



## The Inaccuracy of Sentinel Lymph Node Biopsy of Breast Cancer in the Era of Precision Medicine

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### Editorial

Precision medicine plays a very important role in clinical practice. Its goal is to improve clinical efficacy and minimize unnecessary side effects. Sentinel Lymph Node Biopsy (SLNB) is the standard surgical procedure for early breast cancer [1,2]. Many surgeons have reached a high level of proficiency performing in SLNB; however there is still some variation in the precedence. The clinical practice of SLNB is inaccurate in the era of precision medicine.

It's controversial how many SLNs should be removed. German Gynecological Oncology Group (AGO) recommends that at least two SLNs should be removed [3]. The NSABP B-32 randomized phase III trial reported that the false negative rate was related to the number of SLNs removed [4,5]. The ACOSOG Z1071 study showed that removed more than 2 SLNs could improve the false negative rates [6]. Bonneau and his colleges reported that the number of SLNs was associated with overall survival and the optimal number of sentinel lymph nodes harvested is three [7]. Kim reported that removing at least two SLNs was acceptable [8]. Other reported that terminating the procedure at the 4<sup>th</sup> node may lower the cost of the procedure and reduce morbidity [9]. As SLNs have a clearly defined anatomical location. The number of SLN is individualized and it is unreasonable to say that SLNs must be removed more than certain number. This is out of line with the concept of SLN and does not conform to precision medicine. In our opinion, we couldn't define the number of SLNs that should be removed.

As there is no uniform standard for SLNB procedures, the dyes used in SLNB are also varied. The troubleshooting guide of SLNB showed that dual tracer technique is superior to blue dye alone [10]. Recent studies demonstrated that combination of Indocyanine Green (ICG) and Methylene Blue dye (MB) could improve the detection rate of SLNs [11,12]. Literatures reported that all stained lymph nodes were defined as SLNs [13-15]. Some surgeons may even remove the enlarged lymph nodes closed to stained lymph nodes and defined them as SLNs [15,16]. The lymph edema would increase with the number of removed SLNs. Therefore precise SLNB procedure is urgently needed clinically.

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Received Date: 28 May 2019

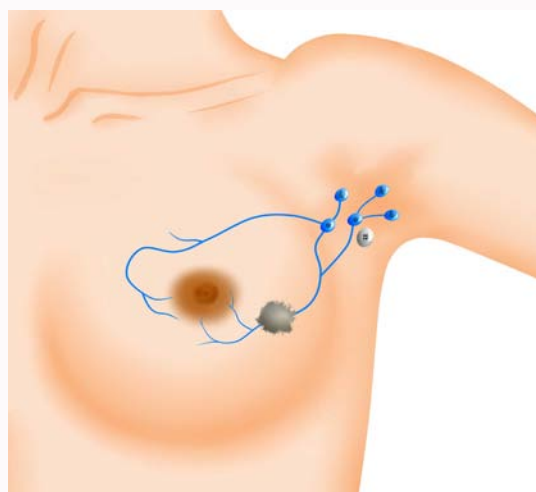
Accepted Date: 25 Jun 2019

Published Date: 03 Jul 2019

#### Citation:

Li X, Wang Y, Yang Q. The Inaccuracy of Sentinel Lymph Node Biopsy of Breast Cancer in the Era of Precision Medicine. *Clin Surg*. 2019; 4: 2500.

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**Figure 1:** Pattern of Sentinel Lymph Nodes (SLNs), po-Sentinel Lymph Nodes (po-SLNs) and para-Sentinel Lymph Nodes (para-SLNs) in breast. SLN is marked by \*; po-SLN is marked by &; para-SLN is marked by #.

In our clinical practice, we conducted precise intra operative SLNB guided by lymphatic drainage. During operation, we used ICG and MB double-tracer technique. We dissected all the lymphatic vessels carefully and found out all the stained lymph nodes. All first lymph nodes that received lymphatic drainage are defined as SLNs. The stained lymph nodes that directly connected the output ducts of SLNs were defined as post-SLNs. The enlarged lymph nodes that closed to SLNs were defined as para-SLNs (Figure 1). When we conducted the SLNB with ICG and MB during operation, we often found some po-SLNs could be stained if the staining time of dyes is too long. Therefore the po-SLNs may be removed and defined them as SLNs. On the contrary, if the staining time is not enough, some SLNs may not be stained and it was not excised. This is very dangerous and may lead to poor prognosis. By using our method, we could distinguish the SLNs, para-SLNs and po-SLNs exactly. Our experience showed demonstrated that not all stained lymph nodes are SLNs. We should identify and preserve the stained po-SLNs during SLNB. In addition, some clinicians may remove these para-SLNs in case of metastasis, we have conducted a clinical trial and our study showed that there was no need to dissect the para-SLNs during SLNB (ClinicalTrials.gov number, NCT02651142). With our novel SLNB technique, we could easily conduct SLNB precisely and it will provide important information to guide precise treatment decisions for breast cancer patients in the era of precision medicine.

Although SLNB is an operation that breast surgeons perform regularly, there is no uniform standard for SLNB procedures. Our precise SLNB procedure guided by lymphatic drainage, as well as preserving po-SLNs and para-SLNs during SLNB are recommended for popularization and application.

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