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Accelerated partial breast irradiation using external beam radiotherapy—A feasibility study based on dosimetric analysis

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ABSTRACT

Aim: To investigate the feasibility of using External Beam radiotherapy for accelerated partial breast irradiation by a comparative tumour and normal tissue dose volume analysis with that of high dose rate interstitial brachytherapy.

Background: Accelerated Partial Breast Irradiation (APBI) is more clinically appealing because of the reduced treatment course duration and the irradiated area. Brachytherapy application is more dependent on the clinician's expertise when it is practised free hand without image guidance and a template. It happens to be an invasive procedure with the use of local anaesthesia which adds patient discomfort apart from its cost compared to External Beam Radiotherapy. But APBI with brachytherapy is more commonly practised procedure compared to EBRT owing to its previous reults. Hence in this research study, we intend to explore the use of EBRT with the radiobiological corrections for APBI in the place of brachytherapy. It is done as a dosimetric comparison of Brachytherapy treatment plans with that of EBRT plans.

Materials and methods: The computed tomography images of 15 patients undergoing ISBT planning were simulated with conformal photon fields. Various dose volume parameters of each structure were obtained from the DVH generated in the brachytherapy and the simulated external beam planning which can correlate well with the late toxicity. The plan quality indices such as conformity index and homogeneity index for the target volume were computed from the dosimetric factors. The statistical *p* values for CI, HI and normal tissue dosimetric parameters were calculated and the confidence levels achievable were analysed. The dose prescribed in brachytherapy was 3400cGy in ten fractions. The equivalent prescription dose for the external beam radiotherapy planning was 3000cGy in five fractions applied with radiobiological correction.

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All the fifteen patients were with complete lung data and six were with left sided tumours having complete cardiac data. The lung dosimetry data and the cardiac dosimetry data of the patients were studied. Lower percentages of lung and cardiac V_{20} and V_5 volumes were obtained with conformal planning. The conformity of radiation dose to the tumour volume was akin to the interstitial brachytherapy planning. Moreover the external beam planning resulted in more homogenous dose distribution. For the sampled population, the statistical analysis showed a confidence level of 95% for using EBRT as an alternate to multi catheter ISBT.

Conclusion: The EBRT planning for Accelerated Partial Breast Irradiation was found to be technically feasible in the institution where the interstitial brachytherapy happens to be the only available technique as evident from the dose volume parameters and the statistical analysis.

1. Background

Accelerated Partial Breast Irradiation (APBI) decreases the duration of entire radiotherapy course.[1] The reduced treatment volume makes APBI more appealing to both clinicians and patients. The uses of brachytherapy either as HDR or LDR interstitial implants have shown promising results which are obvious from the published research works.[2,3] But the interstitial implant technique can be more complex and operator dependent. The implant application is usually done with image guidance (Ultra sound/mammography images) using a template which plays a major role in ensuring uniform and accurate implants. Fewer oncologists prefer doing a free hand application without a template guidance which needs more expertise.

Radiobiological models based comparison of APBI techniques was done by Bovi J et al.[4] Partial Breast Irradiation techniques for early stage breast carcinoma were evaluated by Agata et al.[5] A dosimetric analysis was detailed by Cozzi et al. as a clinical experience of 3D conformal partial breast irradiation.[6] Maia et al. and Vicini et al. studied the accelerated partial breast irradiation using photon fields.[7,8] Dosimetric study of different accelerated partial breast irradiation techniques, such as 3DCRT, IMRT and Mammosite application, was evaluated by Khan AJ et al.[9] Patel RR et al. dosimetrically compared the 3DCRT APBI with that of multi catheter interstitial implant brachytherapy for prone and supine position in helical tomotherapy.[10]

2. Aim

In this study, we explored the feasibility of using external beam radiotherapy using three dimensional conformal photon beams for APBI as an alternate practice to a freehand interstitial brachytherapy with dosimetrical and statistical analysis. The comparison was done with interstitial brachytherapy, since it is the only available APBI technique practiced at the institution.

