Mounting Evidence for Postmastectomy Locoregional Radiation Therapy

Review Article [1] | August 01, 1999
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Marks, Hardenbergh, and Prosnitz provide an excellent overview of the role of postmastectomy radiation therapy for node-positive breast cancer patients. Their review not only summarizes the most recent literature supporting the clearly established benefit of postmastectomy radiation in node-positive patients with respect to locoregional control and overall survival but also offers some meaningful discussion of the pertinent technical issues. Given the delicate balance between the modest, but clinically meaningful and significant benefit of postmastectomy radiation and the potential morbidity of such treatment, attention to detail with respect to the technical aspects of therapy is critical to maintaining a true therapeutic gain.

I will not repeat the points that were outlined so eloquently and concisely by the authors. Rather, I will take this opportunity to elaborate on three issues: (1) patient selection; (2) which radiation fields should be employed; and (3) extrapolation of the results of postmastectomy radiation therapy to conservatively treated node-positive patients.

**Patient Selection**
The authors conclude that all patients with axillary node-positive breast cancer should be considered for postmastectomy radiation. Clearly, patients with four or more positive nodes, with or without a large primary tumor, derive a substantial benefit from postmastectomy radiation with respect to both locoregional control and disease-free survival. Most surgical, radiation, and medical oncologists would concur with the routine use of postmastectomy radiation in this setting.

Although the locoregional control benefit of radiation therapy in patients with T1 or T2 disease and one to three positive nodes is small, the available data suggest that the relative benefit in these patients with respect to overall or disease-free survival is at least as pronounced as the benefit in patients with four or more positive nodes. Data from both the Danish and British Columbia trials demonstrate a benefit with respect to disease-free and/or overall survival in premenopausal patients with one to three positive nodes.[1,2] Although there are conflicting reports, several other studies summarized in the article by Marks et al also support a benefit of postmastectomy radiation in patients with one to three positive nodes, regardless of menopausal status.

However, other factors, including the patient’s overall medical condition, concurrent medical problems, age, and extent of disease at the primary site and nodes, must be taken into consideration when assessing the risk-benefit ratio. In the current era of sentinel node biopsy and increased utilization of immunohistochemical staining of nodal tissue, some patients who are node negative by conventional histologic criteria may be node positive by immunostaining. Whether regional irradiation will benefit this subset of patients remains unclear.

Based on the available data, it is apparent that node-positive patients should be apprised of the potential risks and benefits of postmastectomy radiation in order to make an informed decision. While I concur with the authors that postmastectomy radiation should be considered for all node-positive patients, I must acknowledge that the absolute benefit of this therapy is small in some subsets of patients, and its routine administration in patients with one to three positive nodes is not universally embraced.

In an effort to further investigate this area of controversy, a randomized trial of postmastectomy radiation in patients with one to three positive nodes using current chemotherapy programs and modern surgical and radiation therapy techniques is under development. [personal communication, Lori Pierce, md, May 1999] Hopefully, this trial will identify subgroups of patients who are most likely to benefit from such treatment and perhaps identify a subgroup who derive no significant benefit.
Radiation Fields
Clearly, the optimal technique of regional nodal irradiation following mastectomy remains a controversial issue. Although the Danish and British Columbia trials are often quoted as demonstrating the benefits achievable with postmastectomy radiation, most radiation oncologists do not prescribe radiation in the same fashion as was employed in these trials. Variations from the techniques used in these trials are justifiable based on our attempts to limit morbidity, given current capabilities with computed tomographic (CT) treatment planning and differences in the extent of axillary surgery and chemotherapeutic agents currently employed.

Axillary radiation via an extended supraclavicular field does not appear to be necessary when an adequate axillary dissection is performed. The benefit of a separate internal mammary field remains controversial. An ongoing European trial is randomizing post-mastectomy and postlumpectomy node-positive and high-risk node-negative patients to tangential fields only or to tangential fields with an internal mammary and supraclavicular field. This trial may help resolve the controversy, but it will be several years before the trial closes and the data mature.

