International Journal of Technology Assessment in Health Care, **20:4** (2004), 449–454.

Cost comparison of two surgical strategies in the treatment of breast cancer: Sentinel lymph node biopsy versus axillary lymph node dissection

Lionel Perrier
Karima Nessah
Magali Morelle
Hervé Mignotte
Marie-Odile Carrère
Alain Brémond
Centre Léon Bérard

Objectives: The feasibility and accuracy of sentinel lymph node biopsy (SLNB) in the treatment of breast cancer is widely acknowledged today. The aim of our study was to compare the hospital-related costs of this strategy with those of conventional axillary lymph node dissection (ALND).
Methods: A retrospective study was carried out to determine the total direct medical costs for each of the two medical strategies. Two patient samples ($n = 43$ for ALND; $n = 48$ for SLNB) were selected at random among breast cancer patients at the Centre Léon Bérard, a comprehensive cancer treatment center in Lyon, France. Costs related to ALND carried out after SLNB (either immediately or at a later date) were included in SLNB costs ($n = 18$ of 48 patients).
Results: Total direct medical costs were significantly different in the two groups (median 1,965.86€ versus 1,429.93€, $p = 0.0076$, Mann-Whitney *U*-test). The total cost for SLNB decreased even further for patients who underwent SLNB alone (median, 1,301€). Despite the high cost of anatomic pathology examinations and nuclear medicine (both favorable to ALND), the difference in direct medical costs for the two strategies was primarily due to the length of hospitalization, which differs significantly depending on the technique used (9-day median for ALND versus 3 days for SLNB, $p < 0.0001$).
Conclusions: A lower morbidity rate is favorable to the generalization of SLNB, when the patient's clinical state allows for it. From an economic point of view, SLNB also seems to be preferred, particularly because our results confirm those found in two published studies concerning the cost of SLNB.

Keywords: Breast cancer, Axillary lymph node dissection, Economic evaluation, Sentinel lymph node biopsy

We sincerely thank the members of the biology laboratory and in particular Xavier Greffe, MD, the operating room personnel, and Marie Thérèse Lupo, the anatomic cytopathology laboratory team, and Bernard Fontanière, MD, Isabelle Treilleux, MD, Jean-Philippe Michot, and Frédéric Gomez, MD, Brigitte Carlet, and Murielle Buclon from the Public Health Department, as well as the nuclear medicine staff. We also express our gratitude toward the cost accounting department at the Centre Léon Bérard and the anonymous reviewers of our article.

The sentinel lymph node is the first lymph node that receives lymph flow from a primary tumor. Sentinel lymph node biopsy (SLNB) enables the identification of this node by injecting a radioactive tracer and/or lymphotrophic blue dye. The node is then excised for anatomic pathology examinations. The feasibility of this strategy in the treatment of breast cancer is widely acknowledged today (1;2). The usual identification rate of the sentinel lymph node is greater than 85 percent, whereas false-negative analyses are generally less than 10 percent. In addition, SLNB has proven accurate in determining axillary lymph node status and could replace conventional axillary lymph node dissection (ALND) for the mapping and diagnosis of positive lymph nodes in certain patients. The surgeon's experience is a key factor to the success of this innovative technique: twenty to thirty operations are necessary to attain a positive identification rate higher than 90 percent and a false-negative diagnosis rate of less than 5 percent (10). If these rates are not achieved, it is strongly recommended that ALND be performed as well (10). As the technical constraints related to SLNB have been surpassed and its clinical effectiveness proven, at this stage, it is important to do a cost analysis. The objective of this study was to compare the cost of the two techniques in two patient samples. Quality of life was not taken into account, for this aspect must be studied prospectively, and a relatively long time period is required between the surgical act and the gathering of information to ensure the stability of the data. Nonetheless, initial evaluations appear to be in favor of SLNB, which is less incapacitating in terms of morbidity (e.g., limited mobility of arm and shoulder) (6;9).

MATERIALS AND METHODS

Patient Characteristics

Our study included ninety-one patients who were treated for breast cancer between 1998 and 2001 at the Centre Léon Bérard, a comprehensive cancer treatment center in the Rhone Alps region of France (8). The innovative SLNB technique was introduced at the Centre Léon Bérard in 1999. Today, it is systematically proposed to primary breast cancer patients with tumors of less than 3 cm in the axilla. This technique is not proposed to patients suffering from multifocal cancer, inflammatory cancer, or suspect axillary lymphadenopathy, or to those who are pregnant or who have a history of allergies.

