

Bone Metastases in Primary Operable Breast Cancer. The Role of a Yearly Scintigraphy*

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Abstract—In 231 patients with primary operable breast cancer bone scintigraphies were performed yearly from the second to the 6th year until recurrence irrespective of localization was diagnosed, another cancer was detected, or the patient refused further follow-up or died. During the observation period (from 2 up to 7 years after surgery) 13 patients (5.6%) had bone metastases verified by X-ray or histology within 12 months after the last bone scintigraphy. The scintigraphy was positive in only 7 of these patients. The yearly incidence of bone metastases varied between 0.6 and 2.6%. Due to this low incidence and a low cost/benefit, we conclude that a fixed schedule of repeated scintigraphies in primary operable breast cancer patients otherwise free of apparent disease is not justified.

INTRODUCTION

BONE scintigraphy has for several years been considered the most sensitive of the many biochemical and imaging techniques for the detection of bone metastases in breast cancer patients. Hence, the method has been used increasingly in peri-operative screening for osseous involvement as well as for post-operative evaluation of patients otherwise free of apparent disease.

Previously we have evaluated the diagnostic and prognostic value of bone scintigraphies performed within 30 days of the operation and 6 and 12 months thereafter in breast cancer on a nationwide basis [1-3]. We found, in agreement with others [4, 5], that a fixed schedule of repeated scintigraphies or radiograms in patients with primary operable breast cancer is not justified, at least within 12 months after surgery, because of the small number of patients developing radiographically demonstrable metastases. The purpose of the current study was to examine the value of repeated scintigraphies at fixed intervals in patients with primary operable breast cancer having had a yearly scintigraphy from 2 to 6 years after the operation.

MATERIAL AND METHODS

In 1978 and 1979, 1060 patients with primary operable breast cancer (DBCG stage I and II) entered nationwide randomized adjuvant therapy protocols according to their clinical and menopausal state [6]. The present paper deals with 260 of these patients scanned at 3 nuclear medical centers. Bone scintigraphies were performed at the time of operation, and at 6 and 12 months, 2, 3, 4, 5 and 6 years after surgery, provided that (1) no metastases including local relapse were diagnosed, (2) no other cancer had been detected, or (3) the patient did not refuse further follow-up. The results of the 3 first scintigraphies have been reported previously [1, 2]. Of the 260 patients 29 patients left the program within the first 2 years after operation due to the above-mentioned reasons, leaving 231 patients for the present analysis.

Each scintigram was characterized according to a standardized grading defined previously [1]. The grading can be summarized as follows; grade 0: no abnormal finding; grade 1: benign pathology most likely, but malignancy cannot be excluded with certainty; grade 2: malignant pathology most likely, but benign cause cannot be excluded; grade 3: malignant cause almost certain. For practical purposes grades 0 and 1 were combined as grade 1 (negative scintigraphy). If a patient had clinical symptoms of bone metastases and/or grade 2 or 3

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Table 1. Causes for leaving the fixed schedule of bone scintigraphies and the time of the last scheduled scintigraphy in 81 patients with primary operable breast cancer from 2 to 6 years after operation

Cause	Year for the last scheduled scintigraphy after surgery					Total number of patients
	2	3	4	5	6	
Relapse*	13	8	8	3	3	35
Another cancer	1	1	1	2	—	5
Death†	4	1	2	—	—	7
Did not wish to participate any more	1	11	—	6	3	21
Bone metastases						
positive scintigraphy‡	3	1	2	0	1	7
negative scintigraphy‡	3	1	0	2	0	6
	<div> <div>6</div> <div>2</div> <div>2</div> <div>2</div> <div>1</div> </div>					13

*In these patients no bone metastases were diagnosed within 12 months after the last scintigraphy.

†The death was caused by unrelated disorders, and no bone metastases were detected at possibly autopsy.

‡Results of the last scheduled scintigraphy performed within 12 months before the detection of bone metastases by other methods.

