Bone Scintigraphy in Patients with Operable Breast Cancer Stages I and II. Final Conclusion after Five-year Follow-up

R. M. J. M. BUTZELAAR,* J. A. VAN DONGEN,† P. W. DE GRAAF† and J. B. VAN DER SCHOOT‡ *Department of Surgery, Sint Lucas Ziekenhuis, Amsterdam, The Netherlands, †Antoni van Leeuwenhoek

Ziekenhuis, The Netherland's Cancer Institute, Amsterdam, The Netherlands and ‡Department of Nuclear Medicine, University of Amsterdam, The Netherlands

Abstract—A 5-yr follow-up study was performed in 90 patients with stage I and II breast cancer who had a routine preoperative bone scan. The percentage of positive preoperative scans was 3.4%. Twenty-four of the 90 patients died within 5 yr. In all patients except five a follow-up scan was obtained. The results of our first study were confirmed. In only one of the three patients with a positive preoperative scan suspicious for bone metastases did bone metastases develop in this 5-yr follow-up study. One patient with an equivocal preoperative scan developed bone metastases. In 14 of the 16 patients with bone metastases and a positive scan in the follow-up period the preoperative scan was negative. From the preoperative and follow-up scan results we conclude that in stage I and II breast cancer there is no value in preoperative bone scanning. Routine bone scanning in the follow-up period appears to have little value in the asymptomatic patient.

INTRODUCTION

BONE scintigraphy is considered the best diagnostic method for bone metastases in patients with breast cancer. It is well known that both false-positive and false-negative results can be obtained.

Of all operable patients with carcinoma of the breast, treated in the belief that distant metastasis has not yet taken place, at least 25% will die of distant metastases within 5 yr. In 85% of such patients the post-mortem investigation reveals bone metastases [1, 2]. This was the main reason for assessing bone scintigraphy in patients before surgery. The finding of bone metastases would obviate the need for a patient to undergo a mutilating amputation.

In the period before 1977 most investigators [3-6] found changes indicating bone metastasis in about 25% of the preoperative scans. The advice to perform a routine preoperative bone scan in patients with breast cancer was, at that time, understandable. However, the staging of patients was not always accurate, or patients of all stages

were part of the study. In 1973 Green et al. [7] were the first to report a much lower frequency (10%) of positive preoperative scans in patients with stage I and II breast cancer. He questioned the value of routine bone scintigraphy in preoperative screening in this group of patients.

In the period 1977-1980 a number of publications [8-13] about preoperative bone scanning in breast cancer patients appeared. Although some authors [14] continue to find the same high percentage of positive scans as before, the percentage of positive bone scans in most of the studies varied from 1.8 to 3.5%. So the initial question of whether preoperative bone scintigraphy should be carried out then changed to a rejection of bone scanning as a routine procedure for patients with breast cancer. This is particularly true for stages I and II.

In the present paper we report the results of a follow-up study on the 90 consecutive patients whom we investigated from 1974 to 1976 [8]. At that time routine preoperative examination revealed 3.4% positive scans. In none of the patients with a positive scan suspect for bone metastasis was the existence of metastasis proven, so all patients were operated upon.

MATERIALS AND METHODS

All 90 patients who formed the basis of the publication in 1977 were re-analysed in January 1982. All patients had stage I or II breast cancer. In the follow-up period a bone scan was performed when the complaints of the patients suggested the possibility of bone involvement. A thorough history was taken every time the patient was seen. In the surviving patients a follow-up scan was performed at an average of 61.4 months after the preoperative scan. In the group of patients who died before the end of this follow-up study the bone scan was performed shortly before the patient died, in all but two patients. These two patients died suddenly, one with and one without clinical evidence of bone metastasis. On pathological examination of the surgical specimen, 16 of the 24 patients who died and 18 of the 66 patients who were alive at the end of the study had positive axillary nodes. Scans were made three hours after injection of 555 MBQ (15mCi) of ^{99m}Tc-diphosphonate (EHDP). The scans were made with a Toshiba Jumbo Gammacamera G.C.A. 401 with a 42,000-parallel-hole-resolution collimator (FWHM 8.1 mm on 10 cm). The scans were recorded as negative when no abnormal accumulation of radioactivity was seen and positive when there were clearly discernable hot spots, suggesting bone metastases that could not be explained by radiological features of benign disease. A scan was recorded as equivocal when only slight or questionable local augmentations of radioactivity were seen.

RESULTS

The results of the study are presented in Table 1. On completion of the study 24 of the 90 patients had died, 17 of them with proven bone metastases. Five patients died from causes other than breast cancer, two from cerebral metastases without evidence of bone metastasis. Of the 66 patients alive when the study was completed on 1 January 1982, three patients had proven bone metastases and five patients had non-osseous metastases. In

two of the patients who died and in three of the surviving patients, no follow-up scan was made for various reasons.

Of the 90 patients investigated, 76 had a negative scan preoperatively. Of 71 patients with a negative preoperative scan in which a follow-up scan was made, the scan remained negative in 55. In the remaining 16 patients a positive scan was found. In 14 patients bone metastases were demonstrated, and in two patients the scan was positive because of degenerative disease. Eleven of those 14 patients with bone metastases died before the end of this study.

In three patients who died with bone metastases an early follow-up scan showed no abnormalities, and for various reasons no further scans were made. Three patients with a negative follow-up scan died of unrelated disease.

