Practice patterns of lymph-node mapping and sentinel-node biopsy for breast cancer in British Columbia

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Introduction: Because there is no standardized technique for mapping of lymph nodes and no optimal technique for evaluating the sentinel node, we decided to evaluate practice patterns for sentinel-node biopsy (SNB) for breast cancer in British Columbia 5 years after its introduction in 1996. **Methods:** We carried out mail and telephone surveys of general surgeons performing at least 1 SNB (n = 28) or not performing SNB (n = 50), and carried out telephone surveys or on-site visits with pathologists (n = 7) and nuclear medicine physicians (n = 5) from institutions supporting SNB in the province. We collected data on training, perceived indications and techniques for the surgical, imaging and pathologic assessments of SNB to obtain data on practice patterns in 2001 and the degree of consistency among surgeons and institutions involved in performing SNB and reasons for not adopting the SNB technique. **Results:** By 2001, SNB was incorporated into the practice of 19% of surgeons (28 of 150) performing breast cancer surgery in British Columbia. The survey response rate among SNB surgeons was 89% (25 of 28). Twelve (48%) of the 25 surgeons implemented SNB in the context of a validation study. Ten (40%) of the 25 had no data management support to monitor their results. Surgical training included intraoperative mentoring alone (48%), formal training courses alone (20%), both (24%) and self-teaching (8%). One-third of the surgeons had performed fewer than 10 procedures. Five surgeons had abandoned routine axillary dissection. There was considerable variation regarding the indications for SNB, definition of a sentinel node and surgical techniques. All nuclear medicine departments had a written lymphatic mapping protocol, but each used a different volume and activity of radiotracer. Immunohistochemical evaluation of the sentinel nodes was performed at just 3 pathology laboratories. The survey response rate from surgeons not practising SNB was 54% (27 of 50). Among 24 responders in active practice, 7 (29%) planned to perform SNB; 79% had not decided on the SNB indications. Lack of operating room time was a major limiting factor. **Conclusions:** There was considerable variation in the surgical, nuclear medicine and pathology techniques for SNB in the absence of a planned approach for its implementation in British Columbia. Developing consensus around written guidelines for the indications and techniques of SNB may reduce this variation.

Introduction : Comme il n'existe pas de méthode normalisée de cartographie des ganglions lymphatiques ni de technique optimale d'évaluation du ganglion de Troisier, nous avons décidé d'évaluer les tendances de la pratique relatives à la biopsie du ganglion de Troisier (BGT) pour le dépistage du cancer du sein en Colombie-Britannique cinq ans après son lancement en 1996. **Méthodes :** Nous avons réalisé des sondages postaux et téléphoniques auprès de chirurgiens généraux ayant pratiqué au moins 1 BGT (n = 28) ou n'en ayant pas pratiqué (n = 50) et nous avons procédé à des sondages téléphoniques ou effectué des visites sur place auprès de pathologistes (n = 7) et de spécialistes en médecine nucléaire (n = 5) d'établissements de la province qui appuient la BGT. Nous avons réuni des données sur la formation, les indications perçues et les techniques d'évaluation chirurgicale, radiologique et pathologique de la BGT afin d'obtenir des données sur les tendances de la pratique en 2001 et sur l'uniformité entre

