

Breast conservation treatment and frozen section analysis of margins

Dear Editor,

Re. Surgical margins assessment reduces re-excision rates in breast-conserving surgery

I read with interest the article by Woon et al. published in a recent issue of the *Annals* on the reduction of re-excision rates with the use of intraoperative frozen section (FS) analysis.¹ This certainly has the potential to improve patient outcomes after surgery as their study has demonstrated. It is also likely that a decrease in re-operation rates would have a positive influence on patients' choice to undergo breast conservation treatment (BCT) rather than mastectomy.

However, there are a few points made in this letter by Woon et al. that merit further discussion. The authors cite an article by Fisher et al. published in 2002.² This was a report on a 20-year follow-up of a randomised controlled trial (RCT), which did indeed show equivalent survival following both BCT with radiotherapy and mastectomy. However, in this report, local recurrence following BCT was reported to be numerically lower than after mastectomy.² In Table 2 of the report, it is listed that local recurrence with lumpectomy and radiotherapy was 2.7% while that for mastectomy was 10.2%. Having cited this report in the context of survival, the authors of the letter proceeded to comment that breast conserving surgery is associated with higher local recurrence risk, which may appear contradictory. It should also be noted that this report by Fisher et al. that was cited as a source on higher local recurrence with BCT was based on follow-up information up through 2001. There are more recent studies that demonstrate similar, if not lower local recurrence rates with BCT compared to mastectomy.³

In addition, while it is true that the National Surgical Adjuvant Breast and Bowel Project B-06 study was an RCT, there is now a significant body of contemporary evidence to suggest that BCT may confer superior survival compared to mastectomy. One of the earliest studies was by Martin et al.⁴ in 2007 and more recently, a large study by De la Cruz et al. published in 2022.⁵ Another study reported an overall and breast cancer-specific relative survival gain of 56% to 70% in node-negative patients who underwent BCT compared with those who underwent mastectomy.⁶ This information is relevant for treatment selection and can perhaps provide an alternative view to the long-held but possibly

imprecise belief that BCT and mastectomy result in comparable long-term survival rates, which the authors had expressed.

Time efficiency is a laudable objective. However, this should not supplant good surgical oncology principles. Unless surgeons plan to change instruments intraoperatively, it would be in line with oncologic principles to perform sentinel lymph node biopsy (SLNB) first, as this is more likely to be an unaffected ("clean") operative field, rather than to perform the wide excision first, where instruments may be contaminated with tumour cells. Having performed SLNB first, the sentinel node may also be sent for FS, which would further contribute to a decrease in re-operation rates. Hence, there may be minimal time advantage in performing the wide excision part of the surgery first as the authors have proposed.

Finally, it is possible to further reduce re-excision rates using appropriate techniques.⁷ As the authors have alluded in their article, reduction of re-excision rates improves the patient treatment experience, and I agree that the additional cost and resources required for the routine conduct of FS is likely in totality to be lower than allowing higher re-operative rates without customary intraoperative margin assessment. It is therefore an approach that should be applied until there is clear evidence that another strategy offers better outcomes in terms of cost-effectiveness and surgical results. In this respect, oncoplastic breast surgery may not be the answer, as it contributes to higher resource utilisation, surgical morbidity, and might not serve as a cost-effective means of optimal treatment and appropriate surgical de-escalation.⁸

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Dear Editor,

Re. Authors' reply

We would like to thank the reader for the interest in our article¹ and pertinent points raised. First, in relation to the citation of Fisher et al., the reader highlighted that reporting local recurrence rate as being lower for mastectomy compared to breast conservation treatment (BCT) would be contradictory based on Table 2 of this article.² In this table, local recurrence with lumpectomy and radiotherapy was reported as 2.7% compared to 10.2% for mastectomy. It should be noted however that a caveat under this table stated that tumours in the ipsilateral breast after lumpectomy were not considered recurrences, and women in the lumpectomy groups who had such tumours were classified as event-free. Fisher et al. had separately outlined in Figure 1 of their article, the cumulative incidence of a recurrence in the ipsilateral breast 20 years after surgery at 14.3% among the women who underwent irradiation after lumpectomy.

Similarly, another 20-year follow-up of a randomised trial by Veronesi et al. comparing breast conserving surgery with radical mastectomy for early breast cancer also showed a lower cumulative recurrence at 2.3% for the radical mastectomy group compared to 8.8% in the BCT group, though comparable overall survival and breast cancer-specific survival.³ The strength of both studies with respect to local recurrence and survival lies in their long duration of follow-up of 20 years.

However, we acknowledge the views of the reader that contemporary data from recent studies have been promising, with evidence to suggest that BCT could confer comparable local recurrence rates⁴ to mastectomy with reasons postulated to be multifactorial due to improvements in diagnostic imaging, pathologic margins assessment, precision of radiation therapy delivery, and effectiveness of systemic and targeted therapy. However,

before more long-term data are made available, we prefer to interpret these results with caution. Furthermore, our study is also not designed to compare and address this issue of differences in recurrence rates between BCT and mastectomy.

Second, we applaud the reader for highlighting the need to observe important oncological principles in the conduct of surgery. We acknowledge the theoretical concern of seeding of tumour cells by performing lumpectomy first, followed by sentinel lymph node biopsy. However, this is perhaps analogous to the similar theoretical risk of tumour seeding with preoperative core needle biopsy, which has also not been shown to increase local recurrence rate in breast cancer patients.⁵ The reason for proposing to perform the lumpectomy first and assess the margins before sentinel lymph node biopsy is that in our experience, frozen section (FS) assessment of margins generally takes longer compared to sentinel lymph node biopsy. However, a change of instruments as suggested by the reader can mitigate the risk of tumour seeding.

Finally, while we appreciate the reader's concurrence that intraoperative FS analysis of margins is a valuable technique to decrease re-operation rates, we remain cognisant of the logistical challenges and added pathologist involvement as practical considerations that one may face on the ground. As such, other techniques such as cavity shaving⁶ and oncoplastic techniques,⁷ which have also been shown to decrease positive margins rate deserve mention. Additionally, the choice of technique is best personalised to the individual surgeon's expertise and the healthcare setting. Oncoplastic surgery and FS analysis of margins are not mutually exclusive. Oncoplastic surgery utilised selectively in the appropriate context of large tumour or multifocal ductal carcinoma in situ remains an invaluable tool for the breast surgeon to achieve clear margins while preserving cosmesis for breast cancer patients.

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