

lymph node. The purpose of this study was to identify factors predictive of non-sentinel lymph node involvement after a positive sentinel lymph node.

**Methods:** The medical records of 181 breast cancer patients who underwent sentinel lymph node biopsy examination and ALND were selected from a prospectively collected database and were reviewed for multiple clinicopathologic variables.

**Results:** Univariate analysis showed a significant association between non-sentinel node involvement and primary tumour size ( $p=0.000$ ), size of sentinel node metastasis ( $p=0.000$ ), extracapsular node extension ( $p=0.000$ ) and the number of negative sentinel nodes ( $p=0.002$ ). In a multivariate analysis, only extracapsular extension remained significantly associated with a positive non-SN status.

**Conclusions:** Extracapsular extension is an independent predictor of non sentinel node positivity when a positive sentinel node is found. However, more additional factors need to be identified before in selected cases axillary dissection as a surgical staging procedure can be omitted.

Variable	Univariate	Multivariate	
	<i>P</i>	<i>P</i>	Odds ratio (CI)
Tumour size	0.000*	0.23	1.044
SN metastasis size	0.000*	0.107	1.080
Extracapsular extension	0.000	0.003	0.291
Number of positive SNs	0.096*	0.347	1.347
Number of negative SNs	0.000*	0.076	0.606
Age	0.455		
Tumour type	0.065		
Multifocal	0.796		
Lymphovascular invasion	0.616		
ER positive	0.554		
PR positive	0.568		
Mode of detection	0.133		
Parenchymal invasion	0.081		

Categorical *p*-values were calculated in univariate analysis with Fisher's exact test.

Continues variables (\*) were calculated with Mann-Whitney U-test.

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#### The value of intraoperative frozen section examination of sentinel lymph nodes in breast cancer

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**Background:** Sentinel node biopsy is a standard diagnostic component for the treatment of patients with a primary mammary carcinoma. In an investigation of the prognostic survival of this cohort, a sentinel lymph node biopsy is indicated when a positive sentinel node is discovered. By concomitantly performing intraoperative lymph node biopsy and primary tumor resection, patients with a positive sentinel node are not subjected to the inconvenience and risks of second surgical intervention. The aim of this retrospective study was to determine the sensitivity, accuracy and long-term consequences of the frozen section examination of the sentinel node in breast cancer patients.

**Methods:** Sentinel lymph node biopsy was performed in 616 patients with an invasive tumor of the breast. Frozen sections of the sentinel node were taken from the optimal cross-sectional surface. In the event of a negative node, frozen sections were taken from the remaining sentinel node and stained using hematoxylin-eosin and immunohistochemistry.

**Results:** Sentinel node frozen biopsy accurately predicted the state of the axilla in 560 (90.9%) patients. There were 50 false-negative findings in patients with sentinel node metastases. The sensitivity and specificity of the intraoperative frozen section examination were 71.6% and 100%, respectively. Follow-up (mean 36.3 months) of all false-negative cases showed no development of local axillary recurrence. The results demonstrated no significant relation between tumor size and frozen section sensitivity. Frozen section investigation was less sensitive in ascertaining micrometastases (sensitivity 61.1%) than macrometastases (sensitivity 84.0%,  $p<0.001$ ). The majority of the false-negative results were due to the fact that micrometastases were not localized during intraoperative frozen section examination. However, the presence of micrometastases within the sentinel lymph node is of limited value since a positive sentinel lymph node biopsy was attained in only 30% of micrometastatic patients versus 61% of macrometastatic patients.

**Conclusion:** Intraoperative frozen section examination of the sentinel node is a useful predictor of axillary lymph node status in breast cancer

patients. Seventy-two percent of the patients with metastatic disease were correctly diagnosed and spared a second surgical procedure.

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#### Concordance of Her 2 neu and hormone receptor status between primary tumors and sentinel lymph node metastases

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**Background:** Earlier a 90–98% concordance has been observed between the primary and metastasis in both HER-2 neu and the hormone receptor status, though partly studied only on behalf of the oestrogen receptor (ER) and normally not all these factors simultaneously on the same nodes. Mostly they have included only distant metastases and macrometastasis, or the analysis was only made using immunohistochemistry (IHC).

For these reasons, our aim was to study the concordance in HER-2 neu amplification, as well as ER and progesterone receptor (PR) status between the primary tumours and SN (sentinel node) metastases, including also micrometastases and ITC.

**Methods:** The HER-2 neu amplification status and the status of hormone receptors ER and PR was evaluated in 99 sentinel node metastases from 38 primary tumours that were HER-2 neu positive in chromogenic in-situ hybridisation (CISH) and from 61 primary tumours that were CISH-. They consisted of 23 + 23 = 46 macrometastases, 6 + 28 = 34 micrometastases and 9 + 10 = 19 isolated tumour cells (ITC).

