Mammography Controversy: NIH's Entrée into Evaluating Technology

With what can at best be described as mixed emotions, NIH (the National Institutes of Health) has gone into the business of technology assessment, judging it to be a politically prudent thing to do. Last month, mammography became the first technology to be formally assessed.

At the conclusion of a 3-day public meeting on the use of breast x-rays as a tool for early detection of cancer, a special panel called for new limitations on the National Cancer Institute's (NCI) existing breast cancer screening program and said it never should have been set up the way it was in the first place. The recommendations that emerged from the deliberations of the 16-member panel will affect the use of mammography screening in the federal program and, it is hoped, will apply to private medical practice as well, although the NIH has no legal authority in that area and does not want any.

For years, NIH officials have shied away from attempts to draw the institutes into anything that even smacked of technology assessment for fear that NIH's research mission would be compromised, or at the very least diluted, if they became involved in what amounts to standard-setting and regulation. That fear still prevails, but during the past couple of years, congressional pressure on NIH to do something to assure that research advances hit the medical marketplace neither too late nor too soon has become too great to resist.

More than a year ago, at hearings before the Senate health subcommittee, NIH director Donald S. Fredrickson acknowledged: "It seems clear that in the future, the NIH and the rest of the scientific community must assume greater responsibility for the effect of research on the quality and cost of health care. The need for assuring effective transfer of useful new knowledge across the 'interface' between biomedical research and the health care community and system is a major issue." In short, NIH cannot avoid the business of technology assessment altogether. The question then became, How can NIH make formal assessments of the value of new drugs, new therapies, and new tools for detection or diagnosis of disease without crossing the perilous line to authoritarian standard-setting? As yet, there is no assurance that it can, but NIH is going to make a stab at it with a limited form of technology assessment called "technical consensus"—which means getting a suitably constituted group of people together to decide by consensus what to do about a given issue—short of establishing any procedures for enforcing what they say. One might think of it as standard-setting by indirection; it is going to be a hard role for NIH to play.

Nonetheless, Fredrickson is determined that NIH engage in technology assessment in a more than passing way and formal procedures are already being established to identify issues for future technical consensus meetings. Some 40 topics have been proposed. Mammography may have been an ideal first choice for NIH's first foray into technology assessment. Comparatively speaking, mammography is a newish technology, having been widely available for only six or seven years. It is changing, as radiological refinements make it possible to get good pictures of the breast with lower and lower x-ray dosage. And it's use as a tool for screening apparently healthy women in the NCI program to detect breast cancer early (*Science*, 13 Aug. 1976) has been terribly controversial.

In the two years since controversy over the safety of mammography arose (critics of screening say that the x-rays may cause as many breast tumors as they detect), the NCI has commissioned four studies of its Breast Cancer Detection Demonstration Project which, since 1973, has given breast x-rays to some 270,000 women at 27 centers throughout the country. Sponsored jointly by the American Cancer Society, one point of the project was to demonstrate that mammography is good at finding tiny, and presumably curable, breast cancers that would otherwise be undetected until they had grown into palpable lumps. The four NCI studies were meant to answer questions about just what the benefits and risks of mammography are.

In September, the last of the four studies was released. Taken together, they provided the foundation for assessment by yet one more group—a "consensus"

How Important Is Early Detection?

The premise behind the NCI-ACS Breast Cancer Detection Demonstration Project is that, if cancer is discovered early enough, it can be cured. It follows that if mammography reveals tumors too small to be felt by hand, as a screening technique it should save the lives of countless women.

The logic of this premise is compelling, although there are few clinical data to support it. Now, recent analyses of the four-year-old NCI-ACS project and other findings raise questions about the presumed value of the early detection and whether it is possible that mammography, in its ability to pick up very tiny tumors, may be revealing more than one needs to know. The use of breast x-rays in the screening program, has turned up a new category of tumors that are called, for lack of a better term, "minimal cancers." Sixty-six women in the program with minimal cancers now are known to have been misdiagnosed—the tumors were benign. Another 22 had what reviewing pathologists called "unclear" tumors. Another 374 had minimal cancers that everyone agrees were malignant. The great majority of all these women had surgery. The perplexing question, misdiagnosis aside, is whether surgery and follow-up therapy is really necessary.

