INVITED COMMENTARY

Limited Angle, Limited Approach?

In this issue of *The Journal of Nuclear Medicine*, Murthy et al. (*1*) report on the use of a positron emission mammography (PEM) breast imaging system, PEM-I. Does such a dedicated system have a role next to the well-established roles of SPECT and PET cameras? Before we try to answer this question, let us look at some facts.

Breast cancer is the most common malignant disease in women and, according to the American Cancer Society (*2*), results in an annual death rate of more than 40,000 patients in the United States. Similar data are found for the European Union, with 135,000 new cases each year resulting in 58,000 deaths (*3*). Programs for early diagnosis of breast cancer have been implemented because they facilitate a better prognosis with more therapeutic options and, thus, an enhanced survival rate. Early detection, generally resulting in lumpectomy instead of mastectomy, as well as sentinel node procedures, may also lead to less morbidity (*4*). It is therefore of paramount importance to develop diagnostic techniques with a high sensitivity even for nonpalpable (clinically occult) lesions. The use of mammography in breast cancer screening has been one of the success stories in the medical imaging field over the past century. Small tumors a few millimeters in size or occult carcinomas associated with microcalcifications can be detected, although radiographic patterns are also related to age, menopausal status, race and ethnicity, parous status, and body weight (*5*), leading to differing low- and high-risk populations. To overcome this difficulty, numerous other imaging or detection methodologies for the initial diagnosis of a primary tumor of the breast have been developed (*6*) or are under investigation. These techniques include mammography (digital, with or without core or fine-needle biopsy), sonography (conventional, digital, or Doppler), MRI (conventional or contrast-enhanced), and radionuclide imaging (^{99m}Tc-methoxyisobutyl isonitrile, tetrofosmin, or methylene diphosphonate; ^{201}Tl-chloride; FDG; labeled antibodies or peptides; and receptor ligands). Each strategy has its own limitations and indications, not to mention a wide variation in cost, depending on the combination of procedures used per case.

Although mammography is now the diagnostic method of choice for screening for breast cancer, early studies obtained a positive predictive value of no higher than 10%–40% for mammography. (*7*) Therefore, complementary diagnostic procedures that significantly enhance the positive predictive value of mammography are important for reducing the number of biopsies on benign lesions. Different select subgroups of patients who may benefit from radionuclide imaging have been identified by several investigators (*8*). The most common are patients with dense breast tissue on mammography; patients who have undergone previous breast surgery, radiation therapy, chemotherapy, or biopsy; patients with breast implants; patients with a palpable mass and normal or equivocal mammography findings; and patients suspected of having multifocal disease.

^{99m}Tc-methoxyisobutyl isonitrile and ^{99m}Tc-tetrofosmin (*9,10*) are the most commonly used radiopharmaceuticals in the detection of primary breast cancer. Although the positive predictive value rises considerably when radionuclide imaging is added to mammography, reducing the number of biopsies performed on benign lesions by 30%, the factor limiting scintimammography is spatial resolution. Sensitivity in lesions less than 1 cm in diameter is low. This shortcoming has triggered the development of dedicated cameras for breast imaging.

PET studies using FDG have also shown increased tracer uptake in breast cancer tissue. The size of the primary tumor and the presence of axillary lymph node metastases have been identified as the most important factors determining the prognosis of breast cancer patients (*11*). FDG PET allows the detection of small tumors and axillary lymph node involvement and may provide accurate staging of distant metastases (*12,13*).

The PEM-I system is an interesting concept not only because it offers coregistration of 2 imaging modalities with the potential for detection of small malignant lesions but also because of the revival of what some may consider an outdated technique, limited-angle tomography. The strengths of this technique are the fixed position of the detectors, the rapid acquisition time, and the low cost. However, the weakness of limited-angle tomographic systems lies in the fact that data collection does not span the full range of projection angles needed for accurate image reconstruction, and this weakness may far outweigh the advantages (*14,15*). Unfortunately, the performance of the PEM-I system cannot be accurately assessed, because relevant information has yet to be published elsewhere.

As far as the presumed advantages of coregistration are concerned, we would like to make the following comments. The PEM-I system cannot be considered a screening tool for suspected breast cancer, because in 30% of the cases the initial mammogram will show evidence of either clear-cut malignancy or benign disease, making a subsequent PET examination unnecessary. Because FDG needs to be administered 45 min before the investiga-

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tion, the only suitable subjects for screening with such an approach are those with palpable tumors of a size highly suggestive of malignancy. However, the detection of a positive lesion calls for investigation of the axillae and, thus, for additional imaging with either a PET camera (for which the patient would need to receive an additional dose of FDG) or with a conventional gamma camera using a technetium-labeled radiopharmaceutical. Nonpalpable lesions with a relatively small chance of lymph node involvement would be better served by this technique, were it not for their being generally nonsymptomatic and usually detected on a screening mammogram. The patient group with mammograms that are nondiagnostic or equivocal remains, and the question is raised of whether a nondiagnostic procedure, which in the case of either dense breast tissue or implants cannot be used for finding anatomic landmarks, should be repeated at all.

The results presented in Table 2 of Murthy et al. (1) give rise to some doubts about the solidity of the diagnostic performance of the PEM-I system, the count-rate asymmetry being a questionable index in our opinion. Two false-negative findings in a population of 14 patients, selected on the basis of a palpable mass and a suggestive mammogram, is somewhat high. The authors themselves acknowledge that the system in its present form has major drawbacks, the most important being the limited field of view and the inability to detect lesions close to the chest wall. A positive result is the fact that there were no false-positive findings and, therefore, potentially no unnecessary biopsies.

The information available suggests that the PEM-I system in its present form is of limited value. However, although the clinical implications remain unclear, new developments deserve to be encouraged and followed closely. Until the results of a clinical study using an improved system in a larger group of patients become known, we will reserve final judgment.

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