



## Guidelines for Performing Sentinel Lymph Node Biopsy in Breast Cancer

### Introduction

Sentinel lymph node (SLN) biopsy is a minimally invasive alternative to axillary lymph node dissection (ALND) for staging patients with invasive breast cancer. Multiple studies from a wide range of practice settings confirm that the staging accuracy of SLN is similar to that of ALND (the occasional false negatives are offset by improved detection<sup>1,2</sup>), and is associated with less morbidity.<sup>3,4</sup> For these reasons, SLN biopsy has become the preferred technique of axillary staging. Pre-operative axillary ultrasound to assess for morphological abnormal lymph nodes and biopsy of abnormal lymph nodes is also recommended to assess the axilla if the surgeons or radiologists have experience with axillary ultrasound.<sup>5</sup> This has been shown to decrease the false negative rate of SLN surgery<sup>5-8</sup> and to be cost effective.<sup>9</sup>

### 1) Indications and contraindications:

The current body of reported surgical experience shows that SLN biopsy is suitable for virtually all clinically node-negative T1-2 invasive breast cancers.<sup>3,10,11</sup> Limited data are available regarding suitability for patients with T3 cancers, multifocal/multicentric disease, prior radiation therapy, and prior breast/axillary surgery.<sup>12-15</sup> The published results in these situations have shown equivalent accuracy to ALND, which suggests that SLN biopsy is feasible following axillary surgery of minimal extent, especially previous SLN surgery and radiotherapy. The decision to utilize SLN biopsy in these situations requires individualized surgical judgment and requires an unequivocally successful mapping procedure. If identification of a SLN is doubtful by established technical criteria, standard axillary dissection is advised. SLN biopsy should be performed for DCIS whenever mastectomy is required or when invasive disease is suspected.<sup>16</sup>

The role of SLN biopsy in patients following neoadjuvant therapy remains controversial. A meta-analysis of all published studies demonstrated similar accuracy and false negative rates to SLN biopsy performed before systemic therapy.<sup>17</sup> Patients with documented node-positive disease may be at high risk for a false negative.<sup>18</sup> An American College of Surgeons Oncology Group (ACOSOG) clinical trial is underway to determine the accuracy of SLN biopsy in this clinical scenario.<sup>19</sup> Again, individualized surgical judgment is required. SLN biopsy has no role in inflammatory breast cancer.

### 2) The positive SLN:

The National Surgical Adjuvant Breast and Bowel Project (NSABP) trial B-32 demonstrated that, when the SLN is negative, SLN surgery alone is an appropriate, safe, and effective therapy for breast cancer patients.<sup>20</sup> Additionally, since axillary node metastases are limited to the SLN in more than half of SLN-positive individuals<sup>21</sup>, there may be low-risk subset of these patients for whom the completion ALND may also be omitted. Several nomograms have been developed that attempt to quantify the likelihood of identifying additional positive axillary nodes<sup>22,23</sup>, but their use has not been universally accepted. A recent review of 97,000 patients in the National

Cancer Database indicates that ALND is not routinely necessary in all patients with involved SLNs: completion ALND did not appear to improve outcomes, compared with SLNB alone, for breast cancer patients with microscopic nodal metastases - although a nonsignificant trend toward better outcomes with completion ALND was seen for those with macroscopic disease.<sup>24</sup> This review also showed that fewer ALNDs were being performed for micrometastatic node involvement, without any measurable decrease in survival.<sup>24</sup> The ACOSOG Z-11 trial indicated that omitting routine ALND after identification of a positive sentinel node resulted in residual axillary disease in 27% of patients, but the risk of axillary recurrence was less than 1%, and there was no effect on survival – although long-term results remain to be seen.<sup>25</sup> The decision to omit completion ALND should arise from a balanced discussion between the surgeon and the patient. This discussion should include the risks associated with the additional procedure as well as the potential benefits of information to be gained.