3. Materials and methods

3.1. *Patient selection*

Fifteen patients undergoing the APBI with interstitial brachytherapy technique were enrolled and approved for the feasibility study.[11] The patients underwent partial mastectomy and negative sentinel lymph node biopsy or axillary dissection for T1/T2 invasive duct carcinoma as a part of breast conservation surgery between July 2009 and October 2011 (see Table 1). Pre-treatment computed tomography images were taken as guidance to assess the distance of the tumour bed from the known landmarks or from the skin surface. The distances were marked on the patient body. Flexible plastic implant tubes were inserted into the tumour cavity as a free hand application.

3.2. *Treatment planning*

After the insertion of interstitial tubes, the patients underwent a CT simulation for the treatment planning. The CT images were sent to the PLATO treatment planning system (Version 14.2.6. NucletronBV, the Netherlands). The Clinical Target

Table 1 – Patient selection.

Pt. no	Age (yrs)	Rx site	Lesion size (cm)	No. of negative nodes	Surgical margin
1	61	L Breast	3.0	20	−ve
2	70	R Breast	2.5	25	−ve
3	63	R Breast	1.9	20	−ve
4	65	R Breast	2.8	21	−ve
5	68	L Breast	3.0	23	−ve
6	71	L Breast	2.1	22	−ve
7	69	R Breast	2.7	25	−ve
8	70	R Breast	1.8	20	−ve
9	63	L Breast	1.6	23	−ve
10	61	L Breast	2.5	20	−ve
11	55	R Breast	3.0	22	−ve
12	58	R Breast	2.5	21	−ve
13	60	R Breast	2.7	24	−ve
14	62	R Breast	2.2	23	−ve
15	64	L Breast	1.2	22	−ve

Table 2 – External beam plan parameters.

Pt. no	Rx site	No.of beams	Energy	Coplanar beams	Non coplanar beams	Wedge	Weightings
1	L Breast	7	6 MV	240,10,70,290	20–250 30–320 300–30	–	28:7:7:30:9:9:9
2	R Breast	5	6 MV	55,345,270,231,196	–	15,45,45,15,45	40:04:04:40:12
3	R Breast	4	6 MV	345,40,115,165	–	–	28:24:24:24
4	R Breast	5	6 MV	40,0,280,230	270–320 20–250 266–35 300–30	30,30	20:20:20:20:20
5	L Breast	7	6 MV	225,275,0,60		45,30,30,45	28:7:7:30:9:9:9
6	L Breast	5	6 MV	320,357,141,160, 54	–	45,45,45	18:29:20:20:12
7	R Breast	6	6 MV	60,4,28,0,227	280–110 227–110	45,45,30,30	29:10:10:33:10
8	R Breast	6	6 MV	43,223,4,255	301–90 255–63	45,45	30:30:10:10:10:10
9	L Breast	5	6 MV	319,353,106,162, 55		15,45,45,15 15	32:12:12:33:12
10	L Breast	7	6 MV	238,8,60,280	20–245 30–320 298–25	–	27:8:8:29:9:9:9
11	R Breast	5	6 MV	50,340,270,230, 195	–	45,45,45,45,45,45	35:5:5:30:15
12	R Breast	4	6 MV	340,35,115,160	–	–	20:20:20:20
13	R Breast	5	6 MV	53,345,270,235, 190	–	15,45,45,45 15	35:10:10:30:15
14	R Breast	6	6 MV	40,220,5,255	301–90 255–63	45,45	30:30:10:10:10:
15	L Breast	5	6 MV	320,355,140, 155, 53	–	45,45,45,45	20:20:30:15:15

Volume was delineated as the lumpectomy cavity with a 2 cm margin, modified to 5 mm deep anterior to skin surface and also along the pectoral muscle.[11] Critical organs such as ipsilateral lung and heart for left sided tumour were also marked. The contours were delineated by the same radiation oncologist. The catheters were reconstructed from skin entry to the skin exit in the axial CT images. Dwell positions (step size 2.5 mm) in the catheters were activated in such a way as to fall within the CTV marked. Dose points were computed at 3 mm intervals on the CTV delineated. A dose of 340cGy was prescribed to the target dose points. Then the volume based dose optimisation was done (Fig. 1). The dose volume histograms were generated for the target volumes and the critical structures.

