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Sentinel node localization in patients with breast cancer

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Background Intraoperative lymphatic mapping and identification of the first draining lymph node (the sentinel node) may allow some patients with breast cancer to avoid the morbidity of formal axillary clearance. The aim of this pilot study was to establish the reliability of the technique in predicting axillary node status.

Methods Sixty-eight consecutive patients with breast cancer, 38 undergoing mastectomy and 30 wide local excision, were included. Some 2–4 ml of 2·5 per cent Patent Blue dye was injected into adjacent breast tissue on the axillary side of the primary tumour. After 5–10 min, the axilla was explored. Blue-stained lymphatics were dissected to the sentinel node, which was removed for frozen-section examination, followed by routine histology. Formal axillary dissection was then completed.

Results A sentinel lymph node was identified successfully in 56 (82 per cent) of 68 patients. Histology of the sentinel node accurately predicted axillary node status in 53 (95 per cent). There were three false negatives (5 per cent). In each case, only a single non-sentinel node was tumour positive. Sensitivity and specificity were 83 and 100 per cent respectively.

Conclusion This technique would allow a selective policy of formal axillary dissection in only node-positive patients; however, further experience and refinement are needed.

Axillary node status remains the most important prognostic factor in breast cancer. Formal axillary clearance has remained the best method of breast cancer staging. There is no other reliable method of identifying lymph node-negative patients, using either imaging techniques[1] or pathological characteristics of the primary tumour[2].

Although there is no doubt about the prognostic importance of lymph node status, there is controversy over the extent of axillary surgery required. Axillary dissection is associated with significant morbidity[3,4]. Limited dissection has a lower incidence of morbidity than complete level III axillary clearance. However, axillary node biopsy or sampling has a staging error of 0–42 per cent[5–8] and an increased incidence of axillary recurrence[7,8]. A lower, level II dissection has a staging error of only 2–3 per cent[9,10], and this procedure is preferred by many surgeons.

An alternative strategy of lymph node staging, involving intraoperative lymphatic mapping and identification of the first draining node (the sentinel node), is established in the management of malignant melanoma[11]. Histological evaluation of the sentinel node when compared with the complete lymphatic field shows a high correlation and only a 1 per cent false-negative rate. Preliminary work by Giuliano *et al.*[12,13], using blue dye, suggested that this technique may be applicable to breast cancer. An alternative technique using radiolabelled colloid and a hand-held γ probe has been reported, with similar encouraging results[14,15].

This was a pilot study to verify the reliability of sentinel node localization in predicting axillary nodal status and to carry out a cost analysis in comparison with formal axillary dissection.

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Patients and methods

The study design is summarized in *Fig. 1*. Sixty-eight consecutive patients with primary invasive breast cancer were included. Mean age was 62 (range 33–86) years. Thirty-eight patients underwent mastectomy and 30 wide local excision, in conjunction with axillary exploration. Informed consent was obtained from all patients.

Intraoperative lymphatic mapping involved injection adjacent to the tumour of 2–4 ml 2·5 per cent Patent Blue dye (Laboratoire Guerbet, Aulney-Sous-Bois, France). After 5–10 min the axilla was explored and the lymphatics were identified and dissected to the sentinel node. An effort was made to ensure that the first draining node had been identified by retrograde dissection of the lymphatic track to the tail of the breast. The sentinel node was removed for immediate frozen-section examination, followed by paraffin-section histology (*Fig. 2*). Formal axillary clearance was then completed. In patients who had a wide local excision, this was carried out through a separate incision. In patients who had a mastectomy, the standard incision

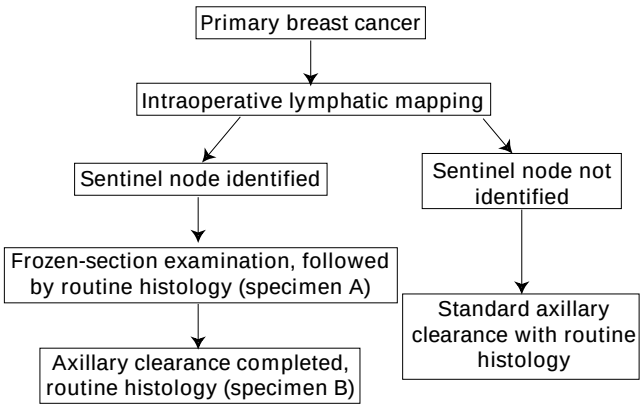

Fig. 1 Design of study to compare intraoperative lymphatic mapping and sentinel node histology with formal axillary dissection in the axillary staging of breast cancer

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Fig. 2 Intraoperative lymphatic mapping. The blue-stained lymphatic track can be seen leading to the sentinel node, which has been dissected from surrounding fat and is held in dissecting forceps (bottom right). This patient then had a mastectomy

was made and inferior and superior skin flaps were dissected before lymphatic mapping.

