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# Impact of SSO-ASTRO margin guidelines on reoperation rates following breast-conserving surgery

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ABSTRACT

*Background:* Re-operation rates following breast-conserving surgery (BCS) for early invasive breast cancer are highly variable, largely due to uncertainty regarding adequate margins. The 2014 SSO-ASTRO guidelines recommended "no ink on tumor" as adequate margins. We evaluated the effect of guideline implementation on re-operation following BCS at our regional cancer center.
*Methods:* Retrospective chart review was performed on records for patients with early invasive breast carcinoma undergoing BCS between February 2011 and May 2017. Time period, pathologic margin status, patient and tumor characteristics were assessed for their impact on re-operation rates.
*Results:* Overall re-operation rate decreased following the guidelines release (OR 0.28, 95% C.I. 0.15–0.51, $p = <0.0001$), with an unadjusted decrease of 3.89%. Re-operations on both close (OR 0.17, 95% C.I. 0.07–0.40, $p = <0.0001$) and widely negative (OR 0.20, 95% C.I. 0.05–0.77, $p = 0.02$) margins decreased in the post-guidelines time period.
*Conclusion:* SSO-ASTRO margins guideline release was associated with decreased re-operation. Furthermore, re-operations rates decreased in patients with pathologically negative margins, the target population the guidelines were meant to address.



## Introduction

Breast cancer is a common malignancy, affecting 1 out of every 8 North American women in their lifetime.[1] Breast-conserving surgery (BCS) is the standard of care for early-stage invasive breast cancer, with two thirds of women pursuing this route.[2] Although maintenance of the breast mound is an obvious benefit, the downside of BCS is the possibility of failing to achieve adequate margins in the index surgery. Positive margins, widely defined as tumor directly abutting the specimen edge during pathological analysis, are associated with a greater than 2-fold increased risk of ipsilateral breast tumor recurrence (IBTR).[3] While the definition of positive margin status may be clear, there has been a lack of consensus on what should constitute an adequate negative margin.[4] As margin status is a significant factor in determining the need for re-operation, this lack of consensus has had the practical consequence of variable re-operation practices. Reported re-operation rates vary widely, with institutions reporting a range of 0–60% and larger population-based studies reporting a range of 17–35%.[5–7] Re-operation has a negative impact, including poor cosmesis, delayed adjuvant treatment, increased surgical complications, increased healthcare costs and costs to the patient, and increased anxiety and stress for the patient and their loved ones.[8–10] Furthermore, 8.5% of patients who undergo BCS will proceed to receive a completion mastectomy.[11]

In 2014, the Society of Surgical Oncology and American Society for Radiation Oncology (SSO-ASTRO) consensus guidelines were released, advocating that negative margins be defined as "no tumor on ink" for patients with early-stage invasive breast cancer undergoing whole-breast irradiation following breast-conserving surgery.[12] While positive margins, defined as the presence of invasive tumor or DCIS on ink, are associated with an increase in IBTR, negative invasive margins of wider than "no tumor on ink" were not found to be associated with reduced IBTR.[3,12] There have

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been several studies published to date suggesting a decrease in overall re-operation rates since the implementation of the "no tumor on ink" standard proposed by the SSO-ASTRO guidelines (range: 1–28%[13,14]), underlining the potential to reduce re-operation without compromising local control.[13–18]

Detailed information regarding the influence of the SSO-ASTRO guideline implementation on a population level is limited, with most coverage coming from single institution studies. Therefore, we aimed to determine the effect of these guidelines in a Canadian health care setting, which has readily available access to robust population level data. In this study, we analyzed the rates of re-operation following BCS for invasive breast cancer before and after the adoption of the SSO-ASTRO margin guidelines with the aim to identify factors associated with need for re-operation.

## Methods

### *Patient selection and identification of cohorts*

Approval from the University of British Columbia Research Ethics Board was obtained for a retrospective chart review of patients referred to the British Columbia Cancer Agency, Sindi Ahluwalia Hawkins Center for the Southern Interior (BCCA SAH-CSI) who were treated surgically by BCS between February 25, 2011 and March 11, 2017. The BCCA is the only institution that provides radiation and medical oncology services within the province, with the BCCA SAH-CSI being one of six regional cancer centers within the province. It functions as the primary referral center for patients undergoing breast cancer surgical services within 10 regional hospitals, representing a blend of urban and rural practice.

