RADIONUCLIDE BREAST SCANNING IN CARCINOMA OF THE BREAST

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Radionuclide breast scans have been found to be positive in a high percentage of patients with carcinoma of the breast. This may be useful in providing independent corroboration in conjunction with other presently performed preoperative tests.

Mammography and thermography currently are the two most important techniques complementing the physical examination in detecting disease of the breast (*1*). Both mammography and thermography are capable of detecting impalpable disease. However, each of these techniques has certain limitations. Mammographic indications of carcinoma are not found in 4–8% of breast cancers (*2*). The false-negatives may lead the clinician to bias his clinical opinion and favor a benign lesion. Adenosis and dense breasts may obscure an underlying neoplasm on mammography. Furthermore, a false-positive incidence of about 6–10% is reported in interpreting mammograms (*2*). Thermography, although sensitive, is not specific. In view of these limitations the need for a complementary test, especially in an equivocal case, is highly desirable.

Radionuclides are currently extensively utilized in the management of breast cancer; however, their role has been relegated mainly to the detection of distal metastasis to bone, brain, or liver. A review of the literature shows many attempts to utilize various radionuclides for the primary detection of breast cancer but most have been relatively unsuccessful. This study reports the use of two scanning agents, ^{99m}Tc-polyphosphate (New England Nuclear) and ^{99m}Tc-diphosphonate (Procter and Gamble and Medi-Physics), in the evaluation of patients suspected of having breast cancer. These agents are normally utilized when performing a bone scan in the staging of patients suspected of having bone metastasis.

In performing the bone surveys, it has been observed that the primary breast lesion could be identified by increased uptake of the bone-scanning agents (*3*). Consequently, a group of 42 patients has been studied to form a preliminary evaluation of the usefulness of the ^{99m}Tc-diphosphonate and polyphosphate compounds in the detection of primary breast cancer.

MATERIALS AND METHODS

Forty-two patients were injected alternately with 15mCi of ^{99m}Tc-polyphosphate and ^{99m}Tc-diphosphonate. Breast images were obtained at 3 hr post-injection. The patients were placed on a canvas stretcher in the lateral decubitus position with the detector of an Anger camera placed beneath the stretcher in close proximity with the breast. A lead sheet with a circular cutout was placed under the thorax so that only the photons emitted from the breast and adjoining anterior chest wall would be detected. A ^{57}Co marker was placed at the level of the nipple to provide an anatomic landmark. A low-energy high-sensitivity parallel-hole collimator was used. The initial breast image was formed with the accumulation of 250,000 total counts. Then the image of the opposite breast was accumulated for an equal time interval. The average time duration for each view was 360 sec.

The results of the breast scans are summarized in Tables 1 and 2. A positive breast scan indicates a focal area of increased radionuclide uptake within the tissues of the examined breast (Figs. 1 and 2). A negative breast scan had no focal areas of increased uptake and the activity appeared homogene-

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TABLE 1. BREAST SCAN POSITIVE

Patient	Age	Solitary mass palpable	Pathology
HE	67	+	Carcinoma
RK	52	+	Carcinoma
PS	66	+	Gynecomastia
IV	63	+	Carcinoma
LC	74	+	Carcinoma
RC	80	+	Carcinoma
ET	83	+	Carcinoma
MG	76	+	Carcinoma
SC	52	+	Carcinoma
MS	69	+	Carcinoma
EH	42	+	Abscess
MF	16	+	Gynecomastia*
BB	75	+	Carcinoma
MG	71	+	Fibrosis
PL	69	+	Carcinoma
AW	74	+	Carcinoma
MS	58	+	Carcinoma
AS	83	—	Carcinoma
FR	59	—	Chronic inflammation and sclerosis

* Indicates histologic correlation was not obtained because either no evidence of breast pathology was thought to be present or the diagnosis could be made on clinical or mammographic criteria or both.

ous within the breast but diminished towards the skin.

RESULTS

Twenty patients having no solitary mass and 22 patients having a solitary mass palpated by the referring physician were studied. In 15 patients histologic correlation was not obtained as either no evidence of any breast pathology was present or the diagnosis of a benign disorder could be made on the basis of the supportive clinical and mammographic criteria. In 14 of the 15 patients no solitary mass was palpable and breast scans were negative. Of these, 11 were felt to be free of breast pathology, 2 had evidence of fibrocystic disease on mammography, and 1 was postpartum and lactating. The remaining patient in this group had a positive scan and evidence of gynecomastia on mammography.

