save countless lives. But women with dense breasts or genetic risk factors require additional imaging, usually with ultrasonography or breast magnetic resonance imaging (MRI). These modalities are also used for clinical staging.

However, the current standard imaging techniques have limitations that can impair their effectiveness as screening and staging tools. Therefore, researchers at The University of Texas MD Anderson Cancer Center and elsewhere are exploring new imaging modalities to determine which techniques are appropriate for which uses.

A palpable mass that was difficult to see on mammography (left) is clearly visible on molecular breast imaging (right) of the same breast. Images courtesy of Dr. Beatriz Adrada.
New Breast Imaging Modalities Show Promise
[Continued from page 1]

Tomosynthesis
Tomosynthesis, also called three-dimensional (3D) mammography, is performed with an x-ray scanner that moves in an arc over the breast. In a few seconds, this technique obtains up to 60 images of the breast rather than the one or two images that would be obtained with the stationary scanner used for standard digital mammography. Tomosynthesis has experienced rapid growth over the past 2 years and is available for breast cancer screening at many centers.

“Tomosynthesis is an important addition for breast cancer imaging,” said Basak Dogan, M.D., an associate professor in the Department of Diagnostic Radiology’s Breast Imaging Section. “It’s used in conjunction with standard mammography for routine screening, where it helps eliminate tissue overlap that obscures masses.”

A retrospective analysis of 13 single-institution studies in which tomosynthesis was added to mammography for routine screening found that the addition of tomosynthesis resulted in a significant increase in the number of invasive cancers identified. The study, which was published in June 2014 in The Journal of the American Medical Association, also found that tomosynthesis significantly reduced the number of women who were recalled for additional testing because of abnormal findings on mammography. Dr. Dogan said, “Avoiding unnecessary recall spares patients the anxiety of undergoing additional testing for a suspected cancer and saves patients and insurance companies the cost of those tests.”

Dr. Dogan added that tomosynthesis is also under investigation as a staging tool. “Dr. Rosalind Candelaria here at MD Anderson is leading an ongoing clinical trial to see if tomosynthesis will improve the accuracy of staging breast cancers,” Dr. Dogan said. “We want to see if we will find additional tumors with tomosynthesis that regular mammography doesn’t catch and how many cancers it will catch in the contralateral breast.”

Other possible uses for tomosynthesis remain to be explored. Dr. Dogan said, “Ultrasonography is currently used to supplement screening mammography in women with dense breasts, and it’s not clear whether ultrasonography is still needed when tomosynthesis is used. This needs to be studied further.”

Dr. Dogan said that the main concern patients and physicians have about adding tomosynthesis to screening mammography is the additional radiation exposure. Each tomosynthesis image carries the same low effective dose of ionizing radiation (0.7 mSv) as a standard 2D mammography view, although performing both techniques using separate scanners doubles the dose to the patient, this dose remains low and is not thought to add to a patient’s lifetime cancer risk. Still, to keep the screening radiation dose as low as possible, new software (C-View, Hologic) allows tomosynthesis scanners to obtain 2D mammograms at the same time as 3D images, thereby keeping the dose approximately the same as that of either scan performed alone. Dr. Dogan said several scanners at MD Anderson will be upgraded with this software by the end of this summer.

Molecular breast imaging
Molecular breast imaging (MBI) is a new imaging technique that can be used as an adjunct to traditional mammography. In a recent screening trial in women with dense breast tissue, the cancer detection rate increased from 3 to 12 cancers per 1,000 women when MBI was added to mammography, said Gaiane Rauch, M.D., Ph.D., an assistant professor in the Department of Diagnostic Radiology’s Body Imaging Section.

MBI uses technetium-99m, a short-lived radioactive tracer that is injected intravenously, after which the breasts are scanned with gamma cameras. The patient is comfortably seated with the breasts lightly compressed while undergoing MBI.

“A mammogram gives an anatomical image,” said Beatriz Adrada, M.D., an associate professor in the Department of Diagnostic Radiology’s Breast Imaging Section. “MBI gives a functional image; tumors take up the radiotracer.”

