Indications and Risk-Benefit of Mammography

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Mammography has recently undergone a striking improvement in image detail along with a corresponding decrease in radiation exposure. Although the data of the Breast Cancer Detection Demonstration Project is tainted by an absence of a control group of women, the high rate of detection of early cancer by mammography alone in the participants above or below age 50 years implies that mammography is useful in detecting breast cancer before the appearance of a palpable mass. Early diagnosis results in higher survival rates. Mammographers should continuously seek the least radiation exposure consistent with a sharp image. Given present knowledge of its benefit and potential risk, mammography should be performed when a significant suspicion of breast cancer exists at *any* age, but it should not be performed *under* age 35 years without such suspicion. A baseline mammogram should be performed in the 35 to 40-year age group. The periodicity of survey mammography in asymptomatic women under 50 years should be determined by analysis of relative risk factors for breast cancer. For asymptomatic women age 50 years and older, periodic screening mammography is sound medical practice.

Historical Perspectives

Mammography is the roentgenologic examination of the breast. Salomon as early as 1913 used x-rays to study gross mastectomy specimens.[1] Warren reported in 1930 on the clinical use of mammography.[2] Thereafter, interest in mammography dissipated because of poor technical quality until 1956 when Egan, after extensive experimentation with various x-ray factors, developed a simple and reproducible mammographic technique, with a great advance in image detail.[3] By 1965, Clark was able to show that Egan's technique was reproducible.[4] A significant step forward in breast cancer detection was achieved.

In the mid 1960s, Gros introduced the use of molybdenum in place of tungsten as a target for mammography x-ray tubes.[5] Image detail was improved; however, one drawback was introduced compared to the Egan technique—an increase in surface exposure to the breast from approximately 4 roentgens to 8 roentgens (R).

The problems of increased dose with the molybdenum tube system diminished when, in

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1973, DuPont marketed a film-screen system consisting of a single-emulsion film and a single high-definition intensifying screen contained in an air-evacuated polyethylene plastic envelope.[6] Surface exposure was reduced to about one eighth of that previously required (from approximately 8 R to 1 R per image), without degradation in image quality. In 1975, the same company brought out a more advanced version of the low-dose film-screen combination requiring only half the exposure (500 mR) of the first version. Other film manufacturers (eg, Kodak Min R) followed suit. Other manufacturers of x-ray equipment now market various machines with molybdenum targets in competition with the Senograph.

Xeroradiography, another new x-ray imaging technique, became widely available in 1972. This electrostatic process results in the enhancement of the edges of anatomic and pathologic structures and was pioneered for mammography by Wolfe[7] and Martin.[8] Through a combination of added filtration and modification of internal parameters of the xeroradiographic system, it is possible to reduce the surface exposure by more than a factor of 2 (from 3 R to less than 1 R per image).[9] By so doing, however, there is visual flattening of the image with decreased image quality. It is possible to further reduce the dose by approximately 30 percent by performing xeroradiography in the negative mode (where the anatomic and pathologic structures appear white and the background structures, blue, instead of vice versa), but there is disagreement among mammographers on whether or not the negative mode degrades the image.

Is Mammography Worth the Risk?

The main purpose of x-ray mammography is to detect cancer before it is palpable and when the disease is potentially curable. Through the use of mammography, moreover, it is possible to detect some cancers when they are still "minimal." So-called minimal breast cancer is defined as invasive or in situ carcinoma without metastasis, that forms a mass no greater than 0.5 cm in diameter as measured pathologically. Women whose lesions are this small have a ten-year survival rate of 95 percent[10]; hence, early detection and treatment are of great importance.

In the past ten years mammography has undergone a striking improvement in image detail along with a corresponding decrease in radiation exposure. The improvement in image detail is obvious in Figure 1. The significance of this improvement can best be appreciated when the results of the ongoing Breast Cancer Detection Demonstration Project (BCDDP) are compared to those of the Health Insurance Plan (HIP) of New York Breast Cancer Detection Project of the 1960s: both projects used a combination of physical examination and mammography. At the first annual screening in the BCDDP, mammography alone was responsible for the biopsy recommendation in 43.7 percent of the cancers, compared with 33.3 percent in the older HIP study. When limited to the age group under 50 years, the corresponding figures were 43.5 percent in the BCDDP and 19.4 percent in the HIP study.

