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The utilization and impact of core needle biopsy diagnosis on breast cancer outcomes in British Columbia

Study results indicate that open surgical procedures are being overused for the diagnosis of breast cancer in BC's more sparsely populated regions.

ABSTRACT

Background: **Numerous studies support the utilization of core needle biopsy rather than open surgical procedures for diagnosis before definitive breast cancer surgery. In British Columbia, a study was undertaken recently to determine the proportions of breast cancer patients diagnosed with core needle biopsy and with open surgical procedures by region, and to establish how each method affected the number of breast cancer surgeries, relapse rates, and sentinel lymph node biopsy results.**

Methods: **BC Cancer Agency databases were used to identify all women with breast cancer in the province in 2006. After excluding patients with metastatic or advanced disease, prior invasive or in situ breast cancer, out-of-province surgery, autopsy-only diagnosis, and incomplete records, 2589 patients were selected for the study and data were analyzed.**

Results: **Of the 2589 patients studied, diagnosis was by core needle biopsy in 58.9% of cases. Utilization of this procedure varied by region from a low of 46.7% to a high of 75.4%. Women diagnosed by core needle biopsy had fewer total breast surgeries, but no difference in relapse rate or the prevalence of pN0i+ disease found on sentinel lymph node biopsy.**

Conclusions: **Core needle biopsies are underutilized in BC, and there is significant regional variation in the use of this procedure. Breast cancer diagnosis with preoperative core needle biopsy was not found to affect relapse rates or the prevalence of micrometastases identified on sentinel lymph node biopsy, and core needle biopsy was associated with substantially fewer breast surgeries per patient. The Provincial Breast Health Strategy has proposed a new Clinical Pathway to ensure that all women suspected of having breast cancer undergo the most appropriate diagnostic imaging workup.**

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Background

Preoperative diagnosis based on a tissue sample prior to definitive breast surgery for cancer or precancerous lesions is considered the standard of care. To establish a preoperative breast cancer diagnosis, a core needle biopsy (CNB), fine needle aspiration (FNA), or both can be clinically-directed or performed under radiological guidance.[1] The BC Cancer Agency (BCCA) recommends using CNB to investigate suspicious breast lesions seen with mammography or ultrasound.[2] Other guidelines

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also support preoperative CNB in the majority of cases.[3-6] An interdisciplinary consensus conference in 2009 concluded that CNB was the favored method of diagnosis for breast lesions found on imaging.[7] European guidelines in 2006 suggested that at least 90% of breast cancers can be diagnosed on a preoperative CNB or FNA.[8] This means breast cancer diagnosis by open biopsy would ideally occur in less than 10% of incident cases.[8] Despite these recommendations, the use of open biopsy is still higher than 10% in North America.[1,5,7] After a diagnosis of breast cancer is confirmed by pathology, patients generally require nodal sampling with either a sentinel lymph node biopsy (SLNB) or axillary dissection. Occasionally, pathologic examination of the excised node(s) identifies isolated tumor cells with a maximum cluster diameter of 0.2 mm, which can be seen on cytokeratin immunohistochemical staining but not with hematoxylin and eosin staining.[9] This finding is referred to as pN0i+ disease and is of uncertain prognostic significance.[9,10] An open biopsy or CNB can result in artifactual displacement of cancer cells in the lymph nodes and lead to pN0i+ findings, although it is unclear whether this is less likely to occur when the breast cancer diagnosis is made with CNB than with open biopsy.[9,10]

More sparsely populated health authorities, such as Interior Health and Northern Health, utilized surgical procedures in more than 40% of initial diagnoses compared with less than 30% in the more densely populated health authorities, Vancouver Coastal and Vancouver Island Health.

To quantify the use of preoperative CNB in BC and the extent of regional variation in its use, and to determine how diagnostic methods may influence outcomes, we designed a retrospective study using data from the BCCA cancer registry and BCCA Breast Cancer Outcomes Unit (BCOU) database. The outcomes of interest were the number of breast and lymph node surgeries performed, the prevalence of pN0i+ found on SLNB, and the rate of relapse for patients with breast cancer.

