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Accelerated partial breast irradiation (APBI): Options and new horizons

After completing this activity, the participant should be better able to:
• Determine good candidates for hypo-fractionated whole-breast irradiation and accelerated partial-breast irradiation
• Differentiate between the various modalities of partial-breast irradiation
• Describe newer modalities and technology currently under investigation for partial breast irradiation

Breast cancer is the second most common cancer diagnosed in women. (Skin cancer is the most common.) With better screening modalities such as annual mammography and MRI, more women are diagnosed with breast cancer at earlier stages. Depending on the location of the tumor and patient breast size, breast conservation therapy is usually an option for many women instead of mastectomy. Several randomized trials have demonstrated that breast irradiation substantially reduces the risk of local recurrence and prevents the need for subsequent mastectomy in patients with invasive breast cancer.1,2 Breast conservation therapy typically requires lumpectomy surgery with or without nodal evaluation and whole-breast radiation treatments. Whole-breast radiation treatments have historically required 6-57 weeks of treatment (30-33 fractions). Hypofractionated whole-breast radiation (involving a higher dose of radiation per fraction, with fewer total fractions), has become another option for early-stage breast cancer, constituting 42.5 Gy in 16 fractions of radiation therapy.3 Whelan et al., in their phase III randomized trial, compared standard fractionation to hypofractionated whole-breast irradiation and found similar local control and cosmetic results at 10 years. However, hypofractionated whole-breast radiation is not an option for every candidate for breast conservation therapy as ASTRO consensus guidelines require favorable dosimetric parameters that usually rely on breast size, T1 or T2N0 disease, age ≥50 years old, and no prior chemoradiation.4

Over the years, it has been discovered that 15-30% of women fail to complete whole-breast radiation therapy treatments as part of their breast conservation therapy (BCT).14 Contributing factors for this high incompletion percentage include inaccessibility to a nearby radiation facility, development of toxicity, and/or the inconvenience of 6-57 weeks of daily radiation treatments. Common early toxicities include fatigue, edema, and skin erythema or blistering, all of which can have an impact on quality of life. Clinical trials evaluating the role of breast irradiation following breast-conserving surgery suggest that if local recurrences occur, they are most likely (70-80% of cases) to develop at the site of the primary tumor with or without radiation therapy. The risk of recurrence in the breast away from the primary tumor site is only 1.5-3.5%.11,12 These observations have led to the hypothesis that limiting radiation therapy to the primary tumor site—a technique called accelerated partial breast irradiation (APBI)—rather than treating the whole breast may result in potentially less morbidity and shorter overall treatments in early-stage breast cancer.

Partial-breast radiation therapy allows for completion of radiation in a faster time frame, thus allowing a more convenient treatment for women. Larger doses per fraction are used while limiting the volume of normal breast tissue exposed to radiation. The lumpectomy cavity is treated with a 1.2-2.5 cm margin, depending on the technique of APBI used. Even though high dose of care is still whole-breast radiation, the frequency of partial-breast radiation in breast conservation therapy has increased due to promising clinical data and perceived patient convenience. Several consensus guidelines outline the ideal candidate for partial-breast radiation outside of a clinical trial setting. As more institutions have started implementing PBI techniques in their practices, different medical societies have published guidelines—among them the American Society for Radiation Oncology (ASTRO), Groupe Europeen de Curietherapie-Europeen Society of Therapeutic Radiation Oncology (GEC-ESTRO), American Society of Breast Surgeons (ASBS), and American Brachytherapy Society (ABS). There are minor variations among the different radiation therapy: Brachytherapy and conventional 3-D external beam radiation therapy treatments are usually given over a five-day period twice per day while intraoperative radiation is delivered at the time of surgery in the operating room in a single fraction. Intertitial brachytherapy is the oldest technique for APBI. This technique uses multiple interstitial catheters that are placed in the breast with either a template or free-hand and usually with some image guidance (ultrasound or CT scan). This technique is very operator-dependent and requires an experienced physician to produce an implant of excellent quality. The catheters can be loaded with either low dose rate (LDR) or high dose rate (HDR) sources. HDR is the most common because iridium-192 sources can be used on an outpatient basis. Intracavitary balloon (Mammosite and Contura) or strut-based brachytherapy (SAVE, Contura, or Mammosite), intraoperative radiation and 3-D external beam radiation. Brachytherapy and conventional 3-D external beam radiation therapy treatments are usually given over a five-day period twice per day while intraoperative radiation is delivered at the time of surgery in the operating room in a single fraction.

Clinical evidence for partial-breast irradiation

The TARGIT, a phase III non-inferiority trial, compared single-dose targeted intraoperative radiotherapy (TARGIT) versus fractionated external beam radiotherapy (EBRT) for breast cancer.15 From 2000-2012, a total of 3,451 patients were randomized between APBI and whole-breast radiation in 33 centers in 11 countries. Fifteen percent of women in the APBI arm were treated with additional EBRT due to adverse pathological features. With a median follow-up of two years and five months for the whole cohort, the five-year risk of local recurrence was 3.3% with TARGIT and 1.3% with the WBRT, (p=0.04). The TARGIT trial using megavoltage electrons has a median follow-up of 5.8 years.15 The five-year risk of ipsilateral breast recurrence was 4.4% with IORT and 0.4% with the standard WBRT. The overall mortality was not different between both groups, with a five-year survival rate around 97%.

Initial phase II trials have reported low rates of local recurrence and acceptable rates of cosmesis (with at least 80% good to excellent cosme- sis outcomes) following APBI with 3D-CRT. Currently, the largest U.S. randomized control trial (RT05 0413 / NSABP 39) comparing whole breast radiation to partial-breast radiation has finished accruing, and we are awaiting final results. More than 4,000 women participated in this trial nationwide. PBI treatments were delivered via interstitial brachytherapy, intracavitary brachytherapy, or 3-D external beam radiation at the discretion of the treating physicians.
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