tion is needed to determine the range of its sensitivity, stratified by the size and type of mammographic abnormalities, for nonpalpable lesions. For patients, breast disease specialists and policymakers, this analysis, although it is not definitive, clarifies and quantifies the trade-offs between strategies. For patients and investigators these results may aid in the recruiting and informed consent process when noninvasive breast techniques are being studied.

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EDITORIAL

A Perspective on Decision Analysis Modeling as It Relates to Sestamibi Imaging of Nonpalpable Breast Abnormalities

Hillner has produced an interesting and provocative manuscript that evaluates the impact of sestamibi breast imaging in patients with nonpalpable breast abnormalities, discovered on mammography (*1*). Mammography has been shown to be an excellent screening test for the evaluation of breast cancer; however, it is nonspecific, with positive predictive values ranging from 10% to 50% (*2–15*). Sestamibi breast imaging has been evaluated in patients with nonpalpable breast lesions that were discovered mammographically (*16–19*). To further assess this new technique, a computer model was developed to answer specific questions relating to forecasting benefits and cost-effectiveness before a randomized comparison is made. It was suggested that the model can be useful to guide scientific evaluation in the trade-offs that occur when using a new test that is "less than perfect."

In any decision model, many assumptions must be made. Some of the assumptions are quite simple, and some are complex and controversial. As Hillner (*1*) points out, a critical assumption is that no change in the stage or prognosis of invasive cancer occurs if a false-negative initial evaluation results in a 6-mo delay in diagnosis. This is controversial, and some investigators suggest that a delay in obtaining a diagnosis of less than 6 mo may result in significant increases in the spread of disease to the axillary nodes (*20*). Hillner (*1*) also makes the assumption that core biopsy equates to sestamibi, with regard to decision-making by referring physicians, in determining if patients need definitive surgery. This is a difficult assumption because many physicians desire "tissue" confirmation before a decision to forego surgery is made. This implies that a sensitivity of 100% for any noninvasive test is required for this conclusion to be reached. As Hillner (*1*) correctly states, the sensitivity reported for core biopsy in invasive cancer has a range of 0.80–0.95. For in situ cancer, the range is 0.70–0.90. It is clear that core biopsy is not a perfect test (*21–25*).

For the model to become functional, it is necessary to input the sensitivity and specificity figures for the individual test in question. Based on the existing literature for core biopsy, Hillner (*1*) has chosen to use a specificity for invasive or in situ cancer of 0.90 and sensitivities of

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0.82 for invasive cancer and 0.77 for in situ cancer. Based upon limited reports in the literature for sestamibi breast imaging in nonpalpable breast abnormalities, base case sensitivities of 0.85 for invasive cancer and 0.80 for in situ cancer were chosen, with a specificity of 0.90.

A large body of information is now emerging with regard to both sestamibi breast imaging and core biopsy. For patients with nonpalpable breast lesions, the most recent reports of sensitivities in the literature for sestamibi imaging in nonpalpable breast abnormalities vary from 25% to 72%. The results obtained by the DuPont/Merck multicenter trial (*26*) demonstrated the institutional sensitivity to be 72%. The institutional values were obtained at specific institutions where the results of physical examinations, as well as prior imaging studies including mammography, were known. Blinded results for the same study were 50%.

Although it is clear that Hillner (*1*) is demonstrating the use of simulation modeling for evaluating new imaging techniques, the choice of base case values of sensitivity and specificity may be inappropriate for this example. To have a more realistic perspective for decision-making with sestamibi as the new imaging technique, the model should be used with a sensitivity equal to or less than 0.72 for the base case sensitivity. With regard to in situ cancer, there is no good statistical number to deal with for this diagnosis. It has been our experience that in situ cancer is poorly detected, with a sensitivity below that for the sensitivity established for sestamibi in nonpalpable breast cancer of an invasive nature.

Cost analysis was based upon the actual cost of performing the individual procedures and not on charges. Knowing the sensitivity and specificity for individual test and the cost, the computer then attempted to assess the impact of sestamibi breast imaging in patients with nonpalpable findings on mammography and compare sestamibi testing with core biopsy in terms of overall impact and cost savings.

Overall, the model presented may have merit from a computer and mathematical viewpoint, if all of the assumptions are agreed on. From a practical perspective, problems that arise help point out the difficulties in using computer models to evaluate specific testing strategies. For example, the choice of sensitivity and specificity for sestamibi breast imaging, as well as for core biopsy, may be influenced by patient selection. Patients selected that are from institutions where the patient prevalence is heavily weighted toward advanced breast cancer will generate statistics different from those patients from institutions where advanced disease is infrequent and benign hyperproliferative breast disorders have the highest prevalence. Most investigators who have published in the area of sestamibi breast imaging have concluded that sestamibi has little merit in detecting tumors smaller than 10 mm in diameter (*19*). Because the majority of nonpalpable breast cancers are much smaller than 10 mm, it is difficult to accept the model's conclusion for invasive nonpalpable breast cancer and especially for in situ breast cancer that two-thirds of the women in the sestamibi strategy will avoid any invasive procedure at all. The conclusions regarding sestamibi depend on the assumptions and values used and are only as good as these parameters.

