Women's Health Issues and Nuclear Medicine, Part II: Women and Breast Cancer

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Objective: This is the second article of a 4-part series on women's health issues and nuclear medicine. This article reviews women and breast cancer. After reading this article the technologist will be able to: (a) discuss breast cancer statistics and potential risk factors for breast cancer; (b) describe the screening tools and diagnostic procedures used for early detection of breast cancer; and (c) explain the role of radionuclide breast tumor imaging in detecting breast cancer.
Key Words: breast tumor scintigraphy; technetium-99m-sestamibi

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According to the American Cancer Society breast cancer is the most common cancer among American women, other than skin cancer, and accounts for 1 in every 3 cancers diagnosed annually in the U.S. (*1*). Since the 1940s the incidence of breast cancer has increased at an annual rate of 1% and, more recently, this rate has increased to 4% per year (*1–3*). Breast cancer will strike 1 in every 9 women in the U.S., accounting for 32% of all cancers and 18% of all cancer deaths in women. Although heart disease is the leading cause of death in all women, breast cancer is the leading cause of death in women ages 40–55 y. Ten to 20 million American women will seek medical care each year to evaluate a suspicious breast abnormality (*2,3*).

Although the cause of breast cancer is not understood, several risk factors have been identified to help physicians determine those women at greater risk of developing the disease. Most of what is known about these risk factors, however, pertains to personal characteristics and are only associated indirectly as a potential cause. Risk factors include: age, gender, genetic factors, family or personal history of breast cancer, race, history of benign breast disease, and hormonal and menstrual history factors (*1,4,5*).

Other risk factors are related to lifestyle and include the use of oral contraceptives, not having children or barrenness, not breast feeding, use of postmenopausal estrogen-replacement therapy, use of alcohol and tobacco, obesity and high-fat diets, physical inactivity, and environmental risk factors such as exposure to toxic chemicals.

At the present there is no means of preventing breast cancer. Since most risk factors are traits, it has not been demonstrated that lifestyle modification prevents the onset of breast cancer (*1,4–6*). There are several ongoing research protocols evaluating different preventative measures such as prophylactic chemotherapies and prophylactic mastectomy for women with very high breast cancer risk (*4,5*). These protocols are experimental, however, and are not recommended yet as a prevention standard.

The best approach for women at average risk is early detection and all women should follow the American Cancer Society's guidelines for early detection given in Table 1 (*1–6*). These guidelines include breast self-examination, clinical breast examination, and a screening mammogram. When diagnosed in its earliest stages, breast cancer has a high survival rate of more than 95%. Statistics also have proven that early detection of breast tumors reduces mortality by at least 30% and, despite the increased use of mammography, 80% of all breast cancers are diagnosed by examination alone. The vast majority of these involve a painless mass detected during breast self-examination (*2,3*).

ROUTINE IMAGING PROCEDURES FOR BREAST CANCER DETECTION

Mammography

Mammography is the most common imaging procedure for diagnosing breast cancer. A screening mammogram is used for asymptomatic patients. Often the earliest signs of breast cancer appear on a mammogram before they can be detected by a woman or her health care provider (*6*). Mammograms also are performed for diagnosing breast cancer in women who are experiencing symptoms such as a lump or swelling in the breast, skin dimpling or puckering, scaling of the nipple or the nipple turned inward, and leakage from the breast that is not associated with breast-feeding (*5*).

Mammography has a moderate sensitivity of 76%–94% as a screening tool for detecting cancer, which is greater than that of

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TABLE 1
American Cancer Society's Guidelines for Early Detection of Breast Cancer (*5*)

Age	Screening guideline
20–39 y	Monthly breast self-examination and a clinical breast examination every 3 y by a qualified health care professional.
>39 y	Monthly breast self-examination; annual clinical breast examination by a qualified health care professional; and an annual screening mammogram.

a breast self-examination alone (57%–70%). Mammography has a moderate specificity (90%) to correctly identify women who do not have breast cancer (*1*). The American College of Radiology implemented a mammography accreditation program in the late 1980s. The Mammography Quality Standards Act (MQSA), first passed by Congress in 1992, requires facilities to meet specific standards of quality to perform mammograms (*1*). These requirements have improved image quality and account for the higher sensitivity and specificity of results.

Despite these improvements, however, mammography may miss 10%–15% of breast cancers. This may be due partially to dense breast tissue observed in young women (*7,8*). Other types of breast tissue that can significantly reduce a mammogram's ability to detect potential malignant tumors include fatty tissue, scarred tissue, tissue with diffuse calcifications, and tissue that is obscured by breast implants (*9*). The presence of these tissue characteristics may hinder diagnosis and lead to unnecessary surgical procedures and increased patient anxiety. Also, the use of mammography cannot accurately differentiate breast cancer from benign breast abnormalities and additional diagnostic steps are needed before treatment can be initiated.

