Accelerated partial breast irradiation with high dose rate brachytherapy for early breast cancer

Globally breast cancer is the most common malignancy among women. In India, it is the commonest cancer in Mumbai, Delhi and Bangalore with Age Incidence Rates (AAR) of 28.6, 28.1 and 22.1 per lac women respectively[1]. Though, majority of patients present in advanced stages, but due to increasing public awareness and better health care facilities, there is a rising trend in early breast cancer (Stage I-II) patients.

The standard management for early breast cancer (EBC) is breast conservation therapy (BCT). Several large prospective randomized trials including National Surgical Adjuvant Bowel and Breast Project study[2] and the European Institute of Oncology trial[3], comparing modified radical mastectomy to BCT, have clearly demonstrated equivalent long-term disease-free and overall survival. BCT characteristically consists of breast conservation surgery (BCS) followed by whole breast radiotherapy (WBRT) plus boost to the lumpectomy site. Traditionally WBRT requires a period of 6–7 weeks, where the patient is treated five times per week. The major advantages of BCT are superior cosmetic outcome and the reduced emotional and psychological trauma afforded by this procedure compared with conventional mastectomy. The principal disadvantage of BCT is its more complex and prolonged treatment regimen requiring approximately 6-7 weeks of external beam radiation therapy (EBRT) which poses problems for some patients such as the working woman, elderly patients, and those who live at a significant distance from a treatment center[4,5]. Thus the logistical problems of BCT are primarily related to the protracted course of WBRT.

To overcome this problem, there has been a steady interest in accelerating the course of irradiation to the site carrying the maximum risk of recurrence i.e. lumpectomy site. By confining treatment to a limited volume of breast tissue adjacent to the lumpectomy cavity, it may be possible to give a larger dose per fraction, decreasing treatment time. Partial breast irradiation as a single RT modality began with interstitial brachytherapy[6]. With the help of brachytherapy, partial breast irradiation (PBI) could be carried out over a 3 to 7 day period immediately following BCS, thus markedly reducing treatment time. Additionally, brachytherapy inherently provides a higher central dose to the volume having a potential risk for recurrence.

Majority of failures are located at the site of surgical resection. In-breast failures located beyond the area of the lumpectomy cavity; occur in only 1.5–3.5% of patients.[7,8,9] The true benefit of WBRT seems to be the reduction of failures in the breast tissue immediately surrounding the lumpectomy cavity. Equivalent local control rates can be achieved with appropriately directed PBI. Two to 5-year follow-up data are now being reported for PBI from several institutions suggesting equivalent safety and efficacy compared with whole breast RT.[10,11] Additionally, several different methods of accelerated breast RT have been described, including both catheter and balloon-based brachytherapy delivering treatment within 4–5 days and intra-operative treatment delivering RT entirely at the time of lumpectomy.[12-16] Multiple-catheter brachytherapy is presently the most widely used technique. Historically this was heavily dependent on operator experience with significant variability in target coverage, homogeneity, and overall outcome. Improvements in the technique of catheter placement using various forms of image guidance coupled with 3D dosimetry now provide the tools for reproducible catheter placement and improved outcome.[17]

In an effort to explore whether BCT could be effectively delivered in an abbreviated time period shortly after lumpectomy, Vicini et al initiated a pilot study in March 1993 testing the technical feasibility and acute toxicity of low dose rate (LDR) brachytherapy as the sole RT modality in 99 patients with Stage I and II breast cancer and reported excellent results.[18,19] In June 1995, they...
began a parallel trial\textsuperscript{20} of outpatient high-dose rate (HDR) brachytherapy as the sole method of RT in the same subset of patients. The principal advantage of this form of brachytherapy was the ability to deliver the RT on an outpatient basis. Thirty-seven patients with Stage I–II breast cancers received radiation to the lumpectomy cavity alone using an HDR interstitial implant with Ir-192. A minimum dose of 32 Gy was delivered on an outpatient basis in 8 fractions of 4 Gy to the lumpectomy cavity plus a 1-2 cm margin over consecutive 4 days. HDR brachytherapy treatment was both technically feasible and well tolerated. Median follow-up was 31 months. There was one ipsilateral breast recurrence for a crude failure rate of 2.6% and no regional or distant failures. Wound healing was not impaired in patients undergoing an open-cavity implant. Three minor breast infections occurred, and all resolved with oral antibiotics. The cosmetic outcome was good to excellent in all patients.

Arthur et al.\textsuperscript{21} reported their experience in 44 patients with partial breast brachytherapy after lumpectomy for selected patients with early-stage breast cancer patients with clear resection margins and 0–3 positive lymph nodes. The HDR PBI dose was 34 Gy in 10 fractions within 5 days in 31 patients, and the LDR dose was 45 Gy given at a rate of 50 cGy/h in 13 patients. After a median follow-up of 42 months (range 18–86), all patients remained locally controlled. The overall rate of good/excellent cosmetic outcome was 79.6% overall and 90% with HDR PBI.

Strnad et al.\textsuperscript{22} treated 176 low risk EBC patients with brachytherapy alone after BCS. None of the patients developed recurrence. Peri-operative breast infection was noted in 0.6% patients. Late toxicity i.e., hypersenssation, hyperpigmentation, fibrosis, or teleangiectasia was observed in 1–12% of all patients. Grade I teleangiectasia was observed in 4.7%, grade II in 0.6%, and grade III also in 0.6% of patients. Excellent or good cosmetic results were observed in 92–95% of patients.

A phase I/II study completed by the Radiation Therapy Oncology Group (RTOG 95-17) has shown promising results.\textsuperscript{23} This trial was conducted from 1997 to 2000 and designed to evaluate the technical feasibility and reproducibility, cosmetic results, complications, and local control rates achieved with APBI. Outcome results from this study are pending as additional follow-up is needed; however, the ability of multiple institutions reproducibly to construct acceptable implants and a report with median follow-up of 2.7 years describing acceptable acute toxicity rates has been published in abstract form.\textsuperscript{23}

Although a variety of dose schedules have been used in PBI treatments with HDR brachytherapy, the most common prescription dose is 34 Gy delivered in 10 fractions, with fractions given twice daily over a period of 5 days. The various other dose schedules used by different authors are 32 Gy in 8 fractions\textsuperscript{20}, 36.4 Gy in 7 fractions and 30.3 Gy in 7 fractions.\textsuperscript{24} American Brachytherapy Society\textsuperscript{25} has recommended 34 Gy in 10 HDR brachytherapy fractions over 5 days (twice daily fractions) to the lumpectomy cavity along with 1-2 cm margin.

The number of published experiences with APBI continues to grow. Although, when considered individually no firm conclusions can be drawn about the validity of this treatment approach, collectively the evidence provides strong support for APBI. The critical components shared by each of these treatment experiences include patient selection and adequate brachytherapy quality assurance. When attention is given to these components, the local recurrence rate is consistently less than 5% with good to excellent cosmetic results recorded in the majority of patients.

Besides clinical benefits, the logistic benefits of PBI in Indian Scenario are manifold. Firstly, due to short treatment period of about 7 days following surgery, the entire local treatment (Surgery + APBI) can be completed in about 10 days time as compared to 2 months with traditional WBRT following surgery. This would avoid the multiple visits required for WBRT especially patients coming from distant place. Secondly, this would reduce the workload of the radiation oncology staff as the resources are limited in our country. Thirdly, this will help in shortening the waiting list for all patients requiring RT since most centers in India are busy and overstressed. Lastly, it can be cost effective too.

**REFERENCES**

8. Clark RM, McCulloch PB, Levine MN, Lipa M, Wilkinson RH, Mahoney