

from each study and used to calculate odds ratios. The random-effects model was used to combine odds ratios to determine the strength of the associations.

**Results:** Fifty-six published series were included in the meta-analysis. The 8 individual characteristics found to be significantly associated with the highest likelihood (odds ratio >2) of NSN metastases are SLN metastases >2 mm in size, extracapsular extension in the SLN, >1 positive SLN, ≤1 negative SLN, tumour size >2 cm, ratio of positive sentinel nodes >50% and lymphovascular invasion in the primary tumour. The histological method of detection, which is correlated with the size of metastases, had a correspondingly high odds ratio.

**Conclusions:** We identified 8 factors predictive of NSN metastases that should be recorded and evaluated routinely in SLN databases. These factors should be included in a predictive model that is generally applicable among different populations.

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### Level III lymph node involvement cannot be predicted following positive sentinel node biopsy

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**Background:** Following a positive sentinel node biopsy, the remaining axillary nodes are usually managed with axillary node clearance or radiotherapy. However variations in hospital radiotherapy protocols and surgeons practice mean that level III lymph nodes are not always treated, raising the concern of inadequate treatment.

**Methods:** A retrospective review of 605 patients undergoing sentinel node biopsy for breast cancer, following normal axillary ultrasound, to identify factors predicting for level III involvement.

**Results:** In total 105 (17.4%) of 605 women undergoing sentinel node biopsy had node involvement. Subsequent completion ANC was performed in 84 (80%) patients. Of patients undergoing completion ANC, 36 (34%) had further axillary node involvement. Further lymph node involvement was not predicted by standard pathological factors (oestrogen/progesterone/Her2 neu receptor status/tumour size/grade). Of patients with only micrometastasis, 7 of 22 (32%) had further axillary node involvement, whereas 10 of 26 (38%) patients with macrometastases had further nodal disease ( $p = 0.6$ ). However 0 of 22 patients with micrometastases had level III nodal involvement and 4 of 26 (15%) with macrometastases had level III nodal involvement ( $p < 0.05$ ). The Memorial Sloane Kettering Cancer Center (MSKCC) breast nomogram for additional node metastases had limited clinical utility. The mean (range) score to predict node involvement in node positive patients was 22% (4–95%) and node negative patients was 12% (3–40%) ( $p = 0.01$ ). 13 (12.4%) of patients had metastatic disease in level III nodes at surgery, following a positive sentinel node biopsy. Level III involvement was not predicted by routine clinicopathological factors, and although the MSKCC breast nomogram gave higher scores for the prediction of patients with subsequent level III involvement (level III positive: 30% (5–95%); negative: 14% (3–69%))  $p = 0.003$ , it was not discriminatory.

**Conclusion:** Neither the MSKCC breast nomogram or standard clinicopathological factors predict for level III node involvement following positive sentinel node biopsy. There is a possible role for more limited axillary treatment in patients with only micrometastases, however with this current data, level III axillary node clearance must be recommended as the gold standard for positive axillary disease to avoid the risk of undertreating over 12% of patients.

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### Sentinel lymph node diagnosis in breast cancer: comparison between two different molecular methods

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**Background:** Considering that the histological method for the intraoperative sentinel node (SN) study seems not to be the gold standard for its evaluation, mainly due to the different ways its study is approached,

and since two new molecular methods have been recently developed to evaluate the presence of metastasis, we hereby try to evaluate the advantages and disadvantages between these two methods when used as a routine procedure.

**Material and Methods:** We compare our experience with the One-Step-Acid-Nucleic-Amplification (OSNA) (Sysmex<sup>®</sup>) procedure against the published data from groups using the GeneSearch Breast Lymph Node Assay (BLNA) (Veridex LLC, Raritan, NJ<sup>®</sup>).

The first method is a one step isothermal RT-Lamp amplification for detection of Cytokeratin 19 mRNA (CK19 mRNA). The second one is a RT-PCR that detects mRNA of both Mammoglobin and CK19.

**Results:** In our experience, the OSNA sensibility up to date is 100% and its specificity 97.2%. The published BLN Assay results have a 95.6% sensibility with a specificity lately not specified.

BLNA, in one hand, offers a relative quantification (related to an internal control) which allows a binary result (either positive or negative). Due to this limitation, it does not differentiate between macro metastasis and micro metastasis, therefore part of the node has to be reserved for a post operative study. On the other hand, the OSNA method gives an absolute quantification of the amount of CK19 mRNA copies offering so a differentiation between micro metastasis and macro metastasis allowing to provide an intraoperative definitive result and diagnosis.

In the technical aspect, BLNA is more complex since nucleic acid extraction requires some experience in molecular handling. This is not the case with OSNA, which has a low technical complexity and high degree of automation, not requiring previous experience in molecular laboratory.

Finally, the timing of the BLNA procedure ranges from 36 to 46 minutes for one to three sentinel nodes. In our experience, OSNA takes a mean of 31 minutes to evaluate up to four sentinel nodes.

**Conclusions:** The OSNA procedure seems to have better sensitivity and specificity than the BLNA. The OSNA discriminate between macro-metastases, micro-metastases and isolated tumour cells (ITC) while the BLNA only offers positive and negative results. Time wise, OSNA procedure is shorter than the BLNA one.

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### Complete axillary lymph node dissection versus clinical follow-up in breast cancer patients with sentinel node micrometastases. Interim analysis of the Spanish multicenter clinical trial. AATRM 048/13/2000

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**Objective:** To assess the impact of SN technique on the wellbeing and performance status of breast cancer patients, specifically targeting the finding of axillary micrometastatic disease.

**Method:** To achieve such objective, a randomized prospective clinical trial was devised with two arms. In one arm, patients with SN micrometastases are the subject of plain clinical follow-up (experimental arm). In the other arm, patients are submitted for second-surgery completion ALND (control arm). All patients are intended for a two-year follow-up period.

**Results:** The accrual phase is completed (1st gen 2002 to 31 dec 2008). A total of 248 patients have been entered. There have been 14 withdrawals in both groups. 113 patients are being followed in the control arm, and 121 in the study arm. In the control arm, 15 completion ALND turned out positive, in 13 only with one additional (non-sentinel) lymph-node metastasis, being a micrometastases in 6 of them. In the study arm, one axillary recurrence has been observed in a single lymph-node, one year after primary surgery.

**Conclusions:** The follow-up phase is not completed. However, the observed data after primary surgery treatment suggest that adjuvant radio-chemotherapy might cure residual axillary minimal disease in those patients not submitted to completion ALND. Primary endpoints analysis, including survival and regional control will have to wait for the study follow-up to be completed.