Dr. Rauch added that radiologists compare the images from mammography and MBI side by side. “Sometimes in patients with dense breast tissue, you cannot see an abnormality on mammography,” she said. “The lesion is hiding behind the dense breast tissue. On MBI, you can see the lesion standing out. It lights up.”

Drs. Rauch and Adrada said that MBI offers a significant advantage over ultrasonography as a supplemental screening modality because MBI can be interpreted rapidly and has fewer false-positive findings, which lead to unnecessary biopsies.

Several studies have found that the sensitivity of MBI and contrast-enhanced breast MRI are similar, but the specificity of MBI is better, decreasing the number of false-positive findings. Another advantage of MBI over MRI, Drs. Rauch and Adrada said, is that MBI is more comfortable for claustrophobic patients and is not con-
traindicated in patients with metallic implants or renal disease. The lower cost of MBI is an additional advantage over contrast-enhanced breast MRI.

Researchers also want to know whether MBI can help gauge treatment response. Dr. Rauch is the principal investigator of a study in which patients undergo MBI after receiving two cycles of neoadjuvant chemotherapy. “The goals of the study are to see if MBI can predict the treatment response to neoadjuvant chemotherapy in patients with invasive breast cancer and help surgeons evaluate residual disease before surgery,” she said.

As with tomosynthesis, some physicians and patients are concerned about the radiation dose from MBI. However, Drs. Rauch and Adrada said the radioactivity from the amount of technetium-99m used in MBI is only 8 mCi (296 MBq), with an effective dose of 2.4 mSv. Although this is higher than the average effective dose from digital mammography combined with tomosynthesis, this effective dose is below the average annual dose of natural background radiation (3 mSv). By comparison, the radioactivity from the amount of technetium-99m used in a cardiac nuclear stress test can be as high as 30 mCi (1,110 MBq).

Other new imaging techniques

While tomosynthesis and MBI are among the more promising new modalities for breast imaging, other new techniques are also under investigation. One such technique is automated breast ultrasonography. Dr. Dogan said, “Automated breast ultrasonography can obtain the same images as classic hand-held ultrasonography in half the time: 20 minutes as opposed to 40. We hope to offer it to patients with dense breasts as a supplemental screening method.”

Another investigational imaging technique is optoacoustic, or photoacoustic, imaging. Optoacoustic imaging uses a pulse of light to heat tissue slightly; the heated tissue generates sound waves that produce functional images similar to MBI, with superimposed ultrasonograms.

Dr. Dogan is the institutional principal investigator of an ongoing study investigating the role of optoacoustic imaging in distinguishing benign breast masses from malignant masses. The study has completed patient accrual, and the results are being analyzed for publication. She added that in another multi-institutional trial, her colleagues are obtaining optoacoustic images through a tomography-based device. “This technique lets us obtain aerial views of the entire breast, not just a lesion, and tell whether any site requires biopsy,” she said.

Dr. Dogan is also the principal investigator of a clinical trial of microbubble-based imaging of the lymph nodes. “This trial involves finding the sentinel lymph nodes using intradermal microbubble contrast under ultrasound guidance,” she said. “The microbubbles are perfluorinated gases surrounded by phospholipids. Those air bubbles in the lymphatic channels make the contrast agent visible. This allows us to find the sentinel lymph node and do a needle biopsy—potentially eliminating the need for the surgeon to find and remove the sentinel lymph node.” Dr. Dogan added that MD Anderson is the first center in North America to use this technique.

Another technique under investigation is not a new modality but one that is usually not applied to breast imaging: diffusion-weighted MRI. Traditionally, contrast-enhanced MRI is used in breast imaging. However, Dr. Dogan is the principal investigator at MD Anderson for a multi-institutional trial in which patients who undergo contrast-enhanced breast MRI also undergo diffusion-weighted imaging. “We’re comparing the two sets of images, and we’re finding that lesions that take up contrast agent but appear benign on diffusion-weighted MRI wind up being benign on biopsy,” Dr. Dogan said. “The limitation of diffusion-weighted MRI is that it misses smaller tumors. I believe that as technology improves, we will overcome this limitation.” She added that the advantage of diffusion-weighted MRI is that the scan is quick and easy to add to any MRI protocol.