### **3) Technique:**

Early studies indicated that the success of SLN biopsy was maximized, and the false-negative rate minimized, by a technique that combined careful intraoperative digital examination, and blue dye and isotope mapping.<sup>11</sup> Lymph nodes identified through this mapping technique and palpably abnormal lymph nodes should be resected and submitted as SLNs. Injection of either isosulfan blue or methylene blue can result in complications: isosulfan blue has been associated with a variety of hypersensitivity reactions, including anaphylaxis<sup>26,27</sup>, and methylene blue, when not diluted, has been associated with skin necrosis.<sup>28</sup> Routine preoperative lymphoscintigraphy does not improve identification of axillary sentinel nodes.<sup>30</sup>

### **4) Morbidity and long-term results:**

Several studies have indicated less morbidity related to sentinel node biopsy than ALND.<sup>4, 31, 32</sup> Lymphedema, parasthesia, seroma, and wound infection have been described following sentinel node biopsy, but generally occur in less than 10% of patients.<sup>31, 33</sup> Axillary recurrences are rare.<sup>34</sup>

### **Conclusion**

Sentinel node biopsy is now established as standard care for most women with invasive breast cancer. Its accuracy has been validated through multiple clinical trials in a variety of practice settings, demonstrating equivalent accuracy to ALND, but with less morbidity. The routine use of ALND after positive SLN is controversial, but is occurring less often, particularly in patients with micrometastatic disease. Several models (nomograms) are available to aid in the decision, but none of these should replace a detailed discussion of risks and benefits.

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This statement updates the Original Guidelines (November 1998), First Revision (August 2000), Second Revision (November 2002), Third Revision (October 2003) and Fourth Revision (December 2005).

## References:

1. Chu KU, Turner RR, Hansen NM, et al. Sentinel node metastasis in patients with breast carcinoma accurately predicts immunohistochemically detectable nonsentinel node metastasis. *Ann Surg Oncol*. Dec 1999;6:756-61.
2. Viale G, Maiorano E, Pruneri G, et al. Predicting the risk for additional axillary metastases in patients with breast carcinoma and positive sentinel lymph node biopsy. *Ann Surg*. Feb 2005;241:319-25.
3. Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med*. Aug 7 2003;349:546-53.
4. Crane-Okada R, Wascher RA, Elashoff D and Giuliano AE. Long-term morbidity of sentinel node biopsy versus complete axillary dissection for unilateral breast cancer. *Ann Surg Oncol*. Jul 2008;15:1996-2005.
5. Sato K, Tamaki K, Tsuda H, et al. Utility of axillary ultrasound examination to select breast cancer patients suited for optimal sentinel node biopsy. *Am J Surg*. Jun 2004;187:679-83.
6. Mathijssen IM, Strijdhorst H, Kiestra SK and Wereldsma JC. Added value of ultrasound in screening the clinically negative axilla in breast cancer. *J Surg Oncol*. Oct 1 2006;94:364-7.
7. van Rijk MC, Deurloo EE, Nieweg OE, et al. Ultrasonography and fine-needle aspiration cytology can spare breast cancer patients unnecessary sentinel lymph node biopsy. *Ann Surg Oncol*. Jan 2006;13:31-5.
8. Deurloo EE, Tanis PJ, Gilhuijs KG, et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. *Eur J Cancer*. May 2003;39:1068-73.
9. Boughey JC, Moriarty JP, Degnim AC, et al. Cost modeling of preoperative axillary ultrasound and fine-needle aspiration to guide surgery for invasive breast cancer. *Ann Surg Oncol*. 2010 Apr;17(4):953-8.
10. Krag DN, Julian TB, Harlow SP, et al. NSABP-32: Phase III, randomized trial comparing axillary resection with sentinel lymph node dissection: a description of the trial. *Ann Surg Oncol*. Mar 2004;11:208S-10S.
11. McMasters KM, Tuttle TM, Carlson DJ, et al. Sentinel lymph node biopsy for breast cancer: a suitable alternative to routine axillary dissection in multi-institutional practice when optimal technique is used. *J Clin Oncol*. Jul 2000;18:2560-6.
12. Intra M, Trifiro G, Viale G, et al. Second biopsy of axillary sentinel lymph node for reappearing breast cancer after previous sentinel lymph node biopsy. *Ann Surg Oncol*. Nov 2005;12:895-9.
13. Knauer M, Konstantiniuk P, Haid A, et al. Multicentric breast cancer: a new indication for sentinel node biopsy--a multi-institutional validation study. *J Clin Oncol*. Jul 20 2006;24:3374-80.
14. Lelievre L, Houvenaeghel G, Buttarelli M, et al. Value of the sentinel lymph node procedure in patients with large size breast cancer. *Ann Surg Oncol*. Feb 2007;14:621-6.
15. Rodriguez Fernandez J, Martella S, Trifiro G, et al. Sentinel node biopsy in patients with previous breast aesthetic surgery. *Ann Surg Oncol*. Apr 2009;16:989-92.
16. Dominguez FJ, Golshan M, Black DM, et al. Sentinel node biopsy is important in mastectomy for ductal carcinoma in situ. *Ann Surg Oncol*. Jan 2008;15:268-73.
17. Xing Y, Foy M, Cox DD, et al. Meta-analysis of sentinel lymph node biopsy after preoperative chemotherapy in patients with breast cancer. *Br J Surg*. May 2006;93:539-46.

