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The sentinel node in breast cancer

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Abstract

Biopsy of the sentinel lymph node now forms part of routine management in many centres dealing with early stage breast cancer. This article seeks to discuss developments over the past number of years and to summarise current practice.

Keywords: *Breast cancer; sentinel node.*

Introduction

The prognosis of breast cancer is determined primarily by axillary lymph node status[1–3]. Axillary lymph node dissection (ALND) surgery carries a significant morbidity with complications such as lymphoedema, pain, numbness and limited shoulder movement[4–7]. The sentinel node is the first draining node on the direct drainage pathway from the primary tumour site[8]. If the sentinel node is positive there is a 40% risk that higher order nodes may also be involved with metastatic disease[9]. Moreover, the frequency of patients with metastatic disease increases significantly if a sentinel lymph node policy is in place[10]. Sentinel lymph node biopsy (SLNB) is a minimally invasive alternative to ALND for nodal staging in breast cancer, which is associated with low post-operative long-term morbidity[11,12]. The technique assumes orderly progression of tumour spread to the regional nodes and biopsy of the first node in the lymphatic chain at risk for metastasis should therefore reflect involvement of the remaining nodes. Early prospective studies validated the concept[13–16]. Subsequent studies have shown that comparing the results of SLNB to ALND indicate that the sentinel node is representative of the presence or absence of metastases in the remainder of the nodal basin (with a false negative rate of less than 2% in most series)[9,17–24]. Current practice is to perform a completion ALND for breast cancer patients although <50% will have non-sentinel node metastases. New models using just three variables have been developed to predict the accuracy of non-sentinel lymph node status[25]. Introduction of SLNB has led to stage migration as is reflected by the small but significant increase in the proportion of patients with positive axillary lymph nodes after adjustment for tumour size and age[26]. In a recent analysis of over 35,000 breast cancer patients diagnosed with T1–T2 tumours, clinically negative nodes and without distant metastases, 70% underwent the procedure and for 65% it was the final axillary treatment[27].

Technical issues

Lymphoscintigraphy

A large choice of dyes and radiopharmaceuticals (usually ^{99m}Tc sulphur colloid) are available. Isosulfan blue dye is safe with anaphylaxis occurring only rarely[28,29]; likewise, with the radiolabelled colloid[30]. The colloid employed should be of a size to be taken up efficiently and retained within the sentinel node. It has been shown that the highest counts in recovered sentinel nodes were from 100 to 200 nm albumin colloid particles[31]. Filtered ^{99m}Tc-sulphur colloid (100 nm filtered) has a faster transport rate to the regional nodes and lower radiation dosimetry. As a result it is the preferred choice if performing surgery within 2 h of injection[9]. The sentinel node is more successfully identified with radiopharmaceuticals than with dyes but a combined technique using both maximises the potential of accurate staging[14,32–37]. Increasing body mass, tumour location outside the upper outer quadrant and non-visualisation of nodes on

preoperative lymphscintigram adversely affect the accuracy of the procedure[35]. Combining the technique of dye, isotope and axillary node sampling improves accuracy further.

A recently published study reviewing 434 patients in a single centre demonstrated a positive axillary node in 13/36 patients with a negative sentinel node[38]. Work performed elsewhere has shown that removal of more than the first four hottest sentinel nodes does not improve staging accuracy[39]. Preoperative lymphoscintigraphy enables faster location of radioactive nodes at surgery and the combined approach results in identification and harvesting of more nodes[40–42]. However, this view is not universally accepted[43].

The injection technique seems to matter little as axillary nodes stained blue by intradermal, peritumoural, subdermal, periareolar and subareolar injections identify the same nodes[33,44–46]. It also appears that there is often more than one sentinel lymph node and using dual agents will assist in identifying all sentinel nodes. In a prospective multi-institutional study of 1436 patients, the false negative rate was 14.3% if a single sentinel lymph node was removed compared with 4.3% if multiple sentinel lymph nodes were removed indicating that there is often more than one sentinel node[47].

Despite variation in mapping techniques results have been similar worldwide with sensitivity and diagnostic accuracy rates greater than 95% and false negative rates ranging from 0 to 10%[48]. Some breast cancer programmes do not routinely utilize preoperative lymphoscintigraphy because of the added time, expense and the fact that the surgical decision making can be performed intraoperatively[9]. Others advocate the concept of the triple-technique comprising preoperative lymphoscintigraphy, injection of radiotracer with use of hand probe and blue dye[49]. Variables such as availability of resources, patient numbers, level of competence and local working practices mean that no standard protocol exists. Nonetheless, it is recognised that identification of the sentinel node in greater than 96% patients and a false negative rate of less than 5% is a desirable outcome[18,50,51].

Using lymphoscintigraphy the surface location of the sentinel node can be marked with some centres marking all sentinel nodes visualised[52,53]. Although high resolution collimators should be used, a medium energy collimator will suffice[53]. The camera is placed as close to the patient as possible and images should be acquired in at least two planes. If the site of injection is close to the nodes, shielding may be necessary to visualise the sentinel node. In one centre analysing the results of 640 patients, 94% demonstrated a sentinel node in the ipsilateral axilla but 46% also had sentinel nodes outside the axilla[53]. The most important site of extra-axillary drainage was to the internal mammary nodal chain and 40% of patients demonstrated a sentinel node in this area[53]. In 5% of patients drainage was exclusively to extra-axillary sentinel nodes. Preoperative lymphoscintigraphy enables these nodes to be identified. In another study comprising 1201 patients lymphoscintigraphy demonstrated extraaxillary lymph node drainage in almost 25% of patients[54]. SPECT CT improves preoperative localisation of draining nodes by detecting nodes missed by planar imaging, excluding non-nodal false positive sites of uptake and accurately localising axillary and extra-axillary nodes particularly in those who are overweight[55,56]. Upright imaging may also be advantageous[57]. Recent work has also shown the potential of the portable gamma camera in theatre over the hand-held probe[58].

Site of injection

Several theories exist concerning lymph node drainage in the human breast[59]. Although Sappey described flow to the subareolar plexus and then to the axilla, this view was not universally accepted[60]. An alternative drainage pattern proposed direct drainage to the ipsilateral axilla avoiding the subareolar plexus[59,61]. A study of 145 dynamic lymphoscintigrams using both intraparenchymal and subdermal injections was unable to visualise the subareolar plexus indicating that it may not act as a conduit to the ipsilateral axilla[62]. Recently published work on breast lymphatic anatomy (24 breasts, 14 patients) demonstrated no significant difference between female and male breasts[63]. Perforating lymphatic tracts tracking internal mammary vessels draining internal mammary lymphatics were identified. In some breasts one sentinel node in the axilla drained almost the entire breast but in the majority more than one sentinel node was represented.