Obstacles and opportunities

The use of new imaging techniques can be limited by their cost. Dr. Rauch said that although MBI can be done at half the cost of breast MRI, patients undergoing screening with MBI may face problems with insurance reimbursement. “For a patient with cancer, MBI for staging is likely to get reimbursed; but for screening, reimbursement can be an issue because MBI is a new modality,” she said.

Dr. Dogan said that insurance companies have similar reservations about covering tomosynthesis for breast cancer screening. To avoid possible hardship for patients owing to insurance denial, MD Anderson charges a standard $60 fee for screening tomosynthesis. “Reimbursement by insurance companies is spotty for screening tomosynthesis because there are not yet any data to show that the procedure has an effect on mortality,” she said. “It’s an extremely new technology that came to the playing field only 2 years ago, so there won’t be any survival data for another 8–10 years.”

Dr. Dogan added that she is confident that screening tomosynthesis will prove to have a survival benefit. “There’s still room for improvement, and there are still unanswered questions,” she said. “But I think tomosynthesis is farther along than the other new technologies. It’s almost resulted in a paradigm shift in screening.”

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Breast Cancer Screening Guidelines


www.mdanderson.org/publications/oncolog 3
The exact prevalence of sexual dysfunction among cancer survivors is hard to pin down—patient populations and definitions of sexual dysfunction vary from study to study—but it is widespread. A 2010 survey by the Livestrong Foundation revealed that nearly two-thirds of the more than 3,100 cancer survivors who responded had at least some impairment of sexual function following treatment.

“Sexual dysfunction is a huge quality-of-life issue in cancer patients,” said Andrea Milbourne, M.D., a professor in the Department of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center. “We’ve had patients who have said their partners leave them because they can’t have sex.”

Moreover, according to the Livestrong survey, 30% of the patients who reported sexual dysfunction also reported that they did not receive care for it.

Physical factors

Driving the high rate of sexual dysfunction among cancer survivors is the fact that some of the most prevalent cancers—particularly cancers of the pelvic region—are linked with treatments that cause sexual dysfunction. Surgery for certain cancers may require the full or partial removal of sex organs. Both surgery and radiation can damage or destroy nerves, vasculature, and other structures that are essential to sexual function and pleasure. Cytotoxic chemotherapy and hormone therapy can cause hormonal changes—temporary or permanent menopause in some women, for example, or low testosterone levels in men—that make it difficult or impossible to have or enjoy sex.

“Most people who undergo cancer treatment can be expected to return to their normal selves, but it depends on the type of cancer, and it depends on the treatment,” said Andrea Bradford, Ph.D., an assistant professor in the Department of Gynecologic Oncology and Reproductive Medicine. “Somebody with an early melanoma on his arm who might get surgery or radiation would not be considered high-risk for sexual dysfunction, but the picture is really different for a person with advanced prostate cancer.”

Other cancer treatment–related conditions, such as fatigue, can also contribute to sexual dysfunction in cancer survivors. In addition, the incidence of sexual dysfunction in the general population is relatively high, which can make it difficult to determine whether the source of the dysfunction is indeed related to the cancer treatment.

In men

Common sexual issues in men following treatment for pelvic cancers—mainly prostate, bladder, and colorectal cancers—include erectile dysfunction, anejaculation, painful ejaculation, and urine leakage during intercourse. The most frequent of these is erectile dysfunction, which can occur as a result of low testosterone levels, damage to the nerves that control erections, or damage to the blood vessels supplying the penis. For patients who were otherwise healthy and did not have erectile dysfunction before treatment and for whom the nerves were saved, a number of treatment options can be used to restore erectile function.

“The patient may respond well to phosphodiesterase type 5 inhibitors such as sildenafil (Viagra), tadalafil (Cialis), avanafil (Stendra), or vardenafile (Levitra). If the medication does not work or if the patient would like his sexual function to return earlier, we do something called penile rehabilitation, where we start the patient on a vacuum erection device and penile injection therapy early,” said Run Wang, M.D., a professor in the Department of Urology. “If none of those options work, we can always do a penile implantation, and the satisfaction rate for that is very high.”