Patients identified as having early invasive breast carcinoma who underwent BCS were included for analysis. Patients were excluded if they had/were: male, less than 18 years of age at the time of diagnosis, neoadjuvant therapy, previous or recurrent breast cancer, micro-invasive carcinoma, T4 cancer on final histology, N3 node status, metastatic breast cancer, indeterminate margin status, bilateral breast cancer, underwent mastectomy or surgical biopsy as their index surgery, or had their initial biopsy or surgical care outside the geographic catchment area of the BCCA SAH-CSI. Notably, we chose to exclude cases in which the first surgery was a diagnostic surgical biopsy, in an attempt to minimize the influence of diagnostic biopsy method on the need for re-operation.

Based on the patient's date of index surgery with respect to SSO-ASTRO guideline for invasive cancer adoption, two time periods were established, with 523 patients in the pre- (February 2011–February 2014) and 589 patients in the post-guideline (August 2014–March 2017) time periods. In the pre-guideline time period, physicians at the BCCA SAH-CSI used a 1–2 mm standard for negative margins. The new standard of "no tumor on ink" was not adopted uniformly across all regional hospitals on a particular date, therefore patients undergoing surgery within 3 months of the May 2014 hard-copy publication of the guidelines were not included for analysis, as we expected data from this period to be convoluted with respect to the effects of guideline implementation.

Furthermore, consideration of patients with ductal carcinoma in-situ (DCIS) at or near the margins was required, as decisions regarding the need for re-excision would not have been made solely based on the status of the invasive component. It should be noted that the SSO-ASTRO guidelines for ductal carcinoma in-situ only became available in November 2016, which suggested that margin considerations should be based primarily on the invasive component rather than the in-situ component.[19] Given the timing of the later guideline, it likely would not have influenced decision making in our cohort of patients with invasive carcinoma. Thus, the presence of DCIS at or near the margins was given consideration along with the invasive component, with the later preferentially considered.

### *Outcomes*

Data collected through chart review included patient age, as well as tumor-related factors (tumor size, grade, histology, pathologic margin status and type, associated DCIS and extensive intraductal component (EIC), multifocality, lymphovascular invasion, estrogen receptor/progesterone receptor (ER/PR) status, human epidermal growth factor receptor 2 (HER-2) status). Pathologic margin status was classified as positive if invasive carcinoma or DCIS abutted the ink-marked specimen edge (0 mm). Pathologically negative margins were further categorized as being close (<1 mm), and widely negative (≥1 mm) for either invasive cancer or DCIS. Further classification of margin status by margin type (i.e. invasive, DCIS, or combination) results in too few events per category, precluding meaningful statistical analysis. In situations where both invasive carcinoma and DCIS were positive or close, the margin was attributed to the histology that was the closest. If they were equidistant, then the margin was attributed to the invasive component. Subsequent breast procedures performed after the initial BCS (revision BCS or completion mastectomy) are considered a re-operation.

### *Statistical analysis*

Patient and tumor factors were summarized by study period, and frequencies between study periods were compared using chi-squared tests. Age and tumor size were categorized, as these variables both had non-linear relationships with probability of re-operation. The association of patient and tumor factors with re-operation was tested first at the univariable level in a model accounting for the clustering effect of surgeons (Generalized estimating equations model). The multivariable model included re-operation as the outcome, margin status, time period and margin status by time period as the main predictors of interest, the clustering effect of surgeon, and other patient and tumor factors associated with the outcome at the univariable level with a $p$-value $< 0.20$. Patient and tumor factors other than the main predictors of interests were removed from the model if $p$-value $< 0.05$ by manual backward selection provided their removal did not change the coefficient estimates of the main effects by more than 20% (which would indicate confounding effect).

