Current Status of Radiation in the Treatment of Breast Cancer

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The role of radiation therapy in the management of breast cancer has continued to evolve over the past several years, in both the breast-conserving and postmastectomy settings. In this issue of ONCOLOGY, Dr. William Small provides a thorough yet concise review of current practices in radiation therapy for ductal carcinoma in situ (DCIS), early-stage invasive breast cancer managed conservatively, and postmastectomy situations. These discussions are supported by a well-selected group of publications on each topic. In addition, the author summarizes the available data and some of the controversies surrounding the use of nodal irradiation, especially in this era of sentinel node biopsy. We would like to mention a few points that warrant further discussion.

Role of Margin Status

The issue of margins in patients undergoing breast-conserving surgery continues to be debated. As mammographic and pathologic evaluation improves, our understanding of the importance of margin status in these patients also improves. Although microscopically positive margins are associated with an increased risk of local recurrence, the best approach for patients with "close" or "focally positive" margins has not been fully determined. In addition, there is no standardized definition of a negative or positive margin (or anything in between).

The most recent update from our institution included patients with stage I or II disease who underwent gross total excision, received at least 60 Gy of radiation to the tumor bed, and had a minimum of 8 years of potential follow-up. Among these patients, those with either close (defined as 1 mm or less from an inked margin) or negative margins had a 7% local recurrence rate.[1] Given this finding, at our institution, we routinely treat patients who have close but negative margins. Patients with margins deemed extensively positive (defined as margin involvement in more than three low-power microscopic fields) or focally positive (defined as margin involvement in three or fewer low-power microscopic fields) had local recurrence rates of 27% and 14%, respectively. Only margins and the use of systemic therapy were associated with local recurrence. Systemic therapy appeared to decrease the incidence of local recurrence in patients with positive margins. Among the 45 patients with focally positive margins who also received systemic therapy, the local recurrence rate was 7% (which is similar to that of patients with negative or close margins). It remains to be seen whether this is a durable finding, and whether others report similar results.

Use of a Boost

The need to employ a radiotherapy boost to the tumor bed in all breast cancer patients managed with conservative surgery has been a matter of continued discussion, as Dr. Small notes. The National Surgical Adjuvant Breast and Bowel Project (NSABP) trials typically have not used a boost. However, data supporting the use of a boost come not only from the Lyon trial, but also from a recently reported study by the European Organization for Research and Treatment of Cancer (EORTC).[2]

In the EORTC trial, 5,569 patients underwent tumorectomy followed by 50 Gy of radiation to the...
whole breast. The 5,318 patients who had undergone a microscopically complete excision were randomized to receive a 16-Gy boost of radiation or no boost. The median follow-up time was 5.1 years. The boost resulted in a 41% reduction in the relative risk of local recurrence and only a slight worsening of cosmetic results. However, the data have been published in abstract form only, and it is unclear how margin width or the presence of DCIS in assessing margin status influenced these results. Our treatment policy continues to be to treat the whole breast with 44 to 45 Gy, followed by a 16-Gy boost.

Impact of Local Control on Survival

Older trials of postmastectomy radiotherapy showed diminished breast cancer deaths but increased non-breast cancer deaths, likely secondary to outmoded radiotherapy techniques. However, recent randomized trials of postmastectomy radiotherapy suggest that in the presence of effective systemic therapy, locoregional radiotherapy improves survival. A recent meta-analysis of 18 randomized trials of patients who received systemic therapy showed a 75% reduction in local recurrence and a 17% reduction in mortality.[3] In addition, preliminary results from the latest Oxford overview also show that the addition of radiotherapy to conservative surgery results not only in decreased local recurrence, but also improved survival.[personal communication, R. Peto, 2000] The above findings are reassuring and support the notion that adjuvant radiotherapy has an impact on survival in breast cancer, both after mastectomy and after conservative surgery.

