

# Dosimetric evaluation of 3Dconformal acceleratedpartial-breast irradiation vs. whole-breast irradiation: A comparative study

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## ABSTRACT

**Background:** Conventional early breast cancer treatment consists of lumpectomy followed by whole-breast irradiation (WBI) therapy. Accelerated partial-breast irradiation (APBI) is also an approach to post-lumpectomy radiation for early breast cancer. **Aim:** The purpose of this study is to compare two different external-beam APBI techniques using three-dimensional (3D) conformal radiation therapy (3DCRT), with conventional whole-breast irradiation based on the radiation conformity index, dose homogeneity index, and dose to organs at risk. **Materials and Methods:** WBI treatment plans were compared with two different 3DCRT APBI plans for each of 15 patients (8 with right sided lesions, 7 with left sided lesions). The first APBI plan (APBI 1) used two small coplanar fields conformed to the planning target volume (PTV) using multileaf collimators (MLCs) and wedges, while the other APBI plan (APBI 2) used three non-coplanar fields conformed to the PTV using MLCs and wedges. **Results:** Both the APBI techniques improved the conformity index significantly over whole-breast tangents while maintaining dose homogeneity and not causing significant increase in dose to organs at risk. **Conclusion:** Both the 3DCRT APBI techniques are technically feasible and dosimetrically appealing, with better target coverage and relative sparing of normal critical organs

**Key words:** Accelerated partial-breast irradiation, planning target volume, whole-breast irradiation, 3D conformal radiation therapy

## INTRODUCTION

The combination of breast-conserving surgery and radiotherapy (RT), known as breast-conserving therapy (BCT), is a widely accepted treatment option for most women with clinical stage I or II invasive breast cancer. Traditionally, patients undergoing BCT have received whole-breast irradiation (WBI). Post-lumpectomy radiation therapy consists of 4–5 weeks of WBI for a total dose of 45–50 Gy in 23–25 fractions, usually

followed by a boost of 10–16 Gy in 5–8 fractions to the tumor bed. Women who choose BCT therefore commit to 6–7 weeks of daily radiation visits to complete local management of their breast cancer.

Accelerated partial-breast irradiation (APBI) is an emerging radiation technique that challenges standard WBI. The volume of breast tissue irradiated is defined by the lumpectomy cavity, identified as the area of postoperative changes evident on a planning CT scan. APBI allows for shorter treatment schemes than does WBI (typically 1–2 weeks), thereby reducing normal-tissue toxicity (i.e., cardiac damage and radiation pneumonitis) due to decrease of the treatment volumes. APBI also reduces the length of the RT course, thereby reducing the overall treatment cost.<sup>[1]</sup>

Several authors have reported APBI both by means of interstitial<sup>[2,3]</sup> and intracavitary brachytherapy with MammoSite<sup>®</sup>.<sup>[4]</sup> The clinical results are promising, although with relatively short follow-up. Intraoperative techniques that utilize electrons or low-energy X-rays have also been

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described.<sup>[5,6]</sup> These three approaches, however, are invasive and costly.

Another approach to APBI has been the use of three-dimensional (3D) conformal external-beam radiation (3DCRT). Different methods of 3DCRT APBI have been proposed by different authors, including Vicini *et al.*, Formenti *et al.*, and Taghian *et al.*<sup>[7-9]</sup> The present study describes the dosimetric parameters of two different 3D conformal APBI techniques—two-field coplanar beam [Figure 1] and three-field non-coplanar beam [Figure 2]—based on the combination of wedges and multileaf collimators (MLCs). The results obtained with regard to dose homogeneity, conformity indices, and organs at risk dose were compared to that with the WBI technique [Figure 3].

## MATERIALS AND METHODS

### Study population

The study population consisted of 15 consecutive women referred for adjuvant RT after lumpectomy between August 2008 and February 2009. All patients had fully excised, unifocal tumors of <4 cm in size; margins were 2 mm or greater.