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les chirurgiens et les établissements pratiquant des BGT, ainsi que sur les raisons pour lesquelles on n'a pas adopté la BGT. **Résultats :** En 2001, 19 % des chirurgiens (28 sur 150) qui pratiquaient des interventions chirurgicales contre le cancer du sein en Colombie-Britannique avaient adopté la BGT. Le taux de réponse chez les chirurgiens pratiquant la BGT s'est établi à 89 % (25 sur 28). Douze (48 %) des 25 chirurgiens ont mis en œuvre la BGT dans le contexte d'une étude de validation. Dix (40 %) des 25 n'avaient aucun soutien en gestion de données pour suivre leurs résultats. La formation chirurgicale a inclus le mentorat intraopératoire seulement (48 %), des cours de formation structurés seulement (20 %), les deux (24 %), et l'autoformation (8 %). Le tiers des chirurgiens avaient pratiqué moins de 10 interventions. Cinq chirurgiens avaient abandonné la dissection axillaire de routine. On a constaté une variation considérable en ce qui concerne les indications en faveur de la BGT, la définition d'un ganglion de Troisier et les techniques chirurgicales. Tous les services de médecine nucléaire avaient un protocole écrit de cartographie des ganglions lymphatiques, mais chacun utilisait un différent volume et une différente activité d'indicateur radioactif. On a pratiqué l'évaluation immunohistochimique des ganglions de Troisier à trois laboratoires de pathologie seulement. Le taux de réponse des chirurgiens qui ne pratiquaient pas la BGT s'est établi à 54 % (27 sur 50). Sur les 24 répondants qui pratiquaient activement, 7 (29 %) prévoyaient pratiquer une BGT, et 79 % n'avaient pas pris de décision sur les indications relatives à la BGT. Le manque de temps en salle d'opération constituait une contrainte importante. **Conclusions :** Comme il n'y a pas de stratégie planifiée de mise en œuvre en Colombie-Britannique, on a constaté une variation importante des techniques de chirurgie, de médecine nucléaire et de pathologie relatives à la BGT. L'établissement d'un consensus sur des lignes directrices écrites traitant des indications relatives à la BGT et des techniques pertinentes pourrait réduire cette variation.

Axillary lymph-node dissection provides important prognostic information[1,2] and guides the selection of adjuvant therapy. However, axillary dissection may cause significant morbidity, including postoperative pain, seroma, neuropathy and lymphedema.

Mapping of the lymph nodes with biopsy of the sentinel node using blue dye or radiocolloid, or both, has recently emerged as an important factor in the surgical management of breast cancer.[3–6] The sentinel node is the first node draining the primary tumour. Its pathologic status may reflect the status of the entire axilla. The goal of sentinel-node biopsy (SNB) is to identify patients with a sentinel node that is free of malignant cells who could avoid the morbidity of further axillary surgery.

In experienced hands, the sentinel node can be identified in over 90% of patients,[7] with a false-negative rate of 5%.[8] It has been proposed that SNB may soon replace axillary dissection as the preferred regional staging procedure for patients with breast cancer.[9] Some surgeons have already abandoned axillary dissection for patients with an uninvolved sentinel node.[4,10] At present, there is no standardization of lymphatic mapping techniques and no consensus on the optimal technique for the pathological evaluation of the sentinel nodes. In Canada, there is also no regulatory body to monitor the introduction of new surgical procedures.

SNB has been gradually implemented in British Columbia since October 1996. In this study we examined how surgeons adopted SNB in British Columbia from 1996 to 2001 and we evaluated the practice patterns of lymphatic mapping and pathological analysis of sentinel nodes for breast cancer in the province.

Methods

The BC Cancer Agency (BCCA) is a provincial organization having a broad-based mandate with respect to cancer control.[11] The BCCA's electronic database of cancer records was used to identify the 150 surgeons who performed 2 or more breast cancer operations in a single year between 1996 and 2000. Twenty-eight surgeons (19%) from 8 of 20 health regions in British Columbia had performed 1 or more SNB procedures by February 2001. A 23-item questionnaire with a covering letter was mailed to these 28 surgeons. If a response was not received within 2 months, up to 3 telephone calls or an on-site office visit, or both, was made.

A separate 8-item questionnaire was mailed to 50 surgeons who were known to perform a substantial volume of breast cancer surgery in British Columbia but who were not practising SNB. They were sent a second mailing if a response was not received within 1 month.

Seven pathologists, 1 from each pathology department where the sentinel nodes were evaluated, were surveyed with a 12-item questionnaire through on-site visits or by telephone, and 5 nuclear medicine physicians, 1 from each nuclear medicine department where lymphatic mapping using radiocolloid was performed, were similarly surveyed with a 12-item questionnaire.

Results

Surgeons performing sentinel-node biopsy

The surgical survey response rate was 89% (25 of 28 surgeons) among those who performed SNB. Twenty-one surgeons (84%) had primary appointments at community hospitals. Twelve (48%) of the 25 responding surgeons participated in an institutional pilot study of SNB. The remaining 13 practised SNB in 7 community practice settings without participation in a feasibility study. Only 3 of these 13 surgeons had data management support to moni-

tor their results. None of the surgeons participated in a randomized clinical trial of SNB.

