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ORIGINAL

Application of Interstitial High Dose Rate (HDR) Brachytherapy with Microselectron HDR for early Breast Cancers

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Abstract

Background: Breast cancer forms a commonest cancer in women, and due to earlier detection and awareness, more patients come to hospital at early stages. Treatments for early breast cancers have evolved from radical mastectomy towards breast conserving surgery (BCS) and radiotherapy. In high-risk patients, a boost dose to tumor bed, 15-20 Gy is required, by high energy electrons or by interstitial brachytherapy (IBT). As our centre did not have high energy electron linear accelerator, we resorted to interstitial brachytherapy for boost dose to tumor bed. The pattern of care followed at our center in early breast cancers and biologically effective doses (BED), efficacy of treatment, needs documentation. **Methods:** From the year 2017, interstitial BT for BCS patients are carried out at our center with microSelectron (M/s Nucletron). A 2-plane template is used to implant needles with treating 'distance' 1.2 cm. 10mm on either side of the catheter was kept cold to avoid excess skin/subcutaneous excess dose, maintain cosmoses and prevent skin spots. Two regimens, 1) HDR BT and External Beam Radiotherapy (EBRT) and 2) Accelerated Partial Breast Irradiation (APBI) with only BT as mono-therapy are followed. 78 patients were treated in 6 years. In 73 patients, doses to 100% covering line was delivered with 6h inter-fraction BT as 8 Gy x 2 fractions(n=1), 4 Gy x 4fr (n=27), 3.65 Gyx4fr (n=24), 3 Gyx4fr (n=19), 3 Gyx3fr (n=2) along with EBRT by Tele-cobalt tangential fields, 5fr/week, breast cone, 40Gy/15 fr equivalent of 46.7 Gy in 2Gy/fr. Second group (mono-therapy) had 5 patients, 3.65 Gy x 10fr (n=1), 3.40 Gy x 10fr (n=3) and 5.88 Gy x 10fr, completing treatment in 5 days. **Results :** BED_{10} for BT = 19.93 Gy for 3.65Gy x 4Fr; This BT dose equal to EBRT dose In 2Gy/fr 8.3 = 16.61 Gy. 40Gy/15Fr @ 2.67Gy/Fr is equal to dose of 42.3Gy at 2Gy/fr. Total dose of whole regimen is 58.9Gy (<1.5% to 60Gy). BED_{10} for BT of 3.65Gy x 10Fr is 49.83G, which is equivalent of 41.5Gy EBRT total dose at 2Gy/fr, 5 fr/week. There was no toxicity recorded on short term follow up. **Conclusion:** As more cancer patients are treated with breast conservation, HDR BT can be practiced, with available brachytherapy machines. Treatment times are very short in breast interstitial BT, and patients tolerate these treatments well. In centres with low energy linacs without electron facility, still this method could help in treatments of early breast cancers.

Key Words: Breast conservation, Breast implants, High dose rate brachytherapy, Early breast cancers

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Introduction

Treatments for early breast cancers have evolved from radical mastectomy towards breast conserving surgery (BCS) and radiotherapy, for more than 40 years. In high risk patients, a localized boost dose to tumor bed, about 15-20 Gy is required. This is achieved by high energy electrons or by interstitial brachytherapy (BT). The EORTC trial investigated the role of boost dose in breast conserving therapy and demonstrated significant better local control rate with higher radiotherapy dose in women of around 50 years age group [1]. They analysed 2661 randomised patients who received a boost dose of 16 Gy to the primary tumor bed after complete tumorectomy and 50 Gy dose by External Beam Radiation Therapy (EBRT). In the above analysis, 63% received boost dose by high energy electrons, 28% with photons and 9% with interstitial brachytherapy. Local recurrences (LR) were compared in these three groups. LR were 4.8% in electron group, photon boost group 4.0%, and interstititial boost 2.5%. Based on the outcome of the above study, they highlighted that interstitital boost has given similar local control and same extent of local fibrosis.

In another report[2], pulsed doserate (PDR) brachytherapy was delivered as boost in 113 patients who received median dose of 50 Gy EBRT(range 46 to 52Gy). 20-25Gy boost dose was based on the pathologic grading, or 15Gy in T2-G3 stage. At median follow up of 61 months, they reported 4.4% local failure, and actuarial 5 and 8 year local recurrence free survival rates 95% and 93% respectively. Cosmesis was 90%, and 14 out of 113 patients experienced Grade III (planar telangiectasia) and none of the

patients had Grade IV late toxicity of the skin. 25 Gy boost dose resulted in significantly higher rate of toxicity. The American Brachytherapy Society (ABS) recommends a dose fractionation scheme that yields early and late effects are approximately equivalent to those of 10 Gy to 20 Gy followed by 45 to 50 Gy of EBRT [3]. In our hospital, linear accelerator with high energy electron facility is commissioned in the year 2023 only. We resorted to boost dose with high dose rate (HDR) in breast conserving treatments during 2017-2023. Our experience is highlighted.