Of the seven patients with a positive preoperative scan, the scan was suspect for bone metastases in only three patients. In the other four patients other reasons for a positive scan were found, namely Paget's disease, pansinusitis, lumbar degenerative change and a rib fracture. In only one of the three patients with a positive scan, suggesting bone metastasis, was bone involvement demonstrated in the follow-up period. This patient died of her disease. In the other two patients the scan turned out to be positive because of degenerative disease in one patient and converted to negative in the other patient. In the four patients with a false-positive preoperative scan the scan remained positive in the patients with Paget's disease, pansinusitis and lumbar degenerative disease. The scan of the patient with a rib fracture became negative.

Of the seven preoperative equivocal scans, four changed to negative in the follow-up period. In one patient, who died of her disease, bone metastases were shown to exist at the same place where the preoperative scan was equivocal. In two patients the scan remained unchanged and equivocal. These two patients died of causes other than cancer.

Table 1

		Follow-up bone scan $(n=85)$			
Preoperative bone scan $(n = 90)$		Positive (benign)	Positive (metastasis)	Equivocal	Negative
Negative	76	2	14		55
Equivocal Positive	7		1	2	4
(benign lesion) Positive	4	3			1
(metastasis?)	3	1	1		1

DISCUSSION

The results of this follow-up study confirm the conclusion of our publication in 1977: routine preoperative bone scanning in patients with stage I and II breast cancer is a superfluous examination.

Only one of the three patients with a preoperative positive scan suspicious for bone metastases eventually turned out to have bone involvement. Of the seven patients with an equivocal scan, the scan became positive and bone metastases were demonstrated in the same place in only one patient. Of the 76 patients with a negative preoperative scan, the scan became positive because of bone metastasis in 14 patients. In three patients who died with bone metastases, an early follow-up scan was negative. So finally, 16 of the 90 patients (18%) developed a positive scan caused by bone metastases in the follow-up period. In these patients the preoperative scan was negative in 14 patients, positive in one and equivocal in one patient.

In evaluating hot spots on the bone scan it is extremely important to use strict criteria. Experience is needed to prevent false-positive conclusions. In the early seventies too liberal interpretation of every radioactive accumulation on the scan might have been one of the reasons for

the many high percentages of positive scans found in some publications. Also, the staging of the patient was inaccurate in some studies and therefore comparison of the results was not reliable.

As mentioned before, no routine bone scans were performed in the follow-up period. The scan was performed for complaints suggesting bone involvement, or when other metastases became manifest. In the patients with bone metastases in this series, pain was the first symptom in nine patients, seven patients had metastases elsewhere before bone metastases became manifest and in two patients abnormal biochemical values were the first sign of bone metastases. In our series the bone scan was the first diagnostic finding in only two patients. At least part of the bone metastases would have been diagnosed earlier if routine follow-up scans were requested. At the moment, however, there is no evidence to suggest that earlier treatment of metastases improves survival. Thus there appears to be no argument for routine follow-up bone scans in patients with stage I or II disease. Only when complaints of the patient or other investigations suggest the presence of bone metastases should a bone scan be made in the follow-up period.

REFERENCES

- 1. Jaffe HL. Tumours and Tumorous Conditions of Bones and Joints. Philadelphia, PA, Lea & Febiger, 1958.
- 2. Robbins GF, Knapper WH, Barry J, Kripalani I, Lawrence J. Metastatic bone disease developing in patients with potentially curable breast cancer. Cancer 1972, 29, 1702-1704.
- 3. Galasko CSB. The detection of skeletal metastases from mammary cancer by gamma camera scintigraphy. *Br J Surg* 1969, **56**, 757-764.
- Citrin DL, Bessent RG, Greig WR, McKellar NJ, Furnival C, Blumgart LH. The application of ^{99m}Tc phosphate bone scan to the study of breast cancer. Br J Surg 1975, 62, 201-204
- 5. Campbell DJ, Banks AJ, Oates GD. The value of preliminary bone scanning in staging and assessing the prognosis of breast cancer. *Br J Surg* 1976, **63**, 811-816.
- 6. Roberts JG, Gravelle IH, Baum M, Bligh AS, Lesh KG, Hughes LE. Evaluation of radiography and isotopic scintigraphy for detecting skeletal metastasis in breast cancer. *Lancet* 1976, i, 237-239.
- 7. Green D, Jeremy R, Towson J, Morris J. The role of fluorine 18 scanning in detection of skeletal metastases in early breast cancer. Aust NZ J Surg 1973, 43, 251-254.
- 8. Butzelaar RMJM, van Dongen JA, van der Schoot JB, van Ulden BJG. Evaluation of routine pre-operative bone scintigraphy in patients with breast cancer. Eur J Cancer 1977, 13, 19-21.
- 9. Baker RR, Holmes ER, Alderson PO, Khouri NFM, Wagner HN. An evaluation of bone scans as screening procedures for occult metastases in primary breast cancer. *Ann Surg* 1977, 186, 363-367.
- Gerber FH, Goodreau JJ, Kirchner PT, Fouty WJ. Efficacy of preoperative and postoperative bone scanning in the management of breast carcinoma. N Engl J Med 1977, 297, 300-303.
- 11. Nomura Y, Kondo, H, Yamagata Y et al. Evaluation of liver and bone scanning in patients with early breast cancer, based on results obtained from more advanced cancer patients. Eur J Cancer 1978, 14, 1129-1135.

- 12. Bishop HM, Blamey RW, Morris AH et al. Bone scanning: its lack of value in the follow-up of patients with breast cancer. Br J Surg 1979, 66, 752-754.
- 13. Wilson GS, Rich MA, Brennan MJ. Evaluation of bone scan in preoperative clinical staging of breast cancer. Arch Surg 1980, 115, 415-418.
- 14. Furnival CM, Blumgart LH, Citrin DL, McKillop JH, Fogelman I, Greig WR. Serial scintiscanning in breast cancer: the indications and prognostic value. *Clin Oncol* 1980, 6, 25-32.