

The Accuracy of Intraoperative Frozen Section Analysis of the Sentinel Lymph Nodes During Breast Cancer Surgery

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ABSTRACT: Background—The sentinel node biopsy (SNB) is a reliable and minimally invasive procedure, representing a new standard of care for patients with clinically node-negative breast cancer. Several studies have confirmed the reliability and the accuracy of this new procedure. Accurate intraoperative evaluation of sentinel lymph nodes (SLNs) can determine the need for immediate axillary node clearance thus reducing arm morbidity in SLN-negative patients and avoiding a second surgical procedure in patients with positive SLNs. The aim of this study is to determine the accuracy and the limitations of intraoperative frozen section (IFS) analysis of SLNs during breast cancer surgery. **Patients and Methods**—96 female patients with clinically node-negative T1-T2 breast cancer who underwent the SNB procedure and IFS analysis by single section standard staining in two hospitals were reviewed. The SNB procedure was performed using the patent blue dye method alone or the combination of the dye and radioactive isotope techniques. The results of IFS and the final histology were compared. **Results**—The mean number of SLNs removed was 2. Overall, 22% (21/96) of patients were found to be SNB-positive on final histology. Based on patients, there was a 96.8% concordance between the results of the IFS and the final histology; the sensitivity was 86% (18/21), and the specificity was 100%. There were 3 cases of false negative all of which contained micrometastases only. When micrometastases were excluded, the sensitivity was 100%. Based on SLNs (n = 196), the sensitivity was 91%, and the specificity was 100%. **Conclusion**—Intraoperative frozen section of sentinel lymph nodes in patients with early breast cancer is highly accurate for macrometastases but not for micrometastases. *Int J Fertil* 49(5):000–000, 2004

KEY WORDS: sentinel node, breast cancer, frozen section, intraoperative

INTRODUCTION

THE SENTINEL NODE BIOPSY (SNB) IS a simple, minimally invasive technique which uses subdermal or peritumoral injection of vital blue dye or radio-labelled colloid, or both substances together, to identify the first lymph node(s) draining the primary tumor. It has been shown to predict accurately the axillary node status in patients with clinically node-negative breast cancer [1–4]. Tumor location, multifocality,

large tumor size, neoadjuvant systemic therapy, and prior breast surgery do not seem to reduce the accuracy of the SNB technique [5–11]. Moreover, prospective observational studies have indicated that the technique is not associated with an increase in axillary recurrence, and have confirmed that it has a low overall morbidity [1–4].

The sentinel lymph node(s) can be examined intraoperatively by frozen section or imprint cytology. Axillary node clearance can be subsequently performed if intraoperative examination of the node

TABLE I
Sensitivity and specificity based on patients.

		<i>Final Histology</i>		
		<i>Pos</i>	<i>Neg</i>	<i>Total</i>
Frozen section	Pos	18	0	18
	Neg	3	75	78
	Total	21	75	96

is positive for malignancy, thus avoiding the need for a second surgical procedure.

PATIENTS AND METHODS

Ninety-six female patients with clinically node negative T1-T2 breast cancer who underwent the

SNB procedure successfully in two hospitals were reviewed. The SNB was performed using the vital blue dye method alone, or the combination of the dye and the radioactive isotope technique. The tracers were injected in subareolar and/or peritumoral locations. The sentinel node was defined as a blue node, a node receiving a blue lymphatic and/or the node with the highest radioactivity counts detected by a gamma probe.

The sentinel nodes were evaluated immediately by intraoperative frozen section (IFS) analysis using a 4- μ m-thick single section (one level) stained with hematoxylin and eosin (H&E). For all sentinel node, the entire node is processed in 3-mm slices into paraffin wax for final histology, including a confirmatory block from the piece taken for IFS. The results of IFS and the final histology were compared with regard to the pathological diagnosis of nodal involvement.

RESULTS

A total of 196 sentinel lymph nodes were identified and examined. The mean number of nodes removed per patient was 2, and the mean size of the SLNs was 17 mm (range: 3–33 mm). Overall 22% (21/96) of patients were found to be SNB-positive on final histology; the sentinel node was the only site of disease in 6 cases (31.6%). The median age was 65 years (range: 41–89), and the mean tumor size was 17.5 mm (range = 7–50 mm). As treatment, 81% of the patients had breast-conserving surgery and 19% had total mastectomy.