### Simulation and treatment planning

The patients were positioned on a breast board with the sternum parallel to the table, and the ipsilateral arm abducted above the head. Before the CT scan, skin marks were placed to enable patient repositioning during treatment. Radiopaque markers were placed to locate the whole breast and lumpectomy cavity on CT images. The patients were scanned from the level of the larynx to the level of the upper abdomen, with a scan thickness and index of 5 mm. The CT scan included the complete left and right lungs, both breasts, and the heart. The CT images were then transferred to the treatment planning system (Varian Eclipse™ 8.6). The gross tumor volume (GTV) was defined by lumpectomy cavity contoured on each CT slice. The clinical target volume (CTV) consisted of the GTV uniformly expanded in three dimensions by 1.5 cm and lay 5 mm within the external contour and up against the pectoralis major muscles. The planning target volume (PTV) was calculated from the CTV using uniform 3D expansion of 1 cm [Figure 4]. The ipsilateral whole breast was defined to lie within the radiopaque markers and as deep as the anterior chest wall muscles. The cranial extent of the heart included the infundibulum of the right ventricle, the right atrium, and the right auricle, but excluded the pulmonary trunk, the ascending aorta, and the superior vena cava. The lowest external contour of the heart was the caudal border of the mediastinum. The pericardium was excluded from the heart volume. In addition, we contoured the lungs and the contralateral breast.

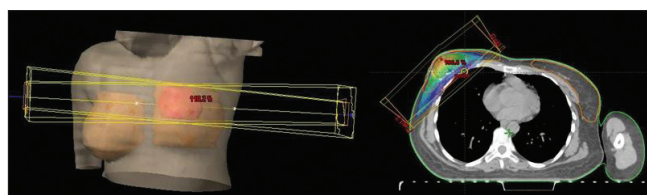


Figure 1: (a) 3DCRT two-field coplanar arrangements (APBI 1); (b) dose distribution in APBI 1

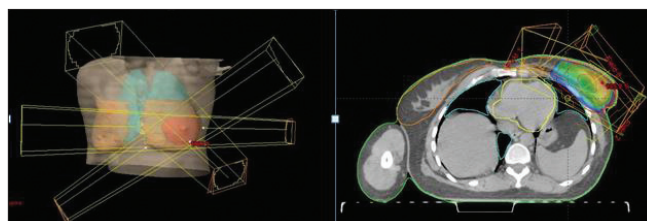


Figure 2: (a) 3DCRT three-field non-coplanar arrangements (APBI 2); (b) dose distribution in APBI 2

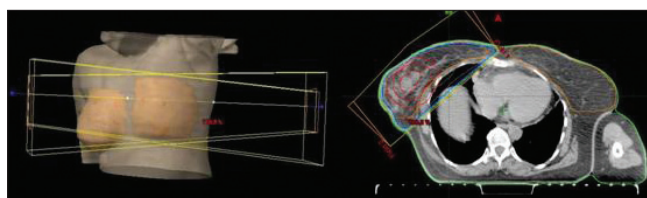


Figure 3: (a) 3DCRT two-tangential field arrangements; (b) field arrangements for WBI

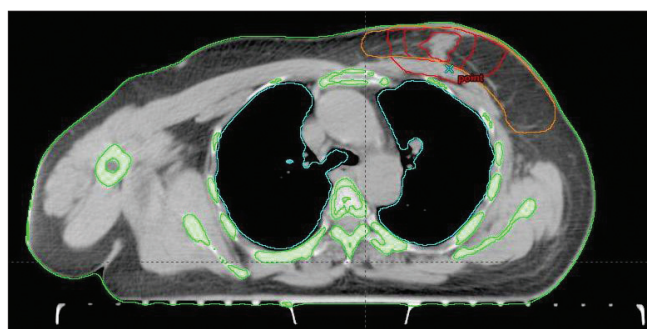


Figure 4: Contouring of target volumes and organs of interest

We generated a rectangular plan for WBI and the two APBI plans based on field arrangements and MLCs. The different 3DCRT APBI field arrangements were as follows: (a) two coplanar fields with MLCs and wedges (APBI 1) and (b) three non-coplanar fields with MLCs and wedges (APBI 2). The dose prescribed was 50 Gy in 25 fractions for whole-breast rectangular plans and 38.5 Gy in 10 fractions in 1 week, with two fractions per day, for 3DCRT APBI plans.

