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## Routine shave margins are not necessary in early stage breast cancer treated with Breast Conserving Surgery

Carla Pajak<sup>a</sup>, JinSi Pao<sup>a, b</sup>, Amandeep Ghuman<sup>a</sup>, Elaine C. McKeivitt<sup>a, b</sup>, Urve Kuusk<sup>a, b</sup>, Carol K. Dingee<sup>a, b</sup>, Rebecca Warburton<sup>a, b, \*</sup>

<sup>a</sup> University of British Columbia, Faculty of Medicine, Division of General Surgery, 950 West 10th. Avenue, Vancouver, BC V5Z 1M9, Canada

<sup>b</sup> Mount Saint Joseph Hospital, 3080 Prince Edward St, Vancouver, BC V5T 3N4, Canada

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## ABSTRACT

**Introduction:** Breast Conserving Surgery (BCS) is considered standard of care for women with early stage breast cancer. Between 20 and 50% of women treated with BCS will require re-operation for positive or close margins and it has been suggested that routine cavity shave margins may reduce the frequency of positive margins.

**Methods:** Retrospective chart review of a prospectively maintained surgical database of patients undergoing BCS for early stage breast cancer, at a single institution, between January 2012 and December 2015. Cohort was followed until June 2016 to capture re-operations.

**Results:** Among 2096 patients with stage 0-III breast cancers, 872 (42%) underwent primary mastectomies and 1224 (58%) underwent primary BCS. Margins were positive in 128 (11%) and close in 442 (36%). Re-operation rate for patients after BCS was 19%.

**Conclusion:** A lower than predicted positive margin rate suggests that routine shave margins are not warranted at our institution.

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### 1. Introduction

Breast Conserving Surgery (BCS) is considered standard of care for women with early stage breast cancer.<sup>1</sup> Microscopically clear margins are an important indicator of completeness of excision<sup>2</sup> and reduce ipsilateral breast tumor recurrence (IBTR) when compared to positive margins. Attempting to achieve negative margins by simply increasing the size of lumpectomy specimens may undermine the conservation and cosmetic goals of BCS without reducing the risk of IBTR.<sup>3,4</sup> A recent meta-analysis found that increasing the radial width of a negative margin had no significant impact on IBTR when risks were adjusted for patients receiving a radiation boost or endocrine therapy.<sup>5,6</sup> Therefore, margin status alone does not determine IBTR which stems from multiple confounding variables such as patient age, tumor size,

tumor biology as well as the use of adjuvant therapies including boost radiation and endocrine therapy.<sup>2,5</sup> While margin width does not appear to have a strictly linear relationship with recurrence risk, positive margins are still a significant prognosticator and may confer up-to a two-fold increase in the risk of IBTR when compared to negative margins.<sup>3,4</sup>

Some debate persists over the optimal negative margin width however the recent Society of Surgical Oncology -American Society of Radiation Oncology (SSO-ASTRO) guidelines recommend the use of no-ink on tumor for invasive disease<sup>3</sup> and 2 mm margins for in-situ disease.<sup>7</sup> To achieve microscopically clear margins, between 20 and 50% of women treated with BCS will require re-operation for positive or, in some cases, close margins.<sup>5,8–10</sup> These repeat surgeries are not without risk and have been shown to increase the risk of complications, threaten the ultimate cosmetic outcome of BCS, induce emotional stress, raise health care costs associated with increased conversion to mastectomy and reduce disease-free survival.<sup>3,11,12</sup>

Routine Cavity Shave Margins (RCSM) have therefore been suggested as a means to potentially reduce the frequency of positive margins and subsequent need for reoperation.<sup>2,13</sup> Prior to adopting the practice of RCSM at our high volume breast center, we

\* Corresponding author. University of British Columbia, Faculty of Medicine, Division of General Surgery, 950 West 10th. Avenue, Vancouver, BC V5Z 1M9, Canada.

E-mail addresses: [carla.pajak@alumni.ubc.ca](mailto:carla.pajak@alumni.ubc.ca) (C. Pajak), [jinsi.pao@ubc.ca](mailto:jinsi.pao@ubc.ca) (J. Pao), [aghuman@alumni.ubc.ca](mailto:aghuman@alumni.ubc.ca) (A. Ghuman), [emckevitt@providencehealth.bc.ca](mailto:emckevitt@providencehealth.bc.ca) (E.C. McKeivitt), [ukuusk@ubc.ca](mailto:ukuusk@ubc.ca) (U. Kuusk), [ckdingee@telus.net](mailto:ckdingee@telus.net) (C.K. Dingee), [rwarburton@providencehealth.bc.ca](mailto:rwarburton@providencehealth.bc.ca) (R. Warburton).

sought to quantify our local rates of positive margins, assess the margin widths for all women who undergo some form of re-operation and quantify the relationship between margin status and the presence of residual disease in re-operative specimens.

## 2. Methods

A retrospective review was performed of a prospectively maintained database of patients undergoing primary BCS for stage 0-III breast cancer between January 2012 and December 2015 at Mount Saint Joseph Hospital. Patients were then followed until June 30<sup>th</sup>, 2016 to capture re-operations. To supplement data where required, individual charts were reviewed. Ethics approval was obtained from the University of British Columbia. Five breast surgeons performed all surgeries. RSCM is not routinely practiced, but rather elective shave margins based on clinical judgement and intraoperative imaging. All specimens were oriented with at least two perpendicular markers. Completeness of excision was confirmed with intra-operative specimen radiographs for non-palpable tumors that required wire localization and by gross inspection and palpation for other tumors.