Nevertheless, as promising as these comparisons seem, the efficacy of mammography in a screening program has yet to be validated in women under age 50 years. The lack of validation results from several factors. First, mortality was not lowered in the age group under 50 years in the HIP screenees, perhaps because very few cancers 1 cm or less were discovered among these screenees, whereas approximately one third of the cancers detected among the BCDDP screenees were less than 1 cm. (Image detail in the HIP mammograms was poor compared to that in the BCDDP mammograms. This is one explanation for the HIP failure to detect cancer less than 1 cm in size, especially in the breasts of younger women which normally contain less fat to serve as a contrasting background upon which to see cancer.) Secondly, the BCDDP is not a case-control study. Screenees lack a suitable control group against which breast cancer mortality may be measured. It is not possible, therefore, to accept the proposition that the high proportion of breast cancers detected in an early stage of disease among the BCDDP screenees provides evidence of benefit. It is not known when and at what stage of disease those cases would ordinarily have been detected without formal screening. Finally, there is a lack of knowledge about the natural history of cases classified as noninfiltrating cancers, some of which might never have become clinically recognized.

What Is the Risk of Mammography?

The report of Dr. Arthur Upton and his National Cancer Institute Working Group on the Risks Associated with Mammography in Mass Screening

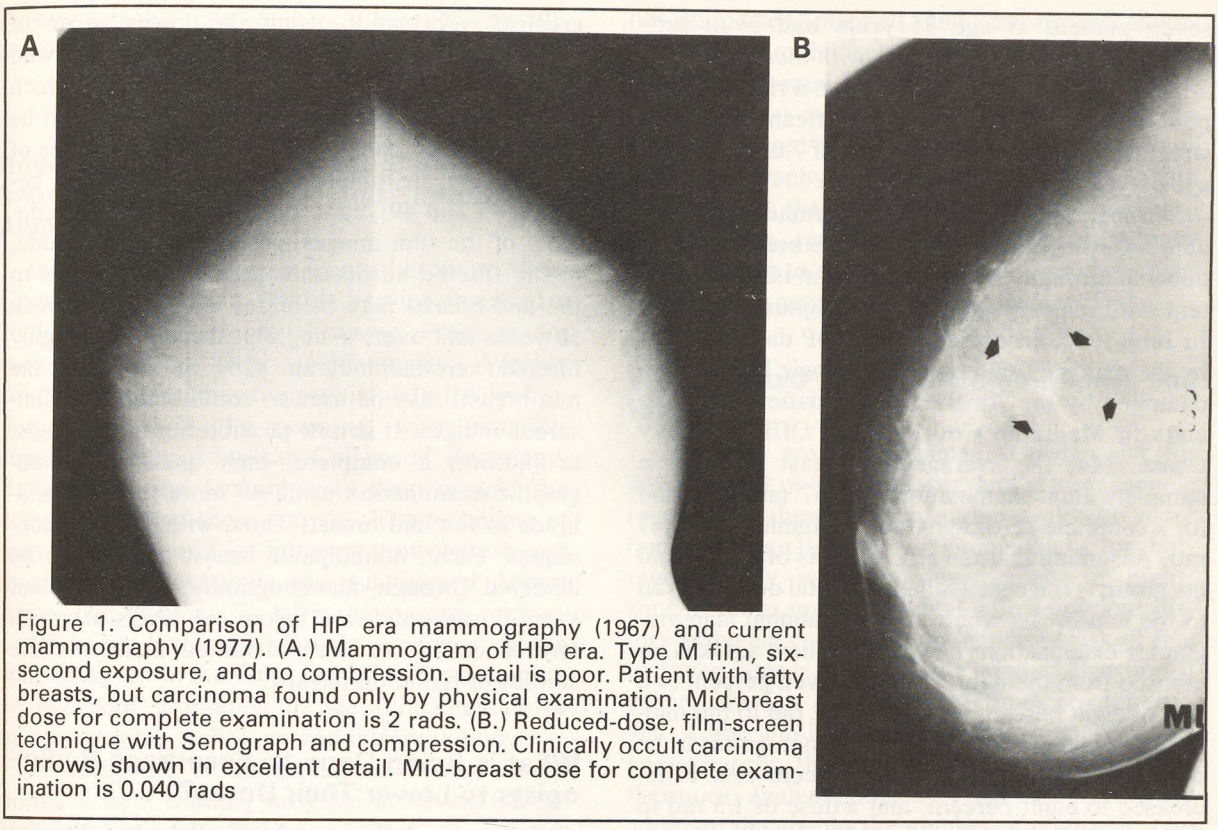

Figure 1. Comparison of HIP era mammography (1967) and current mammography (1977). (A.) Mammogram of HIP era. Type M film, six-second exposure, and no compression. Detail is poor. Patient with fatty breasts, but carcinoma found only by physical examination. Mid-breast dose for complete examination is 2 rads. (B.) Reduced-dose, film-screen technique with Senograph and compression. Clinically occult carcinoma (arrows) shown in excellent detail. Mid-breast dose for complete examination is 0.040 rads

for the Detection of Breast Cancer, issued in February 1977, noted that epidemiological studies revealed an excess of breast cancer in three groups: American women treated with x-radiation of the breast for postpartum mastitis; American and Canadian women subjected to multiple fluoroscopic examinations of the chest during artificial pneumothorax treatment of pulmonary tuberculosis; and Japanese women surviving atomic bomb irradiation.[11]