Methods

An estimated 85% of breast cancer patients in BC are referred to BCCA for consultation and treatment.[11] While these patients are termed "referred cases," those treated solely in the community are termed "non-referred cases." The BCCA cancer registry captures information such as patient demographics, histology, and cause of death on all incident breast cancers.[12] The BCOU prospectively collects additional information, such as tumor characteristics, treatment, and relapse data, but only on referred cases.[11]

For this study, all cases of breast cancer newly diagnosed between 1 January and 31 December 2006 were identified. A cancer was defined as "newly diagnosed" if cancer had not been diagnosed previously in the affected breast. Cases from 2006 were chosen because data from 5 years of follow-up were available.

Cases with advanced disease (pathologic or clinical T4, clinical N2/3, clinical T3N1, or M1) or Paget disease alone, and cases with a prior or synchronous invasive or in situ breast cancer were excluded from the study. Cases with incomplete diagnostic or surgical treatment information were also excluded, including cases where patients were diagnosed or residing out-of-province at the time of diagnosis, and where surgical procedures were performed out-of-province. Cases with patients diagnosed on autopsy only or without pathology records were also excluded.

A total of 3195 cases of breast cancer newly diagnosed in 2006 were identified using the BCCA cancer registry. After excluding patients who did not satisfy study criteria, 2589 patients were selected. All statistical tests used to analyze the data for these patients were 2-tailed, with statistical significance established at $P<.05$. All analyses were performed using SPSS statistical software, version 14.0 (SPSS Inc, Chicago, IL). The UBC BCCA Research Ethics Board approved the study.

Analysis of all cases

For all incident primary breast cancers, the clinical and pathological variables were obtained from the BCCA cancer registry. By matching the procedure date to the breast cancer diagnosis date, we identified the diagnostic procedure(s). Image-guided CNBs were labeled as such if an imaging report was associated with the biopsy, the provider responsible for the biopsy was a radiologist, the radiologist's name or radiological facility was listed on the pathology report, or the pathology report specified that the CNB was performed under ultrasound or stereotactic guidance. Diagnostic CNBs were labeled as clinically-directed if a pathology report, operative report, or surgical consultation indicated that the biopsy was performed by a surgeon. When a CNB could not be identified as image-guided or clinically-directed, further chart review was conducted to guide classification.

The primary endpoint was the number of surgical procedures each patient underwent during diagnostic workup and initial therapy. "Surgical procedure" was defined as fine wire localization (FWL), clinically-directed open biopsy (partial mastectomy, lumpectomy, incisional biopsy, and excisional biopsy), mastectomy, mastectomy with nodal procedures, sentinel lymph node biopsy, axillary lymph node dissection, axillary excision not otherwise specified, and reduction mammoplasty performed on the same day. We excluded procedures that were not part of primary treatment for breast cancer and procedures performed after recurrence or more than 2 years after diagnosis date.

The case data were first analyzed according to method of diagnosis: CNB versus open surgical procedure. CNB cases alone were then analyzed to compare those that were image-guided with those that were clinically-directed. In both analyses, comparisons of patient, tumor, and treatment characteristics between groups were performed using the chi-square test for categorical variables and the student *t* test for continuous variables. Tumor characteristics analyzed included primary tumor histology, tumor size, clinical or pathological nodal status, number of pathologically positive nodes, number of positive nodes in micrometastatic diseases, lymphovascular invasion (LVI) status, tumor grade, ER and HER2 receptor status, and margin status. Treatment characteristics considered included number of breast and nodal surgeries, utilization and type of initial surgery, radiotherapy, and systemic therapy. Differences in patient, tumor, and treatment characteristics identified in the five health authorities in BC were also compared using the chi-square test for categorical variables and the ANOVA method for parametric continuous variables, and the Kruskal-Wallis test for non-parametric continuous variables.

Analysis of referred cases only

We analyzed local and locoregional relapse-free survival on referred cases only as these cases had prospective collection of prognostic factors, treatment factors, and relapse events. Five-year survival curves for local and locoregional relapse-free survival were generated using the Kaplan-Meier method and compared using the log-rank test. Multivariate predictors of local and locoregional relapse were determined using the Cox proportional hazards model (after confirmation of the proportionality assumption). Variables included in the model were HER2 status, ER status, nodal status, LVI, tumor size, tumor grade, type of systemic therapy, and method of diagnosis. A variable's effect on relapse was estimated by the model's hazard ratio. A 95% confidence interval was calculated for each HR.

