

# Feasibility of the use of touch imprint cytology for the assessment of axillary lymph nodes in breast cancer in the rural setting

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## RESEARCH

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## ABSTRACT

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### Background

Sentinel lymph node (SLN) biopsy for the assessment of axillary lymph nodes (ALN) is the gold standard in the management of breast cancer. Patients with a positive SLN will undergo an axillary clearance on a later date. Intra-operative assessment of the SLN is a valuable tool and often performed using Frozen section (FS) in certain tertiary centres. Most rural centres do not have access to this facility due to lack of resources. As patients often travel long distances for specialist treatments within the rural networks, having access to an easy-to-perform intra-operative SLN assessment tool is invaluable.

### Aims

The aim of this study was to assess the feasibility and sensitivity of touch imprint cytology (TIC) and if it can be applied in the rural setting in assessment of SLN in invasive breast cancer.

### Methods

100 patients with newly diagnosed breast cancer were recruited in this cross-sectional study. The management of these patients was not altered in any manner. SLNs were

assessed intra-operatively by TIC prior to being sent for formal histological (FH) analysis. We compared the intra-operative TIC assessment with the formal histopathology. This gave an indication of whether TIC assessment was comparable to alternative intra-operative SLN assessment.

### Results

From the 100 patients selected, seventeen patients were found to be true positive, and 78 were found to be true negative. This gave TIC assessment a positive predictive value (PPV) of 0.89 and a Negative predictive value (NPV) of 0.96. The limitations of TIC were its lack of sensitivity with micrometastasis.

### Conclusion

Our trial was limited by the small number of patients enrolled. TIC lacks the sensitivity in assessing micrometastasis and therefore we do not recommend its use in the intra-operative assessment of SLN.

### Key Words

Touch imprint cytology, invasive breast cancer, sentinel lymph node biopsy

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## What this study adds:

### 1. What is known about this subject?

TIC is a sensitive and specific alternative to frozen section in certain cases of macrometastasis.

### 2. What new information is offered in this study?

We aim to assess the sensitivity and specificity of TIC in the rural setting with a single pathologist.

### 3. What are the implications for research, policy, or practice?

Pathologist need to be adequately trained in cytology to be able to provide accurate TIC interpretation. TIC lacks the required sensitivity in interpretation of micrometastasis.

## Background

In recent times and especially within the rural setting, breast and axillary surgery has become more prevalent in the general surgeon's repertoire. This is mainly due to increases in accessibility of breast screening programs to rural areas and improvements in mobile mammogram technology. Smaller size cancers are picked up earlier allowing for Breast Conservative Surgery (BCS). This being said, approximately 16–19 per cent of patients will have a positive Axillary lymph node (ALN).<sup>1</sup> In the rural setting, these patients travel long distances to get access to medical services. Currently, patients undergo two separate procedures, firstly the breast cancer excision and SLN biopsy.<sup>2</sup> The second for ALN clearance if the SLN biopsy is found to be positive.<sup>3,4</sup> This puts a great physical, financial and psychological burden on these patients and their families. Ideally, these patients would under-go excision of the breast lesion and the SLN biopsy +/- axillary clearance; if the SLN was found to be positive using intra-operative assessment.<sup>5</sup> Often, FS is not available in these rural centres due to lack of resources.

## Method

We recruited 100 patients with early breast cancer with clinically and radiologically negative ALN. These patients gave informed consent for the TIC trial. They were informed that their SLNs would be assessed intra-operatively by a trained pathologist assessing for tumour cells followed by formal histological assessment. Their management would not be altered in any manner. The aim of the trial was to assess the feasibility of TIC.

In suitable patients, the SLN was excised following localization using Patent blue dye injected in the periareolar area and lymphoscintigraphy. A Gamma probe was used to identify and excise blue, "hot" LNs. Each patient had three to four SLNs excised. Once excised, a pathologist examined the LNs by slicing the node thinly and pressing the cut surface of the SLN on a slide. This process was repeated multiple times to allow adequate number of cells to smear onto the slide. The slide was assessed after being fixed using 95 per cent ethanol for 5–6 seconds and stained using haematoxylin eosin. The LNs were reported immediately as either positive or negative for cancer cells. The initial few patients were not included in this study as the pathologist was not familiar with this technique involved in TIC and was not confident enough to deliberate on the status of the LN. The remaining patients were given an interim result. We did not proceed with axillary clearance based on the TIC result alone. Any further surgery was performed after appropriate discussions in a multi-disciplinary meeting and the patient.

