Commentary

Invited commentary on “A prospective study of tumor and technical factors associated with positive margins in breast-conservation therapy for nonpalpable malignancy” by Reedijk et al

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This commentary accompanies the article by Reedijk et al1 in which the authors analyzed prospectively collected data from a randomized trial of radioactive iodine seed versus wire localization to determine factors predictive of positive margins after breast-conserving procedures for nonpalpable breast cancers. Margins were considered positive when disease was found at <1 mm from the inked margin. Given this definition, the rate of positive margins was 20%. Multivariable analysis of pooled data from the 2 arms of the trial revealed that localizations performed using stereotactic guidance, the presence of ductal carcinoma in situ, tumors >2 cm, and multifocal disease were predictive of positive margins.

These data confirmed prior retrospective studies from these same and other authors, who identified young age, the presence of calcifications on mammography, lobular histology, and lymphovascular invasion as predictors of positive margins, in addition to the factors identified earlier in the current article.2–4

The relatively high rate of margin positivity begs 2 questions. The first relates to methods for lowering the risk of positive margins in breast-conserving operations. Pathologic touch preparation cytology and frozen section analyses are used in some centers for intraoperative margin assessment but have not gained wide popularity because of their technical limitations and requirements for specialized pathologists.

Dune Medical (Boston, MA) has developed a probe (MarginProbe) that uses radiofrequency spectroscopy to measure the electromagnetic properties of breast tissue over an area 7 mm in diameter with a 1-mm sensing depth.5 Preliminary testing of this device had high sensitivity and specificity in distinguishing normal from malignant breast tissue.

Optical studies have also been performed to characterize margins after lumpectomy, first by Bigio et al6 using reflectance spectroscopy in the ultraviolet and visible range. More recently, ex vivo lumpectomy specimens have been analyzed by Nguyen et al7 using optical coherence tomographic scanning, a technique that provides high-resolution real-time images of up to a 2-mm tissue depth. In a preliminary clinical study of 37 patients, the sensitivity was 100% and the specificity was 82% in the identification of histologically positive or close margins. Also using ex vivo lumpectomy specimens from 104 patients, Kennedy et al8 showed that a scattering coefficient and the concentration of total hemoglobin were able to differentiate benign from malignant tissues using diffuse reflectance spectroscopy.

The goal of optimizing cosmesis while obtaining wide excision margins after breast-conserving procedures for breast cancer has led to the emergence of oncoplastic surgical techniques.9 Oncoplastic surgery currently includes a wide range of volume displacement and redistribution procedures to restore breast shape and volume after wide-field excision of tumors. For example, reduction mammoplasty resection combines wide local excision with reduction...
mammoplasty for a patient who desires breast reduction. The procedure is frequently combined with contralateral reduction mammoplasty to provide symmetry. An advantage of this procedure is the ability to obtain clear margins of excision for larger tumors, especially those in the lower half of the breast, which might not be amenable to standard lumpectomy through curvilinear incisions. Sun et al recently reported on 119 patients using the “Wise pattern” incision, which created a classic inverted “T” when closed. The median tumor size was 3.3 cm, the mean specimen weight was 147 g, and the overall re-excision rate was 4.2%. In 91 patients with Tis, T1, or T2 cancers, >2-mm margins were achieved in 96%, and the re-excision rate was 0%. Even for 28 patients with T3 cancers, >2-mm margins were obtained in 50%, >1-cm margins were obtained in 29%, and the re-excision rate was 18%. The complications of combined reduction mammoplasty and cancer excision consist of skin and fat necrosis, which were reported in 17% of patients by Munhoz et al, and are more common in smokers and obese patients. However, the long-term cosmetic results after whole-breast radiation have not been well characterized.

The second question raised by this article relates to what constitutes an adequate margin of excision to minimize local recurrence after breast-conserving procedures for breast cancer. It is interesting that many years after randomized trials established the efficacy of breast-conserving surgery the optimal margin width remains controversial. Although a meta-analysis of 21 retrospective studies evaluating the effect of margin width on local recurrence showed an increased risk for positive margins, there was no significant difference in local recurrence rates with margins of 1 mm, 2 mm, or 5 mm. Thus, current evidence does not support the use of margins wider than the National Surgical Adjuvant Breast and Bowel Project definition of margin negativity (ie, “no tumor on ink”). On the other hand, Morrow et al have described the effects of tumor biology and systemic therapy on local control. These authors have proposed that routine requirements for margins wider than negative should be abandoned. Eliminating rules for a specific margin width would significantly reduce the need for re-excision in patients with negative margins while still recognizing the need to selectively apply clinical judgment in the use of re-excision when tumor biology so dictates.

Combining the use of the predictive factors described by Reedijk et al with the selective use of margin re-excision and with newer surgical techniques would go a long way toward achieving best possible long-term results after breast-conserving surgical procedures.

References