### Plan evaluation

Plans were evaluated both quantitatively (dose–volume histograms) [Figure 5] and qualitatively (isodose curves). Plans were checked for radiation conformity and dose homogeneity indices.

### Radiation conformity index

The radiation conformity index (RCI) was first described by Knoos *et al.* A revised definition appears in ICRU 62,<sup>[10]</sup> according to which it is defined as the ratio of the volume of PTV to the volume that receives a dose of 95% of the prescribed dose or higher.

$$\text{i.e., RCI} = V_{\text{PTV}} / V_{95\%}$$

### Dose homogeneity index

The dose homogeneity index (DHI) is defined as the ratio of the dose to 95% of the volume of the PTV ( $D_{\geq 95\%}$ ) to the dose to 5% ( $D_{\geq 5\%}$ ) of the PTV.

$$\text{i.e., DHI} = D_{\geq 95\% \text{ (within PTV)}} / D_{\geq 5\% \text{ (within PTV)}}$$

DHI is an index that typically describes the uniformity of dose within a brachytherapy treatment plan. In this case, it was used to describe the uniformity of dose within the PTV for external therapy plans; this allowed us to better compare dose homogeneity between different plans.

Doses delivered to target and organs at risk were compared between 3DCRT APBI plans and standard rectangular tangential field plans.

## STATISTICAL ANALYSIS

All statistical tests were done using one-way analysis of variance (ANOVA) test and the Fisher's least significant difference (LSD) test as the *post hoc* test for comparison between individual groups. All data was analyzed by SPSS v. 17.  $P < .05$  was considered significant.

## RESULTS

### Patient characteristics

Of the 15 patients, eight (53%) had tumors in the right breast

and seven (47%) in the left breast. All patients were at least 18 years of age (mean age: 47.5 years; range: 35–60 years) and had histologically confirmed, unicentric, stage I or II invasive ductal carcinoma.

The mean PTV was 193.47 cc (range: 95.3–291.6 cc). The mean ipsilateral (whole-breast) volume was 610.6 cc (range: 300–1153.9 cc). The mean ratio of PTV to ipsilateral whole-breast volume (PTV/IB) was 0.33 (range: 0.19–0.56).

### Radiation conformity index

The average RCI for the 15 patients for all the three different techniques evaluated was 1.120, 1.023, and 1.018 for WBI, APBI 1, and APBI 2, respectively. The RCI values of both APBI techniques were significantly superior to the RCI values for WBI ( $P < .001$ ), but there was no significant difference between the RCI values of APBI 1 and APBI 2 ( $P = .77$ ) [Table 1, Figure 6].

### Dose homogeneity index

The average DHI for the 15 patients for the three different techniques evaluated was 78.36, 89.01, and 89.58 for WBI, APBI 1, and APBI 2, respectively. The DHI values of both APBI techniques were significantly higher than the DHI values for WBI ( $P < .001$ ), but there was no significant difference between the DHI values of APBI 1 and APBI 2 ( $P = .77$ ) [Table 1, Figure 7].