With the implanted tubes in situ, an external beam therapy course was planned in the same CT images. The multiple beam arrangement was used with a combination of both coplanar and non coplanar beams.[12–14] The plan data was tabulated in detail (Table 2). An optimal dose distribution with a better coverage and homogeneity was achieved using typical dose weightings with various wedge combination (Fig. 2). An analysis conducted on BED of different fractionation schemes based on available pre-clinical and clinical indications showed that the tumour control in breast carcinoma can be effective with a biological equivalent dose of 75 Gy.[37] According to the LQ model formula, a dose of 30 Gy given in five fractions of 6 Gy over ten days was found to be radiobiologically equivalent in tumour control (75 Gy) to that of 50 Gy/25 fractions over five

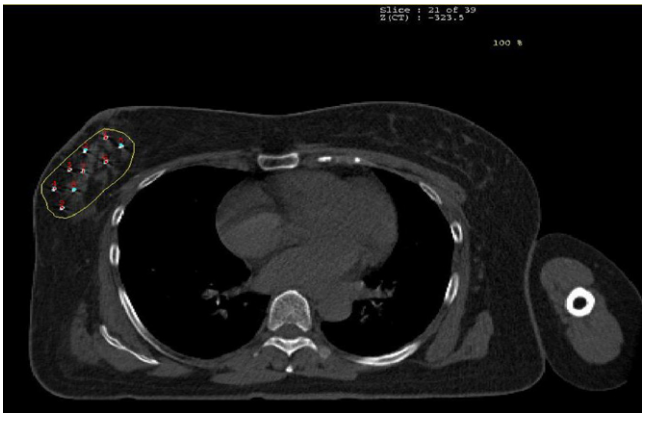


Fig. 1 – Multi catheter interstitial brachytherapy dose distribution-axial view.

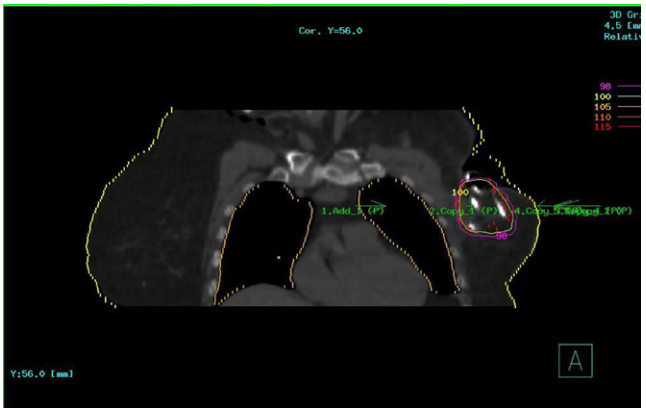


Fig. 2 – 3D conformal EBRT dose distribution-coronal view.

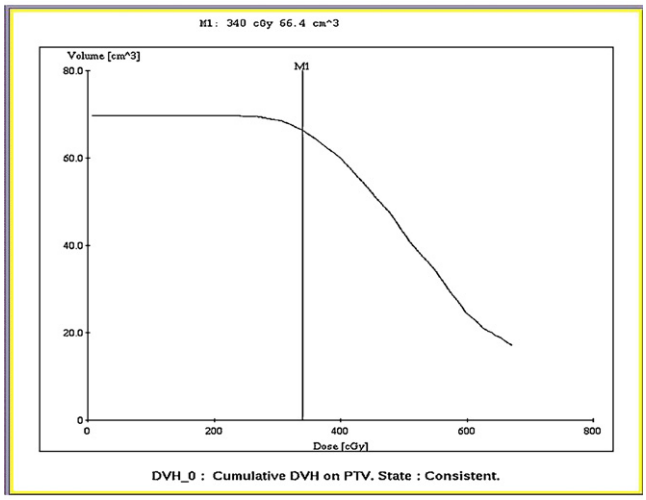


Fig. 3 – Multi catheter interstitial brachytherapy-cumulative dose volume histogram.

weeks.[38] Hence, the dose prescribed was 600cGY × five fractions calculated using linear quadratic cell survival model.[15,16] The five fractions were simulated as an alternate day schedule over ten days. Dose volume histograms were generated for all the structures (both target volume and normal tissues). Since the same CT data sets were used for simulating the EBRT plans, each patient served as their own internal control with respect to anatomy.