Improved Radiotherapy Treatment Planning

As Dr. Small indicates, a detailed discussion of the various planning techniques is beyond the scope of this article. With the advent of computed tomography (CT)-based treatment planning, we now have the ability to evaluate more technical options that allow inclusion of the internal mammary nodes, while reducing cardiac and pulmonary volumes in the treatment fields.

A preliminary study from our group showed a substantial reduction in cardiac volume treated using CT simulation vs conventional simulation.[4] The full importance of minimizing cardiac irradiation remains to be elucidated. However, in this era of cardiotoxic systemic therapy (eg, doxorubicin, trastuzumab [Herceptin]), our policy is to be cautious and employ CT planning in all of our left-sided breast cancer patients when possible.

Treatment of the Axilla After a Positive Sentinel Node Biopsy

In patients with a positive sentinel node, the current standard of care is an axillary node dissection. At our institution, we are evaluating the use of radiotherapy in this situation. Patients in that study undergo sentinel node mapping. If the sentinel node is negative, no further specific axillary treatment is administered. If the sentinel node is positive, three-field radiotherapy is used to treat the axilla and supraclavicular nodes.

This protocol differs from that of the American College of Surgeons, which is randomizing sentinel node-positive patients to either axillary dissection or no further specific axillary treatment. As Dr. Small indicates, however, the lower axilla is often included within tangential breast radiotherapy fields. It remains to be seen whether any or all of these approaches are appropriate in sentinel node-positive patients.

Additional Unresolved Controversies

Dr. Small’s article provides a well-focused list of the major controversies surrounding radiotherapy for breast cancer. Although not mentioned in the article, another issue that we frequently encounter concerns the use of radiotherapy in the reconstructed breast after mastectomy. As plastic surgical technique improves, many women are being offered immediate reconstruction, with either a musculocutaneous (ie, transverse rectus abdominis or latissimus dorsi) flap or a tissue expander/saline implant at the time of mastectomy. While this approach has obvious psychological benefits, it can sometimes limit the radiotherapy planning options. Moreover, although the published literature on this topic is limited, it appears that radiotherapy is associated with increased complications and worse cosmesis, especially in patients undergoing implant placement. The optimal
timing for the various stages of reconstruction also remains unclear. In addition, immediate reconstruction can occasionally result in a lengthy healing process and thus delay the initiation of chemotherapy, but definitive data on this issue are also lacking. At our institution, patients who are likely to require postmastectomy radiotherapy are increasingly involved in some discussion of these issues prior to proceeding with immediate reconstruction. Further study is necessary.

Another area of controversy concerns the use of radiotherapy after neoadjuvant chemotherapy. Increased interest in this approach was probably prompted by the results of NSABP trial B-18, which showed that this practice did not compromise survival.[5] While we apply the same criteria for adequate margins after neoadjuvant chemotherapy as we do for initial surgery, it is unclear whether this strategy is correct or what the best approach is for treatment of the regional lymph nodes.

Pathologic nodal information obtained at the time of diagnosis is typically used to help guide recommendations for the addition of a supraclavicular radiation field, with or without the axilla, after breast-conserving surgery and axillary dissection or sentinel node biopsy. At our institution, patients with four or more positive axillary nodes typically receive irradiation to this additional field. However, as patients receiving neoadjuvant chemotherapy may experience downstaging of their regional lymph nodes, the interpretation of this information in relation to clinical practice remains unclear. For the clinically node-negative patient undergoing neoadjuvant chemotherapy, our preference is to obtain a sentinel node biopsy prior to the initiation of chemotherapy.

Conclusions

Dr. Small provides a balanced, focused discussion of some of the key issues in the use of radiation therapy for breast cancer. He also highlights some of the more common unresolved issues encountered by clinicians. Radiation therapy now plays a major role in the treatment of many breast cancer patients, improving both quality of life and survival. We agree that it is important to offer patients participation in clinical trials.

References:


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