### Planning target volume coverage

The mean PTV coverage of the APBI 1 and APBI 2 was 38.41 and 38.46, respectively. Both the techniques had similar

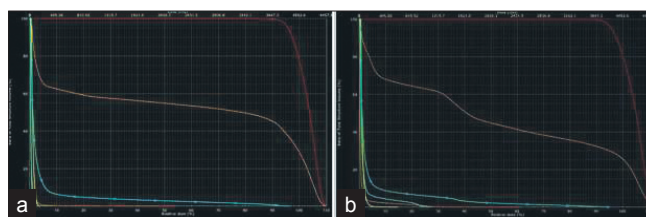


Figure 5: (a) DVH of APBI 1; (b) DVH of APBI 2

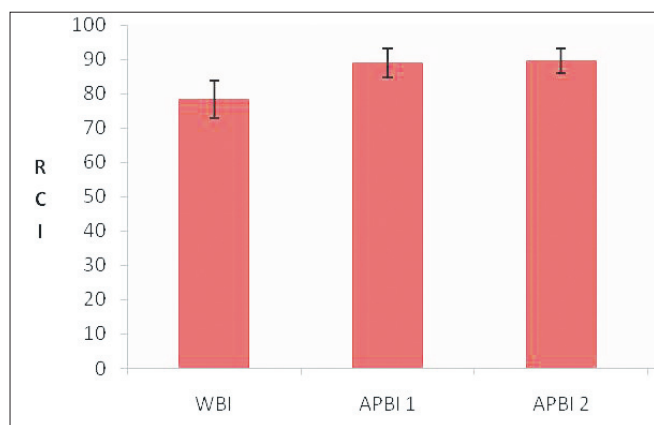


Figure 6: Comparison of RCI of the three techniques

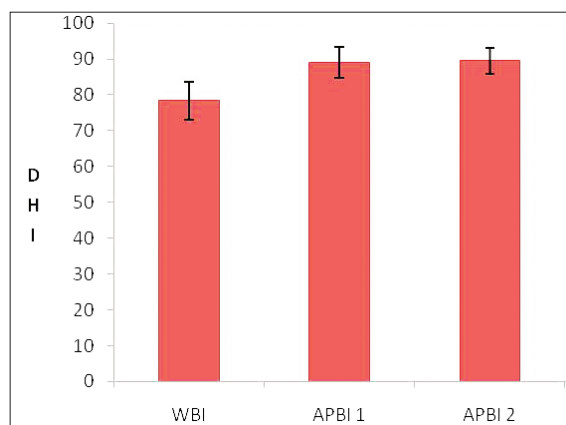


Figure 7: Comparison of DHI of the three techniques

coverage of the PTV, and there was no significant difference between the methods [Table 2].

### Dose to organs at risk

For ipsilateral breast, the mean doses received by the WBI plans were significantly lower than that with the APBI plans ( $P<.05$ ), but there was no significant difference in dose received to ipsilateral breast with the two different APBI plans [Table 3].

Similarly, for contralateral breast, ipsilateral lung, and contralateral lung, the mean doses received by the WBI plans were significantly lower than that with the APBI plans ( $P<.05$ ), but there was no significant difference between the doses received the two different APBI plans. The volume of ipsilateral lung receiving 5 Gy was significantly lower in the APBI 1 plans when compared to the APBI 2 plan ( $P=.048$ ). This may be due to the third field used in the APBI 2 plans [Table 3].

There was no difference between the three different plans with regard to the mean doses received to the heart in case of right-sided lesions. In contrast, for lesions in the left breast, the APBI plans showed significantly lower dose distribution in the heart as compared to the WBI plans. There was no significant difference in dose distribution to the heart between APBI 1 and APBI 2 plans [Table 3].