The findings are discordant with current understanding of lymphatic drainage and may account for a percentage of false negative studies. They also support peritumoural injection as the preferred technique. Variable drainage patterns from injections of localising agents into the subareolar plexus, subdermal breast tissue and the deep breast parenchyma has been demonstrated by several groups[64–67]. Seven sites of injection have been described (peritumoural, subdermal, periareolar, intratumoural, intradermal, subareolar and subtumoural) and one of the factors dictating choice is the intention to locate internal mammary nodes in addition to axillary nodes[68]. Peritumoural injections were the first type of injection used[69,70]. Some groups claim better success with intradermal or subdermal injections than with peritumoural technique when sulphur colloid and blue dye are used[71–73]. Internal mammary node drainage occurs in a significant proportion after peritumoural injection but not after intradermal injection[74–76]. However, the intradermal technique has been shown to identify the SLN in the axilla with a frequency of 98% compared with 90% for peritumoural parenchymal technique[18,77].

A recent study evaluating the success rate of 5 different injection techniques in 192 patients demonstrated that

the highest detection rate for the axilla (98%) was obtained with an intradermal-periareolar injection[76]. The highest detection rate for internal mammary nodes (22%) was achieved using a peritumoural injection. Combining the two injection sites may optimise results. Periareolar injections are made just outside the areolar border at four equally spaced sites. The injections are subdermal although a single subareolar injection lined up with the tumour can also be used[45,46,78]. This technique militates against extra-axillary node identification but is easy and efficient[79–81].

Using a combination of radioisotope and blue dye, the SLN was identified successfully in 98% with no false negative results[82]. Subareolar injection of blue dye alone has been shown to demonstrate a sentinel lymph node in 98% of cases with no false negative sentinel nodes[83,79]. Likewise, it has been shown that subareolar injection of technetium is equivalent to peritumoural injection of blue dye[84,85]. One centre uses the combined intraparenchymal and subdermal injection technique because it more accurately reflects all lymphatic flow from breast tumour[62]. Intraparenchymal injections consistently visualise a more diverse pattern of lymph flow. In particular, the internal mammary chains and supraclavicular nodes are commonly seen after intraparenchymal injection but rarely after subareolar or subdermal injections. Peritumoural and subdermal injection of ^{99m}Tc sulphur colloid combined with periareolar injection of isosulphan blue dye is advocated by another group with extensive experience[51,86–88]. In a recent review of 1019 patients a low overall recurrence (0.5%) and overall false negative rate (1.4%) was shown for the intratumoural injection technique[89].

When should injection be performed?

Comparable accuracies have been shown for same day and day before surgery radioisotope injections[90,91]. After injection, breast massage may be performed to augment lymphatic flow[92]. However, concern exists that tumour cells might be transported from the primary tumour into the lymphatics. Pressure within the lymphatics can increase up to 22-fold following external massage and transport of tumour cells to the lymphatic spaces has been demonstrated[93–95]. However, isolated tumour cells are not true metastases and do not have malignant potential. Intraoperative injection is little used as it requires transfer of radioisotope to the operating theatre, is not as reliable and is complicated by radiation safety issues.

Radiation safety

Several papers have discussed various aspects of radiation safety associated with the sentinel node in detail[96–102]. Radiation doses are low and no additional procedures are required for the protection of staff. The procedure can be performed safely during pregnancy as the foetal dose is very low.

Clinical issues

In a study comparing complete ALND with a two-step procedure in 83 patients there was similar morbidity in terms of lymphoedema, sensory loss, intercostobrachial nerve division rates, impairment of shoulder movement, infection rate or time to resumption of normal day to day activity[7]. The second surgery was associated with increased axillary operative time and total hospital stay. Contrary to some opinions SNLB is not contraindicated in patients with clinically palpable axillary nodes, multicentric breast cancer or who have undergone previous breast cancer surgery[103–105]. Relative contraindications include prior axillary surgery, subglandular breast implants and previous breast irradiation[106]. In one centre, more than 50 patients with subpectoral implants have been associated with 100% SLN identification success rate and no clinically detected recurrences in patients with negative SLN biopsy[9]. Guide wire localisation may adversely influence visualisation of the sentinel node[107].

ALND is the standard treatment for patients with SN metastasis but most of these patients have negative non-sentinel nodes. In a retrospective study of 400 consecutive patients the SLN contained metastases in 148 patients (38.5%)[108]. In this patient group those with T2 tumours, micrometastases in SLNs and extracapsular node extension were more likely to have non-SLN metastases in both univariate and multivariate analyses. Others have devised scoring systems to help identify a subgroup of patients who have a low risk of having non-sentinel node metastases, obviating the need for ALND[109,110].

For patients with a primary tumour greater than 3 cm the success of SLNB shows little difference to those with smaller tumours[20,111]. In patients with multifocal breast cancer sentinel node identification has been reported in 94% and is an accurate predictor of nodal status[112]. This type of cancer favours a periareolar or subareolar injection protocol. Recent published work involving 213 patients found that although patients with large and/or multifocal tumours were more likely to have a positive sentinel node, the findings provide some indication that SNLB may be reliable for staging the axilla in these patients[113]. SLNB performed following excisional biopsy demonstrates satisfactory results[48,114].

Patients with ductal carcinoma-in-situ (DCIS) have an excellent long term prognosis (98% survival) but 10–29% of these patients will have invasive cancer at definitive surgery[115–121]. Analysis of resected nodes from patients who had negative axillary surgery previously demonstrated micrometastases in 13% of nodes but none in patients who had disease recurrence[122]. In a study of 470 high risk patients with DCIS, 43 (9%) had SLN metastases with 21% of this group being upstaged[123]. A recent review of 179 patients who underwent mastectomy with SNLB for DCIS were found to have invasive cancer on final pathology in 11%[124]. The use of SNLB

during mastectomy for DCIS allowed nearly all such patients to avoid axillary dissection. A larger study involving 854 patients with pure DCIS identified SLN metastases in 1.4% of patients[125]. Based on this finding SNLB could not be considered a standard procedure. The sole criteria should be when any uncertainty exists regarding the presence of invasive foci at definitive histology[126].

False negative rate

The false negative rate is the percentage of node positive patients who are missed by mapping[9]. In one centre there has been no axillary recurrence (mean 5 years) following a negative node biopsy in 1914 patients[9]. A more recent study involving 842 patients demonstrated a false negative rate of 9.6% with grade 3 tumours compared with 4.7% in patients with grade 2 tumours ($p = 0.022$)[35]. The false negative rate in patients who had one sentinel node harvested was 10.1% compared with 1.1% in those who had three or more sentinel nodes removed ($p = 0.010$).

Data from case–control studies to date indicate SLN biopsy to be highly predictive of axillary node status with a false negative rate of less than 5%[127]. Reasons for false negative results are attributed to changes in surgical personnel, difficult lymph node location and absence of a thorough histological study[128]. As stated previously factors militating against sentinel node identification are increasing age, increasing body mass index, tumour outside the upper outer quadrant and failure of visualisation on preoperative lymphoscintigraphy[35,129].