(positive) scintigraphy an X-ray of the bone in question was taken.

The records of all 231 patients were reviewed. The clinical course, i.e. relapse with or without bone metastases, occurrence of a different cancer, refusal of further follow-up, or death, from the last scheduled scintigraphy until 12 months later was registered.

RESULTS

A total of 1640 scintigraphies were performed; 693 were done during the first and second years after operation. Fourteen patients had at least 1 positive scintigraphy within the first 2 years, but bone metastases were never proved in these patients, and, additionally, all the scintigraphies performed after the second year were negative.

Sixteen patients had at least 1 positive scintigraphy at 1 of the fixed scheduled examinations performed from 2 to 6 years after surgery. Only 7 of these patients developed bone metastases within 12 months after the positive scintigraphy. A further 6 patients had X-ray or histologically-proven bone metastases within 12 months after a negative scintigraphy. Thus, a total of 13 patients developed bone metastases within 12 months after a scheduled scintigraphy. The yearly incidence of bone metastases was: 3rd year: 2.6%; 4th year: 1.1%; 5th year: 1.1%; 6th year: 1.1%; and 7th year: 0.6%. This results in an overall frequency of bone metastases of 5.6% from 2 up to 7 years after surgery.

Including the 13 patients who had bone metastases, 81 patients were withdrawn from the program from 2 up to 7 years after surgery. The reason and the time for withdrawal appear from Table 1.

DISCUSSION

First of all, the clinical value of repeated pre-scheduled bone scintigraphies in patients with primary operable breast cancer and otherwise considered free of disease should be viewed in the light of the low incidence of bone metastases: for the first 2 post-operative years, around 2.5% per year [2], as well as during the 3rd year, and thereafter about 1.0% per year. Similarly, the Ludwig Breast Cancer Study Group [7] found that 8.5% had first recurrence in bone over a 48-month median observation beyond the first post-operative year.

Secondly, a pre-scheduled scintigraphy is negative in from 33% [2] to 46% of the patients, who within 12 months after the scintigraphy have bone metastases confirmed by other techniques. This could not be explained by an obvious delay between scintigraphy and radiology/histology in both studies. The Eastern Cooperative Oncology Group [8] found that 65% of 66 patients with osseous involvement were first identified through symptoms of the metastatic disease, whereas 18% were recognized by routine scintigraphy. Also Perez *et al.* [5] reported that bone recurrence was symptomatic at the time of diagnosis in most patients.

Thirdly, a single positive scintigraphy seems not to be identical with development of bone metastases when X-ray/histology are used as the 'true' criterion. Fourteen patients of the present study had a positive scintigraphy within the first 2 post-operative years, and 5 years later no bone metastases had been detected by other methods, the patients were without symptoms, and the bone scintigraphies had turned negative. Furthermore, beyond the 2nd post-operative year 9 patients had a positive scintigra-

phy, but no other evidence of bone metastases within 12 months after the scintigraphy.

Fourthly, the cost/benefit is low. Performing 1640 scintigraphies of which 693 were performed within the first 2 postoperative years in 231 patients revealed bone metastases in only 7 patients. Therefore 234 scintigraphies were required to discover 1 case of bone metastases. Others [7] found that the cost of a 1/50 yield was uneconomical. Also the cost of supplementary tests such as X-ray, CT-scanning, and biopsies required to investigate an abnormal scintigraphy should be taken into consideration, making the cost even higher.

Previously we concluded that a fixed schedule of

repeated scintigraphies or radiograms in patients with primary operable breast cancer is not warranted, at least within 12 months after surgery [2, 3]. We can now extend that conclusion to at least within 6 years after operation. We suggest that bone scintigraphies are reserved to patients who have symptoms of bone metastases in agreement with other workers [7, 9]. The usefulness of a peri-operative bone scintigraphy for later comparison with a pathologic scintigraphy is also debatable, since an abnormal scintigraphy will always be followed by X-ray of the bone in question, before the clinical decision is made.

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