MANAGEMENT OF REGIONAL NODES IN BREAST CANCER

N J Bundred, D A L Morgan, J M Dixon

Lymph drainage of breast

Lymph drainage of breast.

Lymph drainage from the breast is important in relation to malignant disease and is via the axillary and internal mammary nodes. To a lesser extent lymph also drains by intercostal routes to nodes adjacent to the vertebra. The axillary nodes receive about three quarters of the total lymph drainage, and this is reflected in the greater frequency of tumour metastases to these nodes.

Levels of axillary nodes.

The axillary nodes, which lie below the axillary vein, can be divided into three groups in relation to the pectoralis minor muscle: level I nodes lie lateral to the muscle; level II (central) nodes lie behind the muscle; and level III (apical) nodes lie between the muscle's medial border, the first rib, and the axillary vein. There are on average 20 nodes in the axilla, with about 13 nodes at level I, five at level II, and two at level III. The drainage from level I nodes passes into the central nodes and on into the apical nodes. An alternative route, by which lymph can get to level III nodes without passing through nodes at level I, is through lymph nodes on the undersurface of the pectoralis major muscle, the interpectoral nodes. The orderly drainage of lymph explains why very few patients with cancer have lymph nodes involved at levels II or level III without involvement at level I. These so called skip metastases are seen in less than 5% of patients with axillary node involvement.

Factors affecting lymph node involvement

Factors associated with lymph node involvement

- Large tumour
- Poorly differentiated tumour (grade III)
- Symptomatic (compared with screen detected) tumour
- Presence of lymphatic or vascular invasion in and around tumour
- Oestrogen receptor negative tumour

Preoperative clinical or radiological assessment of lymph node involvement is inaccurate, with only 70% of involved nodes being clinically detectable. Only histopathological assessment of excised nodes provides accurate prognostic information.

Lymph nodes are ineffective barriers to the spread of cancer, and metastasis indicates biologically aggressive disease that requires systemic adjuvant treatment. Involvement of axillary nodes occurs in up to half of symptomatic breast cancers and in 10-20% of screen detected breast cancers.

Role of axillary surgery in patients with operable breast cancer

Options for axillary surgery

Procedures to stage but not treat the axilla

- Axillary node sampling (removal of at least four lymph nodes)
- Partial axillary dissection (level I or level I and II)

Procedures to stage and treat the axilla

- Level III dissection

Axillary surgery can be used to stage the axilla or to treat axillary disease, or both.

Staging the axilla

The presence or absence of involved axillary lymph nodes is the single best predictor of survival of breast cancer, and important treatment decisions are based on it. Both the number of involved nodes and the level of nodal involvement predict survival from breast cancer. Only nodal involvement that is evident on routine histopathological examination is of proved prognostic importance. The prognostic value of finding microscopic metastases in lymph nodes either by examining multiple sections or by immunohistochemistry remains to be determined.

A single node biopsy does not adequately stage the axilla. Although some centres have found that sampling (dissecting out four separate nodes) provides reliable information on whether axillary nodes are involved, others have found it difficult to identify and dissect out four separate axillary nodes. The probability of a false negative result on sampling decreases as the number of nodes sampled increases. A level I dissection, which should contain at least 10 nodes, provides information on whether there are axillary nodal metastases but does not provide definitive evidence of the number of involved axillary nodes. Level II or III dissections (removing all nodes at levels I and II or I, II, and III) provide more accurate assessments of the number and level of node involvement.

Relation between number of involved axillary lymph nodes and survival after breast cancer.

Relation between level of axillary lymph node involvement and survival after breast cancer.

Treatment of axillary disease

A partial (level I or level II) dissection or sampling of axillary nodes cannot be considered as treatments because even if there is only a single node metastasis at level I there is a 12.5% chance of nodes at level II or III being involved, and if there is metastasis at level II there is a 50% incidence of level III nodal involvement. Thus, patients who are found by axillary sampling or level I and II dissections to have involved axillary nodes require radical axillary radiotherapy; patients with negative nodes after these axillary staging procedures require no further treatment to the axilla.