A review of 10 large observational studies revealed just 10 axillary recurrences in 2664 patients (0.4%) who did not undergo ALND following negative SLN biopsy[130]. A large study comprising 4008 patients and a median follow-up of 31 months had an overall axillary recurrence rate of 0.25%[131]. A further study in 234 patients (median follow-up 42 months) did not find an increased rate of axillary recurrence in patients with negative SLN or SLN micrometastases[132]. As the axillary recurrence rate should not exceed that seen after conventional axillary clearance surgery (1.0–2.3%), the figures quoted above compare favourably with other work published elsewhere[133–135]. In a study involving 335 patients with a median follow-up of 33 months, 15 patients (4.5%) who had negative SLNB and who did not undergo completion axillary dissection developed a cancer recurrence. Only 2 patients (0.6%) had an axillary recurrence. A further study following 95 patients (for up to 5 years) with a negative sentinel node without ALND demonstrated that <1% patients developed nodal extraaxillary recurrence[136]. A multicentre study involving specialised institutions and small community hospitals examined 3534 patients with a median follow-up of 37 months demonstrated that the axilla was the sole site of recurrence in 13 patients (0.6%)[137]. In 7 patients axillary relapse occurred after or concurrently with a local recurrence in the breast and in a further 7 cases it coincided with distant or extra-axillary lymphatic metastases. The overall recurrence rate was 27 (1.2%), overall 5-year survival rate was 91.6% and disease-free survival rate 92.1%. A recent study by Chetty *et al*. involving 434 patients demonstrated a false negative rate of 2.4% with pathological analysis indicating that blockage of the lymphatic tracts was the principal cause[38].A large multicentre randomised trial comparing SLN with ALND in 749 patients revealed a false negative rate of 16.7% in the ALND arm[24]. At a median follow-up of 56 months there were more locoregional recurrences in the SLN arm. The 5-year disease free interval was 89.8% in the ALND arm compared with 87.6% in the SLN arm. Unfortunately, the number enrolled was insufficient to make a definitive conclusion.

Internal mammary nodes

Internal mammary nodes with metastases have been documented as independent predictors of poor outcome for patients with breast cancer[138]. In one centre analysing the results of 640 patients, 94% demonstrated a sentinel node in the ipsilateral axilla and 46% also had sentinel nodes outside the axilla[53]. In 5% of patients drainage was exclusively to non-axillary sentinel nodes. The most important non-axillary drainage was to the internal mammary nodal chain and 40% of patients demonstrated a sentinel node in this area[53]. Sentinel lymph node biopsy of internal mammary nodes is associated with a low morbidity and has been shown to improve staging and change treatment strategy[139,140]. Proponents of evaluating internal mammary nodes argue that this supports lymphatic mapping as it provides more accurate staging although its impact on outcome is less clear[141,142]. Nonetheless, it has been demonstrated that metastases in the internal mammary nodes influence survival in a manner comparable to that of metastases in axillary lymph nodes[143]. A review with 30-year results demonstrated that patients with isolated IMN disease have a prognosis equivalent to that of patients with isolated axillary metastases[144]. Combination of metastatic disease in both axillary and internal mammary nodal chains has an especially poor prognosis with a 10 year survival of 37%[145]. Internal mammary nodes identified on preoperative lymphoscintigraphy require histopathological confirmation of disease before therapy is commenced[146]. Internal mammary nodes are best identified when peritumoural, intratumoural or subtumoural injections are made with some reports visualising these nodes in 10–30% of patients, whereas subdermal, intradermal, periareolar or subareolar injections result in much less frequent visualisation of these nodes[74,87]. A recently published prospective study involving 604 patients demonstrated drainage to internal mammary nodes in 17% resulting in a reduced overall 5-year survival and recurrence free survival[75]. Internal mammary nodal drainage predicted a nearly three-fold increased mortality risk in node positive patients.

Micrometastases

Micrometastases are defined as tumour deposits in nodes ranging from 0.2 to 2 mm with cells less than 0.2 mm, known as isolated tumour cells[147]. Despite the evidence of some retrospective studies there is controversy regarding the prognostic significance of micrometastases found only by immunohistochemistry staining, particularly when only isolated tumour cells are found[148]. A literature review on the clinical significance of micrometastases concluded that they were associated with a poorer prognosis than that associated with no axillary involvement[149]. In a study involving a 15-year follow-up on almost 100 patients and 1539 axillary lymph nodes with pT1 breast cancer, half of the patients developed distant metastases[150]. However, studies involving 234 patients and 84 patients (median follow-up 42 and 40 months respectively) showed that micrometastases were not associated with an increased risk of axillary recurrence or that outcome was significantly affected by the presence of micrometastases[132,151]. A study involving 2150 patients found micrometastases in 23% of involved sentinel nodes and submicrometastases in 16%[130]. Additional macrometastases were found in 15% and 4%, respectively, resulting in altered treatment in 7% of patients. In a recently published study involving 2408 patients detection of micrometastatic carcinoma was a major indicator of poorer survival[152]. In addition, 9.3% of these patients had additional axillary nodal disease on axillary dissection and decreased survival when axillary dissection was omitted. A further study involving the re-examination of axillary node specimens (using modern pathological techniques) obtained surgically 20 years ago revealed that 83 of 368 patients (23%) were converted to node positive[153]. Univariate and multivariate analysis revealed a significant relationship with disease free survival and disease free death.

Neoadjuvant therapy

In published work to date the SLN identification rate has ranged from 84 to 97% implying that the accuracy of sentinel node biopsy is not influenced by neoadjuvant therapy[154–165]. A recent prospective study involving 129 patients with infiltrating breast carcinoma and clinically negative axillary nodal disease demonstrated identification of the sentinel node in 94% following neoadjuvant therapy[166]. Fifty-six of these patients had tumour in the sentinel node with eight having no tumour giving a false negative rate of 14.3%. The false negative patients were correlated with larger tumours and positive nodal status. It would appear therefore that performing SNLB after neoadjuvant therapy can predict axillary lymph nodal status with high accuracy in patients who are clinically node negative at presentation. Questions remain as to whether all nodes respond equally to therapy and a high false negative rate (up to 33%) has been reported in some of these series. Despite recent data, the preferred practice remains performing SLNB prior to commencement of neoadjuvant therapy.

Summary

Lymphatic mapping for early breast cancer has become the standard of care but there is as yet no single study that demonstrates conclusively which particular sentinel node protocol is best for a specific patient.

References

[1] Fisher ER, Costantino J, Fisher B, Redmond C. Pathologic findings from the National Surgical Adjuvant Breast Project (Protocol 4). Discriminants for 15-year survival. National Surgical Adjuvant Breast and Bowel Project Investigators. Cancer 1993; 71: 2141–50.

[2] Fitzgibbons PL, Page DL, Weaver D, *et al.* Prognostic factors in breast cancer. College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med 2000; 124: 966–78.

[3] Singletary SE, Allred C, Ashley P, *et al.* Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol 2002; 20: 3628–36.

[4] Warmuth MA, Bowen G, Prosnitz LR, *et al.* Complications of axillary lymph node dissection for carcinoma of the breast: a report based on a patient survey. Cancer 1998; 83: 1362–8.

