

Lack of Efficacy of Lymphoscintigraphy in Detecting Axillary Lymph Node Metastases from Breast Cancer

M. GASPARINI,* C. ANDREOLI,† A. RODARI,* A. COSTA† and G.L. BURAGGI*

*Nuclear Medicine Division, †Surgical Oncology "C" Division, National Cancer Institute of Milan, Italy

Abstract—Preoperative detection of metastases in regional lymph nodes should constitute a fundamental step towards a better management of breast cancer. The National Cancer Institute of Milan has traditionally been engaged in this particular problem, that is, the search for a new imaging technique for detecting lymph nodal metastases from breast cancer. In 1984 axillary lymphoscintigraphy was performed on 26 patients with operable breast cancer by periareolar injection of 100 μ Ci of ^{99m}Tc sulphur microcolloid. The regional lymph nodes were identified as spot areas and a comparison was made between the number of primary draining axillary lymph nodes and their pathological examination. In only 2 of the 26 patients have more than 3 spot areas been revealed by axillary scintiscan, but this finding did not correspond to metastatic invasion. The lymphoscintigraphy pattern of the other 24 patients did not suggest any pathological condition. From our experience the method does not appear to help either a precise diagnosis of breast disease or the definition of the extent of mammary cancer.

INTRODUCTION

THE IMPORTANCE of the biological aspects of breast cancer has been stressed more and more often in recent studies. This relatively new attitude of the oncologists has been directed not only at the primary disease, but at the whole mammary region. Fisher *et al.* [1] have demonstrated that lymph nodes are not necessarily a compulsory route for the metastatic spread of breast cancer and have suggested that their surgical removal appears to be a useless procedure when breast cancer is, from the beginning, a disseminated, or 'systemic' disease. Veronesi *et al.* [2] have focused their attention on the internal mammary nodes demonstrating that their invasion is not related to the site of the primary tumor. From these data it was assumed that, at the present time, no criteria for the treatment either surgical or radiotherapeutical of the internal mammary nodes is available. Nevertheless, regional lymph nodes and, particularly, axillary lymph nodes, are still the best prognostic factors for breast cancer and their pathological status is considered the main criterion for undertaking or avoiding any adjuvant treatment [3, 4]. On the other hand, axillary and internal

mammary node dissection is not free of complications and both surgery and radiotherapy can leave the patient with permanent lesions, the most critical of which is lymphoedema. However, there being no less invasive method for the assessment of prognosis, axillary lymph node dissection still remains a widely accepted procedure, even in the conservative surgery of breast cancer [5, 6].

After the failure of traditional mammography, xeroradiography, and other special imaging techniques, nuclear medicine has become the spearhead in the endeavor to solve this problem. Lymphoscintigraphy has been used to reveal lymph nodes in several areas of the body. In most studies the objective has been to detect nodal metastases by revealing a defect in a group of nodes on one side and comparing the same nodes on the contralateral normal side. The most significant lymphoscintigraphy study is that of Ege who used antimony sulphide colloid to examine the internal mammary nodes of over 2000 patients with breast masses, including over 1000 with cancers [7]. In 1978, Agwunoby and Black [8] studied a group of 50 patients with breast symptoms by injecting 100 μ Ci of ^{99m}Tc Sb_2S_3 around the areola bilaterally. They considered a photoscan positive if the primary draining axillary lymph node on the symptomatic side gave a lesser image than the corresponding

Accepted 22 August 1986.

Correspondence should be addressed to: Dr. Massimo Gasparini, Divisione Medicina Nucleare, Istituto Nazionale Tumori, Via G. Venezian, 1, 20133 Milano, Italy.

node on the contralateral side: in their pilot study lymphoscintiscanning was superior to mammography, clinical assessment, or combined mammography and clinical assessment in detecting breast carcinoma. Hill *et al.* [9] have utilized periareolar as well as interdigital administration of radiocolloid for more complete visualization of axillary lymphatics; lymphoscintigraphy was accurate in 94% of normal axillas and in 67% of abnormal ones.

Further investigations into the technique of periareolar radiocolloid injection have not confirmed any significant association between the axillary image and the benign or malignant nature of the breast mass.

The aim of this work is to evaluate lymphoscintigraphy as a suitable procedure for the study of axillary nodes drainage and the demonstration of their metastatic involvement in breast carcinoma.

The accuracy of the technique has been determined by correlating the results with pathological findings.

MATERIALS AND METHODS

Twenty-six patients (between 33 and 76 years of age) with operable breast carcinoma ($T_1N_0M_0$ to $T_4N_{1b}M_0$) were studied. Each patient was examined according to UICC criteria to establish the clinical node status: N_0 impalpable; N_{1a} palpable, unsuspected node; N_{1b} palpable and clinically suspected (Table 1). 400 μ Ci of ^{99m}Tc sulphur microcolloid (LYMPHOSCINT-SOLCO) with particle diameter of less than 50 nm, in a volume of 0.5, was injected subcutaneously in 4 fractionated doses around the areolar region (Fig. 1).