Materials and Methods

Implantation Procedure

We have an High Dose Rate(HDR) brachytherapy, 6 Channel MicroSelectron HDR (M/s Nucletron, Netherlands) with Iridium-192, capacity of 10Ci commissioned during 2013. From July 2017 we started interstitial BT for BCS patients and now completed >5 years. A 2 plane template supplied from along with the machine is used, along with flexible plastic catheters (Flexicath Single Leader, Trichy, India). Implantation done with length and number of catheters decided by surgeons based on the extent of primary disease. Dwell points were selected continuous, and the treated length of each catheter determined by the Nucletron Ruler. 10mm on either side of the catheter is left cold, to avoid excess dose to the skin, avoid excess skin/subcutaneous excess dose and to preserve cosmesis. All were two plane implants with treating distance 1.2cm. Sometimes, the treatment distance was altered to avoid increase of hot zones and better uniformity of dose. Dose was prescribed to 100% covering line as per Paris Technique (85% delivering basal dose). For IBT, inter-fraction interval was kept minimum 6 hours, a gap between two successive HDR, IBT fractions

External Beam Radiotherapy (EBRT)

In our center, cobalt bunker houses HDR, BT machine also. EBRT was delivered by Theratron 780E Telecobalt machine, pair of tangential fields with breast cone. Following interstitial brachytherapy (IBT), they received 40 Gy in 15 Fractions, at 5Fr/ week, without treatments on Saturdays, Sundays.

Details of treatments

Two types of regimens were followed, based on the decision by clinical board. As the clinic wanted to evolve an optimal dose prescription, various fraction sizes were prescribed in these patients.

1. In the first group, 73 patients completed HDR BT was followed by External Beam Radiotherapy (EBRT). Following are the details of doses delivered. 8Gy x 2 fr (n=1), 4Gyx 4fr (n=27), 3.65 Gy x 4fr (n=24), 3 Gy x 4fr (n=19), 3Gy x 3fr (n=2)
2. In second group, Accelerated Partial Breast Irradiation (APBI) (only IBT) as mono-therapy was carried out in 5 patients. The doses prescribed in these patients were
3. In these patients were 3.65Gyx10fr(n=1), 3.40Gyx10fr(n=3) and 5.88Gy x 10fr (n=1),. They completed their full course of IBT in 5 days.

The geometry of implanted catheters and the covering isodose pattern are shown in Fig.1. It can be seen that the treatment planning and prescription of dose to 100% covering volume with adequate basal dose of 85% isodose line.

Fig.1 Implant geometry in CT image

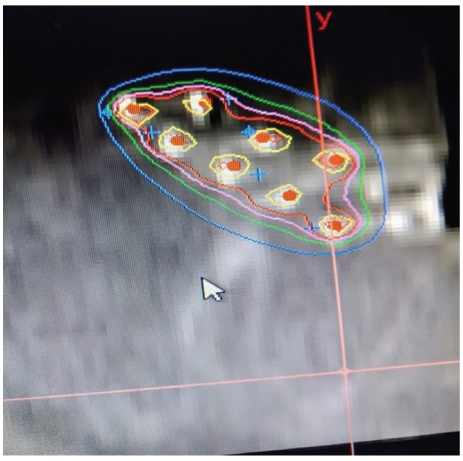

Fig.2 Resultant isodose pattern

Table 1: BED values for all the regimens IBT+EBRT or IBT alone in CCHRC

Group	IBT Dose Schedule Dose /Fr and Number of fractions	EBRT Equiv. BED Gy_{10}	EBRT Dose Gy in total fractions	EBRT Eq. Dose Gy @2Gy/fr	EBRT + IBT Eq. Gy	Pattern of care in our center
1	3.00Gy x 3fr (n=2)	9.75	40 in 15	42.3	52.05	
	3.00Gy x 4fr (n=19)	13.00	40 in 15	42.3	55.30	*Opti-
	3.65Gy x 4fr (n=24) *	16.60	40 in 15	42.3	58.90	mized
	4.00Gy x 4fr (n=27)	18.67	40 in 15	42.3	60.97	
	8.00Gy x 2fr (n=1)	24.00	40 in 15	42.3	66.30	
2	3.40Gy x10fr	45.56		37.97	37.97	*Opti-
	3.65Gy x10fr *	49.82	No EBRT	41.50	41.50	mized
	5.88Gy x10fr**	93.37		77.87	77.87	**Hot

Biologically Effective Doses (BED)

BED values were estimated to see the effectiveness of treatments, using the Linear Quadratic Model (LQ) model (Refer Equations 1,2,3). Table-1 shows the BED values for all the regimens.

$$\mathbf{BED}_{\mathbf{EBRT}} = n.d[\ 1+ d/(\alpha/\beta)] \quad \text{——} \quad (1)$$

$$\mathbf{BED}_{\mathbf{HDR\ BT}} = d[1+d(\alpha/\beta)] \quad \text{——} \quad (2)$$

$$\mathbf{BED}_{\mathbf{EBRT\ Eq\ HDR\ BT}} = \mathbf{BED}_{\mathbf{HDR\ BT}}/[n.2(1+2/10)] \quad \text{——} \quad (3)$$