## Results

2046 patient records were identified in the study time frame, and 934 patients were excluded from analysis. A total of 1112 patients were included for analysis, of which 523 were in the pre-guidelines time period, and 589 patients in the post-guidelines time period. Patients in both time periods were similar with respect to their clinical and pathologic factors except for age (Table 1), where there was a higher proportion of patients aged 65–74 years old in the post-guidelines time period. However, when analyzing age as a continuous variable, the mean age of patients in the pre- and post-guideline time periods did not differ between the two groups ($63.49 \pm 11.72$ pre, $63.49 \pm 10.90$ post, $p = 0.99$). Pathologic margin status was similar between the two time periods ($p = 0.48$), with no apparent change in the proportion of patients with invasive cancer versus DCIS within any of the pathologic margin categories.

After the implementation of the SSO-ASTRO guidelines, the

**Table 1**
Clinical and pathologic factors in pre-guidelines and post-guidelines groups.

| Factor | Pre-guidelines ($n = 523$) | | Post-guidelines ($n = 589$) | | $p$-value[a] |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Age | | | | | 0.01* |
| 0-44 | 20 | 3.82 | 32 | 5.43 | |
| 45-54 | 95 | 18.16 | 84 | 14.26 | |
| 55-64 | 164 | 31.36 | 178 | 30.22 | |
| 65-74 | 157 | 30.02 | 222 | 37.69 | |
| 75+ | 87 | 16.63 | 73 | 12.39 | |
| Invasive tumor histology | | | | | 0.1 |
| Invasive ductal carcinoma | 465 | 88.91 | 507 | 86.08 | |
| Invasive lobular carcinoma | 37 | 7.07 | 41 | 6.96 | |
| Other | 21 | 4.02 | 41 | 6.96 | |
| Associated DCIS | | | | | 0.06 |
| No DCIS | 168 | 32.12 | 210 | 35.65 | |
| DCIS | 304 | 58.13 | 303 | 51.44 | |
| Extensive intraductal component | 51 | 9.75 | 76 | 12.90 | |
| Invasive grade | | | | | 0.94 |
| I | 149 | 28.49 | 168 | 28.52 | |
| II | 222 | 42.45 | 255 | 43.29 | |
| III | 152 | 29.06 | 166 | 28.18 | |
| Invasive carcinoma size (mm) | | | | | 0.35 |
| <10 | 106 | 20.27 | 118 | 20.03 | |
| 10-19 | 243 | 46.46 | 270 | 45.84 | |
| 20-29 | 115 | 21.99 | 125 | 21.22 | |
| 30-39 | 42 | 8.03 | 44 | 7.47 | |
| 40-49 | 6 | 1.15 | 19 | 3.23 | |
| ≥50 | 11 | 2.10 | 13 | 2.21 | |
| Multifocal invasive | 56 | 10.71 | 54 | 9.17 | 0.39 |
| Lymphovascular invasion | | | | | 0.11 |
| Present | 150 | 28.68 | 146 | 24.79 | |
| Absent | 363 | 69.41 | 422 | 71.65 | |
| Undetermined | 10 | 1.91 | 21 | 3.57 | |
| ER subtype | | | | | 0.13 |
| Positive | 466 | 10.90 | 507 | 86.08 | |
| Negative | 57 | 82.03 | 82 | 13.92 | |
| PR subtype | | | | | 0.51 |
| Positive | 429 | 82.03 | 474 | 80.48 | |
| Negative | 94 | 17.97 | 115 | 19.52 | |
| HER-2 subtype | | | | | 0.43 |
| Positive | 67 | 12.81 | 85 | 14.43 | |
| Negative | 456 | 87.19 | 504 | 85.57 | |
| Margin status | | | | | 0.48 |
| Negative (≥1 mm) | 370 | 70.75 | 398 | 67.57 | |
| Close for DCIS (>0–1 mm) | 17 | 3.25 | 19 | 3.23 | |
| Close for invasive (>0–1 mm) | 46 | 8.80 | 46 | 9.34 | |
| Positive for DCIS | 22 | 4.21 | 39 | 6.62 | |
| Positive for invasive | 68 | 13.00 | 78 | 13.24 | |

