

# Sentinel node biopsy for ipsilateral breast cancer recurrence: a review

G. Palit, M.D.; Y. Jacquemyn, M.D., Ph.D.; W. Tjalma, M.D., Ph.D.

Department of Obstetrics and Gynecology, Antwerp University Hospital UZA, Edegem (Belgium)

## Summary

The aim of this study was to review published reports on the feasibility, results, and reliability of sentinel node biopsy in cases of ipsilateral recurrent breast cancer. A Medline search on publications from January 1999 to December 2007 and cross-references in published articles were looked for. We identified 16 reports on sentinel node biopsy in recurrent breast cancer, including a total of 287 patients. In 210/287 (73.2%) a sentinel node was identified, 77/210 (37.7%) had had previous axillary lymph node dissection and 131 (62.3%) a previous sentinel node procedure. Aberrant lymphatic drainage, other than the ipsilateral axilla was noted in 68/210 (32.4%). Of these 16/68 (23.6%) were located in the contralateral axilla. Of the removed contralateral axillary sentinel nodes 8/17 (47.1%) were invaded by cancer. We conclude that sentinel node biopsy in cases of recurrent ipsilateral breast cancer is feasible. In about one out of three cases drainage to the contralateral axilla with invasion in almost half the cases takes place. The therapeutic consequences of these findings need further study.

*Key words:* Sentinel node; Breast cancer; Recurrent; Lymphatic drainage.

## Introduction

Sentinel lymph node biopsy (SLNB) is accepted as the standard procedure for axillary staging in patients with primary operable breast cancer and clinically uninvolved axillary lymph nodes, mainly because of the lower resultant morbidity as compared to complete axillary lymph node dissection (ALND). In most patients this is combined with breast conserving therapy (BCT) and radiotherapy. About 10-15% of these patients will develop locally recurrent disease within ten years [1] and chestwall recurrence after mastectomy is reported to be between 5-10%. If a complete axillary lymph node dissection was previously performed, salvage mastectomy without further lymph node dissection is considered the standard of care. But what after SLNB?

The procedure of SLNB requires an intact lymphatic flow from the tumor site, which can be interrupted or modified by previous surgery and/or radiotherapy. Most breast tumors drain through a few common afferent lymphatic vessels to the common axillary lymph nodes irrespective of tumor location or number of tumor foci [2]. After previous therapy one or more lymphatic channels can be definitely or temporarily interrupted and alternative paths to the sentinel lymph node may occur for migration both of the radio-isotope and tumor cells. The time of restoration of lymphatic drainage after previous surgery or radiotherapy is unknown.

Originally previous breast surgery was considered a contraindication for SLNB, but Luini *et al.* [3] have demonstrated the accuracy of SLNB after previous surgery with results comparable with those obtained in other SLNB validation studies. As SLNB is being performed more and more, patients with local recurrence after breast conserving surgery or after mastectomy (without ALND) will be seen. Also in women with ductal carcinoma in situ (DCIS) who have been treated by wide local excision, most often followed by radiation therapy, or by mastectomy without ALND, 10% to 30% will develop local recurrence, be it DCIS or invasive carcinoma [4].

In the present review we try to evaluate whether SLNB in locally recurrent breast cancer after previous SLNB or ALND is feasible, adds any new information, and might possibly change treatment and/or prognosis.

## Materials and Methods

We performed a Medline search including studies published between January 1999 and December 2007 with the search terms "sentinel" and "recurrent breast carcinoma" or "recurrent breast cancer". Studies were selected on title and abstract (if available). Of all relevant articles the full text was obtained and the reference list checked for other possible relevant publications.

## Results

The original Medline search yielded 17 publications which all seemed relevant. From these 17 publications, two were only comments on other publications [5, 6] and two studies partially reported on the same series of patients, both giving an update with more patients included at a later period in time [7-10], leaving 13 original studies. Reviewing the reference lists revealed three more studies, resulting in a total of 16. An overview of the publications is given in Table 1.

Revised manuscript accepted for publication April 21, 2008

Table 1. — Overview of published studies on SLNB and recurrent breast cancer.