Two samples were drawn at random from two homogenous patient groups: one composed of fifty patients who had undergone ALND, the other of fifty patients who had undergone SLNB. Nine patients were excluded (seven from the ALND group and two from the SLNB group) due to missing data or concomitant noncancerous pathological conditions that required extensive hospital stays. In the SLNB sample, six patients required immediate axillary dissection (extemporaneous examination of sentinel lymph node in the intraoperative phase proved positive), whereas twelve patients required ALND at a later date due to the identification of positive nodes in the final histopathologic examinations. Table 1 presents the main patient characteristics.

Table 1. Patient Characteristics

Characteristics	Technique			
	ALND (n = 43)		SLNB (n = 48)	
Average age in yr (SD)	59.3	(6.9)	62.9	(10.7)
Average size of tumor in mm (SD)	14.02	(4.2)	14.31	(4.3)
SBR = 1	10	(23%)	15	(31%)
SBR = 2	22	(51%)	21	(44%)
SBR = 3	11	(26%)	12	(25%)
Average number of nodes (SD)	16.84	(6.7)	12.5[a]	(12.7)[a]
Negative nodes	26	(60%)	8[a]	(67%)
Positive nodes	17	(40%)	4[(3)]	(33%)

[a] Only concerns patients who underwent ALND at a later date.
ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy; SBR, Scarf-Bloom-Richardson scale.

Cost Evaluation Method

A retrospective study was performed, because the SLNB technique was already in general practice at the Centre Léon Bérard when the study began. The technique had been implemented at the center exclusively on the basis of clinical criteria. The microcosting method was used to evaluate the costs of SLNB and ALND, for this method provides the greatest level of precision in the evaluation of hospital-related costs (4). Only direct medical costs were included to enable a comparison of the real costs for the two strategies. The cost for ALND carried out after SLNB, either immediately or at a later date, was added to the initial cost for SLNB. As the microcosting method requires an extremely detailed breakdown of the production process, all consumed resources were integrated (not only differential items) to determine the total direct medical costs for both procedures. However, neither indirect accounting costs (general hospital administration costs, etc.) nor "indirect costs" as formerly defined in economic evaluation terminology (e.g., loss of income due to sick leave) (4) were included. Information sources included patients' medical files for physical quantities and data from the cost accounting department at the Centre Léon Bérard for prices and unit costs. Prices for 2001 were retained in this economic evaluation. Distributions of total costs (in euros) and hospital stays (in number of days) for the two techniques were compared with the Mann-Whitney nonparametric U-test, using alpha = 0.05. Analyses were performed with the SAS® software (SAS version 8.2, SAS Institute, Carry, NC).

Table 2. Comparison of Unit Costs of ALND and SLNB Strategies

Production process		Technique	
Phase	Title	ALND (in €)	SLNB (in €)
1	Consultation with surgeon	37	37
2	Consultation with anesthesiologist	37	37
3	Preoperative check-up[a]	116	116
4	Biopsy		
	Needle biopsy	41	41
	Ultrasound-guided microbiopsy	107	107
	Macrobiopsy with Mammotome®	571	571
	Surgical biopsy[b]	602	602
5	Anatomic pathology examinations		
	Positive node on first analysis[c]	31	31
	Negative node on first analysis[d]	57	230
6	Consultation with surgeon	37	37
7	Hospitalization[e]	125	125
8	Operating room (total cost)	370	356
	Disposable products and depreciation	158	167
	Surgeon[f]	72	56
	Anesthesiologist[f]	6	6
	Nurses[f]	134	126
9	Postoperative consultation	48	37
10	Nuclear medicine		
	Without X-rays		56
	With X-rays		110

[a] This phase included a blood cell count, haemostasis testing, electrolytogram, glycaemia testing, electrocardiogram and lung X-ray.
[b] The cost for 2.8 days of hospitalisation (the average hospital stay observed in our study) was also included.
[c] We included reception of specimens, gross examination, fixation and slicing, tissue inclusion in blocks, Hematoxylin Phloxin Safran (HPS) staining and slides, interpretation of results and archiving.
[d] Upon initial analysis (positive node), we also included the cost of subsequent slicing, tissue inclusion in blocks and interpretation.
[e] Daily cost excluding medication and the cost of ALND and/or SLNB.
[f] Cost evaluated according to average times reported in the two samples.

