

## Extensive axillary lymph node involvement in breast cancer patients selected for sentinel lymph node biopsy: incidence and implications

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### Abstract

Extensive axillary lymph node involvement in breast cancer patients implies poor prognosis, and is an indication for chest wall irradiation. Patients presenting with small tumors and a negative axillary status clinically, are expected to have a good prognosis. A treatment strategy chosen based on such assumption might prove to be sub-optimal in case of extensive axillary involvement.

Our goal was to determine the incidence of extensive axillary involvement of four nodes or more in patients with T1-T2 tumors, and to evaluate the potential consequences of pre-operatively underestimated extensive axillary disease. We reviewed the charts of patients who underwent sentinel lymph node biopsy for primary T1-T2 invasive breast cancer, with a negative pre-operative axillary assessment. Tumor size, histology, and rates and extent of axillary involvement were noted.

Of 239 patients, 71 (29.7%) had involved axillary nodes. Fifty-eight of these 71 patients had 1-3 involved nodes and the remaining 13 patients had 4 to 18 involved nodes. Of 168 patients with T1 tumors, 3 (1.8%) had 4 to 14 metastatic nodes, and of 71 patients with T2 tumors, 10 (14%) had 4-18 metastatic nodes.

A small percentage of patients undergoing sentinel lymph node biopsy have advanced loco-regional disease due to significant axillary nodal involvement. This should be taken into consideration when planning immediate reconstruction. Prophylactic measures such as contra-lateral mastectomy in patients at high risk for a second primary tumor, when considered, might better be deferred until the final pathology report is available. This is so patients with poor prognosis, evident by extensive lymph node involvement not known pre-operatively, do not undergo unnecessary prophylactic surgery such as contra-lateral mastectomy they will probably not benefit from.

**Key Words:** Breast, Cancer, Sentinel, Extensive, and Under-estimation

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### Introduction

Axillary sentinel lymph node (SLN) biopsy is widely used to identify breast cancer patients who are unlikely to benefit from formal axillary lymph node dissection. The low false negative rate<sup>1-4)</sup> and the low local axillary failure rate<sup>5-7)</sup> have brought about its common use in clinical practice. The available data suggests that the SLN biopsy can be a routine procedure in surgery for early breast cancer patients<sup>8)</sup>.

Most surgeons do not perform the procedure if there is a high preoperative suspicion of axillary nodal involvement. Clinical evaluation is usually done by palpation of the axilla and by ultrasound. Mammography may also indicate presence of involved nodes. When all these are negative, limited or no nodal involvement may

be assumed. Such a preoperative assessment might lead to treatment strategies that are not optimal for a locally advanced cancer. This is in the case that in spite of a negative pre-operative evaluation, multiple metastatic nodes are found. The incidence of any axillary involvement in patients undergoing a sentinel lymph node biopsy is now well known and is in the vicinity of 35%<sup>8)</sup>. Little attention has been given in the literature to rates of extensive axillary involvement in these patients. We refer to metastases in 4 nodes or more as extensive involvement. This is since involvement of 4 nodes or more is considered an indicator of poor prognosis, and may affect decisions regarding surgery and adjuvant treatments. The aim of this study is to determine the incidence of extensive axillary lymph node involvement in breast cancer patients undergoing sentinel lymph node biopsy, and the possible implications of its occurrence.

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## Materials and methods

Of 562 patients treated for invasive breast cancer at the Shaare Zedek Medical Center in the years 1999 to 2003, 238 had a sentinel lymph node (SLN) biopsy. These patients had primary T1-T2 invasive tumors. Patients with micro-invasion were not included in this study. The patients had no clinical evidence of axillary lymph node involvement evaluated pre-operatively by physical examination, mammography and ultrasound. Axillary SLNs were identified by using a combination of radionuclide injection, patent blue dye injection, and intraoperative palpation. SLNs were initially evaluated by frozen section, and then paraffin-embedded at 2mm intervals. All patients with positive SLNs had a formal axillary dissection. Non-SLNs were embedded in paraffin blocks containing the whole node and hematoxylin-eosin stained sections were analyzed from each block. Patient and tumor characteristics as well as rates and extent of axillary involvement were recorded in a prospective database.

## Results

Two hundred and thirty eight patients were included in this study. Average patient age was 59 years (range 31-91). Average tumor size was 2.0 cm  $\pm$  1.1 cm (range 0.4-4.5 cm). The mean number of nodes removed in patients undergoing axillary dissection for involved SLNs was 15.6 $\pm$ 5.7 (range 9-44). Seventy-one patients had positive axillary SLNs (29.8%, Table 1).