Study (author, year, reference)	No. patients	SLNB identification		Aberrant lymphatic drainage		Metastatic SLNB		
		Total	Previous ALND	Previous SLNB	Total	Location (C)	Total	Aberrant SLNB
Chung 2002 [11]	1	1	0	1	0	0	0	0
Lim 2004 [12]	1	1	1 (A)	0	1	1c	1/1	1/1 (1c)
Sood 2004 [13]	4 (B)	4	4	0	4	1i 1c 2m	0/4	0/4
Agarwal 2005 [14]	2	2	2	0	2	2c	1/f2	1/2 (1c)
Taback 2006 [16]	15	11	6	6	8	1s 2i 2p 3c	3/11	2/8 (2c)
Boughey 2006 [17]	21	13	6	7	5	2c 3i	1/13	0/2 (2c)
Milardovic 2006 [18]	1 (D)	1	1	0	1	1e	unknown	unknown
Dinan 2005 [15]	16	11	9	2	8	2s 3c 1sc 1m 1i	0	0
Newman 2006 [19]	10	9	6	1 (E)	7	3 "parasternal"	0	0
Jackson 2006 [20]	1	1	0	1	0	0	1/1	0
Rouwen 2006 [21]	12	10	8	2	7	4c 3i	4/10	biopsied
Port 2007 [10]	117	64	24	40	19	not specified	10/64	2/19
Wellner 2007 [22]	1	1	1	0	1	1c	1/1	1/1
Rozen 2007 [23]	2	2	0	2	0	0	0/2	0
Barone 2007 [24]	19	16	9	7	0	0	2/16	0
Intra 2007 [8]	65	63	0	63	5	1s 4i	7/63	1i others non specified
Total (%)	287	210/287 (73.2%)	77/210 (36.7%)	131/210 (62.3%)	68/210 (32.4%)		31/210 (14.8%)	

s: supraclavicular; i: internal mammary ipsilateral; p: interpectoral; c: contralateral axillary; m: intramammary ipsilateral; e: epigastric; sc: supracervical contralateral.

A: One patient had a mastectomy for ductal carcinoma in situ, but whether an axillary dissection was performed is not mentioned.

B: One patient had undergone previous axillary node dissection for malignant melanoma on the same side as the breast cancer.

C: In the discussion four more patients are mentioned with successful repeat SLNB but no further details are given.

D: Two patients had no previous axillary surgery at all.

Different methods were used in the studies published to perform SLNB, some including lymphoscintigraphy and blue dye injection, but all also used 99 m-technetium sulfur colloid and gamma probe localization. Identification of sentinel nodes was with dye, 99 m-technetium or both. A longer time, necessitating delayed images, for lymphoscintigraphic identification in a repeat procedure has been reported [16].

## Discussion

As a consequence of the frequent application of SLNB a new group of breast cancer patients is emerging without ALND. In case of local recurrence in these patients it seems that clinically involved axillary lymph nodes are a clear indication to perform ALND (although data are lacking whether this significantly improves prognosis). It is unknown what the benefit of adjuvant chemotherapy versus expected management after locoregional resection in these cases is, however a National Surgical Adjuvant Breast and Bowel Project is performing a trial on this. The potential value of SLNB in these cases is to facilitate the identification of nodes that might harbor microscopic metastases that could be prognostically valuable, but this has not yet been proven.

In the very first report on repeat SLNB [11] Chung *et al.* argued their second SLNB was falsely negative. Actually SLNB was performed and the node removed was negative for metastatic disease but ten months later the patient presented with an axillary recurrence, which of course did not prove that there was (microscopic) axillary disease present at the time of SLNB; only a simultaneously performed ALND (which was not done) could have proven this. The only data available are from Port *et al.* [10] in their series on 23 patients where additional (other than sentinel node) lymph nodes were removed concurrently; in two of seven (9%) the SLNB was falsely negative.

Aberrant lymphatic drainage has been published at different sites: contralateral axillary, intramammary, internal mammary, epigastric and contralateral supracervical.

The number (16/68 = 23.6%) of aberrant lymph nodes invaded with cancer in the contralateral axilla was remarkable, and without SLNB all of these cases would have been overlooked. In all studies reported, one out of three (32.4%) of SLNB is at an aberrant location. This may change our idea about the way recurrent breast cancer spreads but it is not yet clear whether this has any therapeutical implications. The number of positive SLNB in recurrent breast cancer was low, around 14.6% in our review. From those publications where it is mentioned, of 17 reported contralateral axillary lymph nodes, eight were positive (47.1%). Boughey *et al.* [16] have concluded that if more than ten axillary lymph nodes are removed at the original operation, or when radiation is part of the previous treatment, the incidence of alternative lymphatic drainage is increased. Port *et al.* [10] concluded that success of reoperative SLNB was inversely related to number of nodes removed previously, and was more likely to be successful after a previous SLNB than ALND (74% vs 38%,  $p = 0.0002$ ).