Referred patients who received an SLNB were compared to determine the prevalence of pN0i+ disease according to method of breast biopsy. Comparisons of tumor characteristics, including pN stage (0 or 0i+), tumor size, LVI status, tumor grade, ER status, and number of open surgical procedures, were performed using the chi-square test for categorical variables and the Mann-Whitney test for continuous variables.

No statistically significant difference in tumor characteristics was found when health authorities were compared.

Results

Compared with patients in the surgically diagnosed group, patients in the CNB diagnosed group were found to have more advanced disease. Ductal and lobular carcinoma were diagnosed in 88.7% of the CNB group

Table 1. BC breast cancer cases (N = 2589), by diagnostic procedure, 2006.

Diagnostic procedure	Number (%) of cases
Image-guided CNB	1408 (54.4%)
Non-image-guided CNB	116 (4.5%)
FNA	223 (8.6%)
Punch biopsy/skin biopsy	5 (0.2%)
Total non-open procedures	**1752 (67.7%)**
FWL biopsy	519 (20.0%)
Clinically-directed open biopsy	262 (10.1%)
Full mastectomy	49 (1.9%)
Reduction mammoplasty	7 (0.3%)
Total open surgical procedures	**837 (32.3%)**

versus 68.1% of the surgically diagnosed group ($P<.001$). The mean tumor size in the CNB group was 2.1 cm versus 1.7 cm in the surgical group ($P<.001$). Positive nodal status was seen in 29.3% of the CNB group versus 13.4% of the surgical group ($P<.001$). Grade 2 and 3 disease were diagnosed in 69.4% of the CNB group versus 57.1% of the surgical group (P .02). Increased LVI was found in 16.3% of the CNB group versus 7.6% of the surgical group (P .001).

Of the 2589 cases studied, 1524 (58.9%) were diagnosed using CNB, either image-guided (54.4%) or clinically-directed (4.5%), 837 cases (32.3%) were diagnosed using an open surgical procedure, and 228 cases (9%) were diagnosed by other means (**Table 1**). Despite the greater number of more advanced disease cases in the CNB group, only 24.3% of cases diagnosed by CNB required two or more separate trips to the operating room for breast and nodal surgeries compared with 73.5% of cases diagnosed by surgical procedure ($P<.001$).

Table 2. Local relapse-free survival in referred patients (N = 2052) diagnosed by CNB versus open surgical procedure.

Diagnostic procedure (n)	Number of events	5-year local relapse-free survival rate (95% CI)	*P* value
Core biopsy (1373)	34	97.4% (96.4-98.2)	.53
Open surgical procedure (679)	14	98.1% (96.8-98.9)	

Table 3. Locoregional relapse-free survival in referred patients (N = 2052) diagnosed by CNB versus open surgical procedure.

Diagnostic procedure (n)	Number of events	5-year locoregional relapse-free survival rate (95% CI)	*P* value
Core biopsy (1373)	47	96.5% (95.3-97.4)	.23
Open surgical procedure (679)	17	97.8% (96.4-98.7)	

Ninety-two percent of all CNBs were performed under image-guidance. Cases diagnosed with clinically-directed CNB were associated with older patient age, more advanced disease (higher percentage of invasive disease, node positivity, LVI, and larger tumor size), and a higher proportion of these cases received total mastectomy as initial treatment. Cases in this group were also more often managed less aggressively, with 12.9% having no surgery versus 3.7% having no surgery in the image-guided CNB group.

Vancouver Coastal Health and Vancouver Island Health, both of which contain densely populated urban centres, had the highest proportion of patients diagnosed by CNB, 70.3% (95% CI, 66.7-74.0) and 75.4% (95% CI, 71.5-79.4), respectively. In comparison, Northern Health, the authority with the lowest population density, had the lowest proportion of CNB diagnoses at 46.7% (95% CI, 37.7-55.6) ($P<.001$).