Scientists say there is not as much information as they would like on the natural development of breast cancer but one NIH official alluded to findings concerning prostate cancer in men that may offer a useful perspective. There have been studies in which pathologists have examined at autopsy the prostates of men who died of something other than cancer. In many cases, they discovered tiny prostate tumors, tumors that had never been detected or suspected. The implication is that one would have done these men no favor by treating them for a disease that was not causing any problem. The question is whether the same might be said for minimal breast cancer in women. No one knows.—B.J.C.

panel. This last group, put together not by NCI but by NIH, through the director's office, was constituted according to the fashion of the times to include ethicists, economists, women, and physicians and researchers who had no particular expertise in breast cancer.

The panel, headed by Samuel Thier, chairman of internal medicine at Yale Medical School, met for 3 days at NIH in an open meeting at which they sifted through available evidence on the pros and cons of mammography as a screening tool, listened to dozens of witnesses (more than 275 individuals and organizations were invited to comment), and worked to come to some agreement about what should be done. To everyone's surprise, including the panelists who were nervous about conducting all of their business with a couple of hundred persons watching, the process worked reasonably well.

To begin with, as Thier noted in a telephone interview with *Science* after the conference, the panelists agreed about what the data on mammography said. (And they agreed that steps previously taken by NCI to modify the program are sound.) The panel agreed there is evidence that screening women over 50 (the group most likely to get breast cancer) is beneficial and should continue. They agreed there is no evidence that exposing younger women to breast x-rays is worthwhile and that there is evidence it may be harmful. In all but a handful of circumstances (see box), it should not continue. They even agreed that if the NCI and ACS had it to do over again, they should not design a screening program like the one they have.

Donald Fredrickson: leading NIH into technology assessment.

One of the controversial points about attacks on the Breast Cancer Detection Demonstration Project is whether it is being unfairly criticized by those who have the benefit of hindsight. Thier says no. "We asked ourselves whether, on the basis of what we know now, we'd endorse a mass screening program like this, and we said 'No,' " he says. "We asked whether we'd have done it this way on the basis of what was known about the value of mammography screening in 1972. We still said 'No'." Thier concludes that "They [the NCI and ACS officials who designed the screening project] way overshot. If there is any lesson, it may be that the real threat is that people of good intentions can be pushed too far on technology transfer. If you're going in for it in a big way, you'd better be sure you know what you're doing scientifically."

Unnecessary Breast Surgery

The question of knowing what one is doing scientifically took on unanticipated immediacy when a group of reviewers reported that, of 1850 women diagnosed as having cancer, a staggering 66 of them did not really have a malignant tumor at all, and in another 22 cases the pathological data were not at all clear. Nevertheless, most of these women had breast surgery, many of them radical mastectomies in which chest muscles were removed along with the breast.

The Thier panel had little trouble reaching a consensus on what to do about this, even though their recommendations are controversial and likely to cause NIH some trouble. First, they agreed that, for ethical reasons, those 66 women who had unnecessary surgery have to be told, as do those whose diagnosis was unclear. Furthermore, the rest of the women should be told that, when their tissues were reexamined by a team of pathologists, the diagnosis of cancer was confirmed. (No one knows yet whether any of the "unnecessary surgery" patients will sue, but the possibility is certainly there.) Second, the panel recommends that, in the future, when breast x-rays reveal a tiny lump—a centimeter or less in diameter—it be examined by no fewer than three pathologists *before* surgery.

The effect of the latter recommendation will be to make the treatment of women with tiny breast lumps at least a two-stage procedure. In current practice, a woman is taken to the operating room and anesthesized, a biopsy is taken, and everyone waits while the hospital pathologist examines the tissue. If he calls it malignant, surgery is performed then and there. If the pathologist is wrong, as was the case at least 66 times, the woman loses her breast for nothing. The Thier panel sees no need for such haste and every reason to seek a second and third opinion, even though many pathologists resent being "second-guessed" and surgeons contend that a two-stage procedure will subject some women to the risk of a second anesthesia. However, as Seymour Perry, special assistant to the NIH director, notes, "We haven't found a single woman who would rather lose her breast unnecessarily than have anesthesia a sec-

The Recommendations

Throughout the past two years, the National Cancer Institute and the American Cancer Society have met frequently to reconsider the guidelines for the Breast Cancer Detection Demonstration Project. Last May the cancer institute issued new regulations limiting the scope of the project. In the main, the Thier consensus panel simply reinforced those limits, although it added a couple of additional restrictions. As they stand now, the principle guidelines, in effect, are these:

1) Mammography screening should be available to women over 50.

2) For women between the ages of 40 and 49, mammography should be used only for those who have had breast cancer or who have a mother or sister who has had the disease.