**Results:** No metastatic tissue for the CISH-analysis was found in 4 macro + 18 micro + 12 ITC = 34 cases. In the CISH+ primary tumours, 26 of 29 metastases were CISH+, including 23 macrometastases, 3 micrometastases and 3 ITC. Three were discordant turning negative in the metastasis. In the CISH- primary tumours, 35 of the 36 examined metastases were CISH-, while one micrometastasis showed a low level amplification of HER 2 neu gene.

The ER/PR status was concordant between the primary tumour and the SN-metastasis in 53/77 (68.8%), consisting of 29 macrometastases, 19 micrometastases and 5 ITC. No metastatic tissue for the analysis was found in 22/99 cases, consisting of 3 macro-metastases, 11 micrometastases and 8 ITC were cut. Altogether 24/77 cases were discordant.

Both the HER-2 neu amplification status and the ER and PR status could be assessed in 62/99 metastases. Full concordance in both HER-2 neu amplification status, that is positive or negative, as well as in the ER and PR status between the primary tumour and metastasis was observed in 38/62 (61.3%), that is 15/26 (57.7%) of the CISH+ cases and 23/36 (63.8%) of the CISH- cases. Of the 38 fully concordant cases were 24 macrometastatic, 13 micrometastatic and 1 ITC.

**Conclusions:** High concordance in HER-2 neu amplification, ER and PR status was observed between the primary tumours and their metastases, even with micrometastases and ITC, when evaluated separately. However, the full concordance between the primary tumour and the metastasis was observed less frequently.

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#### The distribution of axillary lymph nodes metastases and sentinel node biopsy after neoadjuvant chemotherapy in patients with locally advanced breast cancer

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**Background:** The use of neoadjuvant chemotherapy (NCT) becomes more ubiquitous in the treatment of locally advanced breast cancer (LABC), and axillary lymph nodes (ALN) downstage could be obtained in 20–30% pts. To perform SLNB substituting axillary lymph node dissection (ALND) in this pts population, the distribution of ALN metastases, SLNB successful rate (SR) and false negative rate (FNR) should be proved to be similar to that in early breast cancer.

**Methods:** First, we collected data of 370 LABC pts who underwent ALND after 2–3 cycles of NCT from 1996 to 2006. The ALN status at each level was analyzed. Then we performed SLNB followed by ALND in 88 pts after NCT from 2003 to 2007. We used Methylene blue alone in 81 pts and combined with 99mTc-SC in another 7 pts. The SR, FNR and accuracy of SLNB after NCT were evaluated.

**Results:** The distribution of ALN metastases in LABC after NCT was quite the same as that in early breast cancer, with very low incidence of skip metastases. After NCT, 30.3% pts had negative axilla, and ALN were positive only at L1 in 39.5% pts (Table 1).

The SR, FNR, and accuracy of SLNB with Methylene blue alone were 82.7% (67/81), 18.2% (10/55) and 85.1% (57/67), respectively; the rates with Methylene blue combined with 99mTc-SC were 100% (7/7), 16.7%

(1/6) and 85.7% (6/7), respectively. There was a trend for higher SR in the combined detection of SLNB.

The SR, FNR and accuracy of SLNB in 33 pts with obvious clinical ALN downstage were 97.0% (32/33), 15.0% (3/20) and 90.6% (29/32), respectively. The rates in the other 55 pts with no significant ALN downstage were 76.2% (42/55), 19.5% (8/41) and 80.9% (34/42), respectively. The p values were 0.011, 0.667, and 0.247, respectively.

**Conclusion:** The distribution of ALN metastases in LABC after NCT was quite the same as that in early breast cancer, with very low incidence of skip metastases. There was a trend for higher SLNB SR with the combination of Methylene blue with colloid. Significant higher SR was found in pts with obvious clinical ALN downstage, though with similar FNR and accuracy.

Table 1. The distribution of ALN metastases after NCT

Status of ALN at different levels			Patients	
L1	L2	L3	No.	(%)
L1(-)	L2(-)	L3(-)	112	(30.3%)
L1(-)	L2(+)	L3(+)	1	(0.2%)
L1(-)	L2(-)	L3(+)	0	(0.0%)
L1(-)	L2(+)	L3(-)	0	(0.0%)
L1(+)	L2(-)	L3(-)	146	(39.5%)
L1(+)	L2(-)	L3(+)	32	(8.6%)
L1(+)	L2(+)	L3(-)	41	(11.1%)
L1(+)	L2(+)	L3(+)	38	(10.3%)

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#### Preoperative lymphoscintigraphy did not improve the success rate of sentinel node biopsy in breast cancer patients

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**Background:** The role of preoperative lymphoscintigraphy in sentinel lymph node biopsy (SLNB) remains controversial in breast cancer patients.

**Material and Methods:** Firstly, we retrospectively analyzed a database containing 716 breast cancer patients who received SLNB. Secondly, we had a prospective randomized clinical trial, in which 113 patients with breast cancer were randomized into two groups. Preoperative lymphoscintigraphy was done in group one, and no preoperative lymphoscintigraphy in group two. Before SLNB, 99mTc labeled sulfur colloid and blue dye were injected subcutaneously above the primary tumor or around the biopsy cavity in all the patients. Either "hot" or blue nodes were regarded as sentinel lymph nodes (SLN). The success rates of SLNB between two groups were compared. No patients enrolled in the study received neoadjuvant chemotherapy.