Table 1. TNM classification of 26 patients with breast cancer

T	T ₀	T ₁	T ₂	T ₃	T ₄	T _x	Total
No.	—	11	10	1	1	3	26
N	N ₁	N _{1a}	N _{1b}	N ₂	N ₃		Total
No.	10	8	8	—	—		26
M	All patients with M ₀						

Four hours after injection images of the axilla from the frontal and oblique views were obtained using a small field high resolution gamma camera (SELO KR07) with line computerized data processing (DIGITAL PDP 11/34). No adverse reactions and no complications were observed in any of the patients.

The regional lymph nodes were identified as spot areas and a comparison was made between the number of primary draining axillary lymph nodes and the pathological finding after surgery (in order to establish whether there was any relationship between the number of spot areas visualized and the number of pathological lymph nodes).

RESULTS

The results are summarized in Table 2. Only 2 of the 26 patients had more than 3 spot areas in the axillary scintiscan (Fig. 2); these 2 patients had histologically normal lymph nodes.

Sixteen patients (62%) had a lymphoscintiscan in which 1–3 spot areas were visualized (Figs. 3 and 4): in this group the incidence of axillary positivity, after histological examination was 50%.

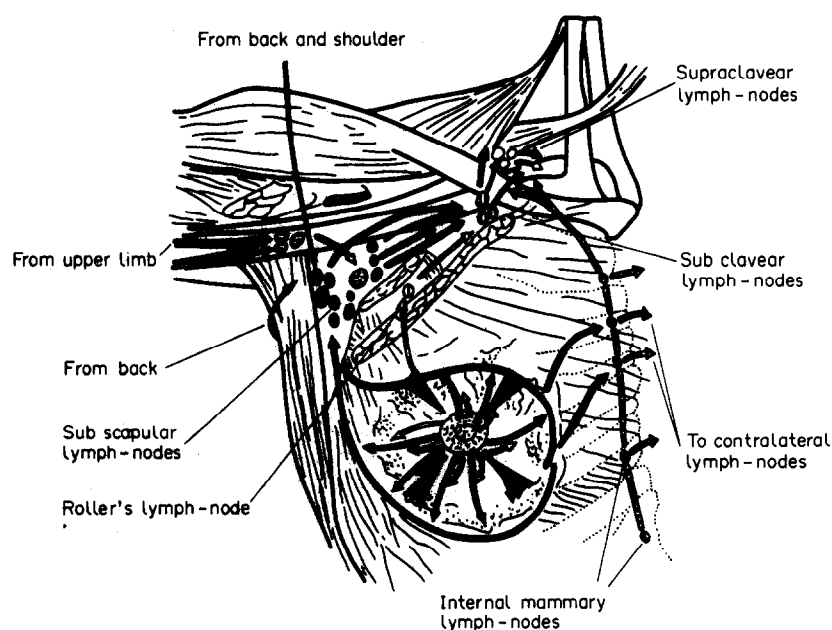


Fig. 1. Lymphatic drainage of mammary gland: the black arrows show the injection side around the areolar area.

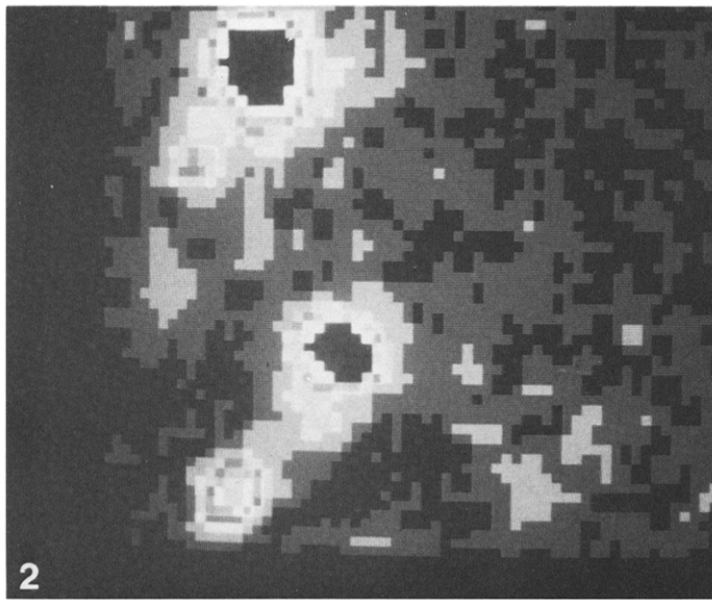


Fig. 2. Axillary lymphoscintiscan in a patient with carcinoma of the right breast: 4 spot areas are visualized.