**Table 1: Radiation conformity index and dose homogeneity index in all three techniques used**

Parameter	Technique	Mean	Range
RCI	WBI	1.120	1.02–1.29
	APBI 1	1.023	1.00–1.15
	APBI 2	1.018	1.00–1.12
DHI	WBI	78.36	69.44–86.49
	APBI 1	89.01	77.98–93.66
	APBI 2	89.58	79.73–95.08

RCI: radiation conformity index; DHI: dose homogeneity index; WBI: whole-breast irradiation; APBI: accelerated partial-breast irradiation

**Table 2: Planning target volume (PTV) coverage at different doses for APBI 1 and APBI 2**

PTV coverage	APBI 1	APBI 2	P value
$V_{100\%}$	93.68 (79.94–99.87)	95.19 (80.84–99.76)	.373
$V_{95\%}$	98.004 (87.61–100)	98.50 (88.60–100)	.659
$V_{90\%}$	99.05 (92.19–100)	99.26 (92.91–100)	.796
Mean dose	38.41 (37.38–39.65)	38.46 (36.69–40.12)	.797

$V_{100\%}$ : Volume receiving a dose of 100%;  $V_{95\%}$ : volume receiving a dose of 95%;  $V_{90\%}$ : volume receiving a dose of 90%; APBI: accelerated partial-breast irradiation. Values in brackets are range

## DISCUSSION

The rationale for partial-breast irradiation is based on the observed patterns of ipsilateral breast recurrences in patients treated with BCT. In the first 5–10 years after BCT with WBI, most tumors recur within or near the original tumor bed.<sup>[11]</sup> The incidence of ipsilateral breast recurrence is dramatically reduced by WBI; however, the incidence of ‘elsewhere’ recurrences after WBI is similar to contralateral breast cancer incidence.<sup>[12]</sup> On the basis of these observations several techniques of APBI have been developed, such as interstitial brachytherapy, MammoSite® radiation therapy system, and intraoperative radiation therapy (IORT).

Interstitial brachytherapy has several disadvantages, including

**Table 3: Dosimetric evaluation in different techniques**

Parameter	WBI	APBI 1	APBI 2
Ipsilateral breast			
$V_{110\%}$	8.02	5.77	6.99
$V_{100\%}$	81.96	45.19	36.45
$V_{75\%}$	97.80	60.16	50.93
$V_{50\%}$	99.61	65.27	62.65
$V_{25\%}$	99.86	69.65	76.57
Mean	49.03	25.07	23.92
Contralateral breast			
$V_{10\text{ Gy}}$	0.44	0.003	0
$V_{3\text{ Gy}}$	2.001	0.01	1.25
Mean	0.66	0.165	0.217
Ipsilateral lung			
$V_{20\text{ Gy}}$	17.03	7.14	6.24
$V_{10\text{ Gy}}$	19.42	8.80	13.44
$V_{5\text{ Gy}}$	23.37	10.46	20.45
Mean	9.20	3.36	3.79
Contralateral lung			
$V_{20\text{ Gy}}$	0	0	0
$V_{10\text{ Gy}}$	0	0	0.14
$V_{5\text{ Gy}}$	0	0	1.85
Mean	0.48	0.15	0.34
Heart (right-sided lesions)			
$V_{20\text{ Gy}}$	0	0	0
$V_{10\text{ Gy}}$	0.004	0	0.02
$V_{5\text{ Gy}}$	0.08	0	0.18
Mean	1.23	0.41	0.41
Heart (left-sided lesions)			
$V_{20\text{ Gy}}$	7.30	0.72	0.19
$V_{10\text{ Gy}}$	9.27	1.27	1.11
$V_{5\text{ Gy}}$	12.62	2.04	7.85
Mean	4.99	0.97	1.26

WBI: Whole-breast irradiation, APBI: Accelerated partial-breast irradiation

invasiveness of the procedure; need for high-quality expertise; need for prolonged hospital stay; risk of wound infections, abscess, fat necrosis; and grade 4 subcutaneous toxicity.<sup>[13-15]</sup> With MammoSite® radiation therapy the infection rates approach 16% and nearly one-third of patients develop postimplantation seromas.<sup>[16,17]</sup> Furthermore, the rate of explantations varies between 20%–27% because of inadequate skin spacing, suboptimal conformance of the surgical cavity to the applicator balloon, and balloon rupture.<sup>[16-18]</sup> The other technique is IORT, which uses either low-energy x-rays at 50 kVp<sup>[6]</sup> or electrons.<sup>[5]</sup> With IORT, dosimetry quality assurance is technically challenging and the final pathologic status of margins and lymph nodes is not available.