3.3. *Target volume dosimetry*

From the Dose Volume Histogram generated from the brachytherapy plans (Fig. 3), the dosimetric parameters such as V_{100}, V_{150} and V'_{100} for the clinical target volume were obtained. Then the dose conformity index (CI) and the dose homogeneity index (HI) for the CTV were calculated from Eqs. (1) and (2) (Table 3).[17]

$$\mathrm{DHI} = \frac{V_{100} - V_{150}}{V_{100}} \quad (1)$$

$$\mathrm{CI} = \frac{V_{100}}{V_{100} - V'_{100}} \quad (2)$$

From the EBRT conformal plan dose volume histograms (Fig. 4), the planning target volume (PTV), reference volume (V_{ref}), D_2 and D_{98} were extracted. The dose conformity and homogeneity index were calculated from the Dosimetric values from Eqs. (3) and (4) [18] and tabulated (Table 3).

$$\mathrm{HI} = \frac{D_2}{D_{98}} \quad (3)$$

$$\mathrm{CI} = \frac{\mathrm{PTV}}{V_{ref}} \quad (4)$$

3.4. *Normal tissue dosimetry*

The dosimetric parameters such as D_{mean}, D_{max}, D_5 and V_{20} were obtained from the lung DVH generated in brachy planning and external beam planning (Table 3). The values of D_{20} and D_{30} from the heart DVH were also obtained in addition to D_{mean}, D_{max}, D_5 and V_{20} (Table 4). These parameters were taken into account since they correlate with late lung toxicity in patients receiving radiotherapy.[19–24,34–36] Cardiac toxicity can be assessed with the available cardiac dosimetry data.[20,25–27,34,36]

3.5. *Statistical analysis*

A summation and a mean calculation were done for the outlined dosimetric data. The paired two tailed student's *t*-tests were performed using Statistica 5.0 (Statsoft Inc) software to assess the significance of difference between the two groups. The *p* values for target dose conformity, dose homogeneity and

Table 3 – CTV dosimetry.

Pt. no	Interstitial brachytherapy planning						External beam palnning				
	V_{100} (cc)	V_{150} (cc)	V'_{100} (cc)	V_{ref} (cc)	C.I.	H.I.	D_2 (cGy)	D_{98} (cGy)	PTV (cc)	C.I.	H.I.
1	27.4	13.2	5.8	33.2	0.8253	0.5182	30.94	28.22	25.5	0.768	1.096
2	115.02	21.82	36.48	151.5	0.7592	0.8102	30.66	28.84	129.2	0.853	1.063
3	145.61	93.59	389	149.5	0.9739	0.3572	32.70	29.52	134.5	0.900	1.107
4	27.51	24.61	0.09	27.6	0.9967	0.1054	33.20	28.64	22.08	0.800	1.159
5	22.70	8.45	8.10	30.8	0.7370	0.6277	31.78	28.14	26.55	0.862	1.129
6	64.91	33.91	2.59	67.5	0.9616	0.4775	32.32	29.84	64.24	0.9665	1.083
7	61.67	43.05	7.53	69.2	0.8911	0.3019	31.60	29.52	64.91	0.938	1.070
8	34.68	28.15	0.15	34.83	0.9956	0.1882	31.40	27.79	28.8	0.827	1.129
9	31.00	19.33	3.80	34.8	0.8908	0.3764	33.30	28.84	29.07	0.8355	1.154
10	30.16	27.14	0.28	35.6	1.009	0.1001	33.16	27.46	34.8	0.978	1.20
11	40.12	30.49	5.64	44.16	1.163	0.2400	32.12	28.48	43.89	0.994	1.128
12	32.13	30.12	6.14	35.75	1.236	0.0625	30.44	29.31	39.71	1.11	1.038
13	28.6	10.12	4.1	30.14	1.167	0.6462	32.60	30.10	32.55	1.08	1.083
14	28.61	20.16	0.5	29.16	1.0178	0.2953	33.15	29.10	30.62	1.05	1.139
15	55.65	40.05	6.00	60.17	1.1208	0.2803	31.48	27.64	59.51	0.989	1.138
Mean					0.9870	0.3591	Mean			0.9301	1.114