18. Shen J, Gilcrease MZ, Babiera GV, et al. Feasibility and accuracy of sentinel lymph node biopsy after preoperative chemotherapy in breast cancer patients with documented axillary metastases. *Cancer*. Apr 1 2007;109:1255-63.
19. ClinicalTrials.gov. Surgery to Remove the Sentinel Lymph Node and Axillary Lymph Nodes After Chemotherapy in Treating Women With Stage II, Stage IIIA, or Stage IIIB Breast Cancer. <http://clinicaltrials.gov/ct2/show/NCT00881361>. Accessed 6 October, 2010.
20. Krag DN, Anderson SJ, Julian TB, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. *The Lancet Oncology*, Volume 11, Issue 10, Pages 927 - 933, October 2010
21. Veronesi U, Paganelli G, Viale G, et al. Sentinel lymph node biopsy and axillary dissection in breast cancer: results in a large series. *J Natl Cancer Inst*. Feb 17 1999;91:368-73.
22. Gur AS, Unal B, Johnson R, et al. Predictive probability of four different breast cancer nomograms for nonsentinel axillary lymph node metastasis in positive sentinel node biopsy. *J Am Coll Surg*. Feb 2009;208:229-35.
23. Pal A, Provenzano E, Duffy SW, et al. A model for predicting non-sentinel lymph node metastatic disease when the sentinel lymph node is positive. *Br J Surg*. Mar 2008;95:302-9.
24. Bilimoria KY, Bentrem DJ, Hansen NM, et al. Comparison of sentinel lymph node biopsy alone and completion axillary lymph node dissection for node-positive breast cancer. *J Clin Oncol*. Jun 20 2009;27:2946-53.
25. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. *Ann Surg*. Sep 2010;252:426-32; discussion 432-3.
26. Albo D, Wayne JD, Hunt KK, et al. Anaphylactic reactions to isosulfan blue dye during sentinel lymph node biopsy for breast cancer. *Am J Surg*. Oct 2001;182:393-8.
27. Leong SP, Donegan E, Heffernon W, et al. Adverse reactions to isosulfan blue during selective sentinel lymph node dissection in melanoma. *Ann Surg Oncol*. Jun 2000;7:361-6.
28. Bleicher RJ, Kloth DD, Robinson D and Axelrod P. Inflammatory cutaneous adverse effects of methylene blue dye injection for lymphatic mapping/sentinel lymphadenectomy. *J Surg Oncol*. May 1 2009;99:356-60.
29. Kang T, Yi M, Hunt KK, et al. Does blue dye contribute to success of sentinel node mapping for breast cancer? *Ann Surg Oncol*. 2010 Oct;17(Suppl 3):280-5.
30. McMasters KM, Wong SL, Tuttle TM, et al. Preoperative lymphoscintigraphy for breast cancer does not improve the ability to identify axillary sentinel lymph nodes. *Ann Surg*. May 2000;231:724-31.
31. Langer I, Guller U, Berclaz G, et al. Morbidity of sentinel lymph node biopsy (SLN) alone versus SLN and completion axillary lymph node dissection after breast cancer surgery: a prospective Swiss multicenter study on 659 patients. *Ann Surg*. Mar 2007;245:452-61.
32. Baron RH, Fey JV, Borgen PI, et al. Eighteen sensations after breast cancer surgery: a 5-year comparison of sentinel lymph node biopsy and axillary lymph node dissection. *Ann Surg Oncol*. May 2007;14:1653-61.
33. Goldberg JI, Wiechmann LI, Riedel ER, et al. Morbidity of Sentinel Node Biopsy in Breast Cancer: The Relationship Between the Number of Excised Lymph Nodes and Lymphedema. *Ann Surg Oncol*. 2010 Jun 24.

34. Langer I, Marti WR, Guller U, et al. Axillary recurrence rate in breast cancer patients with negative sentinel lymph node (SLN) or SLN micrometastases: prospective analysis of 150 patients after SLN biopsy. *Ann Surg.* Jan 2005;241:152-8.