## Results

From the 100 patients who underwent TIC assessment, 81 patients were assessed as TIC negative and 19 were TIC positive (Figure 1). From the TIC positive group, 17 were FH positive and two were FH negative. From the TIC negative group, 3 were FH positive and 78 were FH negative. This gave TIC a positive predictive value of 0.89. And negative predictive value of 0.96. Our small patient population gave the TIC a sensitivity of 85 per cent and specificity of 97.5 per cent. This was calculated after direct comparison of the TIC and FH results (Table 1).

## Discussion

There is no doubt that SLN biopsy is the gold standard in staging the axilla in the clinically and radiologically negative axilla. Often, patients with early breast cancer undergo a two staged procedure which involves a SLN biopsy followed by axillary dissection if metastatic disease is found within the axilla.<sup>6,7</sup> In selected high-volume centres, intra-operative SLN assessment is employed, preventing a second procedure and anaesthetic. This is often done using a frozen section. Doing so requires a number of resources including specialised equipment, laboratory and staff. A small amount of tissue is lost during this time consuming and expensive process. In the rural setting, frozen section is not readily available even though arguably these patients would benefit the most from this facility. Rural patients often travel long distances forgoing family and supports and thus incurring substantial financial and emotional stresses to receive treatment. We aimed to assess TIC as an inexpensive and simple alternative to frozen section. Other advantages are that TIC does not waste any tissue as compared with FS during the assessment.<sup>8</sup> The disadvantages include its dependence of pathologist experience with this technique. Pathologists require specific training in cytology, proper preparation of these slides and adequate experience in accurately identifying malignant cells. Other disadvantages are that the extent of malignant focus is not assessed. As the current guidelines state that this group of patients with micrometastasis and less than 2 foci of micrometastasis can avoid axillary dissection, TIC may alter their correct management.<sup>9</sup>

## Conclusion

Our trial with a small patient population shows a TIC sensitivity and specificity comparable to other larger trials.<sup>10</sup> TIC lacks adequate sensitivity with micrometastasis and has a sensitivity of 70.3 per cent with macrometastasis.<sup>10</sup> TIC would have been a cheap, simple and effective method to assess the SLN intraoperatively but unfortunately lacks the required sensitivity and specificity required to properly

assess the axilla in early breast cancer and therefore cannot be used in intra-operative assessment of the SLN.

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**PEER REVIEW**

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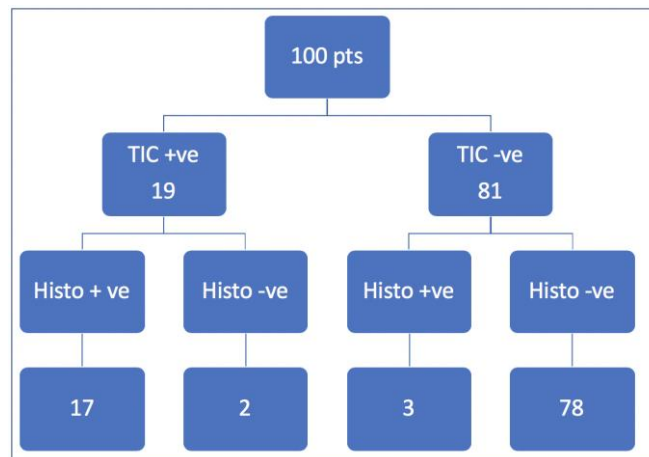
**CONFLICTS OF INTEREST**

The authors declare that they have no competing interests.

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None

**Figure 1: TIC assessment**



**Table 1: Comparison of the TIC and FH results**

|              | Formal Histology Positive | Formal Histology Negative |
|--------------|---------------------------|---------------------------|
| TIC Positive | 17                        | 2                         |
| TIC Negative | 3                         | 78                        |
|              | 20                        | 80                        |

Positive Predictive value - 0.89 Negative Predictive value - 0.96