Early Accelerated Partial Breast Irradiation vs. Whole Breast Irradiation

BY KURT SAMSON

I f treated early enough, low-risk breast cancer patients who receive accelerated partial breast irradiation (APBI) after lumpectomy do just as well over the next decade as women treated with whole breast irradiation, researchers told the 2019 San Antonio Breast Cancer Symposium (Abstract GS4-06).

APBI was associated with significantly fewer adverse events and better cosmetic results than whole breast irradiation (WBI), without increasing the risk of ipsilateral breast tumor recurrence (IBTR) or death. The findings support the use of partial breast irradiation in carefully selected patients, lead author Icro Meattini, MD, of the University of Florence, Italy, told a press conference.

Recent developments in radiation oncology have shown a move toward radiation treatment de-escalation for early breast cancer, including accelerated and nonaccelerated partial breast irradiation, Meattini noted. The 10-year outcomes from the randomized phase III APBI IMRT Florence trial were similar to 5-year results, published in 2015.

“Postoperative radiation still remains a mainstay of adjuvant treatment...and is able to significantly reduce the local relapse occurrence rate,” he said. “What we’ve learned from major phase III trials...is that [with partial breast radiation], disease control is closely related to the adequate selection of patients,” he said. “APBI might be considered a standard alternative to WBI in low-risk and very low-risk early breast cancer patients.”

Study Details

Meattini and his associates analyzed 10-year follow-up data for 520 women enrolled in the trial who, between 2005 and 2013, were randomly assigned to receive either APBI or WBI. All of the patients were over 40 years of age with either stage 1 or stage 2 cancer. The majority of the patients had hormone receptor-positive, HER2-negative breast cancer, and most were over age 50.

Women treated with APBI received a total of 30 gray (Gy) of radiation to the tumor bed in five daily fractions, while WBI subjects received a total of 50 Gy in 25 daily fractions to the whole breast, plus a boost of 10 Gy to the tumor bed in five daily fractions. Both treatment arms were comparable in terms of age, tumor size, tumor type, and adjuvant endocrine treatment, and both achieved a median 10-year follow-up.

After 10 years, breast cancer recurrence in 3.3 percent of women in the APBI arm versus 2.6 percent in the WBI group. However, this difference was not statistically significant and was comparable to the 5-year results. In the earlier analysis, APBI subjects had a 2.4 percent recurrence rate versus a 1.2 rate in the WBI women. Overall survival at the 10-year mark was also very similar, Meattini continued, with rates of 92.7 percent in the APBI group and 93.3 percent in women who received WBI. Breast-cancer-specific survival was 97.6 percent for the APBI cohort and 97.5 percent for women in the WBI arm of the trial, while the distant metastasis-free survival rate was 96.9 percent in both groups.

“These results reinforce the initial promising results from the previous study, that accelerated partial breast irradiation can produce excellent disease control,” Meattini said. “Combined with data from other studies, the findings are part of a growing body of data that can help clinicians make better evidence-based recommendations to their low-risk breast cancer patients.

“In well-selected cases, there is no difference in patients’ outcomes whether they are treated with APBI or WBI," he said. “A once-daily regime of external APBI might also produce an improved quality of life, with less toxicity, and can potentially reduce the overall treatment time.” APBI may also be less likely to cause cosmetic changes and is less expensive to administer than WBI, he added.

“Partial breast irradiation is one of the primary examples of effective de-escalation of treatment in breast oncology. For many patients, partial breast irradiation may be an optimal choice that is cost-effective, safe, and efficacious.”

Methodology

Conducted from March 2005 to June 2013, the trial involved women with a maximum pathological tumor size of 25 mm who were randomly assigned in a 1:1 ratio to receive either WBI using 3-D conformal radiotherapy or APBI using intensity-modulated radiotherapy. The 10-year follow-up included reviews of overall survival, breast cancer-specific survival, distant metastasis-free survival, contralateral breast cancer, and locoregional recurrences.