RESULTS

Unit Costs for Each Phase of ALND and SLNB

Table 2 illustrates the unit costs for each phase necessary to produce ALND and SLNB. The highest unit costs are surgical biopsy (602€), macrobiopsy with Mammotome® (571€), operating room expenses (370€ for ALND versus 356€ for SLNB), anatomic pathology examinations in SLNB when lymph nodes are negative upon first analysis (230€), hospitalization days (125€), and postoperative check-ups (116€). Please note that the cost of ALND and SLNB is not included in hospitalization day costs. Table 2 shows that relatively few unit costs differ; however, this finding does not mean that the quantities consumed by each patient are homogenous. The unit costs that differ are the anatomic pathology examinations (immunohistochemical technique is required when nodes are negative upon first analysis), operating room expenses (the depreciation charge for the probe required in the SLNB procedure increased this unit cost by 9€; however, this extra cost is weighted by shorter interventions), and postoperative consultations (the 11€ difference between the ALND and SLNB techniques was due to the production cost for eventual lymphocele punctures).

Patient Distribution in Each Phase of the Production Process

Regardless of the technique used, all patients had consultations with a surgeon and an anesthesiologist, as well as a preoperative check-up (blood cell count, hemostasis testing, electrolytogram, glycemia testing, electrocardiogram, and lung X-ray). Four of ten patients had percutaneous examinations (essentially needle biopsies) regardless of the procedure applied. Sentinel lymph node mapping was carried out with patent blue dye® injections (colometric method) in all of the patients. This intervention was associated with further isotopic searches in twenty-seven patients. With the SLNB technique, lymph nodes were negative upon first analysis in 83 percent of cases. On the other hand, we observed that the length of hospitalization with ALND differed significantly from that of SLNB (median, 9 days versus 3 days, respectively, $p < 0.0001$, Mann-Whitney U-test). This calculation takes into account the total hospitalization period for

https://doi.org/10.1017/S0266462304001345 Published online by Cambridge University Press

Table 3. Total Direct Medical Cost for ALND and SLNB

Phase	ALND (n = 43)			SLNB (n = 48)		
	Mean cost (€)	in %	SD	Mean cost (€)	in %	SD
1 Consultation 1 with surgeon	37	2%	0	37	2%	0
2 Consultation anesthesiologist	37	2%	0	37	2%	0
3 Preoperative check-up	116	6%	0	116	7%	0
4 Biopsy	90	4%	192	101	6%	193
5 Anatomic pathology exams	57	3%	0	197	11%	75
6 Consultation 2 with surgeon	5	0%	13	8	0%	15
7 Hospitalization	1,150	57%	225	422	24%	300
8 Operating room	471	23%	62	445	25%	75
9 Postoperative consultation	44	2%	14	35	2%	9
10 Nuclear medicine	–	–	–	47	3%	47
Total direct medical cost[a]	2,007	100%	282.99	1444	81%	401
11 Consultation 1 with surgeon	–	–	–	0	0%	0
12 Consultation anesthesiologist	–	–	–	5	0%	12
13 Preoperative check-up	–	–	–	0	0%	0
14 Biopsy	–	–	–	0	0%	0
15 Anatomic pathology exams	–	–	–	0	0%	0
16 Consultation 2 with surgeon	–	–	–	0	0%	0
17 Hospitalization	–	–	–	227	13%	417
18 Operating room	–	–	–	101	6%	179
19 Postoperative consultation	–	–	–	0	0%	0
20 Nuclear medicine	–	–	–	0	0%	0
Total direct medical cost[b]	2,007	–	–	1777	100%	645

[a] For SLNB, this is the mean cost without the 18 patients who underwent ALND either immediately or at a later date.
[b] For SLNB, this is the mean cost with the 18 patients who underwent ALND either immediately or at a later date.
ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy.

the eighteen SLNB patients who underwent ALND (either immediately or at a later date).

Total Direct Medical Costs for ALND and SLNB

The total direct medical cost for ALND differs significantly from that of SLNB (median 1,965.86€ versus 1,429.93€, $p = 0.0076$, Mann-Whitney U-test). SLNB remains less costly than ALND, despite the six ALND procedures carried out immediately after SLNB and twelve others at a later date. A closer look shows that hospitalization represents 57 percent of all total direct medical costs for ALND versus only 37 percent for SLNB (Table 3). This difference begins to fade when we include biopsies (6 percent of total direct medical cost for SLNB versus 4 percent for ALND), anatomic pathology examinations (11 percent of total direct medical cost for SLNB versus 3 percent for ALND), and operating room expenses (25 percent of total direct medical cost for SLNB versus 23 percent for ALND). It is also necessary to take into account the cost of nuclear medicine (3 percent of total direct medical cost for SLNB), which concerned twenty-seven patients in our study. When illustrated as a tree (Figure 1), we see that the average total direct medical cost for the 30 SLNB patients who did not require ALND was 1,349€ (median 1,301€). This figure increases to 2,261€ (median 2,308€) for the six patients who had ALND immediately after SLNB, and to 2,605€ (median 2,763€) for the twelve patients who underwent ALND at a later date. The cumulative cost savings between January 1999 and August 2003 at the Centre Léon Bérard with the introduction of SLNB procedure was 141,554€.