Although not directly addressing technical issues in postmastectomy radiation, the Milan and National Surgical Adjuvant Breast and Bowel Project (NSABP) randomized trials that compared breast-conserving therapy to mastectomy provide some interesting data regarding the issue of regional irradiation. In both of these trials, with respect to disease-free and overall survival, the lumpectomy-radiation arms had a slight advantage over the mastectomy arms in node-positive patients.[3] Since mastectomy patients did not receive radiation and the lumpectomy patients did (and patients in both arms received similar systemic treatment), the survival benefit presumably derived from the radiation administered as part of the breast-preservation program.

Interestingly, in both of these trials, intentional targeting of the internal mammary and/or supraclavicular nodes was not done routinely. In my view, these findings provide at least circumstantial evidence that a significant portion of the benefit is due to the radiation administered to the tangential fields and, possibly, the lower axillary and/or internal mammary nodes, which may be incidentally covered in those fields.

It is apparent that definitive objective data regarding this issue are lacking. Treatment of the chest wall without intentionally targeting the internal mammary chain is widely employed with apparently acceptable results. Advocates of this approach note the exceedingly low rate of internal mammary failures, and point out the potential for added cardiopulmonary toxicity with more comprehensive nodal irradiation, particularly in concert with aggressive chemotherapeutic programs.[4] However, it does appear to be reasonable, as Marks et al suggest, to obtain a treatment planning CT scan in an effort to include the internal mammary chain in the tangential fields, when possible. Alternatively, a separate internal mammary field, carefully matched with appropriate techniques, may be employed. Given the lack of convincing data, and pending the outcome of the European randomized trial addressing this issue, either carefully planned comprehensive nodal irradiation or the use of tangential fields without intentionally targeting the internal mammary chain is an acceptable standard of care. In addition, a carefully matched supraclavicular field without extension to cover the entire axilla results in acceptable morbidity and a high rate of regional control in patients with node-positive breast cancer.

Extrapolation of Results to Conservatively Treated Patients
Numerous randomized trials have established the local control benefit of postlumpectomy radiation, irrespective of primary tumor size and nodal status. Like patients who have undergone a mastectomy, woman who have been treated with a lumpectomy appear to derive a modest distant metastasis and disease-free survival benefit from adjunctive radiation therapy. Since conservatively treated invasive breast cancer patients routinely receive radiation to tangential breast fields, by definition the majority of conservatively treated node-positive breast cancer patients will receive some form of radiation to the breast/chest wall, portions of the lower axilla, and internal mammary chain. As noted above, whether to intentionally target the internal mammary chain and supraclavicular fossa in postlumpectomy patients remains controversial, as it is in postmastectomy patients.

The issue of regional nodal irradiation in conservatively treated patients is further complicated by the cosmetic goals of breast-conserving therapy. If one is to use matching fields, techniques must be carefully designed and carried out in order to minimize overlap between matching fields within the breast tissue. In a recent retrospective analysis of conservatively treated patients at our own institution, we were unable to demonstrate a clear advantage to intentional targeting of the internal mammary chain, irrespective of tumor location or number of lymph nodes involved.[5] Again, the incidental treatment of internal mammary nodes and lower axillary nodes using standard tangential
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fields must be acknowledged. Currently, I approach conservatively treated node-positive patients in a similar manner as postmastectomy patients. As suggested by Marks et al, I obtain a treatment planning CT in an attempt to include the internal mammary field in the tangential fields when feasible. As noted above, the marginal benefit of this approach over tangential fields alone is controversial. Indeed, it must be acknowledged that either tangential fields alone or tangential fields matched to a supraclavicular field with or without intentional targeting of the internal mammary chain is acceptable.

**Summary**

The potential benefit of regional irradiation in both the postmastectomy and postlumpectomy settings can no longer be ignored. The benefits and risks of regional radiation therapy, along with the uncertainties regarding the technical issues and interpretation of the data, are evident. Although controversies and unanswered questions remain, the available data suggest that regional irradiation confers a significant benefit with respect to locoregional control and disease-free survival. Armed with these data, clinicians should inform node-positive patients about the potential benefits of postsurgical radiation therapy and should consider the vast majority for such treatment. Physicians should acknowledge that there remain unanswered questions and should encourage patients to participate in ongoing and future studies addressing the controversies in patient selection and technical issues.

**References:**


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