Using the Kaplan-Meier method when comparing those women diagnosed by CNB with those diagnosed by open biopsy, neither local nor locoregional relapse-free survival was statistically different, with 5-year local relapse-free survival rates of 97.4% and 98.1% ($P=.53$), respectively (**Table 2**), and 5-year locoregional relapse-free survival rates of 96.5% and 97.8% ($P=.23$), respectively (**Table 3**). The impact of diagnostic method on local and locoregional relapse-free survival was also not statistically different when assessed using the Cox proportional hazards model.

There was no evidence that the use of preoperative CNB affected the risk of pN0i+ disease found on SLNB. Of the 515 cases with a CNB diagnosis of breast cancer and a subsequent SLNB, only 22 (4.3%) were identified as pN0i+ cases, compared with 8 (5.3%) pN0i+ in the open biopsy diagnosis group. In a logistic regression model, the method of diagnosis did not significantly affect pN0i+ found on SLNB, with an odds ratio of 0.88 (95% CI, 0.27-2.9) for CNB ($P=.84$).

Conclusions

Numerous studies have supported the benefits of utilizing CNB rather than open surgical procedures for breast cancer diagnosis, citing factors such as the elimination of surgery for benign lesions, superior patient

satisfaction, fewer complications, lower morbidity, better psychological adjustment with earlier treatment discussions, less scarring and shorter recovery time, optimized breast cancer treatment planning, and lower overall treatment cost.[1,5,6,13] Preoperative CNB has also been found equivalent to open surgical biopsy in accurately diagnosing breast cancer.[5-7]

Current guidelines recommend CNB as the initial procedure for diagnosis when investigating suspected breast malignancy based on radiological evidence.[2-7] In some uncommon situations, such as those involving a technically challenging biopsy site,[1,7] a lesion not visualized by ultrasound or mammography, active anticoagulant therapy, or small breast size,[1,14] surgical procedures may be preferred. However, these circumstances should account for less than 10% of all cases according to expert opinion.[1,7,8]

Overuse of surgery for diagnosis

In this study, 58.9% of women diagnosed with breast cancer in 2006 in BC had an image-guided or a clinically-directed CNB, while 32.3% of women were diagnosed with open surgical procedures. Even though the proportion of cases diagnosed with surgical procedures is comparable to the proportion reported in other studies,[1,7,14] it exceeds the "less than10%" recommendation from consensus conferences and national guidelines, and indicates that surgical procedures are overused in BC.

Possible explanations for the high rate of surgical biopsies in BC may include the lack of expertise in providing image-guided CNB, inadequate health care provider knowledge of the benefits of CNB, and financial factors in the decision-making process.[1] Higher rates of surgical biopsies are also associated with non-academic centres and surgeons without breast specialization.[1] Increasing the use of CNB as a diagnostic technique would not only optimize cancer treatment for the patient, it would also decrease costs to the health care system.[15-17] As well, a CNB allows for timely initiation or neoadjuvant systemic therapy when that is the appropriate treatment.

Only 7.6% of all CNBs (or 4.5% of the total number of patients) were performed under clinical guidance, which is appropriate given that clinically-directed CNB has a high false-negative rate of 12% to13%,[18,19] and is less accurate than CNB that relies on imaging modalities such as ultrasound or stereotactic guidance.[18] Even in palpable lesions, clinically-directed CNB is not recommended unless the lesion cannot be visualized with imaging.[18] Although we are unable to report the percentage of palpable lesions that could not be visualized, our other findings indicate there is room for improvement: the use of image-guided CNB needs to be supported and promoted, and the number of clinically-directed CNBs needs to be reduced.