* statistical significance ($p < 0.05$).
[a] Chi-squared test.

overall re-operation rate decreased from 22.56% in the pre-guidelines time period to 18.68% in the post, representing an unadjusted decrease of 3.89% ($p = 0.13$). Of patients who had additional surgery following initial BCS in the post-guidelines time period, only 6.80% went on to receive multiple re-operations. Receipt of a completion mastectomy decreased from 9.94% in the pre-guidelines time period to 7.13% following guideline implementation ($p = 0.09$). In the post-guidelines time period, guideline non-adherence was an uncommon issue with only 12 patients receiving a re-operation on pathologically negative margins (Table 2). It is noteworthy that all cases of guideline non-adherence occurred up until the mid-point of the post-guidelines time period, after which there were no further cases of nonadherence.

Univariable and multivariable analysis was performed to identify clinical and pathological factors that were associated with re-operation in our cohort. On univariable analysis, margin status (close and positive), invasive tumor size (≥50 mm), invasive grade 2 and 3, extensive DCIS, lymph node involvement (involved, and undetermined involvement) and invasive carcinoma multifocality were significantly associated with increased re-operation (Table 3). Age over 74 was found to be significantly associated with decreased re-operation. Margin status, time period, time period by margin status and age category were included in the final multivariable analysis.

On multivariable analysis, patients were less likely to have a re-operation in the time period after guideline implementation compared to the pre-guideline time period (OR 0.28, 95% C.I. 0.15–0.51, $p = <0.0001$) (Table 4). In the overall cohort, close or positive margin status were associated with increased re-operation compared to patients with widely negative margins. However, after guideline implementation, re-operation was reduced in patients with close (OR = 0.17, 95% C.I. 0.07–0.40, $p = <0.0001$) or negative (OR = 0.20, 95% C.I. 0.05–0.77, $p = <0.0001$) margin status compared to this group of patients in the pre-guideline time period. The odds of re-operation did not change between time periods when the margins were positive. Age over 74 was associated with decreased re-operation, compared to patients younger than 45 years old (OR = 0.12, 95% C.I. 0.03–0.77, $p = 0.04$).

## Discussion

Breast conserving surgery (BCS) is the most common procedure performed in patients with early stage breast cancer.[2] Multiple studies have shown significant variability in re-operation rates, with uncertainty regarding pathologic margins considered a major contributor to this problem.[5–7] The SSO-ASTRO margins guidelines consensus statement was developed to help address this issue.[15] To date, there have been several studies addressing the impact of the SSO guidelines on re-operation rates,[13–18] collectively suggesting a decrease ranging between 1 and 28%.

The largest institutional based study to date found that the reoperation rates decreased by 6.3% after guidelines publication (21.4% pre and 15.1% post, $p = 0.006$). Factors associated with re-operation included the introduction of guidelines, positive and close margins for invasive carcinoma and DCIS, as well as multifocal disease, and extensive intraductal component of DCIS.[17] We found that the re-operation rate changed in our patients as well (22.56% pre guidelines and 18.68% post), but to a lesser degree (3.89% decrease). Similar to the report by Rosenberger et al., we also found that close (OR 19.74, 95% C.I. 9.46–41.21, $p < 0.0001$) and positive

**Table 2**
Re-operation rate by pathologic margin status.

| Margin status | Pre-guidelines | Post-guidelines | Unadjusted percentage change |
|---|---|---|---|
| Negative | 13/370 (3.51%) | 3/398 (0.75%) | −2.76 |
| Close for DCIS | 8/17 (47.06%) | 1/19 (5.26%) | −41.80 |
| Close for invasive | 19/46 (41.30%) | 8/55 (14.55%) | −26.76 |
| Positive for DCIS | 20/22 (90.91%) | 30/39 (76.92%) | −13.99 |
| Positive for invasive | 58/68 (85.29%) | 68/78 (87.18%) | +1.89 |
| Overall | 118/523 (22.56%) | 110/589 (18.68%) | −3.89 |