Initial data collection included a compilation of all patients during the study period that underwent BCS as their primary procedure. Margins were defined as positive if there was tumor on ink, close if tumor was within 2 mm of the resection margin and negative if the tumor was greater than 2 mm away. For all patients that had a second surgery we examined the type of re-operations (revision margins or completion mastectomy), the margin width at first surgery and the rates of residual disease in the re-resected specimen. Patients with mastectomy as their first operation, age less than 18yrs, and those who had their first BCS procedure at a different facility were excluded. Patients that had neoadjuvant chemotherapy, hormonal therapy or both and elected for BCS were included.

## 3. Results

Among 2096 patients with stage 0-III breast cancers, 872 (42%) underwent primary mastectomies and 1224 (58%) underwent primary BCS. Baseline patient demographics and pathologic features are shown in Table 1. When reoperations are considered, our overall mastectomy rate for all comers is 949 (45%). Among women initially treated with BCS, 86 (7%) went on to have completion mastectomies.

## 4. Margin status

Within our cohort margins were positive in 128 (11%) and close in 442 (36%). In total 216 (18%) of BCS patients underwent reoperations during the study period, 106 (49%) were for positive margins, 96 (44%) were for close margins and 15 (7%) patients had negative margins. A flowchart outlining re-operation rates and types by margin status is shown in Fig. 1. Among the 131 patients who had a revision of margins as their second surgery, 68 (52%) had positive margins, 57 (44%) had close margins and 6 (5%) had negative margins. Among the remaining 86 who had a completion mastectomy as their second surgery, 38 (44%) had positive margins, 39 (45%) had close margins and 9 (10%) had negative margins. Margin status among revision and completion mastectomy patients is shown in Table 2.

## 5. Reoperation status

A total of 233 repeat surgeries were performed on a total of 216 patients, giving an overall re-operative procedure rate of 19%. Six

patients (3%) had more than one repeat surgery, accounting for 17 (7%) of the 233 total re-operations. Not all positive margins had a second surgery, 17 (22%) did not require a second surgery. Fig. 1 contains a flowchart outlining re-operation rates and types by margin status. In total 86 (7%) cases of primary BCS ultimately ended in mastectomy. Completion mastectomy was more commonly used as a second surgery in the close margin group (41%) versus the positive margin group (36%). The relative risk of having a completion mastectomy among patients with positive margins compared to close is 0.88 [95 CI: 0.62, 1.25],  $p = .48$ , which is not statistically significant.

## 6. Residual disease

Among the re-operative specimens, 116 (54%) contained no residual disease, 39 (18%) contained residual invasive disease, 59 (27%) contained residual DCIS and 2 (1%) contained other residual disease. Chi-square analysis found that margin status was not related to the presence of residual invasive or in-situ disease ( $p > .05$ ) as shown in Table 3.

## 7. Discussion

The rate of positive margins after BCS at our institution is 11%, which is lower than reported in other series, including the rates achieved after the application of RSCM.<sup>13,14</sup> This would suggest that the adoption of RSCM to lower our current rate of positive margins is not indicated at our center. An additional goal of RSCM is to reduce re-operative rates, however this is not uniformly achieved and in some populations RSCM did not decrease re-excision rates.<sup>15</sup> Our re-operation rate for patients after BCS was 19%, which is lower than in previous series that included both selective cavity shave margins and complete cavity shave margins.<sup>15</sup> That said, a recent review of pooled data did demonstrate that re-operation rates could be halved with the application of RSCM.<sup>14</sup> Thus, RSCM may have reduced re-operative rates in our population. Our re-operative rates would have also been lowered by a stricter adherence to the SSO-ASTRO guidelines. If re-operations were confined to only those patients with DCIS and close margins, we would have avoided 59 re-operations, reducing our re-operative rate from 19% to 13%. An additional 21 (10%) of patients had a second operation despite having negative margins. This is an interesting group for further study to ascertain non-margin indications for re-operation. While not captured in our database, we suspect that in our cohort this may occur when patients decide post-operatively that they no longer wish to undergo radiation or to lessen a perceived burden of recurrence risk or need for surveillance. Further study including patient questionnaires would be needed to capture this population.

While important for predicting repeat surgery, the impact of margins on long-term recurrence is not completely clear. In pooled data, RSCM has not been shown to correlate with reduced distant recurrence.<sup>14</sup> In the present study, over half (54%) of all re-operative specimens contained no residual disease and original margin status was not related to the presence of in-situ or invasive disease in re-operative specimens. This finding supports the postulation that the presence of adjacent multifocal disease is likely more significant than margin status in causing disease recurrence.<sup>16</sup> If true, this theory would undermine the potential value of universally adopting RSCM.

Alternative critiques of RSCM, include concerns regarding its impact on cosmetic outcome resulting from the larger specimen volumes taken during RSCM. This size based critique of RSCMs has conflicting data, with some series finding reduced volumes of both lumpectomy and total breast tissue specimens among RSCM groups,<sup>15</sup> while in another series RSCM increased specimen size by

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