It must be noted that in two of these three studies, those on the women who were fluoroscoped and on the Japanese women, the risk of radiation decreased with age. The risk appeared to be greatest in young women, and a considerably lower risk was observed in women over 35 years. In the postpartum mastitis study there was no difference in risk by age, but few women in that study were over the age of 35 years. Furthermore, while the relationship between dose and response (number of cancers) was assumed to be linear, at the lowest dose levels measured or recorded (0 to 9 rads), there was no difference in the number of breast cancers between the women who were not exposed to radiation and those who were exposed. Thus, it seems that women at greatest risk of breast cancer, those over 40 years, have the least risk of developing cancer as a result of radiation to the breast. And, in fact, in two of the three studies evaluated by Upton, little or no risk was observed.

According to Upton, a *single* mammographic examination performed with a technique that involves an average dose to the breast of less than 1 rad should be expected to increase a woman's subsequent risk of developing breast cancer by *much less* than one percent of the natural risk of

seven percent at age 35 years and *by a progressively smaller percentage with increasing age at examination thereafter*, ie, from a risk of seven percent (since 1 out of 14 American women is struck by breast cancer) to a risk of 7.07 percent at age 35 years.

Through the BCDDP data, information is available regarding the least dose to the breast now attainable through mammography that is still consistent with maintenance of high diagnostic quality. In June 1977, according to BCDDP data gathered by the regional Centers for Radiologic Physics and compiled by the American Association of Physicists in Medicine Coordination Office, Chevy Chase, Md, the average mid-breast dose for a complete film examination was 67 millirads and for a complete xeroradiographic examination, 0.61 rad. Assuming that the risk analysis of Upton and his group is the best available, a total dose of 1 rad to the mid-breast would allow 13 annual mammographic examinations before the patient's risk is increased from the natural risk of seven percent to a risk of eight percent. A dose of 1/2 rad to the mid-breast would permit 26 annual mammograms to be performed before this seven percent risk is increased to eight percent; and a dose of 1/3 rad to the mid-breast would permit 39 annual mammograms to occur before the risk is increased to eight percent.