Benefits of CNB diagnosis

In addition to resulting in favorable short-term postoperative quality-of-life scores for domains involving pain, social, and physical performance,[20] preoperative CNB diagnosis assists with treatment planning and has no impact on outcomes such as rate of pN0i+ disease found on SLNB or local and locoregional relapse. Consistent with literature findings,[15-17] women with image-guided CNB had fewer surgeries than women diagnosed by surgical procedure. Seventy-five percent of women with an image-guided CNB had one or less surgical procedure compared with only 26% of women whose diagnosis was made by surgery, despite the image-guided CNB group having larger, more invasive tumors with increased nodal positivity. Major factors contributing to re-excision include tumor histology, the presence of LVI,[21] and positive or close margins after initial surgery.[20,21] Thus, it is no surprise that preoperative histological diagnosis of malignancy is associated with significantly lower rates of re-excision.[20,21]

The aim of the proposed provincial Clinical Pathway is to shorten the wait time from screening or the time of development of symptoms to definitive diagnosis.

Regional variation in BC

We found significant regional variation in the use of CNB for initial diagnosis in British Columbia. More sparsely populated health authorities, such as Interior Health and Northern

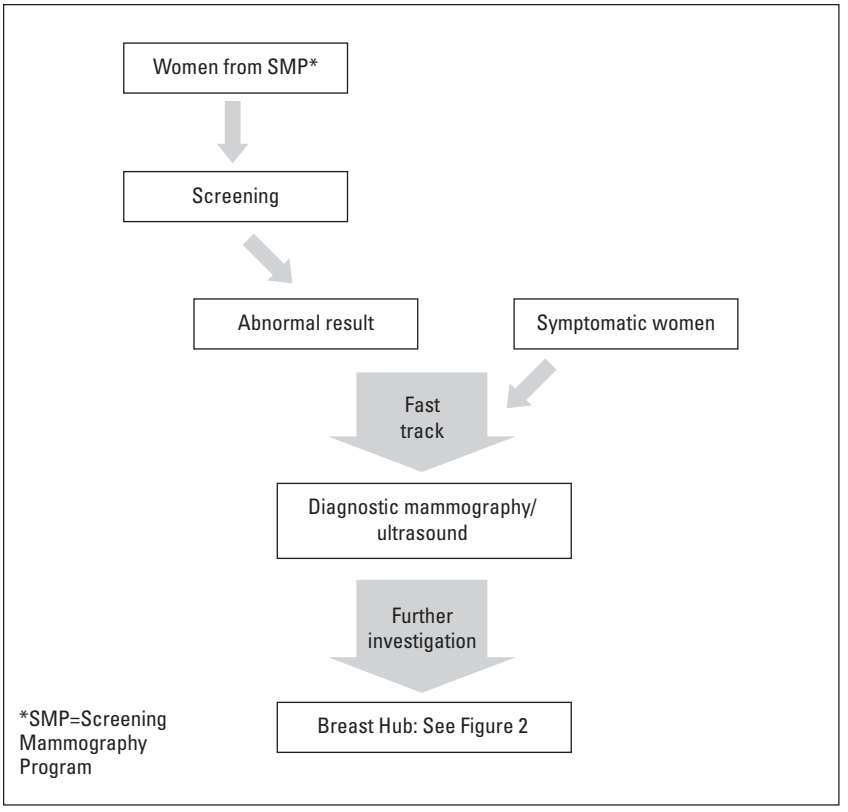

Figure 1. Provincial Breast Health Strategy recommendation: Clinical Pathway.