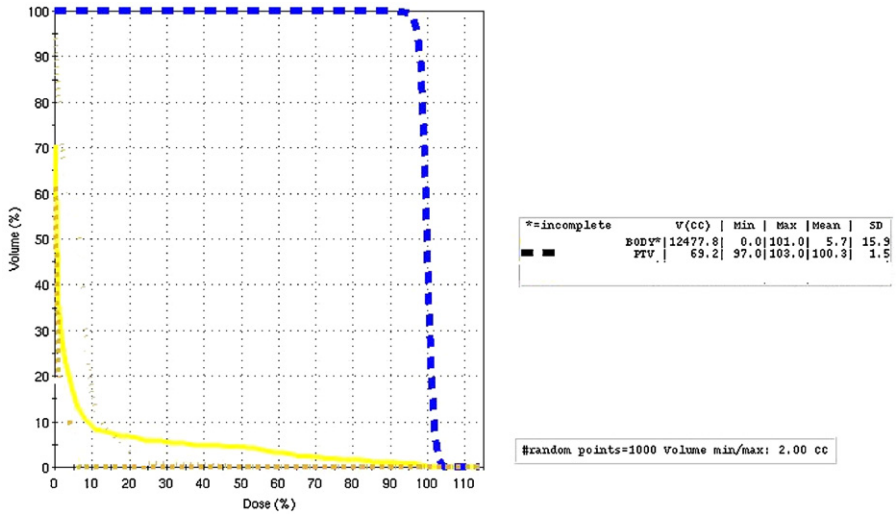


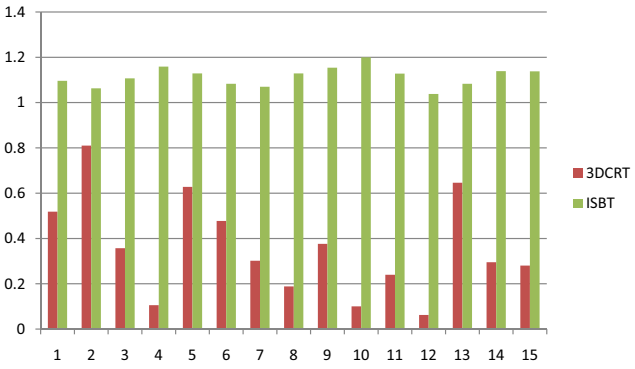
Fig. 4 – 3D conformal EBRT planning-cumulative dose volume histogram.

normal tissue dosimetric parameters, such as D_{mean}, D_{max}, D_5, V_{20}, D_{20}, D_{30} for the normal tissues were computed and analysed (Table 4).

4. Results

The EBRT plans resulted in a more homogenous dose distribution. It is evident from the homogeneity index ($p = 7.255$) (Table 3 and Plot 1). The external beam planning resulted in a conformal dose distribution which was comparable to that of brachytherapy planning ($p = 0.056$) corresponding to a confidence interval of 95%. (Table 3 and Plot 2).

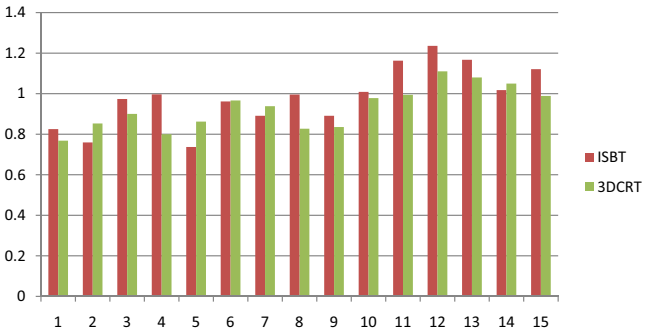
The incidental radiation dose to the lung and the heart using EBRT planning was similar to that of ISBT. A confidence level of 95% was obtained with all the computed dosimetric factors (D_{mean}, D_{max}, D_5, V_{20}, D_{20}, V_5, V_{10} and D_{30}) analysed, which supported the null hypothesis. Hence the normal tissue dosimetry in terms of conformal external beam planning with photon beams was comparable with brachy planning (Table 4).



Plot 1 – Dose homogeneity index.

Table 4 – Normal tissue dosimetry.