[5] Hack TF, Cohen L, Katz J, Robson LS, Goss P. Physical and psychological morbidity after axillary lymph node dissection for breast cancer. J Clin Oncol 1999; 17: 143–9.

[6] Schrenk P, Rieger R, Shamiyeh A, Wayand W. Morbidity following sentinel lymph node biopsy versus axillary lymph node dissection for patients with breast carcinoma. Cancer 2000; 88: 608–14.

[7] Goyal A, Newcombe RG, Chhabra A, Mansel RE. Morbidity in breast cancer patients with sentinel node metastases undergoing delayed axillary lymph node dissection (ALND) compared with immediate ALND. Ann Surg Oncol 2008; 15: 262–7.

[8] Morton DL, Bostick PJ. Will the true sentinel node please stand? Ann Surg Oncol 1999; 6: 12–14.

[9] Jakub JW, Cox CE, Pippas AW, Gardner M, Pendas S, Reintgen DS. Controversial topics in breast lymphatic mapping. Semin Oncol 2004; 31: 324–32.

[10] Madsen AH, Jensen AR, Christiansen P, *et al.* Does the introduction of sentinel node biopsy increase the number of node positive patients with early breast cancer? A population based study form the Danish Breast Cancer Cooperative Group. Acta Oncol 2008; 47: 239–47.

[11] Schulze T, Mucke J, Markwardt J, Schlag PM, Bembenek A. Long-term morbidity of patients with early breast cancer after sentinel lymph node biopsy compared to axillary lymph node dissection. J Surg Oncol 2006; 93: 109–19.

[12] Rutgers EJ. Sentinel node biopsy: interpretation and management of patients with immunohistochemistry-positive sentinel nodes and those with micrometastases. J Clin Oncol 2008; 26: 698–702.

[13] Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymphadenectomy in breast cancer. J Clin Oncol 1997; 15: 2345–50.

[14] Krag D, Weaver D, Ashikaga T, *et al.* The sentinel node in breast cancer–a multicenter validation study. N Engl J Med 1998; 339: 941–6.

[15] Borgstein PJ, Pijpers R, Comans EF, van Diest PJ, Boom RP, Meijer S. Sentinel lymph node biopsy in breast cancer: guidelines and pitfalls of lymphoscintigraphy and gamma probe detection. J Am Coll Surg 1998; 186: 275–83.

[16] Liberman L, Cody HS, 3rd, Hill AD, *et al.* Sentinel lymph node biopsy after percutaneous diagnosis of nonpalpable breast cancer. Radiology 1999; 211: 835–44.

[17] Kapteijn BA, Nieweg OE, Petersen JL, *et al.* Identification and biopsy of the sentinel lymph node in breast cancer. Eur J Surg Oncol 1998; 24: 427–30.

[18] McMasters KM, Wong SL, Chao C, *et al.* Defining the optimal surgeon experience for breast cancer sentinel lymph node biopsy: a model for implementation of new surgical techniques. Ann Surg 2001; 234: 292–9 (discussion 299–300).

[19] Krag DN, Harlow S. Current status of sentinel node surgery in breast cance. Oncology (Williston Park) 2003; 17: 1663–6 (discussion 1669–70, 1675–6).

[20] Jakub JW, Pendas S, Reintgen DS. Current status of sentinel lymph node mapping and biopsy: facts and controversies. Oncologist 2003; 8: 59–68.

[21] Chao C, Wong SL, Tuttle TM, *et al.* Sentinel lymph node biopsy for breast cancer: improvement in results over time. Breast J 2004; 10: 337–44.

[22] Mansel RE, Fallowfield L, Kissin M, *et al.* Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst 2006; 98: 599–609.

[23] Veronesi U, Paganelli G, Viale G, *et al.* Sentinel-lymph-node biopsy as a staging procedure in breast cancer: update of a randomised controlled study. Lancet Oncol 2006; 7: 983–90.

[24] Zavagno G, De Salvo GL, Scalco G, *et al.* A Randomized clinical trial on sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer: results of the Sentinella/GIVOM trial. Ann Surg 2008; 247: 207–13.

[25] Kohrt HE, Olshen RA, Bermas HR, *et al.* New models and online calculator for predicting non-sentinel lymph node status in sentinel lymph node positive breast cancer patients. BMC Cancer 2008; 8: 66.

[26] Maaskant AJ, van de Poll-Franse LV, Voogd AC, *et al.* Stage migration due to introduction of the sentinel node procedure: a population-based study. Breast Cancer Res Treat 2008 [Epub ahead of print].

[27] Ho VK, van der Heiden-van der Loo M, Rutgers EJ, *et al.* Implementation of sentinel node biopsy in breast cancer patients in the Netherlands. Eur J Cancer 2008; 44: 683–91.

[28] Kaufman G, Guth AA, Pachter HL, Roses DF. A cautionary tale: anaphylaxis to isosulfan blue dye after 12 years and 3339 cases of lymphatic mapping. Am Surg 2008; 74: 152–5.

[29] Aydogan F, Celik V, Uras C, Salihoglu Z, Topuz U. A comparison of the adverse reactions associated with isosulfan blue versus methylene blue dye in sentinel lymph node biopsy for breast cancer. Am J Surg 2008; 195: 277–8.

[30] Chicken DW, Mansouri R, Ell PJ, Keshtgar MR. Allergy to technetium-labelled nanocolloidal albumin for sentinel node identification. Ann R Coll Surg Engl 2007; 89: 12–13.

[31] Edreira MM, Colombo LL, Perez JH, Sajaroff EO, de Castiglia SG. In vivo evaluation of three different 99mTc-labelled radiopharmaceuticals for sentinel lymph node identification. Nucl Med Commun 2001; 22: 499–504.

[32] Derossis AM, Fey J, Yeung H, *et al.* A trend analysis of the relative value of blue dye and isotope localization in 2,000 consecutive cases of sentinel node biopsy for breast cancer. J Am Coll Surg 2001; 193: 473–8.

[33] Radovanovic Z, Golubovic A, Plzak A, Stojiljkovic B, Radovanovic D. Blue dye versus combined blue dye-radioactive tracer technique in detection of sentinel lymph node in breast cancer. Eur J Surg Oncol 2004; 30: 913–17.

[34] Pelosi E, Ala A, Bello M, *et al.* Impact of axillary nodal metastases on lymphatic mapping and sentinel lymph node identification rate in patients with early stage breast cancer. Eur J Nucl Med Mol Imaging 2005; 32: 937–42.

[35] Goyal A, Newcombe RG, Chhabra A, Mansel RE. Factors affecting failed localisation and false-negative rates of sentinel node biopsy in breast cancer – results of the ALMANAC validation phase. Breast Cancer Res Treat 2006; 99: 203–8.

[36] Takei H, Suemasu K, Kurosumi M, *et al.* Added value of the presence of blue nodes or hot nodes in sentinel lymph node biopsy of breast cancer. Breast Cancer 2006; 13: 179–85.