Of the 27 patients in whom histologic correlation was available, 14 of 17 patients with carcinoma had positive breast scans. The remaining ten had a variety of benign disorders of which six had negative breast scans. Positive breast scans occurred in four patients with proven benign lesions (gynecomastia, abscess, fibrosis, and chronic inflammation with sclerosis, respectively).

DISCUSSION

The first published report of radionuclide breast scanning was in 1948 by Low-Beer in which ^{32}P was given to 25 patients with breast masses (*4,5*). Of the 17 patients with proven carcinoma, 16 patients showed an increase in activity of 25% or more over the mass when compared with the corresponding area of the opposite breast and adjacent areas of the same breast. All eight patients with benign masses showed an increase in activity of less than 25% over the mass when compared with other areas of either breast. However, further studies done by the same group showed that false-negatives could occur in mucinous carcinomas, deeply situated carcinomas, or very small primary carcinomas. False-positives could occur in benign inflammatory conditions and fibrocystic disease (*6*). Since the maximum range of the beta particles of ^{32}P in body tissue is about 8 mm, it is not surprising that lesions deeper than 0.5 cm from the surface produced no increase in counting rate. Other investigators obtained similar results (*7–10*).

The use of ^{42}K administered to 102 patients with benign and malignant breast tumors was first publicized in 1955 by Baker, et al (*11*). The authors found that 80% of proved malignant breast tumors caused an increase in the local counting rate of greater than 20% over background. However, no patient with a benign breast lesion showed an increase in the local counting rate of greater than 20%.

In 1952, Ruffo and Lundaburn showed that breast carcinoma retained more rubidium than normal breast tissue (*12*). Sklaroff in 1958 used ^{86}Rb in 24

TABLE 2. BREAST SCAN NEGATIVE

Patient	Age	Solitary mass palpable	Pathology
MG	24	—	Normal*
HS	65	—	Fibrocystic disease
ES	64	—	Fibrosis
JS	29	—	Lactating breasts*
JW	24	—	Normal*
DL	25	—	Normal*
FH	24	—	Normal*
MM	56	—	Normal*
PM	46	—	Fibrocystic disease*
DV	27	—	Normal*
AF	37	—	Normal*
LH	81	—	Normal*
MC	69	—	Normal*
BH	74	—	Cellulitis
CW	33	—	Fibrocystic disease*
ER	53	—	Carcinoma
FS	76	—	Normal*
MG	73	—	Normal*
BM	42	+	Fibroadenoma
BM	23	+	Fibroadenoma
IR	47	+	Cyst
HW	68	+	Carcinoma
TS	80	+	Carcinoma

* Indicates histologic correlation was not obtained because either no evidence of breast pathology was thought to be present or the diagnosis could be made on clinical or mammographic criteria or both.

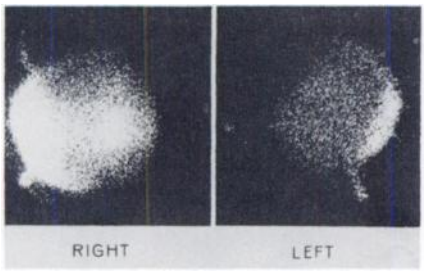

FIG. 1. Focal area of increased radionuclide uptake within carcinoma in right breast in Patient IV.

patients with breast carcinoma and 12 patients with benign breast tumors (*13*). He concluded that the uptake of ^{86}Rb by malignant breast tumors was not sufficient to be of diagnostic value.