Men whose prostate and seminal vesicles are removed or damaged as a result of surgery or radiation therapy may experience anejaculation—the inability to ejaculate with or without orgasm. Although this may take some getting used to, Dr. Wang said, “These patients need to understand that this is the consequence of the surgery and that it is a normal phenomenon.”
An α-adrenergic antagonist (α-blocker) can be prescribed to relieve the pain some men experience during ejaculation. Medication or surgery can be used to prevent urine leakage during sex.

The majority of male cancer patients who have sexual dysfunction after treatment are prostate cancer patients. However, Dr. Wang said, “We commonly see patients with all types of cancers who also have erectile dysfunction.”

In women

Common physical issues among women who have received treatment for ovarian, cervical, or other pelvic cancers include vaginal dryness, stenosis, and foreshortening (particularly in women who have received treatment for cervical cancer), all of which can contribute to pain during intercourse.

“About half of the women I see have some degree of pain with sexual activity,” Dr. Bradford said. “A lot of these women keep their partners at arm’s length because they don’t want to become too intimate for fear that their partner is going to expect them to do something that causes them pain. Their solution to that is often to avoid any kind of intimacy altogether.”

Topical moisturizers can be used to relieve vaginal dryness, and water- or silicone-based lubricants can be used before and during sex. Low-dose vaginal estrogen replacement with a cream, ring, or tablet can also be used to moisturize the vagina and relieve vaginal atrophy. Vaginal dilators may be used to help lengthen and widen the vagina in patients with vaginal scarring, stenosis, or foreshortening resulting from surgery or radiation therapy.

Diminished or loss of interest in sex is also common following cancer treatment.

“What I hear from a lot of my female patients is that they just have no interest in sex after treatment, that if their partners didn’t ask for it, they could go years without it,” Dr. Milbourne said. “Unfortunately, we don’t have a lot that we can offer medically to help women with their lack of libido.”

In some women, the early menopause that results from the removal or damage of both ovaries can cause or exacerbate sexual dysfunction.

Other factors

The scars of surgery and other cancer treatments are often more than just skin deep. Disfigurement or other physical changes can give rise to anxiety, depression, or changes in self-esteem that can inhibit a person’s ability to enter a sexual relationship.

“Sexual desire has so many different facets to it,” Dr. Milbourne said. “Patients who have lost hair, who’ve lost or gained a lot of weight, who have a colostomy—you name it—may think, ‘How can my partner still find me attractive when even I don’t find myself attractive?’ It’s really hard to separate the physical from the mental.”

Dr. Milbourne recalled one patient whose clitoris had to be removed because of vulvar cancer involvement. Afraid of what a partner would think, the patient decided to cease seeking out romantic relationships altogether. Dr. Milbourne said, “That may not have anything to do with what we formally think about as physical sexual function, but because of how she perceives herself, she’s not willing to engage in any relationship, sexual or otherwise.”

An elusive conversation

Telling patients that their treatments may cause sexual dysfunction is part of appropriate informed consent. Nevertheless, this information—and any related concerns patients might have—may get shoved aside when a cancer diagnosis looms large.

“When they’re first diagnosed, many patients are purely focused on the cancer,” Dr. Wang said. “They’re scared, and they can’t even begin to think about the possible sexual side effects down the road.”

Other patients “may want to ask about it but don’t because they feel that it’s frivolous to be asking about sex when they should be concerned...
As physicians, we should be frank, we should be complete, and we should be proactive to bring the topic up.”

– Dr. Run Wang

“Physicians don’t have enough training or time to address these issues in depth or effectively prepare the patient for these issues,” Dr. Milbourne said. “If we can’t treat patients for their sexual dysfunction, we should refer them to a specialist who can.”

Numerous resources are available to men and women experiencing sexual dysfunction after cancer treatment. For example, sexual health counselors and therapists with expertise in treating cancer survivors can be located through the American Association of Sexuality Educators, Therapists, and Counselors or the Society for Sex Therapy and Research.

Additional resources for men can be found at www.sexhealthmatters.org, the Web site of the Sexual Medicine Society of North America. Dr. Wang, the president-elect of the society, also serves as the director of MD Anderson’s Sexual Medicine Program in the Department of Urology, whose services include comprehensive penile rehabilitation and counseling. Although current MD Anderson patients are primarily seen in the clinic, its services are also available to outside patients.

