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Accelerated partial breast irradiation: An advanced form of hypofractionation

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ABSTRACT

Altered fractionation schedules are being increasingly investigated in the treatment of breast cancer. Two such schedules that are frequently compared are hypofractionated external beam radiation therapy (HERT) and accelerated partial breast irradiation (APBI). Though these two modalities are considered separately, APBI is actually an advanced form of hypofractionation, where acceleration of the treatment is possible due to the smaller volume being irradiated. HERT as well as APBI are investigational at present and are being tested in randomized trials. This article looks at the advantages of APBI as a hypofractionation schedule.

KEY WORDS: Accelerated partial breast irradiation, hypofractionation, interstitial brachytherapy

Altered fractionation schedules are being investigated extensively in the treatment of breast cancer with radiation. Two such treatment techniques are hypofractionated external beam radiation therapy (HERT) and accelerated partial breast irradiation (APBI). These two techniques are often compared for their relative advantages and disadvantages, as can be seen from an article in the previous issue of this journal.^[1] Although these two treatment modalities are considered separately, APBI is in fact an advanced form of hypofractionated treatment, wherein further acceleration of the dose is possible as the irradiated volume is less.

Data on both HERT and APBI is still evolving and both these modalities are currently investigational. The randomized trial for HERT by Yarnold *et al.* had cosmesis as the endpoint and therefore valid conclusions for the comparable local control rates cannot be made from this study.^[2] The Whelan trial was designed to detect a 5% difference in the local control rates between the two arms,^[3] but it was done in a very selected group of patients, i.e., those who had small tumors with clear margins and a negative nodal status. Patients with large breasts were also excluded from the study as higher dose per fraction has a negative impact on the cosmetic outcome in women with large breasts. There are large randomized trials going on in UK, and till the data from these trials have been evaluated, this treatment modality remains experimental.^[1,4]

Regarding APBI, apart from the two trials, RTOG and the European trial, there are three more trials in progress (five randomized trials in all), with the expected accrual ranging from 800-3000 patients per trial, which will generate large amount of

data.^[5-9] The TARGIT trial is comparing whole breast radiation therapy with APBI using a 50 kV x-ray source, which is used intraoperatively to deliver the radiation of 5-8.5 Gy in a single fraction. Another trial of intraoperative treatment is ELIOT, in which patients are treated with a single fraction of intraoperative electrons in the experimental arm. Recently, a randomized trial with 258 patients has been published by Polgar *et al.*, which showed comparable outcomes with APBI and whole breast radiation therapy.^[7] As all the techniques involve some form of brachytherapy, which is invasive, there is some concern about the use of such techniques.^[1] Attempts are therefore being made to achieve similar dose distributions with external beam irradiation, in the form of three-dimensional conformal radiation, or intensity-modulated irradiation for APBI.

One of the main advantages with APBI is reduction in the overall time. This has an impact on both the patient and the hospital resources. With the techniques of interstitial implant and mammosite, which are at present the common techniques, the treatment time is reduced to 1 week. In situations where the treatment is done intraoperatively or perioperatively, the entire course, including surgery and radiation is completed in 2-3 weeks. This is definitely a huge advantage over the other regimens of external beam radiation. In the hypofractionation regimens that have been evaluated by Yarnold *et al.*, though the number of fractions is reduced to 13 the overall treatment time is still 5 weeks. In the trial by Whelan *et al.*, the overall treatment time is more than 4 weeks for whole breast radiation. In this trial, boost radiation was not considered. However, with the current

evidence from the EORTC trial in support of the benefit of boost radiation, boost should be considered in all patients and this would add one more week of radiation. Both these schedules will have favorable resource implications for the radiotherapy services but may not have that much impact as far as patients are concerned, especially in the case of those traveling long distances for the treatment.

While there have been concerns about the dose distribution with mammosite, further advances are being explored, wherein the balloon system simulates the multicatheter brachytherapy. With the availability of such techniques, treatment delivery will become more conformal and without much side effects. All these techniques have tremendous potential in the West, where cases are detected at an early stage with screening and the majority of the patients fulfill the criteria for APBI. In addition, APBI will also resolve the problems of sequencing of chemotherapy and radiation, as the radiation is delivered immediately after surgery.

In the Indian context and in other countries where the resources are limited APBI with brachytherapy appears to be more a feasible option than other techniques of APBI, though it requires some technical expertise. Brachytherapy machines are more common than machines for megavoltage irradiation and are less expensive for patients. With the treatment of these patients on brachytherapy machines, the possibility arises for accommodating more numbers of patients on the megavoltage machines, which is also a problem due to limited resources. The safety and feasibility of APBI with brachytherapy in the Indian scenario has been shown by us earlier.^[10]

While interest in HERT is limited to UK and Canada, mostly due to the lack of long-term data on the cardiac effects, APBI is evolving in all parts of the globe as can be seen from the ongoing randomized trials which are being conducted in the different centers. Though the pathological studies by Holland *et al.* have shown the presence of tumor cells outside the tumor bed, this need not be of much concern as there is evidence that 70-90% of the local recurrences are seen at the tumor bed alone, with or without radiation therapy after breast conservation.^[11] The recurrences outside the tumor bed is similar to that of contralateral breast cancer and it is now being questioned whether these are true recurrences or second primaries. The impact of APBI will therefore be definitely more than that of HERT all over the world.

HERT also will have a huge impact on the resource-sparing strategies in countries with limited resources. However, implementation of proper technique and planning at least in two-dimensional view on the treatment planning system, with appropriate normalization and use of tissue compensation for

breast (wedges), will be necessary for all these patients. In a publication from our centre in the earlier years, radiation with a high dose per fraction of 2.5 Gy, treatment without use of tissue compensation in the form of wedges and higher boost dose was associated with impaired cosmetic outcome on univariate analysis.^[12] While HERT appears to be an attractive option, it can have a very serious adverse impact if not done properly.

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