Results

Table-1 highlighted the dose prescriptions and calculated EBRT equivalent total dose to the selected target volume of the breast. 40Gy/15Fr @ 2.67Gy/Fr is equal to dose of 42.3Gy at 2Gy/fr. Total dose of whole regimen (1) is 58.9Gy (which is just <1.5% to 60Gy). For monotherapy, regimen (2), the standardized prescription is 3.65Gy x 10Fr followed at our center. BED_{10} for BT of 3.65Gy x 10Fr is 49.83Gy, which is equivalent of 41.5Gy EBRT total dose at 2Gy/fr, 5 fr/week. There was no short term toxicity recorded on till their last follow up. Patients' compliance was satisfactory.

Discussion

As more patients are seen fit for breast conservation, HDR BT can be practiced for delivering boost dose to high risk group, substituting linear accelerator treatments. Based on our experience on 78 patients highlighted in this study 3.65 Gy/fraction has been standardized for future patients. An earlier study in India, in a non-randomized pilot group of 10 patients [4] reported 100% local control in treated patients. Dose rate effect on total fraction dose delivered with HDR, had not been outlined in literature. It is common that as the Ir-192 high intensity source decays, in a useful span of 4 to 6 months, the BCS patients are treated at different dose rate, with total fraction size remains constant. There was a report based on experience with low dose rate manual Ir-192 implants [5]. They treated with linear activities ranging from 1.3 to 1.8 mCi/cm. In this report, they highlighted that in the patient groups with mean dose rates less than 0.53 Gy/hr local recurrence were encountered, whereas dose rates 0.56 Gy/hr have shown recurrence free. Local failure was more with implant dose rates < 0.3Gy/hr. Incidence of normal tissue complications and poor cosmetic outcome were correlated to high dose rates > 1Gy/hr. In another study [6], the radiation electron boost dose was 16 Gy, and dose by fractionated HDR brachytherapy were 12 to 14.5 Gy in their group of 207 patients. 5 year local control was 91.4% and they reported good cosmetic results in 88.5% of total HDR BT boost groups, which gives confidence to obtain explained consent in favour of interstitial boost brachytherapy in breast conservation. The role of HDR brachytherapy in breast conservation is explained by Polgar et al [7] based on long term results. 100 early breast cancers underwent conservative surgery, with whole breast irradiation and boost implantations. Multi-fractionated HDR boost was delivered with different doses 4Gy x 3 fr (n=19); 4.75 Gy x 3 fr (n=70); 6.4 Gy x 2 fr (n=1). They reported only 7% ipsilateral breast failures 8 year survivals 'disease free' 76.1%; 'cancer specific' 82.8%; and 'overall survival' 80.4%. Cosmetic outcome were, 'excellent' 17%; 'good' 39%; 'fair' 33% and 'poor' in 11%. Late radiation effects in 91% of patients were, Grade 3 Fibrosis in 6.6% and Grade 3 Telangiectasia 2.2%. They concluded good long term tumor control with acceptable cosmetic outcome and low rate of Grade 3 radiation effects. Unlike external radiotherapy boost with electrons, brachytherapy dose pattern is well localized with least peripheral doses to proximal critical structures like heart or contra-lateral breast. Accelerated Partial Breast Irradiation (APBI) (only IBT), 34 Gy delivered in 10 fractions either 2 fractions/day in one week, or once daily fractions for 2 weeks, reported by an image guided clinical protocol in 40 patients [8]. They used paired applicators, and patient-specific 3 dimensional dosimetry to deliver prescribed dose to 100% isodose line. Same researchers reported their results from their further clinical trials [9,10]. In this present study, we also used same total dose of 34 Gy in 10 fractions for APBI group.

From our experience we recommend that implant catheters used for HDR IBT shall be of correct specifications. Otherwise there will be bending of catheters leading to source stuck problems, and probability for incorrect dose delivery. Treatment times are very short even with low activity HDR source also. In some centres where HDR machine is housed inside Cobalt Bunker like ours, EBRT dose could be delivered in succession to HDR fractions. The above treatments were held at our hospital, when linear accelerator facility was not available, therefore no conflicts of interests faced by surgical oncologists, to practice this IBT boost in all breast conservation patients. Also, as the procedure of placement of treatment plastic catheters in situ is intra-operatively carried out, the boost tumor volume could be accurately selected. A preliminary communication on our experience was outlined earlier [11]. The interstitial HDR boost in BCS appears to be easy to practice and could be implemented in all the brachytherapy centres in India. In hospitals who do not have linear accelerators, boost dose can be delivered using HDR brachytherapy machine. In countries with earlier diagnosed breast cancers large in number (such as Middle East Countries), HDR BT can be practiced, as more cancer patients are treated with breast conservation.

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