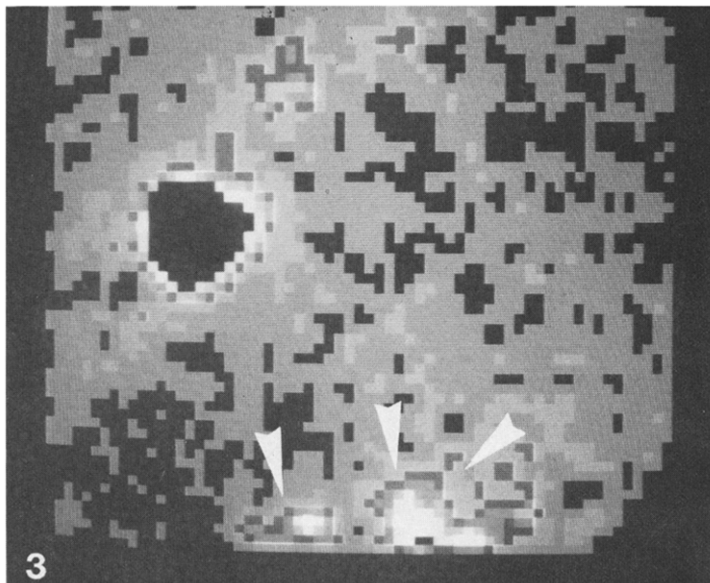


Fig. 3. Axillary lymphoscintigraphy in which 2 spot areas are visualized. In this case the patient had histologically normal lymph nodes. The white arrows indicate the injection site.

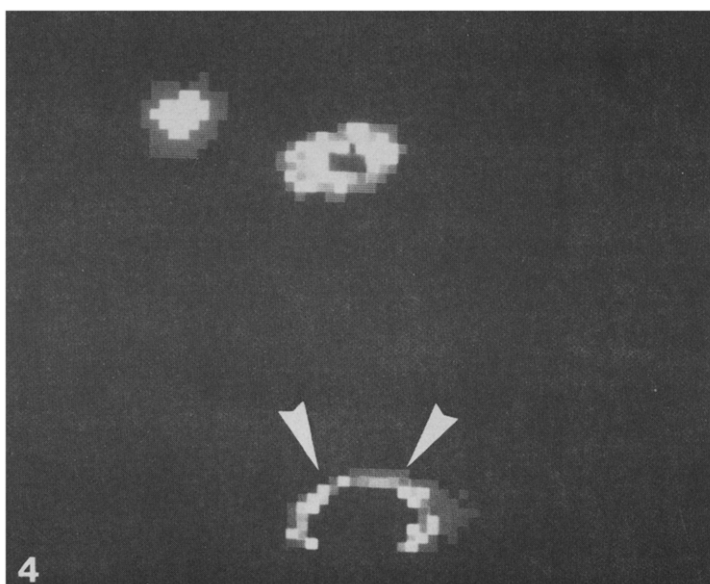


Fig. 4. Axillary lymphoscintigraphy 4 hr after injection of 400 μ Ci of ^{99m}Tc sulphur microcolloid.

Table 2. Correlation between axillary lymphoscintigraphy and histological nodes status

Lymphoscintigraphy No. of spot areas visualized	Histological finding No. of metastatic lymph nodes			Total
0	3	2	3	8
1-3	8	6	2	16
> 3	2	—	—	2
Total	13	8	4	26

The remaining 8 patients (30%) had no visualized lymph nodes: the incidence of axillary positivity, after histological examination, was 62%.

As can be seen, there is no significant difference between the group with 1-3 visualized spot areas and the last group (from 50 to 62% incidence of axillary positivity after histological examination); in the last group of 8 patients, in which spot areas were not visualized, 3 were free of disease, the remaining 5 patients showing one spot area had no lymph node involvement.

DISCUSSION

Metastatic nodal involvement constitutes one of the major prognostic factors in breast cancer. Moreover, the precise knowledge of nodal status influences a rational therapeutic approach to the disease. If there were some procedure by which the axillary node status could be accurately assessed preoperatively, lymphadenectomy, one of the major causes of disability for these patients, could be avoided. In recent years, a further 2 imaging techniques for the detection of metastases from breast cancer in axillary lymph nodes have been investigated at our Institute. The first was xeroradiography, a procedure which Coopmans de Yoldi *et al.* [10] had reported as adding no further precision to the clinical diagnosis. The second was a special radiography of the axilla obtained by means of a water-soluble, radio-opaque molecule injected around the areola and drained by the lymphatic vessels. Musumeci *et al.* [11] were once again unable to add any important information to the clinical examination with this method and since the contrast means was water-soluble, it disappeared as soon as it encountered a vein, after having revealed a few lymph nodes.