For women, help is also available through the Women’s Integrated Sexual Health (WISH) Program in the Gynecologic Oncology Center at MD Anderson. The program’s services, which include sexuality education and counseling, medical evaluation of sexual dysfunction, and short-term psychotherapy for coping with sexual dysfunction, are available to MD Anderson patients and patients in the community alike.

Dr. Bradford, who established and runs the WISH Program along with her colleagues in the Gynecologic Oncology Center, noted that involving the patient’s partner to some extent in the patient’s care is usually very helpful. She said, “I often encourage patients to come in with their partners, because sexual issues belong to the couple; they are not the fault of the cancer survivor.”

FOR MORE INFORMATION
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Dr. Andrea Milbourne ..........713-745-6986
Dr. Run Wang ......................713-745-7575

ADDITIONAL RESOURCES
The Livestrong Foundation survey referred to in this article is available at www.livestrong.org/what-we-do/our-approach/reports-findings/survivor-survey-report.

To locate a sexual health counselor or therapist with expertise in treating cancer survivors, contact the American Association of Sexuality Educators, Counselors, and Therapists at 202-449-1099 or visit www.aasect.org/referral-directory or contact the Society for Sex Therapy and Research at 847-647-8832 or visit www.sstarnet.org/therapist-directory.php.

MD Anderson patients can obtain a referral to the Sexual Medicine Program or the WISH Program from their physicians. Patients in the community can self-refer to the Sexual Medicine Program by calling 713-745-7020 or the WISH Program by calling 713-792-8340.

Dental Hygiene and Care Before, During, and After Cancer Treatment

Measures to protect oral health

Cancer treatment—especially radiation therapy and chemotherapy—can result in dental problems or other serious oral complications. These complications can lead to discomfort, interrupt or delay cancer treatment, and affect daily oral function. Addressing oral health before, during, and after cancer treatment can help prevent or manage oral complications and contribute to improved health and quality of life.

Side effects of radiation and chemotherapy

Radiation therapy to the head or neck or some chemotherapy drugs sometimes damage the salivary glands, reducing the flow of saliva, a natural lubricant that makes it easier to chew, swallow, and speak. This common side effect is called dry mouth (xerostomia). Dry mouth increases the risks of gum disease, tooth decay, and plaque buildup.

Another common complication of chemotherapy or radiation therapy is mucositis. In mucositis, the mucous membranes that line the mouth become inflamed, causing pain and difficulty eating. The resulting loss of appetite and poor nutrition can affect the immune system’s ability to fight infection.

Oral infection by a virus, bacterium, or fungus can become a serious complication. Infections can result from existing tooth decay or compromised teeth, dry mouth, mucositis, or a weakened immune system due to reduced production of blood cells and platelets by the bone marrow.

Some oral complications are specific to radiation therapy to the head or neck. These include radiation-induced cavities and an increased lifelong risk of dental decay. Tissue damage from radiation can lead to an inability to open the mouth properly (trismus or “lock-jaw”) or cell death in the bones of the jaw (osteonecrosis).

Most cancer patients do not experience all these complications, and preventive measures can reduce the risk of complications and help avoid interruptions to their cancer treatment.

Preventive measures

Regular dental treatment is not recommended during cancer treatment because patients’ immune systems may be weakened. Ideally, cancer patients should have oral health issues taken care of before cancer treatment begins.

Before treatment

A visit to a dentist for a comprehensive oral evaluation should occur at least 1 month, or as long as possible, before cancer treatment begins. The dentist can identify existing infections or stabilize areas vulnerable to infection by filling cavities and performing tooth extractions or other dental surgery. One month gives the patient enough time to recover from any invasive dental procedures.

During treatment

Throughout cancer treatment, patients should continue to brush their teeth with fluoride toothpaste. Using an extra-soft toothbrush helps protect the tissues in the mouth that have become sensitive from cancer therapy. Cancer patients should floss daily and avoid using mouthwashes that contain alcohol. Spicy or acidic foods, toothpicks, tobacco, and alcohol may cause irritation and should be avoided as well. Replacing sugary gum, candy, and soda with sugar-free versions helps prevent cavities. Using fluoride gel or treatment helps strengthen the teeth and reduces the risk of developing cavities.

