

Research Article

The Importance of the Sentinel Lymph Node Biopsy

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Abstract

Introduction

The Sentinel Lymph Node Biopsy (SLNB) is based on the idea that tumour cells metastasise first from the original, primary focus to one or a few lymph nodes first, known as the sentinel (gate keeper), before further spreading further to involve other lymph nodes. Mapping and identifying these lymph nodes, enables to predict the status of the lymph nodes after the sentinel LN(s) therefore accurately staging and managing the cancer, gaining loco-regional control and safely preventing the need for unnecessary Axillary Lymph Node Dissections (ALND).

The procedure

The procedure begins with the SLN Mapping Technique which can involve Radioactive Colloid Injection, Blue Dye Injection or both. Radioactive Colloid Injection involves injection of an agent (Technetium sulfur colloid or Technetium-labelled human serum albumin) 2-24hours prior to surgery. Intra operatively a gamma probe is used to identify the SLN location (known as hotspots). Blue Dye Injection occurs at the time of surgery and the agents may include isosulfan or methylene blue.

Intraoperative Evaluation follows which involves excision of SLN(s) identified as all blue nodes, all nodes with afferent blue vessels and all nodes that follow the 10% rule. Then follows a pathologist consultation, where the excised specimen is grossly evaluated and tested for tumor cells/foci with frozen sections and Touch Imprint Cytology (TIC). These results dictate the subsequent surgical management:

Regional LN staging	
pNX	LN's cannot be assessed
pN0:	SLNB negative
pN0(i-)	Histologically -ve LN's
pN0(i+)	Histologically +ve: Isolated Tumour Cells
pN1mi	MICROMETASTASIS (0.2-2mm, >200 cells present)
pN1a	MACROMETASTASIS: 1-3 ALN
pN2a	MACROMETASTASIS: 4-9 ALN
pN3a	MACROMETASTASIS: 10+ ALN

Surgical Management:

- pN0: No ALND
 - pN1a: MACROMETASTASIS: ALND
 - pN1mi: MICROMETASTASIS:
 - > 3 LN positive: ALND
 - < 3 LN positive:
 - Whole Breast Radiation Therapy (WBRT)
- OR
- ≤ 1mm foci: No ALND
 - >1 mm foci: ALND

SLNB Indications and contraindications

Indications involve clinically node negative tumours (T1&T2), In situ lesions (DCIS), multicentric tumours, previous breast biopsies, prior neoadjuvant chemo and High Risk patients (Old age, obese, male).

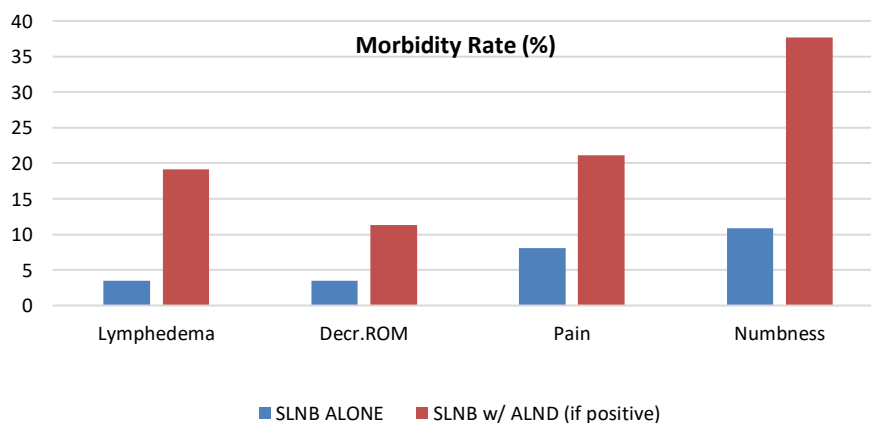
Contraindications include cases where direct ALND is indicated (positive axilla on preop axillary US/FNA), previous non-oncologic breast surgery, inflammatory breast cancer, clinical N2 tumours (4-9 ALN), pregnancy (Isosulfan Blue-Teratogenic, Methylene Blue- Insufficient data).

Methods

SLNB was developed as they were in seek of a method which can result in the same or better success rates (i.e. Disease Free Survival (DFS), Overall Survival (OS), Axillary Recurrence Rate (ARR) and low false negative (FNR) and positive (FPR) rates) as well as less intraoperative and hospitalization time, decreased overall cost of management and most importantly, decreased morbidity and quality of life improvements.

Swiss Multicenter Study:

Comparison of SLNB and ALND



A meta-analysis study and most up to date literature review was carried out to prove the success and validity of the SLNB, identify limitations of the procedure, as well as identify limitations in the data available in order to provide evidence-based recommendations and identify areas for further research.

