Updates from ASCO 2010: Radiotherapy and APBI

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The American Society of Clinical Oncology (ASCO) 2010 Breast Cancer Symposium, held in National Harbor, Maryland, October 1-3, 2010, included 30 presentations on radiation therapy's evolving role in local and regional tumor control.[1] This article reviews presentations on trends in hypofractionated breast radiotherapy and promising findings regarding partial-breast brachytherapy for low-risk recurrent tumors and short-term toxicities for accelerated partial-breast irradiation (APBI).

HYPOFRACTIONATED BREAST RADIOTHERAPY

Hypofractionation—delivery of total therapeutic radiation doses in larger fractions—accelerates total treatment time, reduces treatment costs, and diminishes the risk that tumor cells will develop radioresistance. In August 2010, the American Society for Radiation Oncology (ASTRO) published an evidence-based systematic literature review of whole-breast irradiation (WBI) clinical studies, concluding that WBI hypofractionation is as effective for tumor control and patient survival as conventional radiation therapy regimens.[2]

At the ASCO 2010 meeting, researchers from the University of Iowa reported data from a retrospective single-institutional records review showing that hypofractionated WBI for patients receiving breast conservation treatment has been increasingly common, utilization increased from 3% of patients in 2003 to 40% of patients in March 2010.[3]

Of 55 patients in the study, 32 received hypofractionated WBI (42.56 Gy in 16 fractions), and 23 received conventional WBI. Follow-up durations ranged from 1 to 67 months (median follow-up: 18 months), with no patient in either group experiencing local recurrence and comparable early and late morbidity rates.[3] Hypofractionation reduced treatment expenses by a third compared to traditional WBI, the authors reported.[3]

> Acute skin toxicity is more common in patients irradiated in a prone position.

A recent, well-publicized randomized prospective trial showed hypofractionated WBI is less effective against high-grade tumors than against low-grade tumors.[4] However, a team of researchers at Fox Chase Cancer Center in Philadelphia, Pennsylvania, led by Gary M. Freedman, MD, reported that long-term follow-ups are necessary to determine whether this is due to earlier recurrence of high-grade tumors compared with other tumors, or an intrinsic weakness of hypofractionation in high-grade tumors.[4,5]

Freedman's team analyzed records of patients with early-stage breast cancer treated at Fox Chase and reported that of 144 patients treated with hypofractionation, the 5-year local recurrence rate was 2.6%. The Fox Chase group showed an excess risk of recurrence for high-grade patients, but the difference was not statistically significant in this small sample.[5]

Acute grade 3 skin toxicity is significantly more common in hypofractionated WBI patients irradiated in a prone position (4 of 24 patients) than in those treated in a supine position (1 of 24 patients), a third presentation by University of Chicago researchers noted.[6] "There was a modest increase in skin toxicity and dosimetric parameters for prone treatment, but this did not result in adverse cosmetic outcomes upon long-term follow-up," the authors concluded.[6]

No potential conflicts of interest were reported for the authors of any of the three WBI hypofractionation presentations in the conference's financial disclosure report.[7]

ACCELERATED PARTIAL-BREAST IRRADIATION

Published reports of significant fibrosis-cosmesis and other short-term toxicities for accelerated APBI have overstated actual risks and continued study is "critical" to assess long-term toxicities, reported the authors of an analysis of data from the randomized phase 3 multi-institutional NSABP B-39/RTOG 0413 APBI trial of three-dimensional conformal external beam (CEBT) partial-breast radiotherapy.[8] Previous reports suggesting significant APBI toxicities were based on small, single-institution studies, illustrating the need for larger, randomized, multi-institutional phase 3 trials, reported Drexel University College of Medicine Associate Professor of Human Oncology Thomas B. Julian, MD.

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Analyzing toxicities for 1,367 patients older than 18 years randomized to APBI, at a mean follow-up of 36.7 months, the authors reported "no significant toxicity-related issues." The rates of fibrosis-cosmesis and fibrosis-deep connective tissue toxicities were 11% or lower for grade 2 toxicities and 3% or lower for grade 3 toxicities. No grade 4 toxicities were noted.

"Contrary to findings in recent published reports, the 3D conformal APBI toxicity rates in our trial are acceptably low," Julian reported at the conference. "Our trial surpasses others reported in patient number and length of follow-up, emphasizing the importance of large phase-III randomized trials with rigorous [quality assurance] to determine treatment outcomes and avoid the bias that can arise from small single-institution series. The continuation of accrual to this trial is critical so that APBI efficacy, long-term toxicity and [quality-of-life] outcomes can be accurately assessed."

A separate presentation suggested that salvage high-dose-rate (HDR) brachytherapy is effective for low-risk recurrences after lumpectomy.[9] Preliminary data comparing outcomes for Spanish patients who were treated with total mastectomy or a second conservative surgery plus brachytherapy for local recurrence between 1990 and 2004 showed comparable outcomes for the two strategies.

Of 85 patients with low-risk local recurrence involving tumors smaller than 3 cm, 48 opted for a second conservative treatment rather than total mastectomy.[9] These patients received a second lumpectomy followed by HDR brachytherapy to the tumor bed. A 3-cm margin around the tumor bed was also irradiated. A total of 30 Gy in 12 fractions was delivered to each patient over 5 days.

The comparison group received mastectomy with no radiotherapy. Local control was achieved in 84% of patients who underwent second lumpectomy plus brachytherapy, compared to 71.7% of mastectomy patients; survival after 1-year follow-up was 90.7% for brachytherapy and 88.2% for mastectomy, the authors reported.[9]

Risk of metastasis appeared comparable between the two groups. At follow-up, eight patients from the brachytherapy group had diagnosed metastasis (two regional and six distant), compared with six patients from the mastectomy group (one regional, five distant metastases). One patient from each group died.[9]

HDR brachytherapy is effective for low-risk recurrences after lumpectomy.

No patients in the study experienced high-grade complications. Grade 1 or 2 complications were not detailed, however. No patients experienced arm edema. Cosmetic results were satisfactory in 89.4% of the conservatively treated patients and 13 of 14 patients followed for at least 10 years still had their breast at follow-up. "Lumpectomy and partial-breast brachytherapy can be considered the treatment of choice in selected patients with low-risk recurrent breast tumors," the authors concluded.

The conference financial disclosure report indicates no potential conflicts of interest for the authors.[7]

Always note that findings presented in conferences may not have yet undergone as vigorous an external peer-review process as studies published in the medical journal literature. The ASCO 2011 Breast Cancer Symposium is scheduled for September 8-10 in San Francisco, California. Visit http://breastcasymposium.org/ for more information. ■

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