

Positive Margins: The Challenge Continues for Breast Surgeons

Lisa Jacobs MD

Surgery, Johns Hopkins University, 600 N. Wolfe Street, Osler 624, Baltimore, Maryland 21287, United States

As breast cancer treatment has progressed to offering breast preservation to the majority of patients, a new challenge has arisen. That challenge is adequate margins on the partial mastectomy specimen. The literature reports positive margins in 20–70% of patients, resulting in additional surgery. While the consequences of that additional surgery probably do not affect survival from breast cancer, they do potentially have an affect on cosmesis, wound infection risk, and the confidence that the patient has with the surgeon wondering “why didn’t you get it all?”

The article “Predictors of Re-excision Among Women Undergoing Breast Conserving Surgery for Cancer” by Waljee et al.¹ attempts to identify the factors that increase the risk of a positive margin. This avenue of research is important in clinical management of breast cancer, allowing surgeons to more intelligently counsel patients regarding risk of re-excision. The authors identified several factors that predict a higher rate of positive margins. Smaller breast size, surgical biopsy for diagnosis, use of adjuvant chemotherapy, and lobular histology all predicted a higher rate of positive margins. Another study published in the *Annals of Surgical Oncology* studied the same topic and agreed that method of biopsy and lobular histology result in higher positive margin rates.² A large prospective study reported from the University of Louisville Breast Cancer Sentinel Lymph Node Study included 2658 patients treated with lumpectomy and evaluated factors that resulted in positive margins. They found that larger tumor size and lobular histology both resulted in

higher positive margin rates, but that method of biopsy had no impact.³ While these studies agree on many risk factors for positive margins, unfortunately, these factors, with the exception of biopsy method, cannot be modified.

Few women would agree to undergo mastectomy instead of lumpectomy because of a prediction of positive margins. Because the factors predicting higher re-excision rates are not modifiable, this line of research can only result in providing additional knowledge but cannot result in changes in practice. Efforts to investigate mechanisms that reduce the rate of positive margins have much greater potential to impact treatment. A number of studies have investigated surgical interventions that may reduce the rate of positive margins. Many have investigated intraoperative pathologic assessment as a mechanism to identify positive margins at the time of surgery so that re-excision can be accomplished in the same setting. These have focused primarily on touch imprint cytology, frozen section, and gross examination. Muttalib et al. evaluated intraoperative imprint and scrape cytology to assess margins. While the authors recommend adoption of the technique, the positive margin rate reported in the study remained at 22% with use of the technique.⁴ Intraoperative assessment of gross margins has been reported to result in a final margin positive rate of 25%.⁵ Investigators at MD Anderson Cancer Center evaluated a combination of intraoperative gross margin assessment, specimen radiography, and in some cases frozen section with a final positive margin rate of 20% using these methods.⁶ Others have evaluated intraoperative methods of tumor localization and their impact on positive margins. Tafra et al. completed a randomized study comparing cryoassisted localization with wire localization and demonstrated no difference in positive

Published online March 5, 2008.

Address correspondence and reprint requests to: Lisa Jacobs; E-mail: ljacob14@jhmi.edu

Published by Springer Science+Business Media, LLC © 2008 The Society of Surgical Oncology, Inc.

margins.⁷ Radioguided occult lesion localization was compared with wire localization by Nadeem et al., who demonstrated a positive margin rate of 83% and 57%, respectively.⁸ Other techniques have focused on volume of excision with oncoplastic techniques allowing for larger margin excisions while maintaining the cosmetic appearance of the breast. While these techniques in intraoperative assessment and changes in surgical technique may reduce the rate of positive margins, they have not solved the problem.

Other possible mechanisms that are currently unproven but that may result in lower re-excision rates include improved preoperative imaging to better establish extent of disease and increased use of neoadjuvant chemotherapy. Studies evaluating the utility of magnetic resonance imaging (MRI) find an increased sensitivity for detection of multicentric and multifocal disease. Identifying this situation preoperatively will result in better patient selection for attempted partial mastectomy. We have also found MRI helpful in defining the extent of disease in the breast more accurately identifying the extent of resection required. Improved neoadjuvant chemotherapy regimens have resulted in patients with significantly smaller tumors and in some cases patients with a pathologic complete response. Neoadjuvant chemotherapy regimens that include Herceptin report a pathologic complete response rate of up to 60%.⁹ Of course this would reduce those patients with positive margins by reducing the number of patients with evidence of disease in the breast and also by reducing the tumor volume. In fact, the study by Waljee reported a lower positive margin rate with neoadjuvant chemotherapy.¹

While many of these techniques may reduce the rate of positive margins, the best reports result in at

least 20% of the patients returning to the operating room for re-excision. This rate remains too high despite our best efforts. New innovative surgical techniques, methods of intraoperative margin assessment, imaging for patient selection, and improved neoadjuvant chemotherapies are needed to prevent one in five patients from returning to the operating room.

REFERENCES

1. Waljee J, Hu E, Newman L, Alderman A. Predictors of re-excision among women undergoing breast conserving surgery for cancer. *Ann Surg Oncol* (in press).
2. Smitt MC, Horst K. Association of clinical and pathologic variables with lumpectomy surgical margin status after preoperative diagnosis or excisional biopsy of invasive breast cancer. *Ann Surg Oncol* 2007; 14:1040-4.
3. Chagpar AB, Martin RCG, Hagendoorn LJ, et al. Lumpectomy margins are affected by tumor size and histologic subtype but not by biopsy technique. *Am J Surg* 2004; 188:399-402.
4. Muttalib M, Tai CC, Briant-Evans T, et al. Intra-operative assessment of excision margins using breast imprint and scrape cytology. *Breast* 2005; 14:42-50.
5. Balch GC, Mithani SK, Simpson JF, et al. Accuracy of intra-operative gross examination of surgical margin status in women undergoing partial mastectomy for breast malignancy. *Am Surg* 2005; 71:22-7.
6. Cabioglu N, Hunt KK, Sahin AA, et al. Role for intraoperative margin assessment in patients undergoing breast-conserving surgery. *Ann Surg Oncol* 2007; 14:1458-71.
7. Tafta L, Fine R, Whitworth P, et al. Prospective randomized study comparing cryo-assisted and needle-wire localization of ultrasound-visible breast tumors. *Am J Surg* 2006; 192:462-70.
8. Nadeem R, Chagla LS, Harris O, et al. Occult breast lesions: A comparison between radioguided occult lesion localization (ROLL) vs. wire-guided lumpectomy (WGL). *Breast* 2005; 14:283-9.
9. Buzdar AU, Ibrahim NK, Francis D, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. *J Clin Oncol* 2005; 23:3676-85.