Breast Biopsy

There are several different types of breast biopsies that are performed, including fine-needle aspiration cytology, stereotactic needle biopsy, core needle biopsy, and surgical open-breast biopsy (*3,6*). All of these options offer a means of distinguishing between malignant and benign tumors. These procedures are invasive and require a surgeon, an anesthesiologist and/or a radiologist. They also introduce a complication risk to the patient with an added expense. It has been reported that breast biopsy results are negative for breast cancer in 68%–87% of women. For every 1 woman diagnosed with breast cancer, 5 to 6 will have a biopsy that shows benign breast tissue (*2,3*). Therefore, biopsy may not be the best first choice as a follow-up procedure after an abnormal clinical examination or mammogram.

Breast Ultrasound

Breast ultrasound is sometimes used to evaluate breast abnormalities found during a mammogram or physical examination. Breast masses considered to be cysts can be detected without placing a needle into the breast to aspirate fluid. Ultrasound also can be useful for accurately placing biopsy needles into some breast lesions. It has been suggested that ultrasound can be used as a screening tool for women with dense breasts, however, this has not been recommended because ultrasound cannot detect calcium deposits which are considered to be an early sign of cancer (*6,10*). Calcium deposits are seen on mammograms.

New Experimental Imaging Procedures

Mammography is a good method to detect breast cancer at its earliest and most curable stage (*10*). Mammography does have some disadvantages. It does not detect all breast cancers and has reported false positives. There are several ongoing research efforts in breast imaging to increase diagnostic accuracy for detecting breast cancer.

There have been breakthroughs in many of the imaging modalities, including MRI, computer-aided tomography scanning and PET (*10,11*). All of these modalities have shown some promising results. More research is necessary before the role of each modality in breast cancer diagnosis can be determined. Nuclear medicine also may offer a useful diagnostic tool to be used in conjunction with routine procedures currently being performed.

BREAST TUMOR SCINTIGRAPHY

Technetium-99m-sestamibi first was introduced into nuclear medicine as a myocardial perfusion imaging agent. It is distributed throughout the body in proportion to blood flow, enters cells by passively diffusing across cell membranes, and is fixed intracellularly in proportion to the metabolic activity of the cell (*3,12*). Most cancers have an increased blood flow to facilitate tumor growth and neoplastic cells have a metabolic rate 4–10 times that of normal cells (*13*). These are the suggested reasons breast tumor scintigraphy is possible with ^{99m}Tc-sestamibi. This radiopharmaceutical is available specifically for breast tumor scintigraphy under the trade name Miraluma™ (DuPont/Pharma Radiopharmaceuticals, Billerica, MA).

Imaging Procedure

Breast tumor scintigraphy using ^{99m}Tc-sestamibi is relatively easy to perform and takes approximately 45 min to 1 h. Twenty to 30 mCi ^{99m}Tc-sestamibi should be injected into the arm opposite the side of the suspected breast lesion. It also may be helpful to inject through a butterfly needle followed by a 10-ml saline flush to minimize the possibility of infiltration. Dose infiltration can cause nonspecific axillary node uptake, which may be mistaken for a metastatic lesion.

Imaging should begin 5 min after injection. Three planar images (right lateral, left lateral and anterior) should be acquired using a high-resolution collimator with a 128 $\times$ 128 matrix, using a 10% energy window for 10 min per view (Fig. 1). Lateral images should be obtained in the prone position using a table overlay. The overlay allows the breast to hang freely during the acquisition and allows for visualization of the entire breast separated from the chest and abdominal walls. The anterior image can be acquired in the supine or upright position. The patient's arms should be placed above the head in the supine position or around the camera in the upright position.

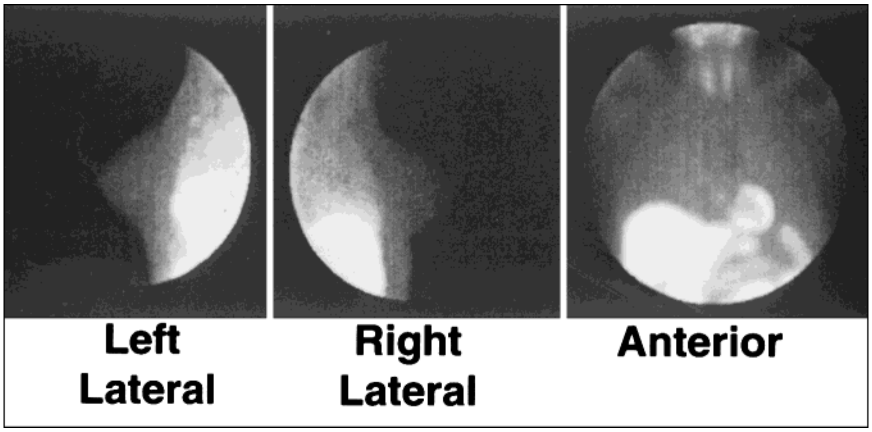

FIGURE 1. Example of normal breast scintigraphy images with optimal image quality. No focal areas of radiopharmaceutical uptake are seen in the breasts nor in the axilla.