**Table 3**
Univariable analysis of factors associated with re-operation.

| Factor | Estimated probability (95% C.I.) | OR (95% C.I.) | *p*-value[a] |
|---|---|---|---|
| Time period | | | |
| Before guidelines | 0.25 (0.20–0.30) | REF | |
| After guidelines | 0.21 (0.16–0.27) | 0.82 (0.63–1.06) | 0.13 |
| Age | | | |
| 0-44 | 0.21 (0.13–0.32) | REF | |
| 45-54 | 0.24 (0.19–0.30) | 1.16 (0.70–1.94) | 0.57 |
| 55-64 | 0.28 (0.22–0.33) | 1.40 (0.86–2.28) | 0.17 |
| 65-74 | 0.21 (0.16–0.28) | 1.00 (0.60–1.70) | 0.99 |
| 75+ | 0.14 (0.10–0.20) | 0.59 (0.36–0.97) | 0.04* |
| Invasive tumor histology | | | |
| Invasive ductal carcinoma | 0.22 (0.18–0.27) | REF | |
| Invasive lobular carcinoma | 0.30 (0.21–0.41) | 1.46 (0.90–2.39) | 0.13 |
| Other | 0.98 (0.35–2.78) | 0.98 (0.35–2.78) | 0.98 |
| Overall margin status | | | |
| Negative (≥1 mm) | 0.02 (0.01–0.03) | REF | |
| Close | 0.26 (0.20–0.34) | 17.11 (10.14–28.89) | <0.0001* |
| Positive | 0.85 (0.81–0.89) | 272.882 (154.60–481.65) | <0.0001* |
| Invasive size (mm) | | | |
| <10 | 0.21 (0.16–0.28) | REF | |
| 10-19 | 0.20 (0.15–0.25) | 0.93 (0.67–1.28) | 0.64 |
| 20-29 | 0.21 (0.16–0.27) | 1.00 (0.70–1.42) | 0.98 |
| 30-39 | 0.27 (0.19–0.36) | 1.35 (0.88–2.07) | 0.17 |
| 40-49 | 0.41 (0.21–0.65) | 2.59 (0.88–7.58) | 0.08 |
| ≥50 | 0.68 (0.38–0.88) | 7.98 (2.19–29.09) | 0.00* |
| DCIS presence and extent | | | |
| No DCIS | 0.17 (0.12–0.24) | REF | |
| Simple DCIS | 0.22 (0.17–0.27) | 1.32 (0.96–1.82) | 0.09 |
| Extensive DCIS | 0.44 (0.32–0.56) | 3.71 (1.93–7.12) | <0.0001* |
| Invasive grade | | | |
| 1 | 0.18 (0.14–0.24) | REF | |
| 2 | 0.25 (0.20–0.30) | 1.45 (1.01–1.94) | 0.01* |
| 3 | 0.25 (0.19–0.31) | 1.45 (1.06–2.00) | 0.02* |
| Lymph node involvement | | | |
| No | 0.20 (0.16–0.26) | REF | |
| Yes | 0.31 (0.24–0.39) | 1.76 (1.16–2.67) | 0.01* |
| Undetermined | 0.05 (0.01–0.17) | 0.21 (0.06–0.74) | 0.02* |
| Multifocal invasive | | | |
| No | 0.20 (0.16–0.25) | REF | |
| Yes | 0.49 (0.38–0.59) | 3.69 (2.50–5.46) | <0.0001* |
| ER status | | | |
| Negative | 0.22 (0.15–0.32) | REF | |
| Positive | 0.23 (0.19–0.27) | 1.02 (0.70–1.49) | 0.91 |
| PR status | | | |
| Negative | 0.25 (0.19–0.33) | REF | |
| Positive | 0.22 (0.18–0.27) | 0.86 (0.63–1.17) | 0.33 |
| HER2 status | | | |
| Negative | 0.22 (0.18–0.27) | REF | |
| Positive | 0.27 (0.20–0.36) | 1.33 (0.96–1.85) | 0.09 |

* statistical significance ($p < 0.05$).
[a] $p$ values calculated for the odds ratios for each factor, compared to its reference.

