Screening for a disease such as breast cancer with multiple test modalities (palpation, mammography, and thermography) will ordinarily have several distinct strategies optimal over the typical range of risk profiles and costs. Computer graphics has played an important role in viewing the complexities of the problem and in making simplified screening recommendations.

INTRODUCTION

The basic process of breast cancer detection is as follows: Several different screening tests are currently available to detect the presence of suspicious masses and/or formations in breast tissue. Those in common use are simple palpation, mammography (film radiography or xeroradiography), and thermography (which produces a map of temperatures within the breast). When one or more of these tests produce a result that suggests the presence of cancer, a biopsy of the lump or region is performed. The results of the biopsy are held to be definitive, and if they are positive, therapy is begun.

While these three screening tests are relatively inexpensive compared to the high cost of a cancer left undetected, they nonetheless do have costs associated with them. First there is the cost of the tests themselves multiplied over the large number of subjects who might be involved in a mass screening program. Second there is the cost of biopsies performed on a certain number of cancer-free individuals as a result of the test outcomes. Third there is a cost associated with the accumulated dose of x-rays used in mammography.

For these reasons, it is clear that an ideal screening program will weigh the costs of mass screening techniques against the benefits to be achieved, in order to determine truly optimal screening strategies.

We have been able to reduce the set of possible strategies to a much smaller set, which we call the non-dominated strategies. Using estimates of cancer incidence and of detection probabilities from the data of the Breast Cancer Detection Demonstration Project 25 (at the Cancer Research Center, Columbia, Missouri), we can then evaluate the cost of each non-dominated strategy over a range of possible screening, biopsy, and incorrect decision costs, to determine domains over which given strategies are optimal. In this last phase, three-dimensional computer graphics has been of great help in visualizing the costs and domains of optimality for strategies.

NON-DOMINATED STRATEGIES

As with most multi-stage games and decision procedures, the number of conceivable decision strategies exhibits dramatic growth as the set of possible tests increases. With three screening tests, there are a total of 16,430 strategies identifiable. Most of these strategies can never be optimal, either because they do not make use of all the information they generate or because they contain at least one illogical decision, calling for biopsy on a given result when a more positive result does not call for biopsy. (Both conditions can even exist within a single strategy.)

When either condition occurs, that strategy can never be optimal because another strategy will have expected cost function lower than its expected cost over the entire domain of cost components. We call strategies that do not create unused test results and that have no illogical decisions non-dominated strategies. By using a one-shot computer program followed by a small amount of hand work, we were able to reduce down from 16,430 strategies to exactly 92 non-dominated, non-equivalent strategies.

For an example of (a) a strategy that does not use all the information it collects, (b) an illogical strategy, and (c) a strategy that dominates both of them, see Figure 1.

ESTIMATES OF CANCER INCIDENCE AND DETECTION PROBABILITIES

Due to the care taken at the BCDDP 25 to have diagnosticians interpret the three screening results independently, we were able to estimate detection probabilities both marginally and jointly. Followup of these women, including recording of malignancies found in the intervals between screens gives a true picture of both incidence of disease and sensitivity of the screening tests.

To obtain estimates as stable as possible, a parsimonious loglinear model was fit to the raw frequencies, and the necessary rates were estimated from the table of expected frequencies. We found it possible to incorporate age (trichomized) into the
model, and found a number of age-specific differences that in turn influenced the probability estimates. There are two reasons age might be expected to be influential. The first is that incidence of the disease increases as a function of age. The second is that the structure of the breast changes with age, generally making it somewhat easier to locate suspicious masses in older women.

DISPLAY OF COSTS AND STRATEGIES

There are three possible sources of cost in the process of screening for breast cancer. The first is the cost of the screening tests themselves. The second is the cost of biopsy. The third and only difficult one to estimate is the cost of an incorrect decision. Two incorrect decisions are possible. A false positive (FP) consists in ordering a biopsy when no malignancy is present. A false negative (FN) consists in failing to order a biopsy when a malignancy is present.

The reason that incorrect decision costs are difficult to estimate is that at least part of the cost is psychological. While it may not be possible to assign precise costs to incorrect decisions, it is clear that the scale of false negative costs is much larger than that of false positive. That is, it is much worse to miss a malignancy, giving it further opportunity to metastasize, than it is to perform a biopsy and find no malignancy.

Since only two sources of cost are not easily fixed, we have used three dimensional graphics to portray the effect of differing incorrect decision costs on the per-person cost of screening. For any single strategy, per-person cost is a linear function of the incorrect decision costs, resulting in a tilted plane as the graph. The different strategies produce different planes, the lowest plane at any point corresponding to the optimal strategy for that pair of incorrect decision costs.

Thus, the graph of minimal cost appears as a polyhedral surface resulting from intersecting a set of plane surfaces. An example of such a graph appears in Figure 2. This graph is for the youngest of the three age categories, 46 years and younger. It involves just two strategies over most of the domain of incorrect decision costs. These two strategies are:

A) Do no tests and no biopsy.
B) Do a mammogram and biopsy if positive.

At the very back of the graph, a third strategy is visible:

C) Do a mammogram first and biopsy if it is positive. If it is negative, perform a physical examination (palpation) and biopsy if it in turn is positive.

The order of these strategies from front to back of the graph is reasonable. Strategy A occurs at the front of the graph, where a low cost is assigned to a false negative, while Strategy C, which gives two opportunities to order biopsy occurs in a rear corner of the graph, where the cost of false negative is high, but the cost of false positive is low.

Figure 3 shows the graph of minimal cost for the oldest of the three age categories, 57 years and older. The same three strategies are involved, but their domains have moved forward dramatically. There are two reasons for the shift. One is the increased incidence of breast cancer among older women, and the other is greater sensitivity of the tests due to changes in the breast.

In each of the figures, the strategy involving palpation alone does not occur. The basic reason is that the three screening tests were each assigned the same cost, and of the three tests, mammography has the highest sensitivity and specificity. However,
Figure 2. Optimal strategies for women age 46 and under.

mammography involves use of radiation, and accordingly might be assigned a higher cost due to the small risk that it itself could induce a tumor at some later time. We have in fact done extensive plots for different costs of the screening tests and have observed 12 different strategies to be optimal at one time or another.

We have found the cubic frame around the graph to be very helpful in portraying our results. At the same time we produce the graph, we also have our program print out a rough map of the strategies involved. This information is used to draw the strategy regions on the top surface of the cubic frame. Since the G3D procedure of SAS does not produce the frame, we are currently using DISSPLA to do the plots.

ACKNOWLEDGMENTS

The work described herein was supported largely by NCHSR Grant RO1HS3255. Additional support was received from American Cancer Society Grant IN-36-R. Cooperation of BCCDP No. 25 and the National Cancer Institute was invaluable.

REFERENCE

Figure 7. Optimal strategy for women age 57 and above.