Only emergency dental treatment is done during cancer treatment, and any emergency dental treatment must be coordinated with a patient’s cancer doctors. The doctors will look at the patient’s most recent blood tests to determine whether the patient can safely undergo the dental procedure. According to Theresa Hofstede, D.D.S., an associate professor in the Department of Head and Neck Surgery at The University of Texas MD Anderson Cancer Center, if a patient has a low level of white blood cells, which fight infection, or platelets, which are necessary for clotting, “then any kind of dental treatment can put the patient at risk for infection or bleeding.”

To relieve dry mouth and other side effects during cancer treatment, patients should drink water frequently throughout the day, suck on ice chips, or use sugar-free candy or gum. A dentist might also prescribe a saliva stimulant or a saliva substitute spray.

Dentures can cause mouth ulcers, and their use should be minimized during cancer treatment. However, if they must be worn, dentures should fit properly, be well cleaned, and not be worn while sleeping.

After treatment

The oral care routine after treatment depends on the type of cancer treatment received and the immune status of the patient. Unresolved oral complications or a weakened immune system can affect a patient’s ability to return to a normal dental care routine. Usually, patients should wait 2 months after treatment to get a teeth cleaning. A patient who has had radiation therapy to the head and neck should be evaluated regularly (at an interval set by his or her dentist). And according to Dr. Hofstede, patients who have received stem cell transplants are usually asked to wait at least 100 days before having any dental treatment.

—U. Arivor

FOR MORE INFORMATION

• Talk to your physician
• Talk to your dentist
• Call askMDAnderson at 877-632-6789
• Visit www.nidcr.nih.gov/oralhealth/topics/cancertreatment
IN BRIEF

New Assay Could Lead to Earlier Ovarian Cancer Detection

Screening for autoantibodies to tumor protein TP53 (also known as p53) could detect ovarian cancer earlier than cancer antigen 125 (CA125) testing, a recent study suggests.

“Ovarian cancer is detected in a late stage in more than three-fourths of patients,” said Robert Bast Jr., M.D., a professor in the Department of Experimental Therapeutics and vice president for the Office of Translational Research at The University of Texas MD Anderson Cancer Center. “Earlier detection could help cure 13%–30% of all patients with currently available surgery and chemotherapy.”

Dr. Bast added that screening with annual CA125 testing and ultrasonography for the early detection of ovarian cancer in women at normal risk for the disease is being evaluated through trials coordinated by MD Anderson in the United States and by University College London in the United Kingdom. However, other biomarkers are needed because CA125 is expressed by only 80% of ovarian cancers.

“(TP53) is the first (biomarker) that has been elevated prior to CA125 in women with ovarian cancer.”

– Dr. Robert Bast

Because TP53 gene mutations and TP53 overexpression occur in virtually all high-grade serous ovarian cancers, Dr. Bast and his colleagues hypothesized that the immune response to TP53 could be used as an ovarian cancer biomarker that is detectable before CA125 levels rise as ovarian cancers grow and spread.

The researchers developed a novel immunoassay for measuring TP53-specific autoantibody titers in small volumes (2 µL) of serum. Using the assay, the researchers analyzed archived blood samples from the United Kingdom Collaborative Trial of Ovarian Cancer Screening.

Elevated anti-TP53 autoantibody titers were detected in about 25% of the samples of women who were later diagnosed with ovarian cancer. In ovarian cancer patients with elevated CA125 levels, anti-TP53 autoantibodies rose a mean of 13.5 months before CA125 levels began to increase. In ovarian cancer patients without elevated CA125 levels, elevated anti-TP53 autoantibodies were detected a mean of 33 months before the cancer was diagnosed.

The researchers concluded that screening for anti-TP53 autoantibodies, used in conjunction with CA125 screening, could aid in the early detection of ovarian cancer. “Among more than 100 biomarkers tested to date, this is the first that has been elevated prior to CA125 in women with ovarian cancer,” Dr. Bast said.

Dr. Bast and his colleagues reported their findings in April at the American Association for Cancer Research Annual Meeting.