In our study with lymphoscintigraphy we followed the methods described by Gabelle *et al.* [12] with only one minor modification (the injection was given around the areola and not into the tumor). They had utilized intratumoral ^{99m}Tc rhenium colloid in 100 patients with 105 breast masses, and reported a correlation between the number of radioactive foci visualized in the axilla and the number of nodes shown to contain metastases. In their work patients who had more than 2 foci of radioactivity in the axilla, generally had either normal nodes, or fewer than 3 nodes with metastases whereas the majority of those with 2 foci or less, had histologic evidence or clinical indications of metastatic involvement of more than 3 nodes.

We did not find any significant relationship between the number of spot areas visualized and the number of histologically positive lymph nodes.

This fact could be due to some factors such as the different injection side, the use of different radiotracers; we used the sulphur microcolloid instead of ^{99m}Tc rhenium colloid. On the other hand, the lymphoscintigraphy could be negative even though one or more micrometastases were present, as there are no significant functional changes in lymph nodes draining a tumor-bearing breast. As Christensen [13] and Peyton [14] also demonstrated, there was no correlation with the presence or absence of lymph node metastases.

These data, though not significant, show that, preoperatively, lymph nodes cannot be assessed with any certainty. In our opinion, it is almost impossible to distinguish completely normal nodes from those affected by metastases by lymphoscintigraphy: we were unable to detect differences between nodes with benign disease and those with malignant disease. In conclusion, as our results prove, we doubt whether there is any pattern of lymphoscintigraphy which is either typical or diagnostic of node involvement. Axillary lymphoscintigraphy does not provide an accurate selection of patients free of nodal involvement: differences in radiotracer distribution are not significantly correlated with axillary lymph node status.

Radical axillary lymphadenectomy remains the mainstay of the staging and treatment of breast cancer.

REFERENCES

1. Fisher ER, Palekar A, Rockette H, Redmond BC, Fisher B. Pathologic findings from the National Surgical Adjuvant Breast Project. *Cancer* 1978, **42**, 2032-2038.
2. Veronesi U, Valagussa P. Inefficacy of internal mammary nodes dissection in breast cancer surgery. *Cancer* 1981, **47**, 170-175.
3. Bonadonna G, Valagussa P, Rossi A *et al.* Ten years' experience with CMF-based adjuvant chemotherapy in resectable breast cancer. *Breast Cancer Res Treat* 1985, **5**, 95-115.
4. Baum M, *et al.* Controlled trial of tamoxifen as single adjuvant agent in management of early breast cancer. *Lancet* 1985, **13**, 836-840.
5. Veronesi U, Del Vecchio M, Greco M *et al.* Results of quadrantectomy, axillary dissection and radiotherapy (QU.A.R.T) in T₁N₀ patient. In: Harris SR, Helman S, Silen W,

- eds. *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*. Lippincott, 1983, 91-98.
6. Fisher B. Breast cancer management: alternatives to radical mastectomy (Editorial). *New Engl J Med* 1979, **301**, 326-328.
 7. Ege GN. Internal mammary lymphoscintigraphy: a rational adjuvant to the staging and management of breast carcinoma. *Clin Radiol* 1978, **29**, 453-456.
 8. Agwunobi TC, Boach JL. Diagnosis of malignant breast disease by axillary lymphoscintigraphy: a preliminary report. *Br J Surg* 1978, 379-383.
 9. Hill NS, Ege GN, Greyson MD, et al. Prediction by lymphoscintigraphy of nodal metastases in breast cancer. *Cancer J Surg* (in press).
 10. Nessi R, Balzarini L, Gilardoni L, Andreoli C, Costa A, Coopmans de Yoldi G. La xeroradiografia dei linfonodi ascellari nelle pazienti con tumore della mammella. *Rad Med* 1983, **69**, 310-315.
 11. Musumeci R, Tesoro Tess JD, Costa A, Veronesi U. Indirect lymphoscintigraphy of the breast with iotasul: a vanishing hope? *Lymphology* 1984, **17**, 118-123.
 12. Gabelle PH, Comet M, Bodin MP, et al. La lymphoscintigraphie mammaire per injection intra-tumorale dans le bilan du cancer du sein. *Nouv Presse Med* 1981, **10**, 3067-3070.
 13. Christensen B, BlichertToft M, Siemssen OJ, et al. Reliability of axillary lymph node scintiphography in suspected carcinoma of the breast. *Br J Surg* 1980, **67**, 667-668.
 14. Peyton JWR, Crosbie J, Bell TK, et al. High colloidal uptake in axillary nodes with metastatic disease. *Br J Surg* 1981, **68**, 507-509.