Accuracy of frozen sections for breast cancer sentinel lymph node biopsies within a peripheral New Zealand hospital

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ABSTRACT

AIM: Intra-operative frozen section is a commonly-used technique for evaluating sentinel lymph node biopsies in breast cancer to determine the need for an axillary node dissection (AND). Frozen section does have drawbacks, including cost and uncertainty around operating time. In addition, recent studies have questioned the benefit of AND in certain cases. The aim of this study was therefore to evaluate the accuracy of frozen section at our institution.

METHODS: All patients who had a sentinel node biopsy for breast cancer in the Hawke’s Bay District Health Board region over a 1-year period were included in the study. Results of intra-operative frozen section were compared to routine paraffin histological analysis.

RESULTS: Eighty patients were eligible. Eighteen had a positive frozen section. There were two false negatives. The sensitivity of frozen section for metastases was 90%, specificity was 100%, and the false negative rate was 2.5%.

CONCLUSIONS: The accuracy of frozen section section for sentinel lymph node biopsies in breast cancer at Hawke’s Bay District Health Board is acceptable by international standards. However, as further evidence against axillary node dissections in those with sentinel node positive disease mounts, their use in the future may be limited.

Sentinel lymph node biopsy (SLNB) is now standard practice for staging of early breast cancer. It allows avoidance of axillary node dissection (AND) in patients with sentinel node negative disease, thereby significantly reducing potential morbidity. Intra-operative frozen section (FS) is one option for evaluation of the SLN providing a rapid result (within 20–30 minutes). Although patients benefit by proceeding directly to AND if positive, and therefore only requiring one operation, there are downsides such as false negatives, increased pathology time and cost, and uncertainty around planning operating theatre time. In addition, recent evidence has questioned the benefit of AND in patients with limited SLNB positive disease, leaving management decisions in this group highly controversial. These decisions may be more appropriately made in a multidisciplinary meeting setting rather than intra-operatively, with subsequent delayed AND where appropriate. In this era of current controversy, audit of practice is more important than ever to justify the ongoing use of frozen section for SLNB.

The aim of our study was therefore to examine the accuracy of frozen section for breast cancer SLNB at a peripheral hospital in New Zealand, and to compare these results to internationally accepted standards.

Methods

All patients with breast cancer who underwent an intra-operative frozen section SLNB between 1 January 2014 and 31 December 2014 in the Hawke’s Bay region...
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(public and private hospitals) were analysed in this prospective, observational study.

All patients had pre-operative scintigraphy to allow localisation of the sentinel node with a hand-held gamma probe. Patent Blue V Dye was also administered in a peri-areolar fashion prior to incision. The sentinel node/nodes were excised in a standard fashion.

Sentinel nodes were sent for immediate frozen section. Frozen sections were prepared using a standard protocol and results relayed to the operating consultant surgeon who proceeded with immediate AND in those with a positive result. All SLNs were then subjected to routine paraffin sectioning with haematoxylin and eosin staining and immunohistological examination. Frozen section results were compared with paraffin section results and sensitivity, specificity and accuracy calculated.

Results

Eighty-one patients were eligible for inclusion in the study. One patient was excluded as the cryostat machine was unavailable at the time of the operation. Summary data is shown in Table 1. Of the eighty SLNBs performed during the 1-year study period, 20 were positive for metastases on paraffin section. Of these, 18 were positive on frozen section. There were two false negatives; one a micro-metastasis and the other a macro-metastasis. There were no false positives.

The sensitivity of frozen section in this study was 90% (95% CI = 68.3%–98.8%);
Figure 1: Paraffin section of a sentinel node with metastatic ductal carcinoma.

Figure 2: Frozen section of a sentinel node with metastatic ductal carcinoma. Note the preparation artefact.
specificity was 100% (95% CI = 94.0%–100%). The negative predictive value of frozen section was 96.8% (95% CI = 88.8%–99.6%). The false negative rate was 2.5% and therefore the accuracy of frozen section in this study was 97.5%.

### Discussion

Frozen section provides a timely result, allowing intra-operative decision making and limiting surgery to a single operation for the majority of patients. However, there are significant trade offs.

Frozen sections are prone to artefact (eg, overlapping of the specimen, frozen water droplets) during preparation, which makes interpretation more difficult (Figure 1). The quality of the slide is also operator dependant. This can lead to inaccuracy in interpretation. Of particular concern is a false negative result, which can falsely reassure patients leading to significant psychological trauma when the final result is explained on top of the need for a second operation. Paraffin sections (Figure 2) are generally of a higher quality, but take longer to prepare without the option of an intraoperative result, therefore resulting in AND as a second procedure in approximately one quarter of patients.

The false negative rate of frozen sections at our institution in this study was 2.5%. This is well within international standards (false negative rates reported between 2.8% and 4.9%).5,6 Of the two false negatives, one was a micro-metastasis and therefore would not have proceeded to AND in our institution. Therefore, only one patient of 80 (1.25%) had management affected by inaccuracy of FS, while FS allowed 18 patients (22.5%) to proceed to immediate AND and therefore avoid the need for a second operation.

Performing frozen section can put a strain on resources. There is a significant amount of pathologist and laboratory technician time required for the procedure. In addition, accurate planning of operating list time is difficult, as the length of the procedure is determined by the outcome of the frozen section. This can result in either under-utilisation of theatre, or overrun lists.

Overall however, the resources saved by avoiding a second operation for a substantial number of patients by utilising frozen section likely outweighs other concerns.

In recent years, deciding which patients should proceed to AND has become less clear. Evidence from the American College of Surgeons Oncology Group Z0011 trial,2 and the International Breast Cancer Study Group Trial 23-013 suggests that, in patients with low volume SLNB metastases, there is no benefit from AND in terms of disease-free survival. The patients who underwent AND had a higher rate of complications. In addition, the AMAROS trial4 has recently demonstrated non-inferiority of axillary radiotherapy compared with AND in terms of axillary recurrence in patients with low-volume SLN disease, but with a lower incidence of lymphoedema in the radiotherapy arm. Radiotherapy may therefore provide a valid alternative to surgery in suitable patients. Based on these trials, some centres have abandoned AND in selected patients with low-volume SLN disease. In our centre, we no longer routinely proceed to AND in patients with micro-metastases. Others argue that trial flaws, in particular underpowering, high rates of adjuvant treatment and poor description of radiotherapy protocols, mean that further evidence is required before changing practice.

Given current controversies, the decision of whether to proceed with AND for an individual patient may be better made in a formal multidisciplinary setting rather than intra-operatively. In the future, this may limit the use of intra-operative frozen section.

In summary, use of FS for SLNB in patients with breast cancer at Hawke's Bay Hospital meets internationally accepted standards. Although not without problems, the overall benefit to patients outweighs these and ongoing use can be justified at present. As evidence mounts against routine AND for those with SLN-positive disease, the role of intra-operative FS may be limited in the future.