All axillary lymph nodes were processed individually for histological examination by a consultant pathologist with a special interest in breast cancer. A full record of operating theatre time was kept to facilitate a cost analysis.

Results

Twenty-one patients (31 per cent) had involved axillary nodes on histology and 47 (69 per cent) were node negative.

Sentinel nodes were identified successfully in 56 patients (82 per cent). In 12, there was more than one sentinel node; a total of 69 was identified.

The histological status of the sentinel node predicted axillary node status accurately in 53 (95 per cent) of 56 patients. There were three false negatives; sensitivity and specificity were 83 and 100 per cent respectively. In five patients the sentinel node was the only positive node recovered from the axilla.

Immediate frozen-section examination of the sentinel node accurately predicted the paraffin-section histology in 53 (95 per cent) of 56 patients. In two patients with positive sentinel nodes, the frozen section was reported as suspicious of metastatic carcinoma. In one, a sentinel node was negative on frozen-section examination, but a single tumour deposit was identified on paraffin section. If formal axillary clearance had been performed on the basis of sentinel node histology, a single patient would have required a second procedure.

Cost analysis

The mean time to dissect and remove the sentinel node was 8 (range 1–18) min compared with 40 (range 20–70) min to complete the axillary dissection. The authors' average theatre costs are £432 per hour. The respective costs of operating time per patient are shown in *Table 1*.

Pathology costs were £95 for frozen section and subsequent histology on the sentinel node, compared with £70 for routine processing of lymph nodes recovered from the axillary dissection specimen.

If sentinel node localization had been used as a staging procedure and a selective policy of formal axillary dissection employed only in node-positive patients, the total operating cost would have been £32 659 compared with £42 106 if routine axillary dissection had been carried out. The respective pathology costs were £7210 and £4760. The combined costs for sentinel node localization were £39 869 compared with £46 866 for routine axillary dissection. The technique of sentinel node localization could have saved £6997 or 15 per cent.

Table 1 Operating time and costs

	Sentinel node localization	Axillary dissection	Total time in operating theatre
Mean (range) theatre time (min)	8 (1–18)	40 (20–70)	86 (60–105)
Cost per patient (at £432 per h)	£57·60	£288·00	£619·20

Discussion

Axillary lymph node dissection is an important staging procedure and has a therapeutic role in reducing the risk of axillary relapse[16]. It is, however, associated with significant morbidity. Seromas requiring aspiration occur in 30–42 per cent of cases[17,18]. Ivens *et al.*[4] found subjective morbidity, interfering with daily living, in 39 per cent of 126 women surveyed 6 months after full axillary clearance.

Reliable prediction of axillary node metastases could help to avoid routine axillary dissection in some patients with invasive breast cancer. However, non-invasive methods have been unsuccessful. Clinical examination[19] and imaging techniques such as ultrasonography, computed tomography and lymphoscintigraphy have largely failed as reliable methods of detecting axillary disease[1].

Limited dissection is an alternative to axillary clearance. In the Edinburgh randomized trial of axillary sampling or clearance[8], a subgroup of 67 patients in whom axillary sampling was performed subsequently went on to have axillary clearance. Twenty-six (39 per cent) had histologically positive nodes and in each case these had been identified on sampling. This contrasts with the results from other studies, showing a staging error rate of 8–42 per cent[5–7]. In one of these studies, involving 473 patients with stage I or II disease, no nodes were identified for histological examination after axillary sampling in 116 patients (25 per cent)[7]. There is conflicting evidence on the value of the qualitative information obtained from axillary sampling. In addition, sampling may not give accurate information on the number of involved nodes, which influences prognosis and often determines the use of adjuvant systemic therapy.

Sentinel node biopsy seems to have sufficient reliability to allow formal axillary clearance to be limited to node-positive patients. Successful lymphatic mapping and localization of the sentinel node is possible in a large proportion of patients and the histology of the sentinel node is highly predictive of axillary node status.

There were three false negatives in this series. However, this rate is low and close to the figure reported for level I and II axillary dissection[9,10]. In each patient only a single non-sentinel lymph node was tumour positive, and in one a micrometastasis was the only evidence of involvement.

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This technique is also cost effective. In addition to the saving in operating time and cost, a reduced inpatient hospital stay may be expected if axillary dissection is avoided. Node-negative patients would avoid the potential morbidity of formal axillary clearance. The two previously reported large studies on sentinel node localization in breast cancer have shown similar encouraging results, using two different techniques[13,15]. The techniques may be complementary; lymphatic mapping using a combination of both blue dye and a radiolabelled colloid may be an improvement.

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