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# Does duration to ipsilateral breast tumor recurrence affect the success of reoperative sentinel lymph node biopsy?

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ABSTRACT

*Background:* Five to ten percent of patients with prior breast cancer treated with breast conservation therapy (BCT) will develop ipsilateral breast tumor reoccurrence (IBTR), requiring reoperative sentinel lymph node biopsy (SNLB). IBTR patients may have a history of prior axillary surgery, which can be a SLNB or an axillary lymph node dissection (ALND).
*Materials & Methods:* A retrospective chart review was conducted on patients with IBTR who received care in the Department of Surgery at William Beaumont Hospital, Royal Oak and Troy, Michigan, from January 2007 to December 2009.
*Results:* Twenty-eight patients were identified and categorized as Prior ALND ($>10$ lymph nodes, $n=14$), Prior SLNB ($\leq 10$ lymph nodes, $n=10$) and an Unknown number of lymph nodes ($n=4$). Among Prior ALND patients, reoperative SLNB success was increased in the $\geq 10$ years group (25% vs. 50%, $p=0.58$). Similarly, among Prior SLNB patients, reoperative SLNB success was increased in the $\geq 10$ years group (71% vs. 100%, $p=1.0$).
*Conclusion:* Increased duration to IBTR may be associated with success of reoperative SNLB in patients with IBTR with prior ALND or SNLB. Further study is required to better understand this relationship.
*Microabstract:* The relationship between timing of and success of reoperative sentinel lymph node biopsy (SLNB) has not been studied. We conducted an observational, retrospective analysis of 28 patients with ipsilateral breast tumor recurrence (IBTR). Our results may suggest a higher rate of reoperative SNLB success with increased ($\geq 10$ years) duration to IBTR among patients who initially underwent breast conserving therapy with initial axillary lymph node dissection or SNLB. Further research is required to characterize this potential relationship.
*Clinical practice points:* Specific mechanisms for the regeneration of lymphatic channels in patients with IBTR after original SLNB or ALND are currently being investigated. The time necessary to reestablish significant lymphatic networks is unknown, but likely impacts the success of reoperative SNLB in ITBR patients. Our results may suggest a higher rate of reoperative SNLB success with increased ($\geq 10$ years) duration to IBTR among patients who initially underwent BCT with original axillary lymph node dissection or SNLB. Although more advanced research is required to better understand the relationship between timing of and success of reoperative SLNB, the results of this study may suggest that the utility of SLNB may be greater with increased length to IBTR. As a result, clinicians should be somewhat skeptical of the success of SLNB in patients with immediate IBTR until further research can be conducted.


## 1. Introduction

An estimated 2.8 million women in the United States are currently undergoing treatment for breast cancer or have a past diagnosis of the disease [1]. Breast conserving therapy (BCT) is becoming a mainstay in the surgical treatment of early breast

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cancers due to the positive oncological and cosmetic results that can be simultaneously achieved [2]. Unfortunately, ipsilateral breast tumor recurrence (IBTR) after BCT and axillary lymph node dissection (ALND) or sentinel lymph node biopsy (SLNB) is estimated to range from 5–10% within ten years of intervention [3,4].

Although reoperative BCT may be appropriate for select patients, mastectomy without axillary surgery is currently the standard of care for localized IBTR. However, the feasibility and validity of reoperative SLNB in patients with IBTR has been reported by several retrospective studies [5–8]. Results indicate that the success of reoperative SLNB is inversely related to the number of lymph nodes removed during prior SLNB or ALND [5,6]. SLNB for tumor staging is critically important in IBTR as these patients are known to be at 3 to 5 fold increased risk for distant metastasis [9].

Specific mechanisms remain to be elucidated but the regeneration of lymphatic channels likely drives the success of reoperative SNLB in ITBR patients [7,10]. The time necessary to reestablish these connections is unknown, however, and may impact the success of reopoerative SNLB depending on how long after the initial procedure the reoperative procedure is conducted. Therefore, the purpose of this study was to determine the relationship between duration to IBTR and successful reoperative SLNB in patients with prior ALND or SNLB.

## 2. Materials and methods

A retrospective chart review was conducted to consecutively identify all patients with IBTR who received care in the Department of Surgery at William Beaumont Hospital, Royal Oak and Troy, Michigan, between January 1st 2007 and December 31st 2009. Patients were included in the analysis if they received initial breast cancer treatment for early-stage breast cancer consisting of BCT (including radiation) with ALND, SLNB or an Unknown number of lymph nodes removed and received reoperative SLNB. Patients were excluded from the analysis if they had a chest wall recurrence following a mastectomy and received reoperative SNLB.