In all, 260 women participated in the APBI arm of the trial while 260 received whole breast treatment. All of the patients achieved median 10-year follow-up and all were comparable with regard to age, tumor size, grade, tumor type, and adjuvant endocrine therapy.

No significant difference in ipsilateral recurrence was found between the two treatment arms. Among women who received APBI, the 5-year IBTR was 1.96 percent (5 events) and the 10-year IBTR was 3.74 percent (9 events). In the WBI group the 5-year IBTR rate was 1.2 percent (3 events) and the 10-year rate was 2.5 percent (6 events). The hazard ratio for women in the APBI group versus WBI patients was 1.33, while the HR for APBI patients was 0.66.

The breast cancer-specific survival rate for subjects in the APBI arm was 98 percent, compared to 97.5 percent among women treated with WBI, while the distant metastasis-free survival rate for the APBI cohort was 97.4 percent compared with 96.1 in the other group. Locoregional recurrences were 3.9 percent in the APBI treatment arm versus 3.0 percent among women treated with whole-breast irradiation.

Cosmetic results were substantially better with APBI versus WBI, as measured by the Harvard Breast Cosmesis Scale, with significantly more physicians and patients having reported “good” or “excellent” outcomes.

Commentary

In addition to the current findings, a number of randomized clinical trials have reached similar conclusions, including phase III trials from the NSABP B-39 in the U.S., the RAPID trial in Canada, the U.K., and European Union, noted Gary Freedman, MD, Professor of Radiation Oncology at the University of Pennsylvania’s Abramson Cancer Center.

“These have confirmed that the long-term overall survival is the same between whole breast and partial breast irradiation for early-stage breast cancer, so I think this has been settled,” he told Oncology Times.

Even so, he said there are several remaining issues to be considered. “There is some uncertainty over how broad we should make the eligibility. Early-stage disease, yes. But what about patients with larger tumor sizes, positive nodes, receptors negative, close margins, and other factors? A problem with many of the trials is they were highly selective for small, very favorable breast cancer in older women—in many cases, women who may not have needed radiation in the first place. Will the results of partial breast be as good if we open it up to more young women <50, with more adverse features to their breast cancers?”

Despite the positive results of these trials, partial irradiation has yet to be widely adopted in the U.S., according to Freedman, who estimated that it is only being used in treating perhaps 5 percent of eligible patients.
Residual Cancer Burden Predicts Outcomes for All Breast Cancer Types

BY KURT SAMSON

Using a breast cancer patient’s residual cancer burden after they have undergone postoperative neoadjuvant chemotherapy appears to be an effective prognostic indicator for both long-term tumor recurrence and survival, regardless of cancer subtype, researchers told attendees at the 2019 San Antonio Breast Cancer Symposium (Abstract GS1-09).

A pooled analysis performed on patient data from 11 cancer institutes and clinical trials was used to assess whether or not residual cancer burden (RCB) index—based primary tumor size, percentage of tumor that is invasive, and involvement of lymph nodes, as well as other clinical and individual risk characteristics such as age, T category, nodal status, and grade—might predict outcomes as earlier research has indicated.

The index was found to be very accurate in predicting both event-free and distant recurrence-free survival (EFS and DRFS). Moreover, the findings were consistent across clinical sites and predictive for all four breast biological cancer subtypes, noted William Fraser Symmans, MD, the study’s lead author, at a press conference.

The findings support a number of other studies that have likewise found accurate prognostics using residual cancer burdens as a means of estimating the trajectory of breast cancer patients as they recover.

“In recent years, many single-institution studies have shown that residual cancer burden after neoadjuvant chemotherapy can tell us a great deal about a patient’s prognosis after surgery,” said Symmans, Professor and Director of Research Operations at The University of Texas MD Anderson Cancer Center’s Department of Pathology. “We undertook this meta-analysis to help determine whether this is true for all subtypes, and how generalizable previous findings might be.”

