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# Is full complete dissection axillary necessary for all patients with positive findings on sentinel lymph node biopsy? Validation of a breast cancer nomogram for predicting the likelihood of non sentinel lymph node

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**Background:** The sentinel lymph node (SLN) procedure is a reliable technique for assessing axillary lymph node involvement in breast cancer. To identify the individual patient's risk for non-SLN metastases, a nomogram was developed by the Breast Service of Memorial Sloan-Kettering Cancer Center. A nomogram is a tool to depict a complicated calculation created using variable following: pathologic size, tumor type and nuclear grade, lymphovascular invasion, multifocality, estrogen receptor status, method of detection of the SLN metastases (frozen section, serial H&E, routine H&E, IHC) number of positive SLNs and number of negative SLNs. The outcome of the nomogram is the predicted probability of non-SLN metastases. This can be determined by the web site <http://www.mskcc.org/nomograms> or through a personal digital compatible application. The aim of this study was to assess to nomogram's predictive accuracy in a population of breast cancer patients from Italy, in our hospital.

**Materials and Methods:** We consider 221 consecutive breast cancer patients that underwent an SLN biopsy for a clinical T1/2N0 breast cancer in the our Breast surgery Division. Data concerning these patients were collected in a database. The biopsy revealed metastatic disease in 61 patients (32%). To be included in the study population, patients had to meet the following criteria: patient had to undergo operation for a primary invasive breast cancer, without neoadjuvant therapy; the SLN biopsy had to be successful and the SLN had to contain any amount of metastatic disease.

Patient and tumor characteristics were collected from the prospective database for each variable of the MSKCC nomogram:

1. tumor type (ductal vs lobular carcinoma), nuclear grade
2. pathologic size
3. presence of lymphovascular invasion
4. multifocality
5. estrogen receptor status
6. method of detection of the SLN metastases (routine histopathology, serial H&E, IHC immunohistochemistry)
7. number of positive SLNs
8. number of negative SLNs

**Results:** The predicted probability of risk to have additional nodal metastases was calculated for each patient:

1. High Risk (57.3%) range 19–66% LNS/PZ (27/35)
2. Medium Risk (24.5%) range 10–18% LNS/PZ (4/16)
3. Low Risk (16.3%) range 3–9% LNS/PZ (0/10)

In the totality of the patients (61) 16% of the patients have found an inferior value to 10% of additional nodal metastases risk therefore consider you like patients with possibility to avoid a complete axillary dissection.

**Conclusions:** This method may allow identification of an individual risk extremely low for which the risks associated with complete dissection can overcome the beneficial effects. The nomogram provides a fairly accurate predicted probability for the likelihood of non sentinel lymph nodes (SLN) therefore in the practical current it would have to be used to avoid the complete axillary dissection, and its complications, in all the patients with low risk (<10%).

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# Axillary recurrence in breast cancer patients after a negative sentinel lymph node biopsy

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**Background:** Sentinel lymph node (SLN) biopsy is an accepted standard of care for patients with clinically node negative breast cancer. Validation studies have revealed false negative rates of 5–10%, but few studies have reported rates of axillary recurrence in SLN negative patients without completion axillary lymph node dissection (ALND).

**Materials and Methods:** A retrospective analysis was undertaken to examine axillary recurrence amongst a group of 314 clinically node negative patients undergoing SLN biopsy for symptomatic and screen-detected breast cancer between January 2004 and December 2006 (median tumour diameter 15 mm). The median age of patients was 64 yrs with a range of 23–88 years. Dual localization methods were used and

all patients were classified as sentinel lymph node negative on H&E step sections but included some patients with deposits of isolated tumour cells on either H&E or immunohistochemistry ( $\leq 0.2$  mm). The median tumour diameter for the invasive component was 15 mm (range 2–40 mm). To allow at least 12 months follow up, patients treated after December 2006 were excluded, together with those patients who had died without evidence of recurrence (4) and patients with DCIS only on final histology (18). This left 292 patients available for analysis, the majority of whom had received some form of adjuvant systemic therapy (262/292). Neoadjuvant patients with a negative sentinel lymph node pre-treatment were included as these did not proceed to axillary dissection after chemotherapy.

**Results:** At a median follow up of 28 months (range 13–48) there has been only one case of axillary recurrence (1/292). This occurred after 4 months and was the first site of treatment failure. Interestingly, the patient had only a single sentinel node harvested and this most likely represented a false negative result (mean number of sentinel nodes 2.9). Eight patients have developed distant disease without evidence of any loco-regional relapse, of whom 6 have since died. Distant relapse occurred after a median interval of 21 months following surgery (with a range of 11–37 months). One patient developed isolated chest wall recurrence after mastectomy and another supraclavicular nodal disease without distant metastases.

**Conclusion:** This low rate of axillary recurrence (0.34%) accords with other reports in the literature and compares favourably with ALND. Finite rates of false negativity associated with the SLN biopsy technique do not appear to translate into higher rates of axillary relapse. However, any residual disease within the axillary nodes will be low volume and longer follow up is required to substantiate these early observations.

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# Validation of a nomogram to predict the risk of non-sentinel lymph node metastasis in breast cancer patients with a positive sentinel node biopsy

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**Background:** Completion axillary lymph node dissection (ALND) remains, according to the Dutch guidelines, the standard of care for patients with a positive sentinel lymph node. However, approximately 40–60% of patients with positive SLNs will have no additional positive nodes. To identify the individual patient's risk for non-SLN metastases, the Memorial Sloan-Kettering Cancer Center (MSKCC) developed a nomogram currently available as an online tool. The purpose of this study was to validate the nomogram in a Dutch population of breast cancer patients.

**Methods:** The medical records of 183 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.

A receiver operating characteristic curve was drawn and the area under the curve was calculated to assess the discriminative power of the nomogram. Also, data of the index and test populations were compared.

**Results:** The area under the ROC curve was 0.704 (range 0.625–0.738), as compared to 0.76 in the MSKCC study. When the tool was applied solely to macrometastases, the area under the ROC was 0.648 (range 0.552–0.745).

**Conclusions:** The MSKCC-nomogram seems to be a useful tool to predict the individual patients risk for positive axillary non-sentinel lymph nodes in a Dutch population of breast cancer patients. Further analysis, however, has to be performed to identify subgroups, in which the nomogram is even more predictive. Predicting the risk of additional nodal metastases will allow the surgeon and patient to make an individualized decision regarding the need for completion axillary lymph node dissection.

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# Predictive factors for non-sentinel lymph node metastasis in breast cancer patients with a positive sentinel node

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**Background:** Axillary lymph node dissection remains the standard of care for breast cancer patients with a positive sentinel node. However, in a significant proportion of patients the sentinel node is the only involved