At the University of California, Los Angeles, (UCLA), using the Kodak Min R film-screen technique with a Senograph x-ray unit, the mid-breast dose is 40 millirads for a complete two-view examination. At this dose level, approximately 300 annual mammographic examinations are possible before risk is increased by one percent.

Xeromammography and film-screen mammography, while excellent methods of breast cancer detection, have their advantages and drawbacks. Relative soft-tissue densities are sometimes more reliably evaluated in film-screen images, while calcifications are sometimes more reliably evaluated in xeromammographic images. Film-screen mammography tends to record fatty or fibrofatty breasts more reliably than xeromammography, while the latter tends to record dense, dysplastic breast tissue more reliably than the former.

At UCLA, both film-screen and xeromammographic techniques are available, and the mammographic examination is tailored to obtain the greatest information using the lowest dose of radiation possible. For women under 35 years who have strong indications for mammography, which usually means signs or symptoms which could be those of breast cancer, two film-screen images of each breast are obtained. For some women between 35 and 49 years, depending upon the contents of the film images, a single negative-mode, highly filtered xeromammogram (150 millirads to the mid-breast) may be added. For some women 50 years and over, a single positive-mode, highly filtered xeromammogram (200 millirads to the mid-breast) may be used to complement the film-screen images. It is now possible for a radiologist to perform a complete, high quality mammographic examination using no more than 500 millirads to the mid-breast. Thus, with current techniques, early, nonpalpable breast cancer can be detected through mammography with resultant x-ray dosages that are below the levels at which any cancers have been identified in any of the studies of radiation hazard.

What Is Being Done to Encourage Radiologists to Lower Their Doses?

Six regional Centers for Radiological Physics have been established by the National Cancer Institute. These centers are charged with the responsibility of providing radiation physics reviews of the Breast Cancer Detection Demonstration Projects. For quality assurance of facilities that are not federally funded, local physicists are available. The Bureau of Radiological Health of the Food and Drug Administration has developed a state-based Mammography Quality Assurance Program to minimize patient exposure for mammography and to improve image quality. The program is known as Breast Exposure: Nationwide Trends (BENT). The program operates in four phases: groundwork, evaluation, follow-up survey, and reevaluation. Facilities are mailed a dosimetry card for each mammographic unit. The card is exposed as if it were a breast and then returned for analysis to the state-based agency. The facility receives a report on its exposure. Very high or unusually low dose reports lead to follow-up visits by state physics personnel. Such vistors recommend how to improve mammographic technique. Finally, the effects of implementing these recommendations are assessed by a sub-

sequent mailing of dosimetry cards several months later.

How Education in Mammography Yields Improved Techniques and Interpretive Ability

In the 1960s, the Cancer Control Program of the United States Public Health Service financed a National Mammography Training Program for radiologists and their technologists. Weekly courses were taught at approximately ten institutions throughout the country, with materials supplied by the American College of Radiology. Radiologists and technologists from around the country attended these courses. The technique of mammography and its interpretation were based largely on the technique and teachings of Robert Egan. The teaching file of mammograms and accompanying text were superb examples of the state of the art in the 1960s and offered radiologists an excellent grounding in the fundamentals of mammographic technique and interpretation.

In 1975, the National Cancer Institute supported a new training program at seven US institutions, one of which was UCLA, in a three-year effort to reorient radiologists and their technologists in more advanced mammographic techniques and interpretation for the detection of *early* breast cancer. At these seven teaching institutions, highly filtered xeromammography, reduced-dose film-screen mammography, physical examination, and thermography were taught through on-the-job training as well as didactic teaching and audiovisual materials supplied by the American College of Radiology. Anatomic, physiologic, and pathologic correlation were stressed, as were the need and reasons for dose reduction. Epidemiology, preoperative needle localization of clinically occult suspicious lesions, and specimen radiography were fundamental components of these one-week-long, continuous training programs.