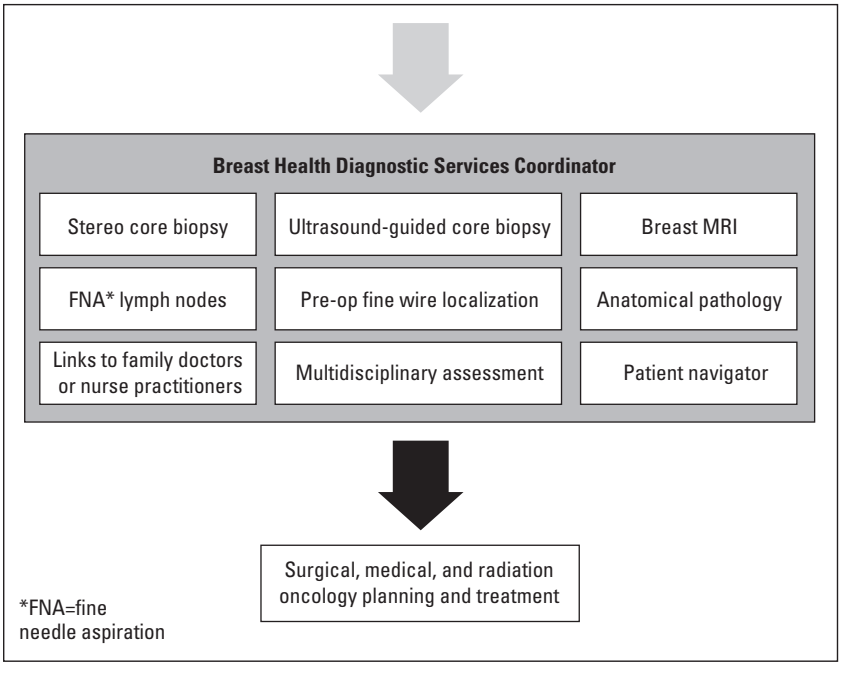

Figure 2. Provincial Breast Health Strategy recommendation: Breast Hub.

Health, utilized surgical procedures in more than 40% of initial diagnoses compared with less than 30% in the more densely populated health authorities, Vancouver Coastal and Vancouver Island Health. No statistically significant difference in tumor characteristics was found when health authorities were compared, suggesting the disparity is due to other factors, such as access to and availability of image-guided CNB or provider and patient attitudes in particular regions. In addition to providing regionally focused provider and patient education, further efforts in standardizing provincial breast cancer diagnostic algorithms are needed. This may be achieved by implementing recommendations from the Provincial Breast Health Strategy for a new Clinical Pathway (**Figure 1**) and the development of Breast Hubs (**Figure 2**).[22] Currently, women in BC receive fragmented care in the diagnosis of breast cancer, whether they present with symptoms (**Figure 3**) or are identified by the Screening Mammography Program (SMP) (**Figure 4**). Approximately 300 000 women per year go through the SMP under the direction of BCCA with approximately 8% (24 000) requiring further diagnostic workup.[23] Of all the women who go through the diagnostic workup from both the screening program and direct referral from physicians due to symptoms, approximately 15% will require further intervention such as a CNB.[23] A proportion of symptomatic women may undergo surgical treatment without any imaging workup.

The aim of the proposed provincial Clinical Pathway is to shorten the wait time from screening or the time of development of symptoms to definitive diagnosis. The EUSOMA (Euoropean Society of Breast Cancer Specialists) guideline for this is 21 days.[8] The Clinical Pathway would

help shorten wait times by ensuring that all women suspected of having breast cancer undergo the most appropriate diagnostic imaging workup. Ultrasound, MRI, CNB, FNA, and preoperative FWL would be provided at Breast Imaging Hubs, one physical location for imaging services, or could be accessed at different institutions with the help of a Breast Cancer Diagnostic Services Coordinator (i.e., through a virtual Breast Hub). The hub would also link directly to and facilitate the referral process for women with a cancer diagnosis for multidisciplinary assessment prior to breast cancer treatment.

Further research

Although it was not an original objective of this study, we are now reviewing our data to determine whether there is a difference between the CNB and the surgical group in the time from cancer diagnosis to completed surgical treatment, as this may have a significant impact on both patient survival and health care delivery planning. As well, a review of the completeness of prognostic information in the diagnostic process may be revealing.

Summary

In BC in 2006, the proportion of breast cancer cases diagnosed with open surgical procedures exceeded the recommended rate of less than 10%. Patients with a surgical diagnosis of cancer were 3 times more likely to have two or more breast cancer surgeries than patients diagnosed with CNB, even though the CNB group had larger, more invasive tumors with increased nodal positivity. There was no difference in disease-free survival or prevalence of micrometastases on SLNB between the two groups. Regional variation was also seen, with a much higher