A potentially valuable use of this technology would be to evaluate sestamibi breast imaging using a family of results for sensitivity and specificity. If a model were to fix the specificity at approximately 85%–90% and vary the sensitivity incrementally from 30% to 85%, it should be possible to determine at what level of sensitivity sestamibi breast imaging could be demonstrated to be effective in terms of medical decision-making, as well as being cost-effective. Using this rationale, it would be appropriate to demonstrate how microsimulation can help determine what the appropriate sensitivity and specificity of sestamibi breast imaging in nonpalpable cancer would have to be, for a given cost of an examination, for the test to be competitive with existing modalities. The model should be able to help us predict what sensitivity and specificity are required at a given test cost for the test to be considered practical for clinical use. Once this is accomplished, the other factors in determining whether a test is usable in the current clinical and economic environment can then be assessed. For example, philosophic issues, such as whether the sensitivity of the test needs to be "perfect," i.e., a 100% sensitivity, before a physician would forego a biopsy can then be discussed. In addition, a computer simulation model may be able to compare the existing modalities and associated cost to determine the optimum sequential strategy for evaluating subjects. This may be important if the sensitivity and specificity results show significant differences between tests.

Hillner (*1*) has demonstrated a potentially powerful technique in evaluating a new test. In this case, the new test is sestamibi breast imaging in evaluating nonpalpable cancer. The key issue is whether sensitivity and specificity values for sestamibi breast imaging in nonpalpable disease can approach the minimum values for "effectiveness," as determined by computer microsimulation. I agree with Hillner's final conclusion that the model demonstrates that, for sestamibi imaging, further investigation is needed to determine the range of the sensitivity stratified by the size and type of mammographic abnormalities for nonpalpable lesions (*1*).

A follow-up article addressing these issues could be most provocative and would allow us to set goals for both efficacy and cost before extensive clinical validation. The use of these powerful computer techniques is heavily dependent upon the assumptions made for all parameters chosen for evaluation. Accurate assessment of many of these parameters may require extensive clinical validation potentially resulting in a catch-22. We may find ourselves in a situation in which extensive clinical validation is required to input accurate parameters into a model, that may then tell us that extensive clinical testing is not warranted.

Overall, the computer simulation models now appearing for evaluating testing strategies are important in determining the "best" approach to managing specific disease processes. The era of corporate medicine will probably demand more of these models be used to effect maximum cost saving. This must be weighed against the possibility that, although the strategy is desirable for 95%–99% of patients studied, 1%–5% of patients may have a serious negative outcome if the most cost-effective strategy is used.

Moral and ethical considerations are sure to cause controversy when cost-effective strategies are applied to a large population base. Hopefully, we will be up to the challenge to use computer decision modeling wisely in our attempt to improve patient care.

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(continued from page 9A)

FIRST IMPRESSIONS
Contamination?

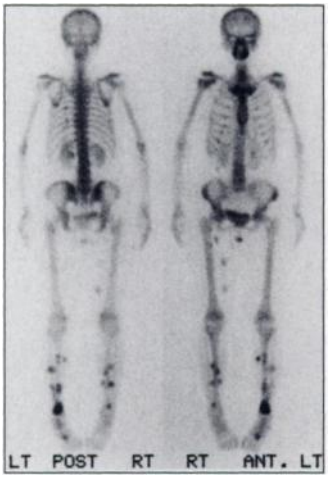

Figure 1.

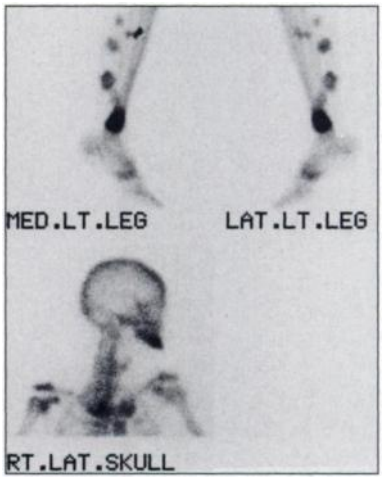

Figure 2.

PURPOSE
Anterior and posterior whole-body bone scan demonstrates multiple foci of activity in both lower extremities in a 40-yr-old woman with mandibulectomy done in 1992 for high-grade sarcoma in the mandible. She developed multiple soft-tissue nodules in both lower extremities since June 1996. Accumulation of ^{99m}Tc-MDP in these nodules is indicative of soft-tissue metastases (Fig. 1). Spot images of the skull and left leg demonstrate status post-mandibulectomy and osseous involvement in the distal left tibia (Fig. 2).

TRACER
Technetium-99m-MDP, 20 mCi

ROUTE OF ADMINISTRATION
Intravenous

TIME AFTER INJECTION
4 hr

INSTRUMENTATION
Elscint Helix dual-headed camera

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