"Early" Breast Cancer Detection Using Techniques Other Than Mammography

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X-ray mammography is the only imaging method currently available with any proven efficacy for screening to detect early-stage, clinically occult breast cancer. Sonography has a limited role in the differentiation of cystic from solid masses and as a guide for aspiration and preoperative localization of selected breast lesions. Computed tomography has a more limited role to determine the spatial orientation of a lesion detected only in the lateral mammographic position. All other imaging methods should be considered experimental at this time.

The past 15 years has seen a burst in technologic activity aimed at the early detection of breast cancer through various imaging methods. Concerns about the possible radiation induction of breast malignancy raised in the 1970s [1] spurred the development and modification of x-ray systems to perform high-quality mammography at low doses, and at the same time stimulated the development of imaging techniques not requiring ionizing radiation.

Since the mortality reduction from screening demonstrated by the Health Insurance Plan of New York study in the 1960s [2], the efficacy of x-ray mammography was demonstrated by the Breast Cancer Detection Demonstration Project (BCDDP) in the 1970s. The BCDDP confirmed the ability of x-ray mammography to detect clinically occult breast cancers 1 cm or less in diameter as well as intraductal carcinoma [3]. With these “early” breast cancers, the incidence of positive lymph nodes in the axilla at the time of diagnosis was 14%-15%. In the BCDDP, larger cancers that were more readily palpable had an incidence of positive lymph nodes that was twice that number. Since the prognosis in breast cancer relates to the size of the tumor and the status of axillary lymph nodes at the time of diagnosis, the term “early breast cancer” as used here will denote tumors that are 1 cm or smaller or those that are totally intraductal.

At present, x-ray mammography remains the only imaging method suitable for screening asymptomatic women, with a proven capability of detecting nonpalpable, clinically occult, early-stage breast cancer. Although carefully executed clinical trials have not yet shown other imaging systems to be suitable for screening, several have adjunctive roles in lesion evaluation.

Detection vs. Diagnosis

In 1979, Moskowitz [4] stressed the important distinction between detection and diagnosis. Inaccurate use of these two terms has led to much of the confusion concerning mammography’s role in breast evaluation. Detection can be defined as the ability to find breast cancer in women who are clinically asymptomatic and in whom the cancer is not detectable by physical examination. Since prognosis relates to the stage of the lesion, an efficacious screening method must be able to detect breast cancer at an earlier stage than palpation.

Diagnosis, on the other hand, relates to the further characterization of the lesion.
whose presence is already manifest. A "diagnostic" evaluation is efficacious if it can lead to a less invasive resolution of the lesion in question. A system, such as mammography, with the demonstrated ability to detect occult cancer may be poor at diagnosis. In fact, unless a lesion has the "classic" appearance of a spiculated, poorly defined mass, mammography is not a truly diagnostic test. Because of the overlapping appearance of benign and malignant lesions (fig. 1), mammography should be used to detect lesions but not to decide that a lesion is benign unless it is a densely calcified, involving fibroadenoma or a lucent lipid lesion. X-ray mammography is primarily a screening method. Even in the symptomatic patient, it should be used to "screen" the rest of the symptomatic breast and the contralateral breast [5]. X-ray mammography should be used to increase the level of concern but should never be relied on to exclude the presence of malignancy.

Conversely, a method such as sonography that is useful in diagnosis by differentiating cystic from solid may have no efficacy in detection. There is persistent confusion concerning this dichotomy. An understanding of the importance difference between detection and diagnosis and the careful clarification of these differences for our clinical colleagues will lead to more efficacious use of the various methods.

**Sonography**

The most useful adjunct to x-ray mammography at this time is sonography. Initial optimism concerning the ability of sonography to detect early breast cancer has not been supported by clinical trials. Despite the development of sono-graphic scanning systems capable of evaluating the entire breast, there is no evidence from objective clinical studies to suggest that sonography can detect clinically occult breast cancer. Our own experience with whole-breast water-path sonography, used in a blind comparison of physical examination, sonography, and mammography, demonstrated that sonography was only capable of detecting palpable breast cancer. Breast cancer is almost always hypoechoic and may be difficult to distinguish from the inhomogeneous, variably hypoechoic regions of the normal breast (fig. 2). Posterior acoustic shadowing, which has been described as a primary sign of carcinoma, is often absent [6] (fig. 3), and benign lesions as well as normal tissue can produce identical shadowing. Sickles et al. [7] reported a similar experience.

Sonography does have a limited role as a diagnostic procedure to differentiate cystic from solid masses. It should be clearly understood, however, that sonography should not be used to differentiate benign from malignant solid lesions. There is a significant overlap in the appearances of benign and malignant solid masses. Sonography only defines shapes and reflecting surfaces, and a round, well circumscribed carcinoma with a homogeneous tissue texture can look identical to a benign fibroadenoma (fig. 4). Furthermore, benign lesions can have the "classic" malignant appearance of an irregularly shaped structure with an inhomogeneous or absent echo texture with posterior shadowing (fig. 5).

The efficacy of sonography lies in the differentiation of cystic from solid lesions [8] and as a guide for aspiration or preoperative localization [9]. Cyst/solid differentiation by sonography can supplement clinically guided needle aspiration. Cysts often have thick walls and, because of their relative mobility in the breast tissue, can be difficult to puncture. Cysts that have eluded clinical aspiration have been successfully aspirated under sonographic guidance, obviating surgical excision.

