Annals of Surgical Oncology, **13**(5): 604–606
DOI: 10.1245/ASO.2006.09.914

Editorial

The Search for Occult Metastatic Disease in Breast Cancer Patients: How Far Should We Go?

Lisa A. Newman, MD, MPH, FACS

Breast Care Center, University of Michigan Comprehensive Cancer Care Center, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109

In this issue of *Annals of Surgical Oncology*, Port et al.[1] present a well-designed prospective study of ^{18}F-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scanning compared with conventional imaging (body computed tomographic [CT] scan plus bone scan) in women with breast cancer. The overall ability to detect metastatic disease was equivalent for these two imaging strategies, but patients undergoing PET scanning were less likely to have false-positive findings that led to additional diagnostic studies or procedures. These data provide a very compelling argument in favor of routinely performing PET scans in selected categories of patients with newly diagnosed breast cancer. Indeed, the American College of Radiology Imaging Network has included the study of functional imaging as one component of their primary overall research strategy for the remainder of this decade.[2] It is essential to underscore a point made by Port et al.[1]: the value of performing the metastatic screen in a patient with newly diagnosed breast cancer is relevant only for the patient with high-risk or advanced-stage disease; an asymptomatic patient with clinically early-stage breast cancer will have only up to a 5% likelihood of having a significant lesion identified on metastatic work-up, whether conventional imaging or PET scanning is used.[3,4] The Centers for Medicare and Medicaid Services approves coverage for PET scanning in women with known advanced or metastatic disease, but not for PET scanning performed at the initial diagnosis of early breast cancer.[5]

As with any investigation that prompts a potential change in practice patterns, the concept must be scrutinized in the context of several other public health-care issues:

1. Cost.
2. Patient satisfaction and tolerance.
3. Availability of technology.
4. Competing technology.
5. Downstream effects on other patient management decisions.
6. Reproducibility of study results.

COST

The "conventional" metastatic imaging work-up for an appropriately selected breast cancer patient would include a chest radiograph, abdominal CT scan, and bone scan, with cost estimates of $160, $1500, and $1300, respectively. The cost of a total body PET scan ranges $1,500–$4,00.[6] The few hundred dollors in difference may appear scanty per patient, but if multiplied over the approximately *20,000* stage III breast cancer patients diagnosed annually[7] that would require a metastatic surgery, and the many more stage II breast cancer patients that may undergo a preadjuvant therapy metastatic screen, and if compounded by the expense of many additional facilities having to purchase and maintain new PET scan equipment, then the cost differential becomes potentially more formidable.

Received October 24, 2005; accepted October 27, 2005; published online March 13, 2006.

Address correspondence and reprint requests to: Lisa A. Newman, MD, MPH, FACS; E-mail: lanewman@umich.edu.

PATIENT SATISFACTION AND TOLERANCE

Both CT and PET necessitate an intravenous injection and are therefore comparable in terms of patient inconvenience and tolerance. The FDG (a glucose analogue) requirement of PET, however, requires that the procedure be coordinated appropriately with the medical needs of the diabetic patient. This risk may still balance out favorably against the potential nephrotoxicity of CT contrast agents.

AVAILABILITY OF TECHNOLOGY

Before any technology can be adopted as a new standard of care, it should be readily available and accessible to at least a reasonable proportion of the breast cancer patient population. At this time, PET scanning equipment is still costly and is available only at selected medical facilities, estimated at approximately 200–250 in the United States.[6,8]

COMPETING TECHNOLOGY

It can be argued that "plain" PET scans have already been rendered obsolete by the combination technology of CT-PET scans, which have the advantage of offering improved morphological and anatomical information in addition to the metabolic clues. Body magnetic resonance imaging has also become popular and is preferred over plain PET scans by many radiologists because of their more precise anatomical information. Also, alternatives to the FDG label are being actively investigated for improved cancer specificity and easier incorporation into the treatment schedules of patients being followed up for chemotherapy response in metastatic lesions. Potential alternatives include ^{18}F-fluoro-L-thymidine, which can target DNA replication; annexin V derivatives that can evaluate apoptosis; and novel tracers that can specifically target estrogen receptors and HER-2/neu receptors.[5] At present, FDG-PET has limited value in the setting of patients actively receiving chemotherapy, because chemotherapy must be withheld for at least 3 weeks before the study. Use of FDG-PET sooner can yield a falsely negative result because metabolic activity in a residual and viable tumor population is paralyzed by the recent chemotherapy cycle.

DOWNSTREAM EFFECTS ON OTHER PATIENT MANAGEMENT DECISIONS

The present study by Port et al.[1] demonstrated a minimal risk of PET-detected false positives that would have generated "unnecessary" diagnostic work-ups. However, it remains valid to question whether widespread adoption of the PET scan as a screen for metastatic disease might result in a decline in its positive predictive value. Detection of indeterminate lesions on PET could result in referrals for other interventions that will have associated costs and risks. Furthermore, inaccurate interpretations of PET findings could lead to inappropriate upstaging of a patient's disease, and this could result in the particularly hazardous scenario of missing an opportunity to treat with curative intent.

REPRODUCIBILITY OF STUDY RESULTS

The Memorial Sloan-Kettering Cancer Center is renowned for its multidisciplinary oncology expertise, and this would certainly include the radiology staff. It is not necessarily clear that other facilities are similarly prepared to handle the workload of PET scanning and PET interpretations.

The rapid evolution of technology makes it very challenging to conduct prospective trials, which can take several years to meet accrual goals, analyze results, and reach publication. Despite the concerns raised, and in light of the difficulties faced by all clinical trial investigators, Port et al.[1] are to be heartily congratulated for their strong results and clean study design. They have made a valuable contribution to our understanding of the comparative value of FDG-PET and conventional imaging techniques.

REFERENCES

1. Port ER, Yeung H, Gonen M, Liberman L, Caravelli J, Borgen P, Larson S. ^{18}F-2-Fluoro-2-deoxy-D-glucose positron emission tomography scanning affects surgical management in selected patients with high-risk, operable breast carcinoma. *Ann Surg Oncol* (in press).
2. Aberle DR, Chiles C, Gatsonis C, et al. Imaging and cancer: research strategy of the American College of Radiology Imaging Network. *Radiology* 2005; 235:741–51.
3. Samant R, Ganguly P. Staging investigations in patients with breast cancer: the role of bone scans and liver imaging. *Arch Surg* 1999; 134:551–3; discussion 554.
4. Weir L, Worsley D, Bernstein V. The value of FDG positron emission tomography in the management of patients with breast cancer. *Breast J* 2005; 11:204–9.

5. Quon A, Gambhir SS. FDG-PET and beyond: molecular breast cancer imaging. *J Clin Oncol* 2005; 23:1664–73.
6. Berger M, Gould MK, Barnett PG. The cost of positron emission tomography in six United States Veterans Affairs hospitals and two academic medical centers. *AJR Am J Roentgenol* 2003; 181:359–65.
7. National Cancer Data Base. Patterns of diagnosis and treatment 1995–2000. Available at: http://web.facs.org/ncdbbmr/ncdbbenchmarks.cfm. [accessed February 23, 2006]
8. Juweid ME, Cheson BD. Positron-emission tomography and assessment of cancer therapy. *N Engl J Med* 2006; 354: 496–507.