In 13 patients (5.4% of all T1 and T2 tumors), 4 to 18 axillary nodes harbored metastasis. Average tumor size in this group was 2.5 cm (range 1.5-4.0 cm). Of the 168 patients with T1 tumors, 39 had involved axillary nodes (23.2%). Three of these patients (1.8% of all, 7.7% of patients with axillary involvement) had extensive axillary involvement: 1 patient with a high grade 1.5 cm invasive duct carcinoma (14 involved nodes), one patient with a 1.5 cm invasive lobular carcinoma (9 involved nodes) and one patient with a 2 cm intermediate grade invasive duct carcinoma (4 involved nodes, Table 2). Of the 71 patients with T2 tumors (size range 2-4.5 cm), 32 had involved axillary nodes (45.1%). Ten of these patients had extensive nodal involvement (14.1% of all T2 patients, 31.2% of those with positive nodes), with tumor size of 2.5 to 4.0 cm and 4 to 18 metastatic nodes (Table 2).

## Discussion

The majority of non-metastatic breast cancer patients with T1-T2 tumors do not have axillary lymph nodes metastasis, but were still exposed to the possible complications of axillary dissection until the introduction of the

**Table 1** Occurrence of lymph node metastases according to tumor size in 239 patients with sentinel lymph node biopsy.

|   | T1 tumors<br>No. (%) | T2 tumors<br>No. (%) | T1 and T2 Tumors<br>No. (%) |
|---|----------------------|----------------------|-----------------------------|
| Patients with involved SLNs                   | 39<br>(23.2%)        | 32<br>(45.1%)        | 71<br>(29.8%)               |
| Patients with extensive axillary involvement* | 3<br>(1.8%)          | 10<br>(14.1%)        | 13<br>(5.4%)                |
| Patients with negative SLNs                   | 129<br>(76.8%)       | 39<br>(54.9%)        | 168<br>(70.2%)              |
| TOTAL (All patients having SLN biopsy)        | 168<br>(100%)        | 71<br>(100%)         | 239<br>(100%)               |

\* $\geq$ 4 involved lymph nodes

SLN = sentinel lymph node

**Table 2** Tumor Characteristics and extensive axillary involvement

| Pt Number | Tumor Size (cm) | Tumor Histology  | Tumor Grade | Number of involved nodes | ER               | PR  | HER 2 NEU |
|-----------|-----------------|------------------|-------------|--------------------------|------------------|-----|-----------|
| 1         | 1.5             | <sup>1</sup> IDC | 3           | 14                       | 3                | 2   | neg       |
| 2         | 1.5             | <sup>2</sup> ILC |             | 9                        | neg <sup>3</sup> | neg | neg       |
| 3         | 2.0             | Mixed IDC+ILC    |             | 4                        | 3                | 3   | 1         |
| 4         | 2.4             | ILC              |             | 18                       | 3                | 2   | 1         |
| 5         | 2.5             | IDC              | 2           | 12                       | neg              | 3   | neg       |
| 6         | 2.5             | IDC*             | 3           | 4                        | 3                | 2   | neg       |
| 7         | 2.5             | IDC              | 3           | 6                        | ?                |     |           |
| 8         | 2.6             | IDC              | 2           | 4                        | 1                | 3   | 2         |
| 9         | 3.0             | IDC              | 2           | 4                        | neg              | neg | neg       |
| 10        | 3.0             | IDC              | 3           | 9                        | 3                | 2   | neg       |
| 11        | 3.0             | ILC              |             | 11                       | 3                | 2   | neg       |
| 12        | 3.5             | ILC              |             | 4                        | 3                | 2   | 2         |
| 13        | 4.0             | ILC              |             | 17                       | 3                | 3   | neg       |

1: Invasive duct carcinoma, 2: Invasive lobular carcinoma, 3: negative, \*: vascular invasion known by core biopsy

sentinel lymph node biopsy in the 1990's. The sentinel lymph node biopsy is usually performed in clinically early stage breast cancer when there is no pre-operative evidence of axillary lymph node involvement. Since usually most of the data regarding tumor characteristics such as size and histology are known before surgery, the main determinant of stage and prognosis that remains unknown at this stage is the status of the axillary lymph nodes. Extensive axillary involvement of 4 or more nodes may dictate irradiation after mastectomy. This may be relevant to decisions regarding type of immediate reconstruction, if chosen. The impact of axillary nodal status is also crucial in determining prognosis. This may be relevant in patients presenting with clinically early breast cancer who might be candidates for curative as well as prophylactic surgery, as patients who have a family history of breast cancer or are BRCA mutation carriers<sup>9</sup>). Such patients may consider bilateral mastectomy for a small unilateral tumor, for future risk reduction. If such a patient actually has a poor prognosis as may be reflected by an extensive axillary lymph node involvement

found at surgery, the likelihood of benefit from such an extensive and mutilative surgery is low.

It is therefore of interest to have an idea of the likelihood of extensive axillary lymph node involvement before a treatment strategy is chosen.

A positive sentinel node is found in approximately 35% of the patients<sup>8)</sup>. In the present study we have shown that in T1 tumors with a negative pre-operative assessment of the axilla by palpation, mammography and ultrasound, extensive axillary lymph node involvement is infrequent: 1.8%. There were no patients with such involvement when tumors were smaller than 1.5 cm. In patients with T2 tumors of up to 4.5 cm, extensive axillary involvement was not infrequent – 14.1%.

This data may be of help when treatment options are discussed with the patient. In some cases, a SLN biopsy for prognostic evaluation might be considered as a first surgical step.

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