DISCUSSION

SLNB Seems to Be Less Expensive Than ALND

From an economic point of view, SLNB seems to be less expensive than ALND. Moreover, we consider that the difference between the total direct medical costs for ALND and SLNB could be even greater for four reasons. First, this cost analysis does not include indirect costs in the accounting sense of the term, which should be lower with SLNB than with ALND because this new technique absorbs a lesser amount of production factors. For example, as hospitalization is longer with ALND, cost-drivers based on length of stay would increase the indirect cost of ALND, for the ALND technique requires more hospital personnel time (e.g., axillary drainage, extensive nursing care of scars, immediate physiotherapy, and a greater number of complications). Second, this cost analysis does not take into account wasted work

https://doi.org/10.1017/S0266462304001345 Published online by Cambridge University Press

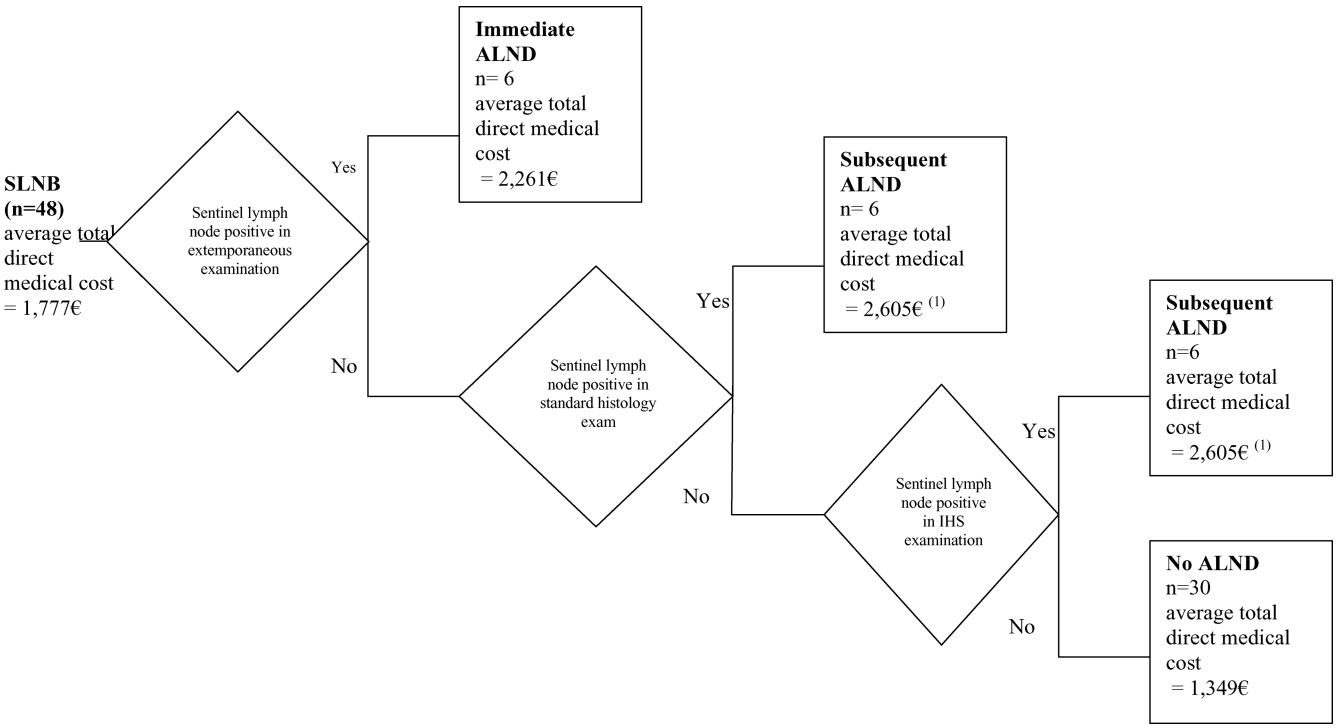

Figure 1. Breakdown of SLNB procedure. SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection. (1), Average total direct medical cost of SLNB with subsequent ALND (n = 12).