One technique of APBI is by 3DCRT, which is noninvasive and employs technology used daily by both academic and community-based radiation oncologists. This technique is attractive to patients as it eliminates the need of further procedural trauma to the breast. It can be initiated after final evaluation of margins, lymph nodes, and other pathologic details.

A few authors have used different methods for 3DCRT APBI. Vicini *et al.* has described a technique of APBI that utilizes 3–5 non-coplanar fields.<sup>[7]</sup> Formenti *et al.* used prone positioning to minimize target-tissue movement during breathing.<sup>[19]</sup> Although this technique provides exceptional sparing of normal heart and lung tissue, specialized prone positioning boards are not widely available. Taghian *et al.* described a 3DCRT APBI technique using photons and electrons.<sup>[9]</sup> The use of electrons can lead to telangiectasia and skin reactions, which may affect cosmesis. Moreover, there are chances of dosimetric uncertainty.

In this study, we have employed two simple APBI technique using 6 MV photons. The APBI 1 plan delivered radiation using two small coplanar beams conformed to the PTV with MLCs and wedges (15°–30°). The APBI 2 plan delivered radiation using three non-coplanar beams conformed to the PTV using MLCs and wedges (15°–30°). These APBI plans were compared with the standard two tangential field plans to the whole breast.

The dosimetric analysis of this study reveals that the conformity index and homogeneity index were significantly superior in the APBI plans as compared to the WBI plans, but there was no significant difference between the APBI 1 and APBI 2 plans.

The PTV coverage for both the APBI plans showed similar PTV coverage, with no significant difference between APBI 1 and APBI 2; however, there was a trend toward better PTV coverage with APBI 2 plans.

Similarly, for doses to organs at risk, the APBI plans delivered significantly lower doses as compared to the WBI plans for doses to ipsilateral breast, contralateral breast, ipsilateral lung, and contralateral lung. However, there was no difference between APBI 1 and APBI 2 plans except for the amount of ipsilateral lung receiving >5 Gy, this being higher with the APBI 2 plan as compared to APBI 1 plan. This is probably due to the third field in the APBI 2 plan.

The doses to the heart varied according to the side of the lesion. For right breast lesions, all the three plans, i.e., WBI, APBI 1, and APBI 2, delivered similar doses to the heart and no significant difference was found. While for lesions of the left breast there was significant reduction in the dose delivered to the heart in APBI plans compared to the WBI plans, there was no significant difference between APBI 1 and APBI 2 plans.

These data indicate that 3DCRT APBI techniques give better dose distribution to the target volume, while delivering significantly smaller doses to the organs at risk. These two different techniques for 3DCRT APBI techniques are simple and efficient.

Despite the appeal of 3DCRT APBI, a setup uncertainty remains between fractions because of organ motion and mobility of breast. There is also a chance of intrafraction setup error due to breathing movement. This may lead to target miss. However, a recent study has shown that intrafraction setup uncertainty was less than interfraction setup uncertainty, indicating that the patient setup should have higher priority than breathing.<sup>[20]</sup> The decision on adequate PTV margin could take into account this setup error. In this study, we have taken a PTV margin of 1 cm as we have used a breast board as the positioning device, which leads to a better reproducibility. Ongoing efforts to improve immobilization and employ real-time image guidance for APBI delivery will further aid in better reproducibility and target coverage.

Thus, the 3DCRT APBI technique described herein provides a technically feasible and dosimetrically appealing strategy for APBI. It results in better target coverage, with relative sparing of normal critical organs. It can be adopted easily by radiation oncologists and physicists.

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