Patients meeting criteria were classified into three groups based on prior lymph node surgery type: Prior ALND ( $>10$ lymph nodes), Prior SLNB ( $\leq 10$ lymph nodes), and an Unknown number of lymph nodes removed. Patients were then characterized in terms of duration to IBTR: $<10$ years vs. $\geq 10$ years. Stratification at 10 years was chosen because breast cancer survival rates are longer than other types of cancers and BCT is associated with an increased risk of IBTR over a 10 to 15 year period of time [3,4]. The primary outcome of interest for this study was reoperative SLNB success, which was defined as the identification of a hot, blue or palpable sentinel lymph node confirmed with intraoperative or final pathology cytology. Chi-squared analysis, and when appropriate Fisher's Exact tests, were used to examine reoperative SLNB success rates across prior lymph node surgery types and duration to IBTR groups.

The standard technique of reoperative SLNB was utilized with intradermal or peri-tumoral injections of 1.1 mCi of technetium-labeled 99 (Tc-99 m) unfiltered sulfur colloid and a single lymphoscintigraphic (LSG) image was taken at 30 to 120 min post injection. Lymphazurin Blue dye or methylene blue dye 1–5 ml (diluted or undiluted) was injected as above after induction of anesthesia. Exploration of the contralateral axilla and non-axillary sites was undertaken at the discretion of the operating surgeon. Cytology was used intraoperatively and was followed by final pathology with Haematoxylin and Eosin and cytokeratin stains.

## 3. Results

Twenty-eight patients with IBTR were identified. Of these patients, 50% ($n=14$) received Prior ALDN, 35.7% ($n=10$) received Prior SNLB and 14.3% ($n=4$) had an Unknown number of lymph nodes removed. Duration to IBTR could be determined for 23 out of 28 patients (12/14 patients with Prior ALDN, 9/10 with prior SLNB, 2/4 Unknown). Duration to IBTR was $<10$ years for 65% of patients ($n=13$) and $\geq 10$ years for 35% of patients ($n=10$). Average patient age at reoccurrence was 61 years.

Reoperative SLNB successfully identified one or more sentinel lymph nodes in 53.6% of patients ($n=15$). The success rate was 70% ($n=7$) among patients with Prior SLNB, 36% ($n=5$) among patients with Prior ALND and 75% ($n=3$) in patients with an Unknown number of lymph nodes removed. Reoperative SLNB success rate did not differ significantly between Prior SLNB and ALND patient groups ($p=0.1$).

Duration to IBTR ranged from 3 to 27 years with a median of 8 years. Overall, reoperative SLNB success rate did not differ significantly between patients with IBTR $<10$ years and $\geq 10$ years (54% vs. 60%, $p=1.0$). Among Prior ALND patients, reoperative SLNB success increased in the $\geq 10$ years group (25% vs. 50%, $p=0.58$), but was not statistically significant. Similarly, among Prior SLNB patients, reoperative SLNB success increased in the $\geq 10$ years group (71% vs. 100%, $p=1.0$l Fisher Exact), but was not statistically significant. See Table 1.

Reoperative SLNB was identified by both radioisotope and blue dye in 7/15 (46.6%) patients, by isotope alone in 5/15 (33.3%) and by blue dye alone in 3/15 (20%) patients. LSG was positive in 15/28 (53%) patients, but only in 12 (80%) of the patients with successful identification of the SLNB to the ipsilateral axilla. Thus, chances of successful axillary identification of the SNLB increased with a positive result of LSG. Three patients were found to have altered lymphatic drainage to supraclavicular, cervical, intramammary or a contralateral lymph node.

## 4. Discussion

Our results may suggest a higher rate of reoperative SNLB success with increased ( $\geq 10$ years) duration to IBTR among patients who initially underwent BCT with ALND or SNLB. Reoperative SNLB success rates were 25% and 29% higher among patients with increased duration to IBTR ( $\geq 10$ years) who underwent ALND and SNLB, respectively. However, these results were not statistically significant. Our analysis also suggests the increased rate of success of reoperative SNLB that may be able to be achieved with the use of dual radioisotope and blue dye (46.6%) compared to radioisotope (33.3%) or blue dye (20%) alone.

Unlike mastectomy, BCT is associated with an increased risk of IBTR over a 10 to 15 year period of time [3,4]. With increasing numbers of patients electing BCT we expect to see a corresponding increase in the number of patients presenting with IBTR in the long term [11]. Reoperative SNLB in this population has been shown to be both feasible and valid, as well as an important tool for tumor staging [5–8]. The occurrence of morbid axillary lymphedema in SLNB is significantly reduced compared to ALND,

**Table 1**
Reoperative SLNB success rate overall, with prior ALND, and prior SNLB by time period.

| | $<10$ years | $\geq 10$ years | $p$-Value |
|---|---|---|---|
| Reoperative SLNB success – overall | 54% ($n=7$) | 60% ($n=6$) | 1.0 |
| Reoperative SLNB success – prior ALND | 25% ($n=1$) | 50% ($n=4$) | 0.58 |
| Reoperative SLNB success – prior SLNB | 71% ($n=5$) | 100% ($n=2$) | 1.01 |

ALDN – Axillary Lymph Node Dissection, SLNB – Sentinel Lymph Node Biopsy