Current Status of Radiation in the Treatment of Breast Cancer

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By Taryn Torre, MD [2] and Louis Potters, MD, FACR [3]

The article by Dr. William Small on the role of radiation therapy in the treatment of breast cancer is a comprehensive review of the current standards of care and highlights the controversies surrounding recent trends. Breast cancer treatment has come full circle in the last 20 years, with emphasis now being placed on technical advances and treatment techniques as new data substantiate the impact of radiation therapy on survival following local surgery and mastectomy.

Ductal Carcinoma In Situ

The effort to define a subpopulation of patients in whom less treatment can be given while maintaining or improving local control and survival rates is noble. Whether moving from mastectomy to breast-conservation therapy or from breast-conservation therapy to excision alone, Dr. Small diplomatically points out the need for caution and the role of good randomized trials. Although breast-conservation therapy has become the accepted standard of care for patients with ductal carcinoma in situ (DCIS), mastectomy remains the procedure that offers the lowest rate of recurrence. National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 data on 22 patients who underwent a mastectomy with negative margins showed that 41% had residual DCIS in the same breast quadrant upon pathologic review.[1] As Dr. Small reported, there are currently no published randomized trials that have compared mastectomy and breast-conservation therapy in patients with DCIS.

The Eastern Cooperative Oncology Group (ECOG) is currently conducting a randomized trial of local excision without breast irradiation in a subgroup of patients with DCIS and favorable factors.[2] Dr. Small's article clearly cautions against making generalizations from nonrandomized trials such as that of Silverstein et al who tried to classify DCIS patients according to their need for mastectomy, local excision alone, or local excision and radiation.[3] The reproducibility of such data is a major concern.

Silverstein's results (and findings from other nonrandomized trials), however, do provide an excellent foundation on which to base future randomized studies. Until the ECOG data have matured, management of DCIS should conform to the results of the NSABP B-22 study, which, to date, has provided the clearest guidelines. Routine radiation to the breast following a lumpectomy remains the current standard of care for all patients with this disease.

Invasive Breast Cancer

Full axillary dissection for invasive breast cancer is slowly being replaced by sentinel lymph node biopsy, although no randomized trial has established that the two procedures are equivalent. The NSABP B-32 and American College of Surgeons Oncology Group (ACOSOG) trials are currently addressing this issue and hopefully will determine the efficacy of the axillary dissection procedure itself.[2] Now that immunohistochemical staining can identify single metastatic cells in lymph nodes, we are faced with new challenges in defining the role of chemotherapy as well as the addition of nodal irradiation. The above-mentioned trials will be investigating patient outcomes related to immunohistochemical studies.

The traditional lumpectomy cavity radiation boost has also been challenged for patients with stage...
I/I breast cancer. Nevertheless, recently presented data from the European Organization for Research and Treatment of Cancer (EORTC) "boost vs no boost" trial[4] showed that boost radiation decreased the risk of local failure and had the greatest impact in younger women. The study also found that local failure increased the risk of systemic metastasis by 8.3%. The best method for delivering the boost has yet to be determined, but generally, direct electron fields are used.

**Postmastectomy Radiation**

While the role of radiation in DCIS and early-stage invasive breast cancer has been challenged, the role of postmastectomy chest wall radiation has been expanded over the last 2 years. During the era from the 1960s through the late 1970s when the Haagensen surgical criteria for breast cancer were used, it became apparent that chest wall recurrence was a significant problem for patients with class C or D disease and that the addition of chest wall and nodal irradiation was important for local control and survival.[5] With the advent of chemotherapy, the survival advantage associated with radiation was lost, thereby decreasing the use of radiation over the last 10 to 15 years.

As Dr. Small has pointed out, results from both the Danish Breast Cancer Cooperative Group Trial and the British Columbia study document a survival advantage in premenopausal, node-positive women who underwent mastectomy, chemotherapy, and radiation of the chest wall and regional nodes. In fact, the Canadian study implies a survival benefit for chest wall radiation following mastectomy in patients with one to three positive nodes, as compared to those with four or more nodes (whose risk of systemic failure is significantly higher). The Intergroup trial is investigating postmastectomy radiation in women with one to three positive nodes. The radiation fields in this study include the internal mammary nodes. This highlights yet another question[whether radiation to the internal mammary nodes contributes to survival. These and other recent trials further support the paradigm that local control remains paramount for overall survival and that chemotherapy, although important for control of systemic disease, has less of an impact on local control.

**Radiation Techniques**

Techniques for delivering radiation have thus become a focal point, in light of the younger population and the increased survival of these patients. Dr. Small mentions his preference for the Marks’ technique in treating the internal mammary nodes.[6] This approach, which eliminates the need for matching internal mammary fields, becomes even more significant when one considers recent data from the Joint Center of Radiation Therapy.[7] These data revealed that younger patients (< 50 years) treated with breast irradiation had a 43% increase in unexpected second, nonbreast malignancies.

Among seven patients who developed sarcomas, four developed the sarcoma within an area of match-line fibrosis. The authors postulate that the fibrosis was related to an older matching technique and conclude that perhaps newer methods of delivering radiation to the breast and lymph node areas may reduce the risk of secondary nonbreast malignancies.[7]

**Conclusions**

Clearly, the current investigational focus is on reproducibly defining the subpopulations for whom a particular therapy offers optimal local and survival benefit while limiting the toxicities of treatment. The pendulum continues to swing as technical advances are made. If one could more specifically define the region that needs to be treated, coupled with the advent of the technology that allows our treatments to be more focused (such as with intensity-modulated radiation therapy, deep inspiration breathhold, and brachytherapy), then our goals may be achieved.[8-11]

While preliminary studies of intensity-modulated radiation therapy using conventional field arrangements have demonstrated improved dose homogeneity within the breast, the potential advantage of this technology lies in its ability to deliver doses differentially with combinations of photons and electrons. With the apparent need to continue using tumor boosts, intensity-modulated radiation therapy can selectively treat the boost volume while simultaneously treating the whole breast volume. Also, defining the volumes of interest to include the nodal sites in higher-risk patients, with inverse planning, may help to develop novel radiation field arrangements. However,
the question remains: Is less really more?

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