Dosimetric parameters	External beam APBI		ISBT APBI		*p*-Value
	Mean	Range	Mean	Range	
Lung $n = 15$					
D_{mean} Gy	5.1	3.2–12.2	4.0	2.0–6.14	0.047
D_{max} Gy	36.3	8.0–48.0	34.56	7.2–46.1	0.122
V_{30} (%)	0.5%	0–1%	0.4%	0.0–0.65%	0.107
V_{20} (%)	1.09%	0–3%	1.1%	0–2%	0.924
V_{10} (%)	10%	0–15%	8.5%	0–14.1%	0.141
D_5 Gy	12.1	6.0–16	10.94	6.0–15.6	0.050
Heart $n = 6$					
D_{mean} Gy	3.2	2.7–5.1	2.8	1.7–4.8	0.089
D_{max} Gy	15.6	11.1–28.4	14.3	10.6–26.7	0.094
V_{20} (%)	0.15%	0–0.5%	0.11%	0.0–0.4%	0.047
V_{10} (%)	2.8%	0–8.2%	2.5%	0–8.0%	0.153
V_5 (%)	20.8%	11.5–31.6%	19.5%	9.6–30.1%	0.608
D_{20} Gy	7.9	6.0–15.5	7.49	5.89–14.9	0.142
D_{30} Gy	7.27	6.8–10.4	7.0	6.0–9.9	0.218



Plot 2 – Dose conformity index.

5. Discussion

From this feasibility study, it was inferred that the simulated EBRT plans gave low doses of radiation to the critical organs, such as the lung and heart, which was comparable with the brachy planning. EBRT planning with conformal photon fields resulted in a very low percentage of volume receiving a dose of 20 Gy having a confidence level of 95% from the sampled population, which correlates with the lower incidence of lung toxicity.[26,28,29,31–35] There was no prominent difference in heart maximum and minimum dose in both treatment planning techniques.

The dose conformity index (CI) and the dose homogeneity index (HI) are the quality indicators of the best treatment plan. Conformity index measures the degree of conformity of the radiation dose prescribed to the clinical target volume. Ideally, CI should be unity or the nearest value to unity in case of a better treatment plan. More conformal dose distribution can be achieved with the use of multiple photon beams which gives an analogous dose distribution as brachytherapy treatment plans (Table 3 and Plot 2).

Homogeneity index (HI) measures the radiation dose uniformity in the clinical target volume. The HI values calculated from the EBRT plans showed the values nearing to one (Table 3 and Plot 1), which is ideal for a homogenous dose distribution. Brachytherapy dose distributions are more heterogeneous around the catheter in nature which results in a poor cosmetic effect in the patients. Hence, it is of major concern in the brachytherapy, particularly when a free hand application happens to be the only available option in the institution.

The use of EBRT in APBI resulted in more homogenous dose distribution without compromising the dose conformity. The critical organ doses were also minimal which was similar to the dose distribution achieved with brachytherapy interstitial implants. It was clearly manifested by statistically less significant p values and optimal confidence level ($t_{0.975}$ or $t = 0.05$) attained with the dose volume parameters.

The dose escalation of about 600cGy per fraction with conformal external beam radiotherapy paves the way for a better tumour control. Hence, it can be treatment of choice when a non invasive procedure is preferred. The set up uncertainties in the external beam radiotherapy procedure can be effectively overcome by daily treatment verification methods (Port films, EPID), immobilisation devices and with an added target volume margins.

6. Conclusions

This is a small sub set treatment planning feasibility study comprising of fifteen patient cases simulated with EBRT plans. The dose distribution planned was compared with the high dose rate brachytherapy planning. It gives satisfying results of dose conformity and dose homogeneity to the tumour volume with acceptable sparing of normal tissues based on the statistical analysis. Hence, the APBI can be effectively planned using the three dimensional conformal external beam radiation therapy. Patient discomfort during brachytherapy procedures involving sedation and a poor cosmetic effect after irradiation can be avoided. Conformal EBRT course is more cost effective when compared to brachytherapy. Hence, it can be suggested as an alternative treatment modality where brachytherapy procedures are performed freehand which is tedious in nature. Enduring research will focus on the evaluation of Tumour Control Probability and Normal Tissue Complication Probability in EBRT and brachytherapy plans.

Conflict of interest

None declared.

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