[37] Buscombe J, Paganelli G, Burak ZE, *et al.* Sentinel node in breast cancer procedural guidelines. Eur J Nucl Med Mol Imaging 2007; 34: 2154–9.

[38] Chetty U, Chin PK, Soon PH, Jack W, Thomas JS. Combination blue dye sentinel lymph node biopsy and axillary node sampling: the Edinburgh experience. Eur J Surg Oncol 2008; 34: 13–16.

[39] Boileau JF, Easson A, Escallon JM, *et al.* Sentinel nodes in breast cancer: relevance of axillary level II nodes and optimal number of nodes that need to be removed. Ann Surg Oncol 2008; 15: 1710–6.

[40] Mariani G, Moresco L, Viale G, *et al.* Radioguided sentinel lymph node biopsy in breast cancer surgery. J Nucl Med 2001; 42: 1198–215.

[41] Motomura K, Noguchi A, Hashizume T, *et al.* Usefulness of a solid-state gamma camera for sentinel node identification in patients with breast cancer. J Surg Oncol 2005; 89: 12–17.

[42] Marchal F, Rauch P, Morel O, *et al.* Results of preoperative lymphoscintigraphy for breast cancer are predictive of identification of axillary sentinel lymph nodes. World J Surg 2006; 30: 55–62.

[43] Shoher A, Diwan A, Teh BS, Lu HH, Fisher R, Lucci A, Jr. Lymphoscintigraphy does not enhance sentinel node identification or alter management of patients with early breast cancer. Curr Surg 2006; 63: 207–12.

[44] Borgstein PJ, Meijer S, Pijpers RJ, van Diest PJ. Functional lymphatic anatomy for sentinel node biopsy in breast cancer: echoes from the past and the periareolar blue method. Ann Surg 2000; 232: 81–9.

[45] Pelosi E, Baiocco C, Ala A, *et al.* Lymphatic mapping in early stage breast cancer: comparison between periareolar and subdermal injection. Nucl Med Commun 2003; 24: 519–23.

[46] Pelosi E, Bello M, Giors M, *et al.* Sentinel lymph node detection in patients with early-stage breast cancer: comparison of periareolar and subdermal/peritumoral injection techniques. J Nucl Med 2004; 45: 220–5.

[47] Wong SL, Edwards MJ, Chao C, *et al.* Sentinel lymph node biopsy for breast cancer: impact of the number of sentinel nodes removed on the false-negative rate. J Am Coll Surg 2001; 192: 684–9 (discussion 689–91).

[48] Pendas S, Giuliano R, Swor G, Gardner M, Jakub J, Reintgen DS. Worldwide experience with lymphatic mapping for invasive breast cancer. Semin Oncol 2004; 31: 318–23.

[49] Torrenga H, Meijer S, Fabry H, van der Sijp J. Sentinel node biopsy in breast cancer patients: triple technique as a routine procedure. Ann Surg Oncol 2004; 11: S231–5.

[50] Cox CE, Salud CJ, Cantor A, *et al.* Learning curves for breast cancer sentinel lymph node mapping based on surgical volume analysis. J Am Coll Surg 2001; 193: 593–600.

[51] Aarsvold JN, Alazraki NP. Update on detection of sentinel lymph nodes in patients with breast cancer. Semin Nucl Med 2005; 35: 116–28.

[52] Uren RF, Thompson JF, Howman-Giles R. Lymphatic drainage of the skin and breast: locating the sentinel nodes. Amsterdam: Harwood Academic; 1999.

[53] Uren RF, Howman-Giles R, Chung D, Thompson JF. Nuclear medicine aspects of melanoma and breast lymphatic mapping. Semin Oncol 2004; 31: 338–48.

[54] Kawase K, Gayed IW, Hunt KK, *et al.* Use of lymphoscintigraphy defines lymphatic drainage patterns before sentinel lymph node biopsy for breast cancer. J Am Coll Surg 2006; 203: 64–72.

[55] Lerman H, Metser U, Lievshitz G, Sperber F, Shneebaum S, Even-Sapir E. Lymphoscintigraphic sentinel node identification in patients with breast cancer: the role of SPECT-CT. Eur J Nucl Med Mol Imaging 2006; 33: 329–37.

[56] Lerman H, Lievshitz G, Zak O, Metser U, Schneebaum S, Even-Sapir E. Improved sentinel node identification by SPECT/CT in