With respect to the technical training and educational support about the technical aspects of SNB received by the 25 surgeons before practising SNB independently, 12 (48%) of the 25 surgeons received intraoperative mentoring alone, 5 (20%) attended a formal training course alone and 6 (24%) had both forms of training. Two surgeons (8%) had neither form of training, and 1 of them had abandoned the procedure (Table 1).

The number of SNB procedures performed by the 25 surgeons to February 2001 ranged from 1–78 per surgeon (Fig. 1); 9 (36%) had performed fewer than 10 SNBs, and 21 (84%) had performed fewer than 30.

Twenty surgeons (80%) routinely performed a completion axillary dissection after SNB. The remaining 5 (20%) did not perform an axillary dissection if the sentinel node was uninvolved. These 5 surgeons had performed 14, 21, 49, 56 and 78 SNB procedures respectively. Two surgeons used intraoperative imprint cytology to guide them on whether to proceed with a completion axillary dissection.

Twenty surgeons (80%) reported that they had decided on the indications for SNB. Table 2[12] shows the factors considered to be indications for SNB by the surgeons. All but 1 considered patients with invasive breast cancer classified as T1–2 and a clinically uninvolved axilla to be suitable candidates. Eight surgeons (32%) stated that they would perform SNB in pure ductal carcinoma in situ if the lesion was larger than 2 cm or there was comedo-necrosis, or both.

All 25 surgeons used blue dye (isosulfan blue 1%) to localize the sentinel node. Twenty surgeons (80%) also used radiocolloid, and 19 surgeons (76%) used preoperative lymphoscintigraphy routinely. Seven surgeons (28%) who used radiocolloid would biopsy an internal mammary sentinel node. Two of the 5 surgeons who used blue dye only did not have access to a nuclear medicine facility at their community hospital. Table 3 shows the different injection sites used by the surgeons. The total volume of blue dye injected per procedure also varied among the surgeons (≤ 2 mL, 4 surgeons; > 2–5 mL, 14 surgeons; > 5–10 mL, 3 surgeons; not specified, 4 surgeons). Breast massage after injection of the blue dye was practised by 16 surgeons (64%).

Table 1

Training on the Techniques of Sentinel-Node Biopsy (SNB) in Breast Cancer Received by 25 Surgeons in British Columbia

No. of procedures with intraoperative mentoring	Attendance at formal training course, no. (and %)		
	Yes	No	Total
0	5 (20)	2 (8)	7 (28)
1–5	5 (20)	7 (28)	12 (48)
6–10	0 (0)	2 (8)	2 (8)
> 10	1 (4)	0 (0)	1 (4)
Missing data	0 (0)	3 (12)*	3 (12)
Total	11 (44)	14 (56)	25 (100)

*Two surgeons were trained during residency; the third surgeon learned the technique during the institutional feasibility study.

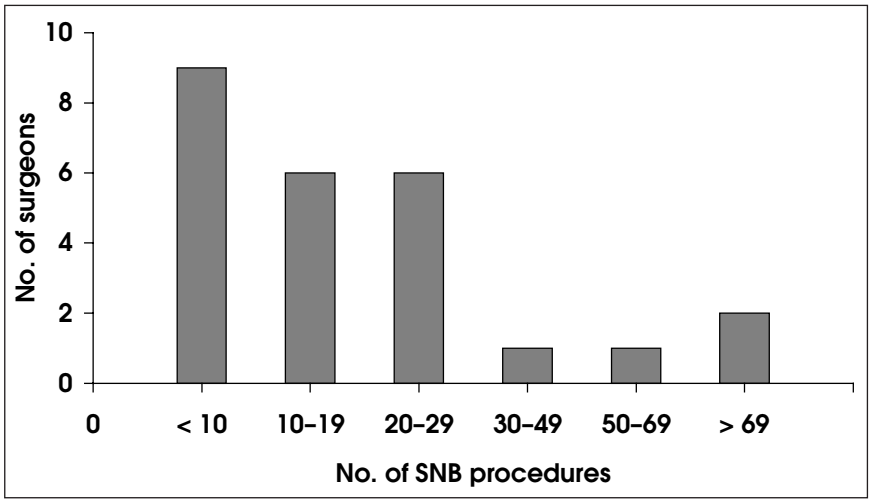

FIG. 1. Number of sentinel-node biopsy (SNB) procedures performed by 25 surgeons in British Columbia by February 2001.

