Local Recurrence Risk Factors in Women Treated With BCT for Early-Stage Breast Cancer

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The article by Revesz and Khan is an excellent summary of the state of our knowledge of margin width in relation to breast cancer recurrence. The importance of preventing local recurrence in women who undergo breast-conserving therapy (BCT) for early-stage breast cancer is underscored by the fact that local recurrence is associated with increased cost, psychosocial distress for the patient, and potentially worse distant disease-free and overall survival.[1] With early breast cancer, adequate local control, and more specifically, adequate surgical margins, are arguably key components of therapy. What constitutes an adequate surgical margin in breast-conserving surgery remains controversial, however. Some have advocated for margins of 10 mm or greater for ductal carcinoma in situ (DCIS), but there are no data from large randomized controlled trials to guide us as to what are safe margins for resection in BCT. In National Surgical Adjuvant Breast and Bowel Project (NSABP) trials, which demonstrated the safety and efficacy of BCT, local recurrence rates were low, and a negative margin was defined as simply no tumor cells at the inked edges of the specimen.[2] Revesz and Khan note that a 2-mm margin is generally considered acceptable for DCIS, although the evidence in favor of a 2-mm margin over a 1-mm margin is primarily derived from retrospective, single-institution studies, not all of which demonstrate an advantage for greater margin width.

Margins Greater Than 1 mm Are Not Necessarily Better

More recently, Houssami et al performed a meta-analysis of 21 trials in which both microscopic surgical margins and recurrence rates were reported. While these were mostly retrospective analyses, the pooled data from these 14,571 women with early breast cancer treated with BCT (1026 of whom developed local recurrence) demonstrated that a positive margin or a margin less than 1 mm was associated with increased risk of local recurrence, but the odds of local recurrence did not differ significantly with surgical margin widths greater than 1 mm. In other words, a 2-mm margin is not necessarily better than a 1-mm margin, and a 5-mm margin is not better than a 2-mm margin.[3] If we mandate at least 2-mm margins in BCT, however, then re-excision rates would most assuredly be greater than if a 1-mm margin is accepted as safe. Re-excision is costly from both an economic and a cosmetic standpoint, as resection of greater than 15% of the breast volume increases the risk of unacceptable cosmesis and patient dissatisfaction after BCT.[4,5] The likelihood of finding residual disease is also relatively low (12% to 31%) when surgical re-excision is performed for initial margins of at least 1 mm.[6,7]

Patient Characteristics and Tumor Biology Affect Local Recurrence

In addition to surgical margins, patient and tumor characteristics may modify local recurrence risk. A number of studies suggest that younger patients (< 50 years old, especially those < 35 years or younger at diagnosis) treated with BCT are at increased risk for local recurrence. Higher tumor grade, the presence of lymphovascular invasion, and larger tumor size have also been linked to increased local recurrence risk, but not as consistently as age.[8-10] Analyses of local recurrence by molecular subtype and hormone receptor status indicate that estrogen receptor (ER)- and progesterone receptor (PR)-negative cancers, especially the basal subtype, and HER2-positive breast cancers may also be associated with greater risk of local recurrence after BCT.[10-12]

Adjuvant Therapy Decreases Local Recurrence Risk

Because tumor biology seems to influence local recurrence risk, it is only logical that adjuvant therapy decreases the risk of local recurrence. NSABP trials and other randomized trials have
demonstrated that the risk of local recurrence is about threefold higher in patients who do not receive radiotherapy than it is in patients who do. Patients who received systemic therapy with tamoxifen for ER-positive breast cancers and/or combination chemotherapy in the NSABP trials also had lower rates of local recurrence: 6.6% vs 12.3% without systemic therapy. While side effects are common, adherence to endocrine therapy for women with ER-positive breast cancers is high in both the clinical trial (about 75%) and community (58% to 88%) settings.

In summary, negative surgical margins are important for local control of breast cancer. Nevertheless, a variety of other factors affect the risk of local recurrence in women with early-stage breast cancers treated with BCT. In regard to the width of safe surgical margins in women treated with breast conservation, bigger is not always better, and a 1-mm surgical margin may be adequate in most circumstances.

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cancer who have human epidermal growth factor receptor 2-positive, node-negative tumors 1 cm or smaller. J Clin Oncol. 2009;34:5700-6.


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