overweight patients with breast cancer. J Nucl Med 2007; 48: 201–6.
[57] Tsushima H, Takayama T, Kizu H, *et al.* Advantages of upright position imaging with medium-energy collimator for sentinel node lymphoscintigraphy in breast cancer patients. Ann Nucl Med 2007; 21: 123–8.
[58] Paredes P, Vidal-Sicart S, Zanon G, *et al.* Radioguided occult lesion localisation in breast cancer using an intraoperative portable gamma camera: first results. Eur J Nucl Med Mol Imaging 2008; 35: 230–5.
[59] Tanis PJ, Nieweg OE, Valdes Olmos RA, Kroon BB. Anatomy and physiology of lymphatic drainage of the breast from the perspective of sentinel node biopsy. J Am Coll Surg 2001; 192: 399–409.
[60] Turner-Warwick RT. The lymphatics of the breast. Br J Surg 1959; 46: 574–82.
[61] Shen P, Glass EC, DiFronzo LA, Giuliano AE. Dermal versus intraparenchymal lymphoscintigraphy of the breast. Ann Surg Oncol 2001; 8: 241–8.
[62] Kaleya RN, Heckman JT, Most M, Zager JS. Lymphatic mapping and sentinel node biopsy: a surgical perspective. Semin Nucl Med 2005; 35: 129–34.
[63] Suami H, Pan WR, Mann GB, Taylor GI. The lymphatic anatomy of the breast and its implications for sentinel lymph node biopsy: a human cadaver study. Ann Surg Oncol 2008; 15: 863–71.
[64] Nieweg OE, Jansen L, Valdes Olmos RA, *et al.* Lymphatic mapping and sentinel lymph node biopsy in breast cancer. Eur J Nucl Med 1999; 26: S11–16.
[65] Canavese G, Gipponi M, Catturich A, *et al.* Pattern of lymphatic drainage to the sentinel lymph node in breast cancer patients. J Surg Oncol 2000; 74: 69–74.
[66] Byrd DR, Dunnwald LK, Mankoff DA, *et al.* Internal mammary lymph node drainage patterns in patients with breast cancer documented by breast lymphoscintigraphy. Ann Surg Oncol 2001; 8: 234–40.
[67] Estourgie SH, Nieweg OE, Olmos RA, Rutgers EJ, Kroon BB. Lymphatic drainage patterns from the breast. Ann Surg 2004; 239: 232–7.
[68] Nieweg OE, Estourgie SH, van Rijk MC, Kroon BB. Rationale for superficial injection techniques in lymphatic mapping in breast cancer patients. J Surg Oncol 2004; 87: 153–6.
[69] Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. Ann Surg 1994; 220: 391–8 (discussion 398–401).
[70] Albertini JJ, Lyman GH, Cox C, *et al.* Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. JAMA 1996; 276: 1818–22.
[71] Lin KM, Patel TH, Ray A, *et al.* Intradermal radioisotope is superior to peritumoral blue dye or radioisotope in identifying breast cancer sentinel nodes. J Am Coll Surg 2004; 199: 561–6.
[72] D'Eredita G, Giardina C, Ingravallo G, Rubini G, Lattanzio V, Berardi T. Sentinel lymph node biopsy in multiple breast cancer using subareolar injection of the tracer. Breast 2007; 16: 316–22.
[73] Varghese P, Abdel-Rahman AT, Akberali S, Mostafa A, Gattuso JM, Carpenter R. Methylene blue dye – a safe and effective alternative for sentinel lymph node localization. Breast J 2008; 14: 61–7.
[74] Park C, Seid P, Morita E, *et al.* Internal mammary sentinel lymph node mapping for invasive breast cancer: implications for staging and treatment. Breast J 2005; 11: 29–33.
[75] Yao MS, Kurland BF, Smith AH, *et al.* Internal mammary nodal chain drainage is a prognostic indicator in axillary node-positive breast cancer. Ann Surg Oncol 2007; 14: 2985–93.
[76] Mudun A, Sanli Y, Ozmen V, *et al.* Comparison of different injection sites of radionuclide for sentinel lymph node detection in breast cancer: single institution experience. Clin Nucl Med 2008; 33: 262–7.
[77] Borgstein PJ, Meijer S, Pijpers R. Intradermal blue dye to identify sentinel lymph-node in breast cancer. Lancet 1997; 349: 1668–9.
[78] Krynyckyi BR, Kim CK, Mosci K, *et al.* Areolar-cutaneous "junction" injections to augment sentinel node count activity. Clin Nucl Med 2003; 28: 97–107.
[79] Kern KA. Lymphoscintigraphic anatomy of sentinel lymphatic channels after subareolar injection of technetium 99m sulfur colloid. J Am Coll Surg 2001; 193: 601–8.
[80] Kern KA. Breast lymphatic mapping using subareolar injections of blue dye and radiocolloid: illustrated technique. J Am Coll Surg 2001; 192: 545–50.
[81] Vargas HI, Tolmos J, Agbunag RV, *et al.* A validation trial of subdermal injection compared with intraparenchymal injection for sentinel lymph node biopsy in breast cancer. Am Surg 2002; 68: 87–91.
[82] Kern KA. Concordance and validation study of sentinel lymph node biopsy for breast cancer using subareolar injection of blue dye and technetium 99m sulfur colloid. J Am Coll Surg 2002; 195: 467–75.
[83] Kern KA. Sentinel lymph node mapping in breast cancer using subareolar injection of blue dye. J Am Coll Surg 1999; 189: 539–45.
[84] Klimberg VS, Rubio IT, Henry R, Cowan C, Colvert M, Korourian S. Subareolar versus peritumoral injection for location of the sentinel lymph node. Ann Surg 1999; 229: 860–4 (discussion 864–5).
[85] Chagpar A, Martin 3rd RC, Chao C, *et al.* Validation of subareolar and periareolar injection techniques for breast sentinel lymph node biopsy. Arch Surg 2004; 139: 614–18 (discussion 618–20).
[86] Alazraki NP, Styblo T, Grant SF, Cohen C, Larsen T, Aarsvold JN. Sentinel node staging of early breast cancer using lymphoscintigraphy and the intraoperative gamma-detecting probe. Semin Nucl Med 2000; 30: 56–64.
[87] Alazraki NP, Styblo T, Grant SF, *et al.* Sentinel node staging of early breast cancer using lymphoscintigraphy and the intraoperative gamma detecting probe. Radiol Clin North Am 2001; 39: 947–56 viii.
[88] Styblo T, Aarsvold JN, Grant SF, *et al.* Sentinel lymph nodes: optimizing success. Semin Roentgenol 2001; 36: 261–9.
[89] van der Ploeg IM, Kroon BB, Antonini N, Valdes Olmos RA, Rutgers EJ, Nieweg OE. Axillary and extra-axillary lymph node recurrences after a tumor-negative sentinel node biopsy for breast cancer using intralesional tracer administration. Ann Surg Oncol 2008; 15: 1025–31.
[90] McCarter MD, Yeung H, Yeh S, Fey J, Borgen PI, Cody 3rd HS. Localization of the sentinel node in breast cancer: identical results with same-day and day-before isotope injection. Ann Surg Oncol 2001; 8: 682–6.
[91] Babiera GV, Delpassand ES, Breslin TM, *et al.* Lymphatic drainage patterns on early versus delayed breast lymphoscintigraphy performed after injection of filtered Tc-99m sulfur colloid in breast cancer patients undergoing sentinel lymph node biopsy. Clin Nucl Med 2005; 30: 11–15.
[92] Bass SS, Cox CE, Salud CJ, *et al.* The effects of postinjection massage on the sensitivity of lymphatic mapping in breast cancer. J Am Coll Surg 2001; 192: 9–16.
[93] Ikomi F, Hunt J, Hanna G, Schmid-Schonbein GW. Interstitial fluid, plasma protein, colloid, and leukocyte uptake into initial lymphatics. J Appl Physiol 1996; 81: 2060–7.
[94] Carter BA, Jensen RA, Simpson JF, Page DL. Benign transport of breast epithelium into axillary lymph nodes after biopsy. Am J Clin Pathol 2000; 113: 259–65.
[95] Diaz NM, Cox CE, Ebert M, *et al.* Benign mechanical transport of breast epithelial cells to sentinel lymph nodes. Am J Surg Pathol 2004; 28: 1641–5.
[96] Fitzgibbons PL, LiVolsi VA. Recommendations for handling radioactive specimens obtained by sentinel lymphadenectomy. Surgical Pathology Committee of the College of American Pathologists, and the Association of Directors of Anatomic and Surgical Pathology. Am J Surg Pathol 2000; 24: 1549–51.