During the time that these major training efforts were underway and during the interval between them, the American College of Radiology and many interested mammographers and technologists have presented local postgraduate refresher courses and workshops in mammography. For the past 16 years, the American College of Radiology has supported, planned, and coordinated annual week-long multidisciplinary conferences and workshops aimed at earlier detection and treatment of breast cancer. While all of these programs have stimulated the training of radiology residents in mammography, a simple but equally important stimulus was the decision of the American Board of Radiology, several years ago, to present questions relating to mammography in both their written and oral certifying examinations.

Who Should Have Mammography and When?

Are there groups of women at higher risk for development of breast cancer, and is it reasonable to examine these women earlier and with more regularity than the average? Some risk factors correlate highly with the development of breast cancer: for example, a patient with a previous history of breast cancer has an increased risk of five to seven times; if a patient's mother had breast cancer, there is a two to three times greater risk; and if the mother had bilateral premenopausal breast cancer, the increased risk is ninefold. Furthermore, evidence indicates that risk factors are additive; the greater the number of relatively low-level risk factors, the greater the chance of breast cancer.

While the BCDDP data are tainted by the absence of a control group of women, the high rate of detection of early cancer in women below 50 years of age merits further evaluation. Summing up his personal views of the current mammography controversy, Samuel Thier, Chairman of the 1977 Blue Ribbon National Institutes of Health/National Cancer Institute (NIH/NCI) Consensus Development Panel stated:

> It seems ethically defensible to re-evaluate the benefits of screening for women in the group 40 to 49 years old and to design the evaluative study to answer questions on the relative contributions of physical examination and x-ray mammography in screening. . . .It is hard to accept the idea that only expensive, lengthy, randomized clinical trials stand between the present controversy and the answers to the key questions. However, if such trials are the only solution, the sooner they are begun the sooner answers will be available.[12]

Clearly, with the striking technical advances and lower doses that are now possible in mammography compared with the HIP experience, randomized controlled trials under the age of 50

years, as advocated by the Beahrs Group and by Dr. Thier, are defensible. They are the only way to resolve questions concerning: (a) the magnitude of benefit achieved in screening with mammography and physical examination under the age of 50 years; (b) the magnitude of benefit due to mammography alone in this age group; and (c) the effect on benefit when screening is scheduled less frequently than annually. The next move seems to be up to the National Cancer Institute.

What can now be considered a reasonable policy for the performance of mammography? Dr. Richard Lester,[13] Chairman of the American College of Radiology Committee on Mammography and Diseases of the Breast, has proposed the following policy, one which this author believes is reasonable, given the present knowledge of benefit and potential risk:

A. Mammography should be performed at any age when clinical findings indicate a significant suspicion of cancer. *The importance of this indicator for mammography has been reiterated over and over again, most recently by the Consensus Development Panel in the NIH/NCI hearings of September 1977.* No criticism has ever been leveled at this indicator for mammography.

B. Mammography should not be performed in women under the age of 35 years except when there are specific strong clinical indications. The incidence of carcinoma in this age group is low.

C. A baseline mammogram should be performed in the age period 35 to 40 years because:

1. A small and significant number of early cancers will be detected.
2. A baseline study provides the groundwork for assessing subtle changes in subsequent mammograms that may indicate mammary cancer.
3. There is increasing evidence that the radiologic appearance of breast patterns can be used as indicators of higher or lower risk categories.

D. Periodic mammography at low-level radiation factors may be performed in women between the ages of 35 to 49 years, but the periodicity of such examinations should be determined by analysis of relative risk factors.

E. For women 50 years of age and older, the National Cancer Institute agrees that annual or other periodic mammography is statistically justified to screen asymptomatic women for breast cancer.

Conclusions

Early diagnosis when cancer is localized to the breast without axillary metastasis has been proved to result in much higher survival rates. Mammography is capable of detecting breast cancer in a preclinical state, before the appearance of a palpable mass. That the performance of mammography in such women will result in higher survival rates appears incontrovertible. The radiologist is responsible for performance of the highest quality of examination with the lowest dose feasible. In such a setting, the risk-benefit ratio appears clearly favorable.

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