The studies reported have clearly demonstrated the feasibility of SLNB both after previous SLNB and after previous ALND. It has become clear that aberrant breast lymphatic drainage is more common in cases of local recurrence both after SLNB and ALND.

Publication bias can influence the reported incidence of aberrant lymphatic drainage as it is reasonable to expect cases with “normal” drainage not to be published.

This aberrant drainage can result both from surgical scarring or radiotherapy-induced fibrosis. It is not known whether a patient that had a previous SLNB and then demonstrates a local recurrence should also undergo ALND as a means of documenting false-negative repeat SLNB? Probably the surgical morbidity of ALND outweighs the risk of understaging with a false-negative result, but there are no real data to corroborate this statement [6]. If a positive sentinel node is identified in a contralateral axilla it has not been documented if there is any advantage in performing complete ALND of the contralateral axilla. Not performing SLNB could lead to not diagnosing metastasis to aberrant lymph nodes, but it is not yet clear how this might influence treatment (surgically but also considering contralateral radiotherapy and adjuvant chemotherapy) and prognosis.

There is some discussion on how patients with positive contralateral axillary lymph nodes should be staged, as M or as N1; some have proposed that this should be considered a direct drainage pathway (N1) and not a distant metastasis (M) [22].

## Conclusion

In conclusion repeat SLNB can demonstrate aberrant lymphatic drainage and metastasis that could otherwise have been overlooked, however the clinical significance of this is quite unclear. The risk of false-negatives has been poorly studied. Perhaps the best way at this time is to perform SLNB for aberrant lymphatics and concurrent ipsilateral ALND in case this was not performed at the original surgery.