production factors. Third, it does not include non-hospital-related costs reimbursed by the public health-care system, which would have further increased ALND costs in relation to SLNB. For example, twenty sessions of physical therapy are systematically prescribed to patients who undergo ALND during their postoperative hospitalization or after discharge from the Centre Léon Bérard. If these sessions were valued according to French Social Security tariffs, the difference between the two techniques would increase by 282€. Fourth, our evaluation does not include "indirect costs" as formerly defined in economic evaluation terminology, such as loss of income due to sick leave (4). According to both the literature (10) and the initial analyses at the Centre Léon Bérard, ALND is more incapacitating than SLNB. This finding means that costs generated by sick leave, for example, would in all probability have been greater for ALND.

Comparison and Comparability of our Results With Other Studies

Two articles concerning the cost of SLNB were found in the literature (3;5). The approach used by Chirikos et al. (3) evaluates the global cost for SLNB and ALND over 44 months. Due to a different evaluation method and study timeframe, these results are not comparable with ours in terms of absolute value. Nonetheless, this study shows that the average cost for SLNB represents 91 percent of the average cost for ALND, a figure that is similar to ours (89 percent). Here too, the cost of SLNB differs significantly from that of ALND. The approach used by Gemignani et al. (5) is also difficult to compare with ours, despite a similar study time frame, for these authors base their research on the extemporaneous examination of the lymph node with frozen-section analysis. This technique enables a complete and rapid analysis but requires a higher work factor, which increases the cost of SLNB. Furthermore, the authors use a global cost method. As such, we cannot yet compare our results with other cost analyses. This finding is particularly unfortunate because the approach applied here contains no bias related to indirect costs, which tend to fluctuate greatly from one hospital to another for two principal reasons. First, the allocation of indirect costs (in the accounting sense of the term) is carried out according to various arbitrary cost-drivers. Second, they depend upon the cost-containment measures implemented by the hospital. Such measures might aim, for example, at eliminating inefficiency related to internal communication problems. Qualified by Leibenstein as X-inefficiency (7), these problems are generally an increasing function of the size of the health-care establishment.

POLICY IMPLICATIONS

The SLNB strategy enables physicians to determine the axillary status of a patient with a lower morbidity rate. The economic dimension appears to be an additional element in

https://doi.org/10.1017/S0266462304001345 Published online by Cambridge University Press

favor of generalizing SLNB, for this practice reduces hospital costs by around 10 percent. The surgeon's experience seems to further increase the difference in cost between the two techniques (37,820€ saved in 2002 with 178 SLNBs and 44,450€ between January and August 2003 with 109 SLNBs). It would be of interest to perform a cost utility analysis that includes long-term quality of life assessment. Future modifications to hospital management, notably regarding outpatient surgery, could also improve quality of life and increase the cost variation between the two techniques.

REFERENCES

1. Agence Nationale d'Accréditation en Santé. *La technique du ganglion sentinelle dans le cancer du sein*. Evidence based recommendation (ISBN: 2-914517-23-8). Paris: ANAES; 2002.
2. Albertini JJ, Lyman GH, Cox CE, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA*. 1996;276:1818-1822.
3. Chirikos TN, Berman CG, Luther SL, Clark RA. Cost consequences of sentinel lymph node biopsy in the treatment of cancer. A preliminary analysis. *Int J Technol Assess Health Care*. 2001;17:626-631.
4. Drummond MF, O'Brien BJ, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press; 1997.
5. Gemignani ML, Cody HS, Fey JV, et al. Impact of sentinel lymph node mapping on relative charges in patients with early-stage breast cancer. *Ann Surg Oncol*. 2000;7:575-580.
6. Giuliano AE, Haigh PI, Brennan MB, et al. Prospective observational study of sentinel lymphadenectomy without further axillary dissection in patients with sentinel node-negative breast cancer. *J Clin Oncol*. 2000;18:2553-2559.
7. Leibenstein H. Allocative efficiency vs X-efficiency. *Am Econ Rev*. 1966;56:392-415.
8. Philip T. The Léon Bérard cancer center. *Pediatr Hemat Oncol*. 1996;13:477-486.
9. Pressman P. Surgical treatment and lymphedema. *Cancer*. 1998;83:2782-2787.
10. Schwartz GF, Giuliano AE, Veronesi U. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast April 19 to 22, 2001 Philadelphia, Pennsylvania. *Cancer*. 2002;94:2542-2551.