Some surgeons deliberately limit their axillary dissection to level II, arguing that this carries a lower incidence of complications than a level III dissection and that patients with nodal involvement at level II will receive adjuvant systemic treatment that will control residual apical nodal disease. Both assumptions are unproved, and residual disease at the apex of the axilla can cause distressing symptoms that can be difficult to treat. Although axillary radiotherapy given after a level II dissection will control metastases at level III, this combination of procedures is associated with high rates of lymphoedema (>30%).

Control of axillary disease

Axillary recurrence in 10 years after level III axillary clearance, radiotherapy, or watch policy*

	Clearance	Radiotherapy	Watch policy
Axillary relapse	3%	8%	21%
Uncontrolled axillary relapse	1%	5%	12%

*Data compiled from reports from several centres relating to series of symptomatic patients, of whom about half had histologically positive nodes. No patients received adjuvant systemic therapy, which reduces rate of regional node relapse.

The options for treating involved axillary nodes are radical radiotherapy or a level III axillary clearance. Both options provide satisfactory rates of disease control, but a level III axillary clearance seems to provide a lower rate of axillary recurrence. Radiotherapy to the axilla cannot be repeated.

Axillary recurrence causing lymphoedema.

Ulcerating, uncontrolled axillary recurrence.

Some clinicians believe that surgeons should not enter the axilla and that patients should have either radical radiotherapy or a watch policy—treatment of only those patients who develop symptomatic axillary relapse. A watch policy, however, prevents the acquisition of important information that is used both to decide adjuvant treatment and to discuss prognosis with the patient. Uncontrolled axillary recurrence, which can manifest as ulceration or brachial neuropathy, is unpleasant and difficult to treat and is seen more commonly after a watch policy than after an axillary node clearance or radical axillary radiotherapy. The aim of treating the axilla is to minimise axillary relapse; it is evident that such treatment almost certainly has no effect on overall survival.

Morbidity of axillary treatments

Lymphoedema due to recurrent axillary disease.

Damage to nerves in the axilla may occur during surgery, the most common being division of the sensory intercostobrachial nerve. Radiotherapy may result in brachial plexopathy. This complication may be due in part to overlap of fields, which can result in high doses of radiation being delivered to the brachial plexus. With modern planning techniques, treatment schedules, and newer equipment this complication is rare. Brachial plexopathy can also be due to apical axillary recurrence; this complication is much less common if initial treatment of axillary disease has been optimal. Many surgeons take care to preserve the intercostobrachial nerve during axillary node surgery, which reduces the number of patients who develop numbness and paraesthesiae down the upper inner aspect of the arm.

Wound infection complicates about 5% of axillary surgical procedures and is more common after axillary clearance than sampling: about one third of patients develop seromas after a level III axillary clearance compared with less than 5% of patients who undergo four node sampling.

Reduced range of movement—Both surgery and radiotherapy are associated with a reduction in the range of movement of the shoulder in some patients, and about 5% develop a frozen shoulder. This can be minimised with regular exercise programmes developed and supervised by physiotherapists, and patients with a frozen shoulder require a prolonged course of intensive physiotherapy.

Symptomatic lymphoedema occurs in less than 5% of patients treated by a level II or III axillary dissection or by radical radiotherapy. It is much more common when an extensive axillary dissection (such as a level II dissection) is combined with radical radiotherapy. Radiotherapy should not be given after a level III axillary dissection. Recurrence in the axilla produces the most extreme lymphoedema. There is no satisfactory treatment for this problem, but symptoms can be improved and, in some patients, the lymphoedema controlled.

Methods for control of lymphoedema

- Oral bioflavonoid oxerutins or coumarin
- Bandaging arm
- Elasticated compression sleeve (should be individually measured for each patient)
- Multiple chamber Flowtron pumps (must be used for at least two hours a day to maintain improvement)

Treatment of internal mammary and supraclavicular nodes

The value of prophylactic irradiation of the internal mammary and supraclavicular nodal areas is unproved. For anatomical and geometric reasons the supraclavicular nodes can readily be included when axillary radiotherapy is given and, providing there is no overlap of fields, adds little in the way of morbidity. Such treatment reduces the rate of supraclavicular recurrence but has no impact on survival.

