

ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

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Breast Cancer In Focus

The Need for Postoperative Radiation Therapy

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H&O What is the current standard of care for postmastectomy treatment?

BM The American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), and the American Society for Therapeutic Radiology and Oncology (ASTRO) guidelines state—and most clinicians agree—that any patient with 4 or more involved positive lymph nodes should receive postmastectomy radiation. However, the controversy arises in patients who present with 1–3 positive lymph nodes. At the moment, there is no consensus on the use of adjuvant radiation for such patients, once they have completed any planned systemic therapy.

H&O Why are the data unclear on whether radiotherapy is needed after mastectomy?

BM My colleagues and I at the Radiation Therapy Oncology Group, as well as other cooperative groups, have pondered this question. Approximately 15 years ago, results from 3 major randomized controlled trials were presented; 1 study was conducted in Canada and 2 in Denmark. These prospective trials evaluated a relatively low-risk group of women who received cyclophosphamide, methotrexate, and fluorouracil chemotherapy and had a mastectomy; these women were randomized to receive radiation or no radiation. The findings showed

a benefit in local control and a modest improvement in survival (approximately 10%). However, it was also noted that the local recurrence rate in the women who were randomized to not receive radiation was exceptionally high. This finding led to much criticism about the quality of the surgeries being performed in Canada and Denmark. Accordingly, many of the breast cancer cooperative groups in the United States joined to create a similar trial with the same objective as the Danish and Canadian trials. The trial opened, and it closed a year later with less than 100 patients accrued due to the fact that physicians felt very strongly about either giving or not giving radiation in this group of patients. Since that time, we have had to depend on retrospective studies, which has detracted from the clarity of the issue of whether radiotherapy is needed after mastectomy.

H&O What factors need to be considered when deciding whether or not to administer postmastectomy radiotherapy?

BM There are a number of factors that are considered when debating the appropriate course of treatment; however, they have all been derived from various retrospective studies, and there is no consensus on these factors in the medical community.

In general, patients who are younger tend to have a higher local recurrence rate than patients who are older,

thus age is a factor. We also look at the number of lymph nodes that are involved: when a patient has closer to 4 positive nodes, I would be more likely to recommend radiation. Information about the number of nodes removed by the surgeon is also of importance: the lower the number of nodes, the higher the risk. The proportion of nodes is also considered: a breakpoint of 20–25% positive nodes over the overall denominator of nodes removed influences risk of local recurrence. There are also other histologic or pathologic factors that are evaluated, such as the size and grade of the tumor, lymphovascular invasion, multicentric disease, and margin and nipple involvement. These are some of the factors that we evaluate, but none of them have been adapted to any kind of algorithm or nomogram.

Some groups are now studying molecular subtyping and trying to identify its relationship to the risk of local recurrence.

H&O What data have been presented on the use of postoperative radiotherapy?

BM The SUPREMO (Selective Use of Postoperative Radiotherapy after Mastectomy) trial is a phase III randomized trial that is evaluating the role of adjuvant chest wall irradiation following mastectomy in intermediate-risk breast cancer patients. This large study is currently ongoing, and we are awaiting results.

The MA.20 study was a trial conducted in Canada around the same time the US cooperative group trial failed to accrue. This study looked at the benefit of regional nodal irradiation in patients with 1–3 positive nodes who have had a lumpectomy. Dr. Tim Whelan presented the findings from this trial at the 2011 ASCO meeting. In this trial, women were randomly assigned to receive whole breast irradiation plus regional node irradiation or whole breast irradiation alone. Dr. Whelan reported that the women who were managed with whole breast irradiation plus regional node irradiation had improved disease-free survival and showed a trend toward improved overall survival, when compared to those women who received whole breast irradiation alone.

H&O It appears that there is nonadherence to evidence-based guidelines that support the use of postmastectomy radiotherapy. Why is that?

BM There may be a gap between the evidence suggesting the benefits of postmastectomy radiation therapy and its use in everyday clinical practice for several reasons. Although the ASCO, NCCN, and ASTRO guidelines are in agreement regarding radiation therapy for patients with more than 4 positive lymph nodes, there are areas where the guidelines may be open to interpretation, such as the need for radiation therapy in patients with 1–3 positive nodes. For example, both the NCCN and ASCO guidelines recommend treating a patient with 4 or more positive lymph nodes with radiation, but the ASCO guidelines do not comment on patients with 1–3 positive nodes, and the NCCN guidelines suggest considering radiation in patients with 1–3 positive nodes. Furthermore, there are concerns of possible risks from radiation, and patients may refuse this type of treatment.

A multidisciplinary approach is necessary in order to evaluate each individual patient and to tailor his or her treatment. At Memorial Sloan-Kettering Cancer Center, we consult with all node-positive patients, including those who have 1–3 positive lymph nodes, but we do not treat them all.

Suggested Readings

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