Table 2

Factors Considered by 25 Surgeons in British Columbia to Be Indications for Sentinel-Node Biopsy (SNB) in Patients With Breast Cancer

Indications for SNB	No. (and %)		
	Yes	No	Not sure
Invasive tumour (TNM classification[12])			
T1	24 (96)	0 (0)	1 (4)
T2	24 (96)	0 (0)	1 (4)
T3	15 (60)	6 (24)	4 (16)
T4	3 (12)	18 (72)	4 (16)
Ductal carcinoma in situ	8 (32)	15 (60)	2 (8)
Multifocal invasive tumours	6 (24)	15 (60)	4 (16)
Clinically uninvolved axilla	24 (96)	0 (0)	1 (4)
Clinically involved axilla	4 (16)	17 (68)	4 (16)
Gross intraoperative finding in nodes of cancer cells	13 (52)	11 (44)	1 (4)

The definition of a sentinel node varied. All 20 surgeons who used both blue dye and radiocolloid designated a blue *and* hot node as a sentinel node. If none of the nodes was hot, 16 (80%) of them biopsied *any* blue nodes as sentinel nodes. In the absence of a blue-stained node, 16 surgeons (80%) would label *any* hot nodes as a sentinel node, whereas the other 4 surgeons (20%) would designate the hottest node *only* as the sentinel node. The numbers of surgeons who removed the sentinel node before the tumour or breast excision in patients who underwent a partial mastectomy, simple mastectomy and modified radical mastectomy were 19 (76%), 15 (60%) and 11 (44%), respectively.

Surgeons not using sentinel-node biopsy

The response rate from 50 surgeons who performed a substantial volume of breast cancer surgery but not SNB was 54% (27 surgeons). Among 24 who responded to the survey and were still practising breast cancer surgery, 7 (29%) stated that they planned to incorporate SNB into their practice, 3 (13%) stated that they did not intend to use SNB and 12 (50%) were undecided. Five (21%) of the 24 surgeons had decided on the indications for SNB, but 79% had not. Preferred training techniques included formal training courses and intraoperative mentoring. The factors limiting the implementation of SNB included the following: lack of operating room time (54%); difficulty in obtaining adequate training (38%); lack of nuclear medicine (42%) or pathology (21%) support; and a problem securing funding for the purchase of a gamma probe (17%). Ten surgeons (42%) were awaiting the results of prospective randomized trials before considering SNB.

Nuclear medicine survey

A written protocol for sentinel-node localization was available at all 5 nuclear medicine departments. Filtered technetium-99m (^{99m}Tc)-labelled sulfur colloid was the radiotracer used at all 5 departments. ^{99m}Tc-labelled antimony sulfide colloid was used for a short time at 1 department.

The activity and volume of the ^{99m}Tc-labelled sulfur colloid injected varied among the 5 nuclear medicine departments (Table 4). The radiocolloid was injected peritumorally, in 4–6 aliquots, into the breast parenchyma, and in 1 department a subdermal injection overlying the breast tumour was also administered. All departments used breast massage after injection. Preoperative lymphoscintigraphy was routinely performed in all departments.

Pathology survey

A written protocol for the pathological evaluation of sentinel nodes was available in 4 of 7 pathology departments. Most departments consisted of more than 1 laboratory facility, and as a result, 8 of 11 hospital laboratories providing sentinel-node evaluation services had a written protocol. In all 7 pathology departments, the sentinel nodes were submitted and reported separately from the non-sentinel nodes. Immunohistochemical evaluation of the sentinel nodes was performed in 3 of 7 pathology departments. In these 3 departments, 3 or 4 hematoxylin and eosin-stained sections of each sentinel node were evaluated. In the 4 pathology departments where immunohistochemical examination was not performed, the sentinel node was evaluated with a single hematoxylin and eosin-stained section at 3 departments, and 3 such sections at the remaining department. Intraoperative evaluation of the sentinel nodes by frozen section or imprint cytology was available to just 2 surgeons.