Sonography has also been useful in a selected number of patients to permit the positioning of a wire guide through a needle to direct the surgical excision of nonpalpable solid masses or suspicious masses for which aspiration attempts have failed.
Computed Tomography

Although it is an x-ray technique, computed tomography (CT) should be considered a nonconventional radiographic method. Work done by Chang et al. [10] suggests that breast cancer may have an avidity for intravenously administered iiodinated contrast material. This has not yet been confirmed by other investigators due to the limited availability of CT scanners and the rigorous and tedious pre- and postcontrast scans that are required. In addition, the radiation dose from CT is higher than conventional mammography and exposes the entire thorax to the radiation.

It has been our experience that computed tomography of the breast is most useful in determining the three-dimensional location of a lesion that is seen only in the lateral conventional mammographic views (fig. 6). Using a technique previously described [11], accurate placement of wire guides can be performed under CT guidance to locate these lesions for surgical excision.

Thermography

In theory, thermography is ideal because it is a totally safe, passive system for measuring the temperature of the skin. To be detected, breast cancer has to generate greater heat than normal breast tissue, and this heat must reach the skin through conduction or convection. Rapidly growing breast cancers seem to be hypermetabolic and generate more heat. However, there are significant numbers of breast cancers that do not. Furthermore, the breast is an excellent insulator, and heat from small deep lesions may not reach the skin. There are no data to prove that thermography is useful as a screening method to detect clinically occult, early-stage breast cancer. Several investigators have suggested that an abnormal thermogram may be a strong indicator of risk for the subsequent development of breast cancer [12]. This is paradoxical when it is acknowledged that small cancers that are detected by other means often do not alter the thermographic pattern. The suggestion that thermography may detect more rapidly growing tumors because of their increased metabolic production bears further investigation. The high false-positive and false-negative rates for thermography make it unjustifiable at this time for screening. Thermography should still be considered experimental until its role (if any) is more clearly defined [13].

Transillumination

Much interest has been generated in the past few years concerning the use of transmitted "visible" light through breast tissue. This technique was originally described in the 1920s and has been recently reevaluated making use of new technology that permits the selection of the longer, far-red and near-infrared wave lengths of light that are more readily transmitted through breast tissue. In some instruments, computer manipulation is used to enhance this effect. The basic weakness of transillumination is that only a very small fraction of 1% of this light is directly transmitted through the breast. This severely compromises the resolving power of such a system due to the overwhelming scattering and diffusion of the light. The equipment available today for transillumination uses a diffuse light source, further degrading any resolving capability. Sickles' [14] experience with over 1000 women having high-quality x-ray mammography and transillumination demonstrated the inability of transillumination to detect small early breast cancer. Bartram and Crow [15], however, using computerized equipment, believe that by firm compression of the breast, lesions can be brought closer to the skin surface opposite the incident light and thus one can take advantage of the light-scattering in the rest of the breast to silhouette a
lesion just beneath the skin. This possibility remains to be conclusively demonstrated, and a clinical trial is underway.

If, in fact, there is any unscattered light that passes through the breast, it is possible that using the coherent light of low-energy lasers and scatter elimination techniques, transillumination might one day have a significant role in screening. Until proof is available from blind clinical trials, however, transillumination should be considered a totally experimental technique with no proven clinical efficacy.

Magnetic Resonance Imaging

Evaluation of the breast by MRI is currently at a very early stage. Preliminary work by El Yousef et al. [16] has demonstrated a morphologic difference between some benign and malignant lesions, characterizing the irregular margins of breast cancer. This alone will probably be insufficient to justify the expense of MRI. Unique tissue signatures, differentiating benign from malignant lesions, would be of major importance by reducing the excision of benign masses, but these have not yet been proven in vivo. It seems that high-resolution surface coil equipment will probably be necessary for breast evaluation. Because of the cost and cross-sectional imaging nature of MRI, it is unlikely that it will develop into a screening method in the future, but a role in diagnosis is a distinct possibility.

Immunodetection

This is a category of techniques that relies on the as yet undemonstrated possibility that breast cancer cells have unique surface antigens. If such tumor-specific antigens are identified, monoclonal antibodies could be produced and labeled with radionuclide tracers. Administered intravenously, these labeled antibodies theoretically would adhere to breast cancer cells. With sufficient concentration of radionuclide and sensitive imaging systems, early detection of small lesions may be a possibility. To date, however, there have been no unique surface antigens discovered in human breast cancer [17]. In addition, the surface antigens of breast cancer cells seem to change over time. The most likely initial application for immunomaging will be the noninvasive evaluation of the axilla to establish prognosis by detecting cancer cells in axillary lymph nodes [18].

Minimal-Dose Digital Breast Radiography

The greatest impact in the near future in detecting breast cancer will most likely come from advances in digital radiography specifically designed for breast evaluation. A solid-state detector with a capability of spatial resolution greater than 5 line pairs/mm is currently under development (unpublished data). The coupling of high detector efficiency with scatter-reducing pre- and postcollimation slit scanning will permit high-resolution radiographic imaging at doses that are significantly lower than currently available film/screen technology. If successful, minimal dose digital breast radiography will virtually eliminate the issue of radiation risk. The wide dynamic range of such a system and the ability for computer manipulation will combine the best characteristics of film/screen and xeromammographic imaging. The potential for dual-energy subtraction and further testing of Chang's hypothesis [10] using intravenous contrast material may produce significant improvements in radiographic detection of breast cancer.

REFERENCES