They analyzed data on 5,161 breast cancer patients who had been treated at 11 cancer centers or had participated in clinical trials, using mixed effect models that included both fixed and random events. There were 950 EFS and 876 DRFS events during follow-up (median 65 months).

Symmans and his colleagues with the I-SPY Clinical Trials Consortium next used a special calculator created at MD Anderson to evaluate each patient’s RCB index value. Results from the 10-year follow-up analysis were then used to classify each patient’s status as RCB-I (minimal burden), RCB-II (moderate burden), or RCB-III (extensive burden). Once categorized, the team then compared each patient’s RCB status with the pathologic complete response (pCR) rates for each category.

Subtype Analysis

At 10 years, 69 percent of patients were classified as having a pCR, including 11 percent within the RCB-I category, 16 percent classified as RCB-II, and 4 percent who were determined to have had RCB-III. Seven percent of the pCR group had a recurrence or had died, compared with 15 percent of the RCB-I group, 37 percent of the RCB-II group, and 40 percent of those in the RCB-III category.

For patients with HR-negative/HER2-positive breast cancer, 43 percent had a pCR at 10 years, including 12 percent of women with an RCB-I rating, 33 percent of those rated as RCB-II, and 11 percent of those in the RCB-III group. After a decade, 14 percent of the pCR group had had a recurrence or had died, including 25 percent of the RCB-I group, 39 percent of RCB-II women, and 75 percent of patients in the RCB-III group.

Among women with HR-positive/HER2-negative cancer, 11 percent had a pCR and their 10-year EFS rate was 86 percent, which fell as RCB index increased. Among the other patients, 11 percent were classified as RCB-I, 53 percent as RCB-II, and 25 percent as RCB-III. In all, 19 percent of the pCR group had a recurrence or had died, compared with 14 percent of the RCB-I group, 31 percent of the RCB-II group, and 48 percent of the RCB-III group.

For patients with HR-positive/HER2-positive cancer, 38 percent of were determined to have had a pCR, including 20 percent of those women classified as RCB-I, as well as 33 percent of those rated RCB-II and 8 percent rated RCB-III. At the 10-year follow-up, 9 percent of the pCR group had a recurrence or had died, compared with 17 percent of the RCB-I group, 36 percent of the RCB-II group, and 55 percent of the RCB-III group.

“The measurement of the RCB index is strongly prognostic, allowing us to measure risk of recurrence with confidence,” said Symmans. “This meta-analysis of residual cancer burden provides real-world evidence of how patients are responding to neoadjuvant treatments, and calibration of RCB index to prognostic risk enables us to determine the most appropriate next steps for breast cancer patients.”

He noted that, although not all cancer centers routinely collect data on residual cancer burden, the new review and analysis demonstrates that pathologists can use this technique to get relatively accurate results to predict recurrence in women across different breast cancer subtypes.

However, the study was not without limitations, Symmans said. These included the fact that the findings were based on data from multiple institutions, which can lead to some variation in clinical methods, the handling of specimens, and other potential factors. Moreover, some of the RCB data were collected prospectively while others were collected retrospectively.

“Long-term prognosis after pCR was similarly excellent in all phenotypic subtypes. RCB index and classification was independently and strongly prognostic in all subtypes, and generalizable to multiple practice settings,” Symmans said. “Looking ahead, if we can standardize the reporting of residual cancer burden, that will only improve its usefulness in determining long-term prognosis.”

Kurt Samson is a contributing writer.

The Florence trial researchers said the cosmetic results are as good between partial breast and WBI, while the Canadian trial said the opposite. We don’t know what factors—size of the breast cancer, surgery technique, or radiation technique—determine how to get the best cosmetic result.”

How radiation is paid for is another factor, he added. “It is currently paid for by the number of treatments—if whole breast radiation pays 16-30 treatments, there is a possible bias against changing to a Florence regimen of only five treatments. More patient education about this shorter and convenient option for radiation is needed so that they feel empowered to ask if it is right for them.”

Kurt Samson is a contributing writer.