The IFS analysis showed 96.8% concordance with the final histology on paraffin sections. The sensitivity was 86% (18/21) and the specificity was 100%. The negative predictive value was 96.2% and the positive predictive accuracy was 100% (Table I).

There were three cases (3.2%) in which the IFS findings were discordant with those of the final histology. The latter revealed small groups of atypical epithelial cells in the subcapsular sinus which were determined to represent micrometastases on further immunohistochemical (IHC) staining in two patients. The third patient had a micrometastatic deposit (less than 2 mm) in one half of the SLN. When micrometastases were excluded, the sensitivity was 100%.

Based on sentinel lymph nodes removed ($n = 196$), the sensitivity was 91%, the specificity was 100% (Table II).

DISCUSSION

This study shows that IFS analysis of sentinel lymph nodes has a high sensitivity and specificity, especially for the detection of macrometastases. The reported sensitivity of intraoperative examination ranges from 52% to 100% [12]. The imprint cytology method seems to be less sensitive than frozen section, but can be used as an alternative when the latter is not possible. Frozen section offers the advantage of visualizing nodal architecture but has the disadvantages of frozen-tissue artifacts and consumption of some tissue [13].

Extensive histopathological examination of the sentinel lymph nodes can increase the accuracy of axillary staging in breast cancer and can identify more patients with lymph node metastases, especially micrometastases, compared with routine histological examination of lymph nodes [14]. Immunohistochemical (IHC) examination of SLNs using anti-cytokeratin antibodies can also increase

TABLE II
Sensitivity and specificity based on sentinel lymph nodes.

		<i>Final Histology</i>		
		<i>Pos</i>	<i>Neg</i>	<i>Total</i>
Frozen section	Pos	39	0	39
	Neg	4	153	157
	Total	43	153	196

the detection rate of nodal micrometastases [15,16]. However, the clinical and prognostic significance of such occult disease remains uncertain [15–19]. Several retrospective studies suggest that micrometastases are associated with poor outcome [15,16] but numerous other studies could detect no association between micrometastases and diminished survival [17–18]. The College of American Pathologists has affirmed that the prognostic and predictive value of micrometastases identified in deeper sections using IHC in sentinel nodes is still unproven, and therefore basing therapeutic decisions on such findings is not recommended until further studies demonstrate their clinical significance [19].

Examining a single central cross-section was advised against as early as 1961, but it is still routine in many laboratories [17]. In our practice, a single block is taken from the sentinel node for IFS, but the entire node is processed for subsequent histological analysis in accordance with the National Health Service breast cancer screening program guidelines [20]. Multiple levels sectioning of individual blocks may result in nodal upstaging due to the presence of micrometastases [21,22]. Since in addition to the high cost of such processing, the biological significance of this occult disease is still uncertain [17–19].

Axillary node clearance can be performed if IFS of the sentinel lymph node(s) is positive for malignancy, because at least 25% of these patients will have further positive nodes [23]. This avoids the need for a second surgical procedure and leads to cost savings estimated to be 15% [24].

Our retrospective study showed a high accuracy for IFS analysis of sentinel nodes with no false positive results when compared with the final histology. This means that no patient is subjected to unnecessary axillary clearance with its attendant arm morbidity. The sensitivity was 100% when micrometastasis cases were excluded. The incidence of non-sentinel node involvement seems to be related to the number of positive sentinel lymph nodes, tumor size, and the size of metastases in the node [25,26]. If a primary breast tumor is small and if the sentinel node involvement is micrometastatic, then tumor cells are unlikely to be found in other axillary lymph nodes. This suggests that axillary lymph node dissection may not be necessary in patients with sentinel node micrometastases from T1-T2 lesions or in patients with sentinel node metastases from T1a lesions [25,26]. Prospective randomized studies are required to address the clinical relevance of nodal micrometastases and the need for axillary node clearance in such cases.

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