Other radionuclides have also been used for external counting over breast masses: ^{131}Cs, ^{197}Hg-chlormeridrin, ^{67}Ga-citrate, and ^{206}Bi-citrate (*8,14–16*). However, it wasn't until 1966 that Whitley, et al reported a photoscan that showed increased ^{99m}Tc-pertechnetate activity in a case of breast carcinoma (*17*). In the following year, Bonte, et al reported two fair and two poor rectilinear scans of breast carcinomas using ^{131}I-human serum albumin (*18*). In 1969 Buchwald reported 18 out of 26 breast carcinomas visualized by rectilinear scan using $^{197}HgCl_2$ (*19*). In 1972 Sannazzari, et al using $^{197}HgCl_2$ were able to show increased activity in the breast of nine out of ten patients with breast carcinoma by rectilinear scan (*20*). Papavasiliou, et al reported increased activity when imaging ^{87m}Sr in the breast of two patients with breast carcinoma (*21*). Winchell, et al in 1970 imaged ^{67}Ga-citrate in a patient with breast carcinoma but this failed to show any uptake in the tumor (*22*). The following year Lavender, et al reported very poor results using ^{67}Ga-citrate with only 4 of 25 patients with breast carcinoma showing localized uptake (*23*). Later in the same year, Fogh showed that ^{67}Ga-citrate could be imaged in five out of seven patients with breast carcinoma but not in eight patients with benign tumors (*24*). This was the first reported series of cases using a scintillation camera. Somewhat later, Langhammer, et al reported poor results when imaging breast cancer using ^{67}Ga (*25*).

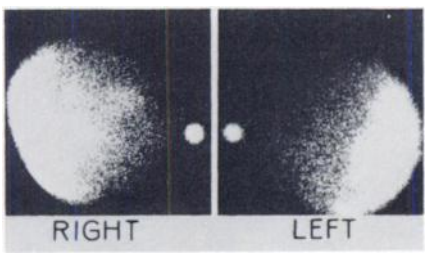

FIG. 2. Focal area of increased radionuclide uptake within carcinoma in right breast in Patient HE.

Eskin and Parker have been using ^{131}I to obtain iodine uptakes over each breast. They found that uptakes of less than 5% are normal whereas uptakes greater than 9% are usually associated with dysplasia or neoplasia (*26*). They suggested that variations in iodine metabolism may be the reason for this difference. Recently, Eskin has been using ^{123}I instead of ^{131}I with similar results (*27*).

Cancroft and Goldsmith reported visualization in each of four breast carcinomas using ^{99m}Tc-pertechnetate scintigraphy (*28*). Villarreal, et al reported the use of ^{99m}Tc-pertechnetate as a breast-imaging agent in 18 women with breast nodules including 3 patients with proven breast carcinoma (*29*). All three patients with breast carcinoma had positive localization by breast scintigraphy whereas 14 of the remaining 15 showed no localization. Matsui, et al reported negative results in a single case using ^{99m}Tc-diphosphonate to scan a breast tumor (*30*). However, the breast had not been examined histologically. Berg, et al recently reported ^{99m}Tc-diphosphonate concentration in two patients with primary breast carcinoma (*3*).

Our findings show that ^{99m}Tc-diphosphonate and ^{99m}Tc-polyphosphate both concentrate in tumors of the breast. In this series a positive breast scan was obtained in 82% of the patients with histologically proven carcinoma. Although 36% of patients with non-neoplastic lesions demonstrated positive scans, no normal patients had a positive scan. The study shows that the scan is fairly sensitive in demonstrating an underlying disorder of the breast, however, it is not sufficiently specific to allow differentiation of benign from malignant lesions. Although the study alone may be of limited value in detecting carcinoma of the breast, a positive or negative breast scan may be useful in conjunction with other tests.

Considering the relatively poor resolution of currently available radionuclide scanning instrumentation, we are led to expect that much smaller lesions could be detected with thermography or mammography. However, the degree of local involvement in the patient with known carcinoma of the breast is quite readily apparent in the scintiphotos of positive cases and may be more extensive than previously indicated by thermography or mammography. As such, this may be a useful test for evaluating the extent of the local disease and therefore selecting the type of surgery. This, in conjunction with the fact that distal bone metastasis can be simultaneously evaluated, makes it useful in the staging of patients preoperatively.

The mechanism of localization of both agents in

the lesions is not understood at this stage. Although increased vascularity may be a factor, a number of patients have demonstrated no abnormalities on the thermograms. This would suggest that local vascularity to the lesion may not be the sole factor. Other mechanisms such as selective uptake related to tissue factors or increased vascular permeability secondary to inflammation or associated with neovascularity must also be considered.

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