Over 90% of women with metastases to the internal mammary nodes have axillary node involvement. Of the 5–10% who have internal mammary node involvement in isolation, most have tumours involving the medial half of the breast. Some surgeons take biopsy samples from the internal mammary chain (through the second intercostal space) of patients aged under 60 who have medial tumours. Such patients are candidates for systemic chemotherapy if they are node positive.

Internal mammary nodes can be irradiated only by means of complex fields that include the heart and are no longer routinely covered in radiotherapy fields after mastectomy or wide local excision.

Recommended management of axillary nodes

Recommended management of axillary nodes in patients with operable invasive breast cancer

Premenopausal women

Axillary staging

- Mandatory for all patients

Level III dissection

- Patients with palpable clinically involved nodes
- Patients undergoing mastectomy and reconstruction

Choice of level III dissection or axillary sampling

- All other patients

Postmenopausal women

Level III dissection

- Patients with palpable clinically involved nodes

Choice of level III dissection or axillary sampling

- All other patients with palpable breast cancers

Choice of axillary sampling or watch policy

- Patients with impalpable cancers (<1 cm in diameter)

Premenopausal patients must all have a surgical axillary staging procedure, and a level III axillary dissection has the advantage that it permits identification of patients with a poor outlook—more than 10 nodes positive—who might benefit from aggressive systemic treatment. Removal of nodes at all levels is preferred after mastectomy because it allows all patients to avoid axillary radiotherapy and most to avoid chest wall radiotherapy—this is particularly important for patients who undergo immediate breast reconstruction by tissue expansion.

Postmenopausal women with symptomatic and palpable screen detected cancer should have some form of axillary surgery. As with younger women, full level III axillary clearance is usually preferred after mastectomy. For patients with impalpable tumours (<1 cm in size) the choice is between axillary node sampling (level I dissection or four node sampling) and a watch policy because of the low incidence of axillary node metastases in these patients (<10%). Axillary sampling can be performed at the same time as a therapeutic wide local excision of an impalpable breast cancer that has been diagnosed by image guided fine needle aspiration cytology. If a diagnostic excision of an impalpable breast cancer shows it to have risk factors for nodal involvement the options for treatment are full axillary clearance or axillary sampling.

Presentation of breast cancer with enlarged axillary nodes

Less than 1 in 300 patients with breast cancers present with nodal metastases and an occult primary cancer. Up to 70% of women shown histologically to have metastatic adenocarcinoma in the axillary nodes will have an occult breast cancer, most of which will be visible on mammography. Treatment of these 70% is as for breast cancer with palpable nodal metastases. In the remaining 30% axillary node clearance (level I, II, and III dissection) should be performed and the breast kept under regular observation. Both groups of patients should receive appropriate adjuvant systemic treatment.

Treatment of axillary recurrence

Treatment depends on whether recurrence occurs in isolation or in association with other sites of recurrence. If initial axillary therapy has been suboptimal, axillary disease can represent residual untreated disease rather than recurrence. Isolated mobile axillary recurrences should be excised and combined with a level III dissection if this has not already been performed. Patients with isolated inoperable recurrence may be given radiotherapy (if not previously given) or systemic treatment, or both; these are sometimes effective at palliation but rarely produce long lasting control of disease. When the disease occurs in association with metastases at other sites systemic treatment is indicated. The most effective strategy is to try to prevent recurrence by ensuring adequate initial treatment.

J M Dixon acknowledges the support of the Cancer Research Campaign. Photographs were prepared by Mr D Dirom, Medical Illustration Unit, University of Edinburgh. The picture of axillary recurrence causing lymphoedema has been reproduced from N J Bundred and R E Mansell, eds, *Wolfe coloured atlas of breast disease* (London: Wolfe Medical Publications) 1994 with permission of the publishers.

N J Bundred is senior lecturer in surgery at University Hospital of South Manchester and Christie Hospital, Manchester; D A L Morgan is consultant clinical oncologist at Nottingham City Hospital; and J M Dixon is senior lecturer in surgery at Edinburgh Royal Infirmary and honorary consultant surgeon at Western General Hospital, Edinburgh.

The ABC of Breast Diseases has been edited by J M Dixon.

Malignant axillary node visible on mammography with no associated breast lesion.