margins (OR 515.43, 95% C.I. 285.27–931.26, $p < 0.0001$) were highly associated with increased re-operation rates. However, more importantly, in multivariable analysis the odds of re-operation significantly decreased following the guidelines release (OR 0.28, 95% C.I. 0.15–0.51, $p < 0.0001$), in a vastly different practice setting than the aforementioned academic breast surgical oncology division. Breast surgical services in our region are performed in 10 different hospitals, with radiation treatment and other adjuvant care primarily provided and integrated within one referral facility. Specifically, compared to the pre-guideline time period, patients treated after guideline implementation were less likely to receive a re-operation if they had negative (OR 0.20, 95% C.I. 0.05–0.77, $p = 0.02$) or close margins (OR 0.17, 95% C.I. 0.07–0.40, $p < 0.0001$). This decrease in re-operation did not extend to patients with positive margins. While no other pathologic factors reached statistical significance in multivariable analysis, we identified that age over 75 years was negatively correlated with reoperations.

These results are in stark contrast to a larger Surveillance, Epidemiology and End Results (SEER) population-based study by Morrow et al.[16] Over a similar time period they noted a 16% decrease in reoperations following BCS. It is notable that this was a survey-based study of patients identifying the need for reoperation following BCS, which would potentially be subject to response bias. Furthermore, the re-operation rates were much higher prior to the guidelines release (34%) than in our cohort (22.56%), potentially accounting for a large part of the discrepancy (16% vs 3.89% overall change in reoperation rate). There were also no pathological details available, but the authors did state the "pathological margin positivity rates remained stable over this time period." Despite these limitations, this study by Morrow et al., suggests that the effect of the guidelines is generalizable to the community.

The diversity in reported changes in reoperation rates (1%–28% decrease) that can be attributed to the guidelines requires a detailed understanding of the diverse pathologic factors influencing the decision to re-operate, most notably the pathologic margin status with respect to invasive cancer. The SSO-ASTRO

**Table 4**
Multivariable analysis of factors associated with re-operation.

| Factor | Estimated probability (95% C.I.) | OR (95% C.I.) | p-value[a] |
|---|---|---|---|
| Time period | | | |
| Before guidelines | 0.33 (0.27–0.41) | REF | |
| After guidelines | 0.12 (0.07–0.19) | 0.28 (0.15–0.51) | <0.0001* |
| Overall margin status | | | |
| Negative | 0.01 (0.01–0.02) | REF | |
| Close | 0.19 (0.13–0.27) | 19.74 (9.46–41.21) | <0.0001* |
| Positive | 0.86 (0.80–0.91) | 515.43 (285.27–931.26) | <0.0001* |
| Age | | | |
| 0-44 | 0.33 (0.13–0.62) | REF | |
| 45-54 | 0.19 (0.11–0.30) | 0.47 (0.14–1.61) | 0.23 |
| 55-64 | 0.35 (0.28–0.43) | 1.10 (0.29–4.18) | 0.89 |
| 65-74 | 0.26 (0.18–0.36) | 0.72 (0.19, 2.68) | 0.62 |
| 75+ | 0.06 (0.03–0.09) | 0.12 (0.03–0.77) | <0.001* |
| Margin status, negative | | | |
| Before guidelines | 0.03 (0.02–0.04) | REF | |
| After guidelines | 0.01 (0.002–0.02) | 0.20 (0.05–0.77) | 0.02* |
| Margin status, close | | | |
| Before guidelines | 0.37 (0.25–0.50) | REF | |
| After guidelines | 0.09 (0.05–0.16) | 0.17 (0.07–0.40) | <0.0001* |
| Margin status, positive | | | |
| Before guidelines | 0.89 (0.80–0.94) | REF | |
| After guidelines | 0.83 (0.75–0.89) | 0.64 (0.28–1.50) | 0.31 |

* statistical significance ($p < 0.05$).
[a] $p$ values calculated for the odds ratio for each factor, compared to its reference.

guidelines were developed to help with decision making in clinical scenarios where margins generally ranged between “no tumour on ink”, and up to 1 or 2 mm, depending upon individual surgeon and institutional practices. The guidelines would likely not influence management in cases with margins positive for invasive disease, whom would generally be expected to undergo further surgery, or alternatively no further surgery if considered widely negative. Thus, changes that occur over time would reflect both changes in the margin positivity rate as well as adherence to the guidelines recommendations. Studies with low baseline re-excision rates likely have fewer cases that would be influenced by the guidelines and smaller potential impact,[18] while in comparison those with higher baseline re-excision rates may realize a larger benefit.[14] While the absolute change in re-excision rates was modest in our cohort of patients, it was not related to a change in the margin positivity rate, but rather the impact of the guidelines in a subset of patients it was designed to address.