Discussion

The surgical management of patients with breast cancer is rapidly evolving. SNB is emerging as an alternative to routine axillary dissection and has the potential for changing the standard of surgical care for breast cancer.[3–7,13,14]

The present study identified several issues about the introduction of SNB in British Columbia. As of February 2001, just 19% of surgeons

Table 3

Blue-Dye Injection Sites Used by 25 Surgeons in British Columbia in the Localization of Sentinel Lymph Nodes in Patients With Breast Cancer

	No. (and %)		
Injection site	Intraparenchymal	Subdermal	Total
Peritumoral (all 4 quadrants)	15 (60)*	2 (8)	17 (68)
Lateral to breast tumour only	5 (20)†	1 (4)	6 (24)
Overlying breast tumour	—	1 (4)	1 (4)
Intratumoral only	—	—	1 (4)
Total	20 (80)	4 (16)	25 (100)

*Two surgeons also injected blue dye intratumorally.
†One surgeon also injected blue dye intratumorally.

Table 4

Activity of Technetium-99m-Labelled Sulfur Colloid and Total Injection Volume* Administered Per Lymphatic Mapping Procedure for Breast Cancer in 5 Nuclear Medicine Departments

Department	Activity, MBq	Injection volume, mL
1	15	3
2	15	6
3	20	3
4	28	10–12
5	30	6

*Sulfur colloid with or without local anesthetic

performing breast cancer surgery in the province had implemented SNB in their practice. The majority of these were in community practice. In contrast, 77% of 410 randomly selected fellows of the American College of Surgeons who responded to a recent questionnaire had performed SNB for breast cancer.[13] The major factors limiting the introduction of SNB in British Columbia included operating room time, access to training and educational support and to on-site nuclear medicine and pathology facilities. Another major factor was uncertainty about the role of SNB for patients with breast cancer.

The training received by those who performed SNB in British Columbia varied. It included formal courses, on-site mentoring by an experienced colleague and self-teaching. Of the surgeons who performed SNB in British Columbia 48% implemented the new technique in the context of a feasibility study approved by an institutional review board with prospective monitoring of outcomes.[14] These surgeons practised within 2 health regions in British Columbia. For the other 52% of surgeons, the technique was incorporated into their practice without the rigours of a prospective study, and 10 surgeons began to use SNB without data management support to document their results. It has been suggested that documentation to establish the mapping success and false-negative rates for the individual surgeon and multidisciplinary team is critical to the success of an SNB program.[3,15–17] The ramifications of inadequate treatment based on a false-negative SNB could be significant.

The published reports validating the accuracy of SNB as a staging procedure have come largely from surgeons who extended their SNB experience from patients with melanoma to patients with breast cancer, usually in a university-hospital setting. Despite the concerns expressed about the use and credentialling of SNB in a low-volume setting, it is increasingly being adopted by general surgeons in community practice.[13,14,18]

SNB is a technically challenging procedure associated with a learning curve.[15] It has been shown that surgeons performing fewer procedures have a lower sentinel-node identification rate[19–21] and a higher false-negative rate than surgeons performing larger numbers of SNBs.[10,21] It has been recommended that surgeons who perform breast cancer surgery infrequently should not perform SNB.[3] However, the level of experience necessary to perform SNB reliably and accurately is less well quantified. In the present study, 84% of the surgeons had performed fewer than 30 SNB procedures each and 5 surgeons (20%) had adopted SNB in lieu of an axillary dissection as the regional staging procedure of choice for patients with invasive breast cancer.

The American Society of Breast Surgeons (ASBS) first put forward the criterion that each surgeon should document an individual experience of at least 30 cases, in which both SNB and axillary dissection were performed with a success rate of 85% or greater in identifying an axillary sentinel node and with a false-negative rate of 5% or less. This recommendation was endorsed by Health Canada's Canadian Breast Cancer Initiative[3] and an Australasian consensus group.[17] More recently, the ASBS has suggested that an individual experience of 20 or more cases of SNB with completion axillary dissection was necessary to minimize the risk of false-negative results.[16]

