In the most recent NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer, there were updates pertaining to various radiation treatment options, including whole-breast radiotherapy (RT), accelerated partial-breast irradiation (APBI), or regional nodal irradiation (RNI), said Kilian E. Salerno, MD, Associate Professor, Radiation Oncology, and Director, Breast Radiation and Soft Tissue/Melanoma Radiation, Roswell Park Cancer Institute, and a member of the NCCN Breast Cancer Panel.

Adjuvant RT After Breast-Conserving Surgery

In short, the NCCN recommendations for RT of invasive breast cancer after breast-conserving surgery include RT to the whole breast, with or without a boost; APBI in select patients; and omission of RT in select patients.

The NCCN recommendations on special considerations for use of breast conservation include 2 new category 2B updates on contraindications for use of RT after breast-conserving surgery in patient subsets. An absolute contraindication for the use of radiation is the presence of a homozygous ATM mutation. Patients with Li-Fraumeni syndrome have been included as a relative contraindication to radiation.

The NCCN recommendations on appropriate margins for breast-conserving surgery have been updated for both ductal carcinoma in situ (DCIS) and invasive breast cancer in patients who will receive whole-breast irradiation. The appropriate surgical margins for lumpectomy are now defined as 2 mm for DCIS and "no tumor on ink" for invasive carcinoma. These recommendations are not applicable for APBI or patients who have received neoadjuvant chemotherapy.

Hypofractionation: Preferred for Whole-Breast RT

For most women receiving whole-breast irradiation, hypofractionation is preferred by the NCCN panel. Hypofractionation is a shorter treatment course using slightly higher doses per fraction (>2 Gy/fraction) and fewer fractions compared with conventional fractionation (1.8–2.0 Gy/fraction). According to Dr. Salerno, for many patients, hypofractionation achieves results that are “at least equivalent to or better than” those seen with conventional fractionation in terms of local control, breast cosmesis, and toxicity. The recommendation

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Who Needs RNI?

The guidelines regarding RNI in the treatment of patients with node-positive and/or high-risk, node-negative disease have been updated on the basis of many studies, including the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) meta-analysis and the MA.20 and EORTC 22922 trials.

In EBCTCG’s analysis of 22 randomized trials of 8,135 patients undergoing mastectomy and axillary dissection, RT reduced locoregional recurrences, overall recurrences, and breast cancer mortality in women with ≥4 positive nodes or 1 to 3 positive nodes. The absolute difference in breast cancer mortality was 7.9% at 20 years. Similar effects were seen for those with 1 positive node. Benefit was not seen in patients with node-negative disease.

After 10 years of follow-up in MA.20 and in EORTC 22922, RNI was associated with improvement in locoregional and disease-free survival and lower breast cancer mortality, but not overall survival. These 2 studies evaluated similar approaches to RNI, although their patient populations were different.

A focused guideline update on postmastectomy RT (PMRT) was recently published addressing the role of radiation in patients with T1–2 breast cancer and 1 to 3 positive nodes. The panel recognized that use of PMRT reduces locoregional recurrences and improves breast cancer mortality. Treatment recommendations for use of PMRT or not should include clinical judgement and assessment of individual risk.

“We have all these trials that interplay and influence our thinking about what to do for node-positive disease; we have to interpret them and reconcile the differences in trying to determine individual treatment recommendations,” Dr. Salerno said. Clinicians should determine the individual patient’s risk for recurrence and whether the patient fits the eligibility criteria of these studies.

RNI should be used in patients with ≥4 positive nodes or locally advanced tumors, should be strongly considered for patients with 1 to 3 positive nodes, and may also be considered for select patients with node-negative disease at high risk. Clinicians should assess individual patient risk for recurrence and apply RNI accordingly, considering age, life expectancy, comorbidities, tumor size, lymphovascular invasion, number and size of positive lymph nodes, response to...
neoadjuvant chemotherapy, extent of residual disease, management of the axillae, and intrinsic tumor type. RNI includes treatment of the supraclavicular area, infraclavicular region, internal mammary nodes, and any part of the axillary bed considered at risk.

RT After Neoadjuvant Treatment
Following neoadjuvant chemotherapy, indications for RT should be guided by maximal disease stage from either prechemotherapy tumor characteristics at diagnosis or postchemotherapy pathology results. Patients with residual nodal disease after neoadjuvant systemic therapy should receive RNI.

Recurrence risk may be lower for patients who experience a pathologic complete response, but at this time, this does not negate the need for RT if indications for treatment were present at diagnosis.

Studies evaluating management of the regional nodes in the setting of neoadjuvant chemotherapy are ongoing, including NSABP B-51/RT0G 1304 and the Alliance 011202 trials. Clinicians are encouraged to enroll patients on these studies.

Optimizing RT Treatment
Numerous treatment modalities and techniques are available for breast radiation with the intent to provide homogenous dose to targets and minimize toxicity to adjacent normal tissues. “Radiation oncologists have a broad spectrum of options,” Dr. Salerno noted, including prone positioning in select patients, use of respiratory control techniques, and CT-based treatment planning.

References