While the SSO-ASTRO invasive cancer management guidelines suggest there are few clinico-pathologic situations in which a re-excision is required in the setting of pathologic margins that are negative for invasive disease, each case requires individualization.[12] One particular situation that was not addressed by this guideline was that in which DCIS is either at, or near the margins.[19] We found that the presence of DCIS at, or near the margins influenced management in a similar fashion to those of invasive disease. In the post-guidelines era, patients with isolated DCIS near the margins (Table 2) underwent reoperation at a similar rate to invasive cancer for both positive margins (76.9% vs 87.2%), as well as those under 1 mm (5.3% vs 14.6%). It is noteworthy that the reoperation rate in the 1 mm margin group was significantly higher prior to the guidelines(47.0% and 41.3%) though, suggesting the guidelines are impacting both groups of patients. This finding is supported by the study of Rosenberger et al., who found that DCIS under 1 mm from the margin had a larger effect on re-excision rates than that of invasive cancer both before (OR 68.4 vs 13.0) and after the guideline release (OR 24.6 vs 4.2)[17]. This suggests that DCIS influences management considerations when at or near the margins, irrespective of the invasive cancer status. This clinical scenario was addressed in the subsequent release of the SSO-ASTRO guidelines statement for patients with DCIS which suggests that the margin status of the invasive disease takes precedence over the DCIS.[19] Whether the release of this later guideline affects this clinical situation will require further exploration in a more contemporary cohort of patients.

The strengths of this study are that this patient cohort represents a diverse population of patients, with multiple community surgeons, and is likely reflective of what is occurring outside of high volume, academic institutions. This context is important given that the majority of breast cancer surgery occurs in this setting, and many surgeons may not have readily accessible multidisciplinary rounds for case discussions, making availability of guidelines may especially helpful in these circumstances. Potential weaknesses of this study include the low number of events, which required combining invasive carcinoma and DCIS margin status for meaningful analysis. Other concerns relate to noncentralized pathology review and non-standardized reporting, which could influence the accuracy and interpretation of reports. Furthermore, case conferences or reviews are available to all surgeons in the region but are used to varying degrees, which may have affected results.

In conclusion, re-operation rates decreased following the SSO-ASTRO margins guideline release. Furthermore, implementation of the SSO-ASTRO guidelines was associated with a significantly decreased rate of reoperation in patients with pathologically negative margins, the target population it was meant to address.

## Conflicts of interest

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter discussed in this manuscript.