The present study demonstrated variation in perceived indications for SNB. Although most surgeons agreed that SNB was indicated for T1–2, clinically node-negative, invasive breast cancer, there was disagreement on other indications and contraindications. The appropriate upper size limit of invasive breast cancer for SNB and the role of SNB in patients with intraductal disease were contentious issues. Sixteen percent of the surgeons considered patients with a clinically involved axilla, and 24% considered patients with multifocal invasive breast cancer as suitable candidates for SNB. The ASBS recommended against SNB in patients with a clinically involved axilla, and noted that SNB might be unreliable for patients with multifocal disease.[16]

Our study showed that the surgeons and nuclear medicine physicians used a variety of techniques to localize the sentinel nodes. Eighty percent of the surgeons used both blue dye and radiocolloid in lymphatic mapping. Studies have shown that the 2 techniques are complementary in localizing the sentinel nodes,[4,10,22] but a randomized trial did not confirm this finding.[19]

Seventy-two percent of the surgeons who practised SNB in British Columbia would not biopsy internal mammary sentinel nodes that were identified at preoperative lymphoscintigraphy. In addition to its morbidity, the impact of internal mammary node dissection on survival remains controversial.[23–25] It has been shown that internal mammary nodal metastases have prognostic significance[24,25] and are clinically relevant, especially in the context of a negative axillary dissection. The evaluation and treatment of the internal mammary lymph nodes are subjects for further investigation.

The present study also documented variation in the techniques used in the pathological evaluation of sentinel nodes. Immunohistochemical examination of the sentinel nodes was performed in just 3 of 7 pathology departments. The prognostic significance of isolated tumour cells identified by immunohistochemical methods in axillary nodes is unclear.[26] The number of hematoxylin and eosin-stained sections examined per node also differed among the departments. The optimal intensity and most cost-effective technique for the pathological analysis of sentinel nodes have not been defined. Two surgeons in British Columbia who had abandoned routine axillary dis-

section adopted intraoperative sentinel-node examination by imprint cytology to guide them on whether to proceed with a completion axillary dissection. The reliability of intraoperative frozen section and imprint cytology has not been determined.[3,27,28]

The literature suggests that in experienced hands, SNB is accurate in determining the regional nodal status of patients with breast cancer. However, before SNB is accepted as the standard of care for patients with breast cancer, further efforts are required to refine the selection criteria for SNB and standardize the optimal approach in each discipline. Each multidisciplinary team should develop a standardized approach and document success in identifying the sentinel node and be able to consistently achieve false-negative rates of 5% or less.[3] Until then, SNB should not be offered as the sole regional staging procedure. Surgeons are encouraged to participate in the ongoing randomized trials to validate the clinical utility of SNB.