Results

The success and validity of the SLNB

The evidence collected in support of the SLNB is, primarily the decreased arm morbidity, relative to that encountered after complete ALND. Specifically, in a prospective Swiss multicentre study comparing SLNB alone versus SLNB followed by ALND, presence of lymphedema was 3.5% vs. 19.1% (P < 0.0001) respectively, impaired shoulder range of motion was 3.5% vs. 11.3% (P < 0.0001), shoulder/arm pain was 8.1% vs. 21.1% (P < 0.0001) and numbness was 10.9% vs. 37.7% (P < 0.0001), indicating that ALND should be avoided using SLNB, where possible [1]. In addition, the percentage of node positive patients who benefit from ALND is constantly decreasing as breast cancer is increasingly detected at an early stage; therefore, BCT with SLNB can be sufficient [1].

The Disease Free Survival (DFS) and Overall Survival (OS) between SLNB followed by ALND (ALND group) and SLNB followed by ALND only if the SLN is positive (SLNB group), have been examined in numerous trials, namely the NSABP B32, EIO, ACOSOG Z0010 and ACOSOG Z0011 and have shown that there is no significant difference between the two groups.

The ARR (Axillary Recurrence Rate) after negative SLNB varies widely and after a positive SLNB it was proven to be 2.8 % after a median follow-up of over 5 years. The axillary recurrence rate continued to occur up to 63 months, demonstrating the importance the length of follow-up is in investigating axillary recurrence [2].

Limitations of the procedure

This work has also attempted to identify, collect and redress the pitfalls of the procedure as well as to investigate the limitations of studies and data associated with it;

The False Negative Rate (FNR), is defined as detection of negative sentinel lymph nodes on intraoperative evaluation (i.e. frozen section or TIC at time of surgery) but metastasis is found on evaluation of the permanent section (after surgery). An axillary false-negative finding in the absence of metastasis on evaluation of a permanent section but tumour-positive non-SLN in the completion ALND specimen are found. These range from 5,1-7,3 % [2].

The False Positive Rate (FPR) of 14% was reported in a recent meta-analysis of 15 studies which examined the accuracy of SLNB after chemotherapy in clinically node-positive patients. This was higher than that for node-negative patients who underwent chemotherapy (4-5%) or node-negative patients who did not undergo chemotherapy (7%) [3].

Surgeon's technique, skill and experience, independently of the method(s) implemented, showed to be one of the most important factors influencing the success of SLNB [4].

The SLNB causes an increased intraoperative time and cost when compared to a simple mastectomy or BCT. However, it was found that it is cost-minimizing compared to the ALND-only treatment option. The costs of treating postoperative complications did not contribute to the incremental average cost [5].

The contraindications to SLNB limit the use of this method greatly. However, the overall percentage of patients unsuitable or with multiple risk factors that may compromise the success of the sentinel lymph node biopsy is very small. Nevertheless, these patients need to be successfully identified, appropriately informed and warned about the possible risks [6].

Limitations of the data

A major drawback encountered when investigating into published data and clinical trials were the number of enrolled patients. In most trials, the most important one being the Sentinella-GIVOM randomised clinical trial, the results were not sufficient enough to draw definitive conclusions.

In addition, the validity of the data and information collected regarding the SLNB comes from studies and trials that include many variables including materials used (radio colloid, blue dye or both), injection site, surgeon's experience, high risk or low risk patient, different age groups and different ethnicities. All these factors can influence the outcome of SLNB result, ARR, DFS and OS.

Conclusions, Recommendations and Further Research

With emerging data and completion of major trials in the future as well as more familiarisation with the technique and its outcome, a more uniform and solid protocol for the implementation of the SLNB, especially in controversial indications, can be developed and followed.

Decreasing the FNR: The most important and feared drawback of SLNB is the FNR. One measure suggested in literature to decrease the false-negative findings involves sampling more nodes [3]. The FNR was also significantly lower when a dual-agent mapping technique (10.8%) vs a single-agent mapping (20.3%; $P = .05$) technique was used [7]. This is particularly true after chemotherapy, when the axilla often has more fibrosis, making evaluation of lymphatic drainage and surgical dissection more challenging.

Using 2 mapping agents with different molecular sizes and transit times is an important surgical standard that should be adhered to for SLN surgery after chemotherapy [7].

Lastly, in locally advanced tumours (≥ 3 cm) and in clinically suspicious nodes, additional Axillary Sampling (AS) has proven to be beneficial in decreasing the False Negative Rates.

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