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## References


1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. cancer.ca/Canadian-CancerStatistics-2017-EN.pdf. Accessed October 18, 2018.
2. Porter G, Wagar B, Bryant H, et al. Rates of breast cancer surgery in Canada from 2007/08 to 2009/10: retrospective cohort study. *CMAJ Open*. 2014;2(2): E102–E108. https://doi.org/10.9778/cmajo.20130025.
3. Houssami N, Macaskill P, Marinovich ML, Morrow M. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol*. 2014;21(3):717–730. https://doi.org/10.1245/s10434-014-3480-5.
4. Lovrics PJ, Gordon M, Cornacchi SD, et al. Practice patterns and perceptions of margin status for breast conserving surgery for breast carcinoma: national Survey of Canadian General Surgeons. *Breast Edinb Scotl*. 2012;21(6):730–734. https://doi.org/10.1016/j.breast.2012.07.017.
5. Spilsbury K, Semmens JB, Saunders CM, Hall SE, Holman CD. Subsequent surgery after initial breast conserving surgery: a population based study. *ANZ J Surg*. 2005;75(5):260–264. doi:ANS3352 [pii].
6. Wilke LG, Czechura T, Wang C, et al. Repeat surgery after breast conservation for the treatment of stage 0 to II breast carcinoma: a report from the National Cancer Data Base, 2004-2010. *JAMA Surg*. 2014;149(12):1296–1305. https://doi.org/10.1001/jamasurg.2014.926.
7. Cancela M de C, Comber H, Sharp L. Hospital and surgeon caseload are associated with risk of re-operation following breast-conserving surgery. *Breast Canc Res Treat*. 2013;140(3):535–544. https://doi.org/10.1007/s10549-013-2652-5.
8. Wazer DE, DiPetrillo T, Schmidt-Ullrich R, et al. Factors influencing cosmetic outcome and complication risk after conservative surgery and radiotherapy for early-stage breast carcinoma. *J Clin Oncol Off J Am Soc Clin Oncol*. 1992;10(3): 356–363. https://doi.org/10.1200/JCO.1992.10.3.356.
9. King TA, Sakr R, Patil S, et al. Clinical management factors contribute to the decision for contralateral prophylactic mastectomy. *J Clin Oncol Off J Am Soc Clin Oncol*. 2011;29(16):2158–2164. https://doi.org/10.1200/JCO.2010.29.4041.
10. Pataky RE, Baliski CR. Reoperation costs in attempted breast-conserving surgery: a decision analysis. *Curr Oncol Tor Ont*. 2016;23(5):314–321. https://doi.org/10.3747/co.23.2989.
11. McCahill LE, Single RM, Bowles EJA, et al. Variability in reexcision following breast conservation surgery. *Jama*. 2012;307(5):467–475. https://doi.org/10.1001/jama.2012.43.
12. Moran MS, Schnitt SJ, Giuliano AE, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *J Clin Oncol Off J Am Soc Clin Oncol*. 2014;32(14):1507–1515. https://doi.org/10.1200/JCO.2013.53.3935.
13. Gladden AAH, Sams S, Gleisner A, et al. Re-excision rates after breast conserving surgery following the 2014 SSO-ASTRO guidelines. *Am J Surg*. 2017;214(6):1104–1109. S0002-9610(17)30451-8 [pii].
14. Bhutiani N, Mercer MK, Bachman KC, et al. Evaluating the effect of margin consensus guideline publication on operative patterns and financial impact of breast cancer operation. *J Am Coll Surg*. 2018;227(1):6–11. https://doi.org/10.1016/j.jamcollsurg.2018.01.050.
15. Schulman AM, Mirrielees JA, Leverson G, Landercasper J, Greenberg C, Wilke LG. Reexcision surgery for breast cancer: an analysis of the American society of breast surgeons (ASBrS) mastery(SM) database following the SSO-ASTRO "No ink on tumor" guidelines. *Ann Surg Oncol*. 2017;24(1):52–58. https://doi.org/10.1245/s10434-016-5516-5.
16. Morrow M, Abrahamse P, Hofer TP, et al. Trends in reoperation after initial lumpectomy for breast cancer: addressing overtreatment in surgical management. *JAMA Oncol*. 2017;3(10):1352–1357. https://doi.org/10.1001/jamaoncol.2017.0774.
17. Rosenberger LH, Mamtani A, Fuzesi S, et al. Early adoption of the SSO-ASTRO consensus guidelines on margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: initial experience from memorial sloan kettering cancer center. *Ann Surg Oncol*. 2016;23(10): 3239–3246. https://doi.org/10.1245/s10434-016-5397-7.
18. Patten CR, Walsh K, Sarantou T, et al. Changes in margin re-excision rates: experience incorporating the "no ink on tumor" guideline into practice. *J Surg Oncol*. 2017;116(8):1040–1045. https://doi.org/10.1002/jso.24770.
19. Morrow M, Van Zee KJ, Solin LJ, et al. Society of surgical oncology–American society for radiation oncology–American society of clinical oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. *J Clin Oncol*. 2016;34(33): 4040–4046. https://doi.org/10.1200/JCO.2016.68.3573.