**Results:** In the retrospective study, the success rate of SLNB was 98.2% (703/716). SLNs were well imaged by lymphoscintigraphy in 86.6% patients, and SLNs were located extra-axilla in 36 patients. The visualization of SLN in lymphoscintigraphy was not associated with histopathologic type, location and stage of primary tumor, and time interval from injection of radiocolloid to surgery. However, the negative lymphoscintigraphy results were associated with excision biopsy before injection of radiocolloid and axillary node metastases. Failure of surgical identification of axillary SLN was associated with whether hot spot was imaged by lymphoscintigraphy. In the prospective study, the total success rate of SLNB was 96.4% (109/113). There are 62 patients were randomized into group with preoperative lymphoscintigraphy (well imaged by lymphoscintigraphy in 88.7% patients) with the success rate of SLNB of 96.8% (60/62), and 52 patients were randomized into group without preoperative lymphoscintigraphy with success rate of 98.0% (50/51). There was no significant difference between two groups in success rate of SLNB (fisher exact test, p = 1.00).

**Conclusion:** Although preoperative lymphoscintigraphy was helpful in finding extra-axillary SLN. However, it could not improve the success rate and reduce the false negative rate of SLNB in breast cancer patients. Considering the complexity, time consumes, and cost of preoperative lymphoscintigraphy, it should be undergone for investigation purpose only at present.

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#### Sentinel node biopsy in patients with prior aesthetic breast surgery

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**Background:** Sentinel lymph node biopsy (SLNB) is the standard method for axillary staging in early-stage breast cancer. Recent studies have tried to elucidate controversies about initial contraindications to the technique. Up to date, there is little data to recommend sentinel node biopsy in patients with previous aesthetic breast surgery. Here we discuss our experience on sentinel node biopsy in patients with previous aesthetic breast surgery.

**Materials and Methods:** Between April 2001 and June 2007, 70 patients with previous breast aesthetic surgery underwent SLNB. Seventy five percent of patients had had a previous breast augmentation and 25% a breast reduction mammoplasty. All patients underwent lymphoscintigraphy with 99Tc the day before surgery. Sentinel node biopsy was performed in all patients and followed by axillary dissection when it was positive.

**Results:** The mean time from aesthetic surgery to tumour diagnosis was 10 years. Mean age at cosmetic surgery was 38 years old. Seventy percent of patients underwent conservative breast surgery and 30% mastectomy. The sentinel node identification rate was 100%. Lymphoscintigraphy showed bilateral drainage in two patients and drainage to the ipsilateral internal mammary chain in one case. The SLNB was positive in 23 cases (32%), of which 5 (7%) had micrometastasis, and 18 (25%) had macrometastasis. After a median follow up of 19 months no axillary recurrences were observed. One patient developed an ipsilateral breast local recurrence and one patient a distant metastasis.

**Conclusions:** Lymphoscintigraphy and sentinel node biopsy can accurately stage the axilla in patients with early-stage breast cancer and a previous aesthetic breast surgery. The presence of breast augmentation or reduction surgery is not a contraindication to SLNB technique.

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#### Axillary recurrence of breast cancer after negative sentinel lymph node biopsy

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**Background:** Sentinel lymph node biopsy (SLNB) is gaining popularity over axillary lymph node dissection for the detection of node-negative breast cancer, as it is less invasive and false negative results are generally less than 22%. However, regional node recurrence is a major concern for those whose cancer is detected by SLNB. We conducted a retrospective analysis of patient outcomes for those who had received SLNB to assess the rate of recurrence.

**Materials and Methods:** We examined the charts of 720 patients who had been diagnosed with breast cancer between December 2003 and January 2006 and whose SLNB was negative. Of this sample, 174 underwent the SLNB and axillary dissection; 453 patients had an SLNB and node sampling; 93 received only the SLNB. The SLNB was performed using a 99mTc-radiocolloid subareolar injection.

**Results:** The mean number of sentinel lymph nodes removed was 2.1 per patient. At a median follow up of 26 months (range 16-48 months), recurrence appeared in only 3 cases. All three had originally received only the SLNB; all three were also hormone receptor negative. Two of the cases were also c-erbB2 negative. All three recurrences occurred in the axilla; in two of the cases, there was also a recurrence in the internal mammary lymph node.

**Conclusion:** Axillary recurrence of breast cancer is low in patients who receive an SLNB. For those who are also hormone receptor negative, however, it may be important to also sample lymph nodes and examine internal mammary lymph nodes.

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#### Breast cancer patients with micrometastases versus non-metastatic lymph nodes – what is different?

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**Background:** Characterization of Breast Cancer (BC) patients (pts) with micrometastases (micm) in Sentinel Lymph Nodes (SLN) and comparison with BC pts with non-metastatic SLN (pT1 BC).

**Material and Methods:** Analysis of 312 BC pts diagnosed and treated in our department from January 1998 to October 2007.