[97] Nugent N, Hill AD, Casey M, *et al.* Safety guidelines for radiolocalised sentinel node resection. Ir J Med Sci 2001; 170: 236–8.
[98] Morton R, Horton PW, Peet DJ, Kissin MW. Quantitative assessment of the radiation hazards and risks in sentinel node procedures. Br J Radiol 2003; 76: 117–22.
[99] Gentilini O, Cremonesi M, Trifiro G, *et al.* Safety of sentinel node biopsy in pregnant patients with breast cancer. Ann Oncol 2004; 15: 1348–51.
[100] Michel R, Hofer C. Radiation safety precautions for sentinel lymph node procedures. Health Phys 2004; 86: S35–7.
[101] Law M, Chow LW, Kwong A, Lam CK. Sentinel lymph node technique for breast cancer: radiation safety issues. Semin Oncol 2004; 31: 298–303.
[102] Nejc D, Wrzesien M, Piekarski J, *et al.* Sentinel node biopsy in patients with breast cancer – evaluation of exposure to radiation of medical staff. Eur J Surg Oncol 2006; 32: 133–8.
[103] Specht MC, Fey JV, Borgen PI, Cody 3rd HS. Is the clinically positive axilla in breast cancer really a contraindication to sentinel lymph node biopsy? J Am Coll Surg 2005; 200: 10–14.
[104] Knauer M, Konstantiniuk P, Haid A, *et al.* Multicentric breast cancer: a new indication for sentinel node biopsy – a multi-institutional validation study. J Clin Oncol 2006; 24: 3374–80.
[105] Ruano R, Ramos M, Garcia-Talavera JR, *et al.* Staging the axilla with selective sentinel node biopsy in patients with previous excision of non-palpable and palpable breast cancer. Eur J Nucl Med Mol Imaging 2008; 35: 1299–304.
[106] Koizumi M, Koyama M, Tada K, *et al.* The feasibility of sentinel node biopsy in the previously treated breast. Eur J Surg Oncol 2008; 34: 365–8.
[107] Jansen JE, Bekker J, de Haas MJ, *et al.* The influence of wire localisation for non-palpable breast lesions on visualisation of the sentinel node. Eur J Nucl Med Mol Imaging 2006; 33: 1296–300.
[108] Ozmen V, Karanlik H, Cabioglu N, *et al.* Factors predicting the sentinel and non-sentinel lymph node metastases in breast cancer. Breast Cancer Res Treat 2006; 95: 1–6.
[109] Barranger E, Morel O, Coutant C. Axilla scoring systems predicting risk of non-sentinel-node metastasis in breast cancer patients with a positive sentinel node. Ann Surg Oncol 2008; 15: 1261–2 (author reply 1263–4).
[110] Coutant C, Rouzier R, Fondrinier E, *et al*., Validation of the Tenon breast cancer score for predicting non-sentinel lymph node status in breast cancer patients with sentinel lymph node metastasis: a prospective multicenter study. Breast Cancer Res Treat 2008 [Epub ahead of print].
[111] Schule J, Frisell J, Ingvar C, Bergkvist L. Sentinel node biopsy for breast cancer larger than 3 cm in diameter. Br J Surg 2007; 94: 948–51.
[112] Tousimis E, Van Zee KJ, Fey JV, *et al.* The accuracy of sentinel lymph node biopsy in multicentric and multifocal invasive breast cancers. J Am Coll Surg 2003; 197: 529–35.
[113] Behm EC, Buckingham JM. Sentinel node biopsy in larger or multifocal breast cancers: to do or not to do. ANZ J Surg 2008; 78: 151–7.
[114] Haigh PI, Hansen NM, Qi K, Giuliano AE. Biopsy method and excision volume do not affect success rate of subsequent sentinel lymph node dissection in breast cancer. Ann Surg Oncol 2000; 7: 21–7.
[115] Cox CE, Nguyen K, Gray RJ, *et al.* Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): why map DCIS? Am Surg 2001; 67: 513–19 (discussion 519–21).
[116] Burak Jr WE, Owens KE, Tighe MB, *et al.* Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. Arch Surg 2000; 135: 700–3.
[117] Lee CH, Carter D, Philpotts LE, *et al.* Ductal carcinoma in situ diagnosed with stereotactic core needle biopsy: can invasion be predicted? Radiology 2000; 217: 466–70.
[118] Klauber-DeMore N, Tan LK, Liberman L, *et al.* Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion? Ann Surg Oncol 2000; 7: 636–42.
[119] Darling ML, Smith DN, Lester SC, *et al.* Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. AJR Am J Roentgenol 2000; 175: 1341–6.
[120] Renshaw AA. Predicting invasion in the excision specimen from breast core needle biopsy specimens with only ductal carcinoma in situ. Arch Pathol Lab Med 2002; 126: 39–41.
[121] Mendez I, Andreu FJ, Saez E, *et al.* Ductal carcinoma in situ and atypical ductal hyperplasia of the breast diagnosed at stereotactic core biopsy. Breast J 2001; 7: 14–18.
[122] Lara JF, Young SM, Velilla RE, Santoro EJ, Templeton SF. The relevance of occult axillary micrometastasis in ductal carcinoma in situ: a clinicopathologic study with long-term follow-up. Cancer 2003; 98: 2105–13.
[123] Moore KH, Sweeney KJ, Wilson ME, *et al.* Outcomes for women with ductal carcinoma-in-situ and a positive sentinel node: a multi-institutional audit. Ann Surg Oncol 2007; 14: 2911–17.
[124] Dominguez FJ, Golshan M, Black DM, *et al.* Sentinel node biopsy is important in mastectomy for ductal carcinoma in situ. Ann Surg Oncol 2008; 15: 268–73.
[125] Intra M, Rotmensz N, Veronesi P, *et al.* Sentinel node biopsy is not a standard procedure in ductal carcinoma in situ of the breast: the experience of the European institute of oncology on 854 patients in 10 years. Ann Surg 2008; 247: 315–19.
[126] van Deurzen CH, Hobbelink MG, van Hillegersberg R, van Diest PJ. Is there an indication for sentinel node biopsy in patients with ductal carcinoma in situ of the breast? A review. Eur J Cancer 2007; 43: 993–1001.
[127] Mansel RE, Goyal A. European studies on breast lymphatic mapping. Semin Oncol 2004; 31: 304–10.
[128] Vidal-Sicart S, Pons F, Puig S, *et al.* Identification of the sentinel lymph node in patients with malignant melanoma: what are the reasons for mistakes? Eur J Nucl Med Mol Imaging 2003; 30: 362–6.
[129] Cox CE, Dupont E, Whitehead GF, *et al.* Age and body mass index may increase the chance of failure in sentinel lymph node biopsy for women with breast cancer. Breast J 2002; 8: 88–91.
[130] van Rijk MC, Peterse JL, Nieweg OE, Oldenburg HS, Rutgers EJ, Kroon BB. Additional axillary metastases and stage migration in breast cancer patients with micrometastases or submicrometastases in sentinel lymph nodes. Cancer 2006; 107: 467–71.
[131] Naik AM, Fey J, Gemignani M, *et al.* The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection: a follow-up study of 4008 procedures. Ann Surg 2004; 240: 462–8 (discussion 468–71).
[132] Langer I, Marti WR, Guller U, *et al.* Axillary recurrence rate in breast cancer patients with negative sentinel lymph node (SLN) or SLN micrometastases: prospective analysis of 150 patients after SLN biopsy. Ann Surg 2005; 241: 152–8.
[133] Recht A, Pierce SM, Abner A, *et al.* Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. J Clin Oncol 1991; 9: 988–96.
[134] Fredriksson I, Liljegren G, Arnesson LG, *et al.* Consequences of axillary recurrence after conservative breast surgery. Br J Surg 2002; 89: 902–8.
[135] Nieweg OE, van Rijk MC, Valdes Olmos RA, Hoefnagel CA. Sentinel node biopsy and selective lymph node clearance-impact on regional control and survival in breast cancer and melanoma. Eur J Nucl Med Mol Imaging 2005; 32: 631–4.
[136] Domenech A, Benitez A, Bajen MT, Pla MJ, Gil M, Martin-Comin J. Patients with breast cancer and negative sentinel lymph node biopsy without additional axillary lymph node