3) For women between the ages of 35 and 39, mammography should be used only if a woman has previously had cancer in one breast. (Here the panel is taking a tougher stance than the NCI had previously, when it said mammography should be given to these younger women if they had a family history of breast cancer.)

4) Thermograph—the examination of breast tissue by heat rather than x-ray—has not been proved to be valuable and should be dropped from the program, although it should still be studied.

5) Mammography should never be used to screen women under 35.

6) Mammography *should* be used for women of any age to aid in the diagnosis of a suspected tumor.—B.J.C.

ond time if surgery really is needed."

Although the panel reached a consensus on most issues, there were some on which they did not. They could not agree about what to do with respect to following the women in the current project who have had breast x-rays and are under 50. If breast x-rays do, in fact, *cause* breast cancer, it will be some of these women who get it. But careful follow-up for 20 years or more would be, as Thier put it, "exquisitely expensive" and might not be scientifically worthwhile. The number of women involved may be too small to make it possible to draw conclusions about whether there really is a cause-effect relationship between mammography and the development of breast cancer. Still, those women, he says, "should not be ignored."

The other question that eluded consensus was whether it would make sense to design a new breast cancer screening program—a randomized controlled trial—to try to figure out if there really is some benefit to screening younger women that simply has not been demonstrated by existing data. The NCI-ACS project was not designed to answer the question of benefit to younger women; it assumed that benefit would be shown. So, there is no way of getting the answer without a new, huge trial. But it too would be enormously expensive, with no guarantee of producing an answer.

Thier thinks that these two issues can be satisfactorily resolved—there was, he noted, consensus that they are important. "But after being bombarded with data for three days, we were too numb to design new studies or agree they would make sense economically."

—BARBARA J. CULLITON

Famous War General Due to Take Over Vietnamese Science

The Vietnamese will soon write their own unique chapter in the annals of science and development by appointing as their next minister for science the redoubtable General Vo Nguyen Giap, the military strategist of the North's 30-year fight against the French, the Americans, and the government of the South.

This was the word brought back recently from Vietnam by Arthur W. Galston, the peripatetic Yale biology professor who was one of the two first Americans to be admitted to China in 1971 and who has been in Hanoi in 1971, 1975, and again for 3 weeks last summer. Galston is one of the few Americans who have been allowed glimpses of Vietnam's attempts to rebuild after the war's end, in this period in which American-Vietnamese relationships have been strained. His trip was sponsored by the Scientists' Institute for Public Information.

Galston has been able to visit with the prime minister, Pham Van Dong, on each of his trips to Hanoi; and this time Van Dong spoke at length about the fact that, when the current minister of science, Tran Di Ngieh, retires, General Giap will succeed him. The job puts him in charge of all basic and applied science, and much of the country's technology effort; besides the directorship of the booming new Science Research Center outside Hanoi, General Giap will have the ministers of public health and agriculture—and their associated laboratories—reporting to him.

In a major speech last December, General Giap called for a science and technology revolution that would be central to modernizing Vietnam "within 15 to 20 years." He listed several ambitious developmental goals, such as national electrification by building hydroelectric dams and a nationwide survey of the country and its continental shelf. Giap also called for the country to develop more electronics know-how and more engineers to help modernize the means of production. Mathematics and cybernetics, he said, are needed to modernize methods of organization. Of the other disciplines, he said biology should be "a leading scientific branch, highlighting all the advantages of a tropical country that favor agriculture, fisheries, forestry, the food processing industry, medicine, and pharmacy." General Giap's detailed plans are not yet known, but if he displays toward development anything like the military ingenuity that won him world fame for his surprise defeat of the besieged French army at Dien Bien Phu in 1954, and for sustaining his resource-scarce, guerrilla force against the French, Vietnamese, and American armies over the ensuing 20-year struggle, his impact on Vietnam's economic development could be interesting.

The Giap appointment is only one sign of the priority the Vietnamese are giving to science and technology, Galston says. At the time of his last visit (*Science*, 29 August 1975, p. 705), the Science Research Center had just been built; now it is teeming with hundreds of scientists and technicians and seems even crowded.

The Vietnamese seem to be building up their scientific activities in areas where they have a preeminent figure who can lead the research, Galston says, and they seem to devote fewer resources to other fields. For instance, at the Science Research Center, the physics institute is led by Dubna-trained physicist Nguyen Van Hieu, and is the largest of the institutes there. There are also substantial institutes of biology and of earth sciences, led by established figures. The other centers, for mathematics (in Hanoi), for applied mathematics and cybernetics (in

Arthur W. Galston (left) meets with Prime Minister Pham Van Dong.