To optimize image quality, the technologist should make certain the imaging table is locked securely and the overlay is firmly attached to the table. The technologist also should verify that the patient's breast is not pinched by the overlay or table and that the detector head is positioned as close to the patient's breast as possible. It is also important to optimize the patient's comfort during the procedure. The technologist should stay with the patient at all times and make sure the patient is comfortable and in a relaxed position. The technologist should tell the patient how long the procedure will take, dim the lights, and play quiet music, if possible. Most importantly the technologist should always maintain the patient's privacy.

An artifact that may occur is a vertical line visualized through the breast. This artifact can occur when imaging is performed in the prone position and can make image interpretation difficult (*9*). The artifact is due to low-energy scatter caused by the table. Avoid this potential artifact by ensuring a 10% energy window is used and position the patient's chest and shoulder flat against the table.

Clinical Role of Breast Tumor Scintigraphy

The growing awareness and education among women concerning early detection of breast cancer is helping reduce the morbidity and mortality of this disease. Current procedures for early detection are not always accurate or reliable in all women. Breast tumor scintigraphy can be used as an adjunct tool for diagnosis in women who have a borderline abnormal breast examination, a marginally abnormal mammogram, or in whom breast tissue composition results in an uninterpretable mammogram in the presence of a palpable abnormality. Normal breast tumor scintigraphy may eliminate the need for an invasive biopsy (*3*).

Clinical Studies

Breast tumor scintigraphy represents an important step in evaluating breast lesions. The diagnostic accuracy was evaluated in 2 multicenter trials involving 563 female patients from 42 clinical sites (*9*). The presence or absence of malignancy was determined by core histopathology laboratory evaluations of excisional biopsy tissue slides. The results were good, reporting a positive predictive value (PPV) for palpable lesions of 83% and negative predictive value (NPV) of 78%. Sensitivity and specificity were also good (76% and 85%, respectively). The results for nonpalpable lesions were similar (PPV = 79%; NPV = 80%; sensitivity = 52%; specificity = 94%). Other independent studies have been performed with similar results.

Villanueva-Meyer et al. (*14*) evaluated 64 patients who had mammography, breast tumor scintigraphy and surgical biopsy. Of these, 47 patients had a palpable breast mass and 19 had mammographic abnormalities. Breast tumor scintigraphy showed a good sensitivity (83%) and a high specificity (93%) for detecting breast cancer. The sensitvity in patients with palpable lesions was 94%.

Palmedo et al. (*15*) performed a similar study consisting of 54 patients with a suspected breast abnormality. Of these, 40 patients had a palpable breast mass and 14 had abnormalities shown by mammography. Overall the studies showed a good sensitivity (83%) and specificity (88%) for diagnosing breast carcinoma. The sensitivity increased to 100% when palpable masses alone were considered.

In other published research, breast tumor scintigraphy has demonstrated a high sensitivity and specificity in differentiating benign versus malignant lesions when compared to microscopic evaluation of breast tissue after biopsy (*3*). Breast tumor scintigraphy is generally more accurate when evaluating breast abnormalities found by physical examination than by mammography alone. Diagnostic sensitivity has been shown to decrease in masses less than 1 cm in diameter (*9*).

CONCLUSION

Breast cancer patients have a high survival rate if the cancer is detected in its earliest stages. Women should follow the American Cancer Society's guidelines for early detection of breast cancer to increase the chances of detection and, therefore, survival. These guidelines include breast self-examination, breast examination by a qualified health care professional, and a screening mammogram at various time intervals depending on age.

Although mammography has been proven to have a good sensitivity and specificity for detecting breast cancer, a mammogram can be uninterpretable and unreliable in women with dense breasts or abnormal breast-tissue composition. Breast tumor scintigraphy has been reported to have an important adjunctive role in diagnosing malignant breast tumors in these women. It is most helpful in those women who have a palpable breast mass by physical examination. Breast tumor scintigraphy is an easy procedure to perform and, because it is noninvasive, it does not create the risk of complication for the patient. In the future, breast tumor scintigraphy may be used as the intermediate step between mammography and biopsy and it may eliminate the need for many unnecessary biopsies now performed routinely.

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