dissection: a follow-up study of up to 5 years. Oncology 2007; 72: 27–32.
[137] Bergkvist L, de Boniface J, Jonsson PE, Ingvar C, Liljegren G, Frisell J. Axillary recurrence rate after negative sentinel node biopsy in breast cancer: three-year follow-up of the Swedish Multicenter Cohort Study. Ann Surg 2008; 247: 150–6.
[138] Shen J, Hunt KK, Mirza NQ, *et al.* Intramammary lymph node metastases are an independent predictor of poor outcome in patients with breast carcinoma. Cancer 2004; 101: 1330–7.
[139] Tanis PJ, Nieweg OE, Valdes Olmos RA, *et al.* Impact of non-axillary sentinel node biopsy on staging and treatment of breast cancer patients. Br J Cancer 2002; 87: 705–10.
[140] Noguchi M. Relevance and practicability of internal mammary sentinel node biopsy for breast cancer. Breast Cancer 2002; 9: 329–36.
[141] Galimberti V, Veronesi P, Arnone P, *et al.* Stage migration after biopsy of internal mammary chain lymph nodes in breast cancer patients. Ann Surg Oncol 2002; 9: 924–8.
[142] Fabry HF, Mutsaers PG, Meijer S, *et al.* Clinical relevance of parasternal uptake in sentinel node procedure for breast cancer. J Surg Oncol 2004; 87: 13–18.
[143] Bevilacqua JL, Gucciardo G, Cody HS, *et al.* A selection algorithm for internal mammary sentinel lymph node biopsy in breast cancer. Eur J Surg Oncol 2002; 28: 603–14.
[144] Veronesi U, Marubini E, Mariani L, Valagussa P, Zucali R. The dissection of internal mammary nodes does not improve the survival of breast cancer patients. 30-year results of a randomised trial. Eur J Cancer 1999; 35: 1320–5.
[145] Veronesi U, Cascinelli N, Bufalino R, *et al.* Risk of internal mammary lymph node metastases and its relevance on prognosis of breast cancer patients. Ann Surg 1983; 198: 681–4.
[146] Benda RK, Cendan JC, Copeland EM, *et al.* Should decisions on internal mammary lymph node irradiation be based on current lymphoscintigraphy techniques for sentinel lymph node identification? Cancer 2004; 100: 518–23.
[147] Hermanek P, Hutter RV, Sobin LH, Wittekind C. International Union Against Cancer.Classification of isolated tumor cells and micrometastasis. Cancer 1999; 86: 2668–73.
[148] Quan ML, Cody 3rd HS. Missed micrometastatic disease in breast cancer. Semin Oncol 2004; 31: 311–17.
[149] Sakorafas GH, Geraghty J, Pavlakis G. The clinical significance of axillary lymph node micrometastases in breast cancer. Eur J Surg Oncol 2004; 30: 807–16.
[150] Susnik B, Frkovic-Grazio S, Bracko M. Occult micrometastases in axillary lymph nodes predict subsequent distant metastases in stage I breast cancer: a case-control study with 15-year follow-up. Ann Surg Oncol 2004; 11: 568–72.
[151] Martin 2nd RC, Chagpar A, Scoggins CR, *et al.* Clinicopathologic factors associated with false-negative sentinel lymph-node biopsy in breast cancer. Ann Surg 2005; 241: 1005–15.
[152] Cox CE, Kiluk JV, Riker AI, *et al.* Significance of sentinel lymph node micrometastases in human breast cancer. J Am Coll Surg 2008; 206: 261–8.
[153] Tan LK, Giri D, Hummer AJ, *et al.* Occult axillary node metastases in breast cancer are prognostically significant: results in 368 node-negative patients with 20-year follow-up. J Clin Oncol 2008; 26: 1803–9.
[154] Breslin TM, Cohen L, Sahin A, *et al.* Sentinel lymph node biopsy is accurate after neoadjuvant chemotherapy for breast cancer. J Clin Oncol 2000; 18: 3480–6.
[155] Fernandez A, Cortes M, Benito E, *et al.* Gamma probe sentinel node localization and biopsy in breast cancer patients treated with a neoadjuvant chemotherapy scheme. Nucl Med Commun 2001; 22: 361–6.
[156] Haid A, Tausch C, Lang A, *et al.* Is sentinel lymph node biopsy reliable and indicated after preoperative chemotherapy in patients with breast carcinoma? Cancer 2001; 92: 1080–4.
[157] Brady EW. Sentinel lymph node mapping following neoadjuvant chemotherapy for breast cancer. Breast J 2002; 8: 97–100.
[158] Stearns V, Ewing CA, Slack R, Penannen MF, Hayes DF, Tsangaris TN. Sentinel lymphadenectomy after neoadjuvant chemotherapy for breast cancer may reliably represent the axilla except for inflammatory breast cancer. Ann Surg Oncol 2002; 9: 235–42.
[159] Miller AR, Thomason VE, Yeh IT, *et al.* Analysis of sentinel lymph node mapping with immediate pathologic review in patients receiving preoperative chemotherapy for breast carcinoma. Ann Surg Oncol 2002; 9: 243–7.
[160] Julian TB, Dusi D, Wolmark N. Sentinel node biopsy after neoadjuvant chemotherapy for breast cancer. Am J Surg 2002; 184: 315–17.
[161] Piato JR, Barros AC, Pincerato KM, Sampaio AP, Pinotti JA. Sentinel lymph node biopsy in breast cancer after neoadjuvant chemotherapy. A pilot study. Eur J Surg Oncol 2003; 29: 118–20.
[162] Patel NA, Piper G, Patel JA, Malay MB, Julian TB. Accurate axillary nodal staging can be achieved after neoadjuvant therapy for locally advanced breast cancer. Am Surg 2004; 70: 696–9 (discussion 699–700).
[163] Mamounas EP, Brown A, Anderson S, *et al.* Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer: results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol 2005; 23: 2694–702.
[164] Kinoshita T, Takasugi M, Iwamoto E, Akashi-Tanaka S, Fukutomi T, Terui S. Sentinel lymph node biopsy examination for breast cancer patients with clinically negative axillary lymph nodes after neoadjuvant chemotherapy. Am J Surg 2006; 191: 225–9.
[165] Newman EA, Sabel MS, Nees AV, *et al.* Sentinel lymph node biopsy performed after neoadjuvant chemotherapy is accurate in patients with documented node-positive breast cancer at presentation. Ann Surg Oncol 2007; 14: 2946–52.
[166] Gimbergues P, Abrial C, Durando X, *et al.* Sentinel lymph node biopsy after neoadjuvant chemotherapy is accurate in breast cancer patients with a clinically negative axillary nodal status at presentation. Ann Surg Oncol 2008; 15: 1316–21.