## References

- [1] Fisher B., Redmond C., Poisson R., Margolese R., Wolmark N., Wickerham L. *et al.*: “Eight-years results of a randomised clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer”. *N. Engl. J. Med.*, 1989, 320, 822.
- [2] Kumar R., Potenta S., Alavi A.: “Sentinel lymph node biopsy in multifocal and multicentric breast cancer”. *J. Am. Coll. Surg.*, 2004, 198, 674.
- [3] Luini A., Galimberti V., Gatti G., Arnone P., Vento A.R., Trifiro G. *et al.*: “The sentinel node biopsy after previous breast surgery: preliminary results on 543 patients treated at the European Institute of Oncology”. *Breast Cancer Res. Treat.*, 2005, 89, 159.
- [4] Bijker N., Meijnen P., Peterse J.L., Bogaerts J., Hoorbeek I. van, Julien J.P. *et al.*: “Breast conserving treatment with or without radiotherapy in ductal carcinoma in situ: ten years results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853”. EORTC Breast Cancer Cooperative Group; EORTC Radiotherapy Group”. *J. Clin. Oncol.*, 2006, 24, 3381.
- [5] Zgajnar J., Gatzemier W., Costa A.: “Will the sentinel lymph node (SLN) stand a second time-SLN biopsy in breast cancer patients with isolated local recurrence following breast conserving therapy and previous SLN procedure”. *Ann. Oncol.*, 2001, 12, 723.
- [6] Newman L.A.: “Lymphatic mapping and sentinel lymph node biopsy for locally recurrent breast cancer: new clues to understanding the biology of chest wall relapse”. *Ann. Surg. Oncol.*, 2007, 14, 2182.
- [7] Intra M., Trifiro G., Viale G., Rotmensz N., Gentilini O.D., Sotledo J. *et al.*: “Second biopsy of axillary sentinel lymph node for reappearing breast cancer after previous sentinel lymph node biopsy”. *Ann. Surg. Oncol.*, 2005, 12, 895.
- [8] Intra M., Trifiro G., Galimberti V., Fentillini O., Rotmensz N., Veronesi P.: “Second axillary sentinel node biopsy for ipsilateral breast tumour recurrence”. *Br. J. Surg.*, 2007, 94, 1216.
- [9] Port E.R., Fey J., Gemignani M.L., Heerd A.S., Montgomery L.L., Petrek J.A. *et al.*: “Reoperative sentinel lymph node biopsy: a new option for patients with primary or locally recurrent breast carcinoma”. *J. Am. Coll. Surg.*, 2002, 195, 167.
- [10] Port E.R., Garcia-Etienne C.A., Park K., Fey J., Borgen P.I., Cody N.S.: “Reoperative sentinel lymph node biopsy; a new frontier in the management of ipsilateral breast tumor recurrence”. *Ann. Surg. Oncol.*, 2007, 14, 2209.
- [11] Chung H.A., Cady B.: “Caution urged with repeat sentinel lymph node biopsy”. *Ann. Oncol.*, 2002, 13, 1951.
- [12] Lim I., Shim J., Goyenechea M., Kim C.K., Krynycky B.R.: “Drainage across midline to sentinel nodes in the contraateral axilla in breast cancer”. *Clin. Nucl. Med.*, 2004, 29, 346.
- [13] Sood A., Youssef I., Hecke S.I., El-Zeftawy H., Axelrod D., Seigel B. *et al.*: “Alternative lymphatic pathway after previous axillary node dissection in recurrent primary breast cancer”. *Clin. Nucl. Med.*, 2004, 29, 698.
- [14] Agarwal A., Heron D.E., Sumkin J., Falk J.: “Contralateral uptake and metastases in sentinel lymph node mapping for recurrent breast cancer”. *J. Surg. Oncol.*, 2005, 92, 4.
- [15] Dinan D., Nagle C.E., Pettinger J.: “Lymphatic mapping and sentinel node biopsy in women with an ipsilateral second breast carcinoma and a history of breast and axillary surgery”. *Am. J. Surg.*, 2005, 190, 614.
- [16] Taback B., Nguyen P., Hansen N., Edwards G.K., Conway K., Giulino A.E.: “Sentinel lymph node biopsy for local recurrence of breast cancer after breast-conserving therapy”. *Ann. Surg. Oncol.*, 2006, 13, 1099.
- [17] Boughey J.C., Ross M.I., Balzera G.V., Bedrosian I., Feig B.W., Hwang R.F. *et al.*: “Sentinel lymph node surgery in locally recurrent breast cancer”. *Clin. Breast Cancer*, 2006, 7, 248.
- [18] Milardovic C., Castellon I., Mills, Altinyay E., Raphael B., Abdel-Dayen M.: “Scintigraphic visualisation of an epigastric sentinel node in recurrent breast cancer after lumpectomy and postoperative radiation therapy”. *Clin. Nucl. Med.*, 2006, 31, 207.
- [19] Newman E.A., Cimmino V.M., Sabel M.S., Diehl K.M., Frey K.A., Chang A.E., Newman L.A.: “Lymphatic mapping and sentinel lymph node biopsy for patients with local recurrence after breast conservation therapy”. *Ann. Surg. Oncol.*, 2006, 13, 52.
- [20] Jackson B.M., Kim S., Davidson R., Schuchter L., Acs G., Czerniecki B.J.: “Repeat operative sentinel lymph node biopsy”. *Clin. Breast Cancer*, 2006, 6, 530.
- [21] Roumen R.M.H., Kuijt G.P., Liem I.H.: “Lymphatic mapping and sentinel node harvesting inpatients with recurrent breast cancer”. *Eur. J. Gynaecol. Oncol.*, 2006, 32, 1076.
- [22] Wellner R., Due J., Kim U., Menes T.S.: “Altered lymphatic drainage after breast conserving surgery and axillary node dissection: local recurrence with contralateral intramammary nodal metastases”. *Clin. Breast Cancer*, 2007, 7, 486.
- [23] Rozen W.M., Chow Y.: “Role of reoperative sentinel lymph node biopsy in locally recurrent breast cancer”. *Breast J.*, 2007, 13, 629.
- [24] Barone J.L., Feldman S.M., Estabrook A., Tartter P.I., Rosenbaum Smith S.M., Boolbol S.K.: “Reoperative sentinel lymph node biopsy in patients with locally recurrent breast cancer”. *Am. J. Surg.*, 2007, 194, 491.

Address reprint requests to:  
Y. JACQUEMYN, M.D.  
Department of Obstetrics and Gynaecology,  
Antwerp University Hospital UZA  
Wilrijkstraat 10 - 2650 Edegem (Belgium)  
e-mail: yves.jacquemyn@uza.be