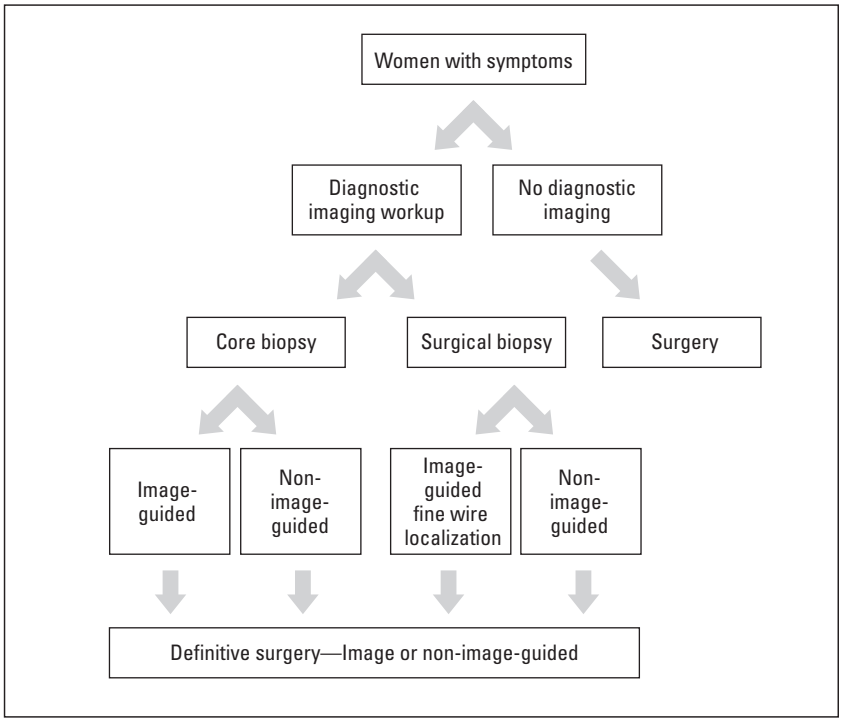

Figure 3. Current breast cancer management pathway for BC women with symptomatic disease.

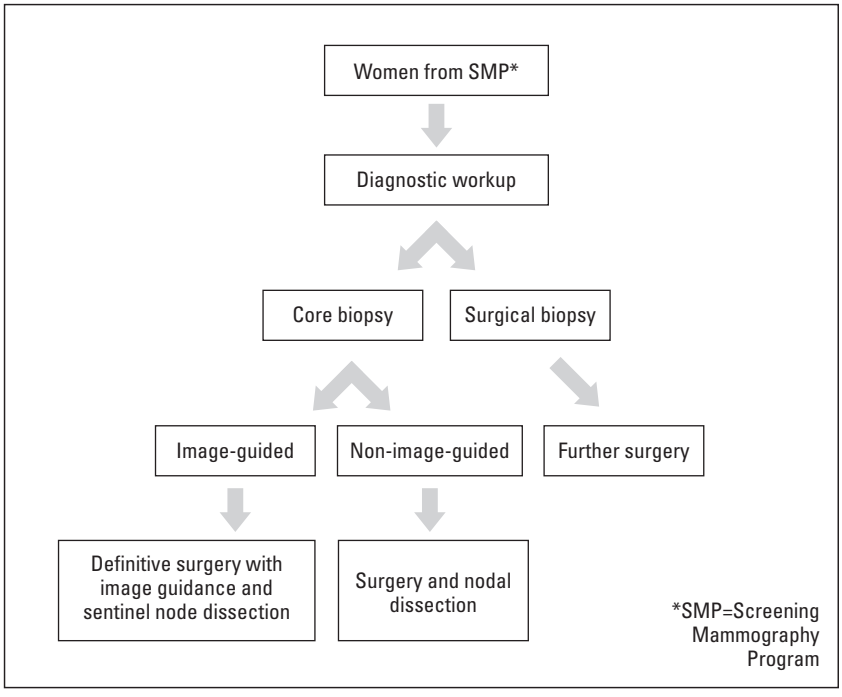

Figure 4. Current breast cancer management pathway for BC women identified through Screening Mammography Program.

utilization of CNB in Vancouver Coastal Health and Vancouver Island Health.

Education is needed in the province for care providers and patients alike regarding the benefits and utilization of CNB in breast cancer diagnosis. To provide timely access to image-guided CNB throughout the province, additional funding is needed to purchase equipment, train personnel, and implement recommendations from the Provincial Breast Health Strategy.

Competing interests

None declared.

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