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References

1. Carter CL, Allen C, Henson DE. Relation of tumour size, lymph node status and survival in 24,740 breast cancer cases. Cancer 1989;63:181-7.
2. Fisher ER, Sass R, Fisher B. Pathologic findings from the National Suirgical Adjuvant Project for Breast Cancers (protocol no. 4). X. Discriminants for tenth year treatment failure. Cancer 1984;53:712-23.
3. Cantin J, Scarth H, Levine M, Hugi M. Clinical practice guidelines for the care and treatment of breast cancer: 13. Sentinel lymph node biopsy. *CMAJ* 2001; 165:166-73.
4. Giuliano AE. Mapping a pathway for axillary staging. A personal perspective on the current status of sentinel lymph node dissection for breast cancer. *Arch Surg* 1999; 134:195-9.
5. Krag D, Weaver D, Ashikaga T, Moffat F, Kilmberg VS, Shriver C, et al. The sentinel node in breast cancer: a multicentre study. *N Engl J Med* 1998;339:941-6.
6. Veronesi U, Paganelli G, Viale G, Galimbert V, Luini A, Zurrida S, et al. Sentinel lymph node biopsy and axillary dissection in breast cancer: results in a large series. *J Natl Cancer Inst* 1999;91:368-73.
7. Hsueh EC, Hansen N, Giuliano AE. Intraoperative lymphatic mapping and sentinel lymph node dissection in breast cancer. *CA Cancer J Clin* 2000;50:279-91.
8. Miltenburg DM, Miller C, Karamlou TB, Brunicardi FC. Meta-analysis of sentinel lymph node biopsy in breast cancer. *J Am Statist Soc* 1999;84:138-42.
9. Habal N, Giuliano AE, Morton DL. The use of sentinel lymphadenectomy to identify candidates for postoperative adjuvant therapy of melanoma and breast cancer. *Semin Oncol* 2001;28:41-52.
10. Cody HS 3rd, Hill AD, Tran KN, Brennan MF, Borgen PI. Credentialing for breast lymphatic mapping: How many cases are enough? *Ann Surg* 1999;229:723-8.
11. Carlow DR. The British Columbia Cancer Agency: a comprehensive and integrated system of cancer control. *Hosp Q* 2000;3 (3):31-45.
12. Wittekind C, Sobin LH, editors: *TNM classification of malignant tumours*. 6th edition.Geneva: International Union Against Cancer; 2002.
13. Lucci A Jr, Kelemen PR, Miller C 3rd, Chardkoff L, Wilson L. National practice patterns of sentinel lymph node dissection for breast carcinoma. *J Am Coll Surg* 2001;192:453-8.
14. Smillie T, Hayashi A, Rusnak C, Dunlop W, Donald J, van der Westhuizen N. Evaluation of feasibility and accuracy of sentinel node biopsy in early breast cancer. *Am J Surg* 2001;181:427-30.
15. Cox CE, Salud CJ, Harrinton MA. The role of selective sentinel lymph node dissection in breast cancer. *Surg Clin North Am* 2000;80:1759-77.
16. American Society of Breast Surgeons. Revised Consensus Statement on Guidelines for Performance of Sentinel Lymphadenectomy for Breast Cancer, September 1, 2000. Available: www.breastsurgeons.org/sentinel.shtml (accessed 2002 Jul 7).
17. Kollias J, Gill G, Chatterton B, Raymond W, Collins PJ. Sentinel node biopsy in breast cancer: recommendations for surgeons, pathologists, nuclear physicians and radiologists in Australia and New Zealand. *Aust N Z J Surg* 2000;70:132-6.
18. Wong JH. Sentinel lymphadenectomy in breast cancer. University research tool or community practice? *Surg Clin North Am* 2000;80:1821-30.
19. Morrow M, Rademaker AW, Bethke KP, Talamonti MS, Dawes LG, Clauson J, et al. Learning sentinel biopsy: results of a prospective randomized trial of two techniques. *Surgery* 1999;126:714-22.
20. Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymphadenectomy in breast cancer. *J Clin Oncol* 1997;15:2345-60.
21. Orr RK, Hoehn JL, Col NF. The learning curve for sentinel node biopsy in breast cancer: practical considerations. *Arch Surg* 1999;134:764-7.
22. Cox CE, Pendas S, Cox JM, Joseph E, Shons AR, Yeatman T, et al. Guidelines for sentinel node biopsy and lymphatic mapping of patients with breast cancer. *Ann Surg* 1998;227:645-51.
23. Veronesi U, Marubini E, Mariani L, Valagussa P, Zucali R. The dissection of internal mammary nodes does not improve the survival of breast cancer patients: 30-year results of a randomised trial. *Eur J Cancer* 1999;35:1320-5.
24. Klauber-DeMore N, Bevilacqua JLB, Van Zee KJ, Borgen P, Cody HS. Comprehensive review of the management of internal mammary lymph node metastases in breast cancer. *J Am Coll Surg* 2001;193:547-55.
25. Cody HS 3rd, Urban JA. Internal mammary lymph node status: a major prognostic factor in axillary node-negative breast cancer. *Ann Surg Oncol* 1995;2:32-7.
26. Hermanek P, Hutter RV, Sobin LH, Wittekind C. Classification of isolated tumour cells and micrometastasis. *Cancer* 1999;86:2668-73.
27. Viale G, Bosari S, Mazzarol G, Galimberti V, Luini A, Veronesi P. Intraoperative examination of axillary sentinel lymph nodes in breast carcinoma patients. *Cancer* 1999; 85:2433-8.
28. Van Diest PJ, Torrenga H, Borgstein PJ, Pijpers R, Bleichrodt RP, Rahusen FD. Reliability of intra-operative frozen section and imprint cytological investigation of sentinel lymph nodes in breast cancer. *Histopathology* 1999;35:14-8.