

Forward-planned intensity modulated radiation therapy using a cobalt source: A dosimetric study in breast cancer

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ABSTRACT

This analysis evaluates the feasibility and dosimetric results of a simplified intensity-modulated radiotherapy (IMRT) treatment using a cobalt-therapy unit for post-operative breast cancer. Fourteen patients were included. Three plans per patient were produced by a cobalt-60 source: A standard plan with two wedged tangential beams, a standard tangential plan optimized without the use of wedges and a plan based on the forward-planned “field-in-field” IMRT technique (Co-FinF) where the dose on each of the two tangential beams was split into two different segments and the two segments weight was determined with an iterative process. For comparison purposes, a 6-MV photon standard wedged tangential treatment plan was generated. D_{mean} , $D_{98\%}$, $D_{2\%}$, $V_{95\%}$, $V_{107\%}$, homogeneity, and conformity indices were chosen as parameters for comparison. Co-FinF technique improved the planning target volume dose homogeneity compared to other cobalt-based techniques and reduced maximum doses ($D_{2\%}$) and high-dose volume ($V_{110\%}$). Moreover, it showed a better lung and heart dose sparing with respect to the standard approach. The higher dose homogeneity may encourage the adoption of accelerated-hypofractionated treatments also with the cobalt sources. This approach can promote the spread of breast conservative treatment in developing countries.

Key words: Breast neoplasms, cobalt machine, intensity-modulated radiotherapy, radiotherapy

Introduction

Breast cancer is a common cancer in any region of the world. The incidence of this cancer is even high in developing countries.^[1,2] Standard conservative treatment includes

lumpectomy followed by radiation therapy. Although the linear accelerator is the preferred equipment, telecobalt machines may be considered as an acceptable alternative for the post-operative radiotherapy.^[3]

Post-operative radiotherapy is based on the use of tangential beams with the wedge filters. Recently, the use of intensity-modulated radiotherapy (IMRT) was also evaluated. Some other studies have shown a dosimetric advantage over the traditional technique in terms of improved dose homogeneity^[4-9] and reduced dose to the organs at risk.^[5,6,8-12] Other studies also documented some clinical advantages like reduction in skin acute toxicity^[13-15] and late toxicity.^[16] In some situations, a simplified technique for IMRT has been used. This technique, sometimes referred to as “field in field (FinF),” is based on forward planning, unlike the classic inverse-planned IMRT.^[8,9,11,14,15,17-20] In developing countries, there are serious technical and logistical limitations for radiotherapy.^[21] In many centers only two-dimensional (2D) techniques are available, based on the traditional simulators and telecobalt equipment.

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In some situations, the limitations are even more serious, with only obsolete equipment without wedge filters being available.^[22]

It can be assumed that the use of FinF technique can be adapted also to less advanced technology levels. The use of forward planning can be accomplished even without advanced treatment planning systems (TPS). It is conceivable that this technique can improve also the quality of treatments using the cobalt equipments; however, the possibility of FinF technique with a cobalt source is not granted due to lack of 2 useful elements to this technique: (a) The use of multileaf collimators (MLC) for the design of conformal treatments and (b) the possibility of photons of different energies. Therefore, before testing the FinF technique in the clinical trials, dosimetric evaluations, and comparisons with the standard (wedged fields) technique are needed.

Thus, given these premises, the purpose of this analysis is to evaluate the feasibility and the dosimetric results of a simplified IMRT treatment for breast cancer with a cobalt-therapy unit.

Materials and Methods

A retrospective cohort of 14 patients who underwent conservative surgery and adjuvant breast irradiation with three-dimensional conformal radiotherapy (3D-CRT) technique were selected for this study. This group included seven patients with the left side involvement and seven with the right side involvement. The patients had different characteristics in terms of anatomical site of the tumor and the size of the residual breast.

In order to perform a dosimetric comparison, a computed tomography (CT) -simulation was carried out with patients positioned supine on breast board with the ipsilateral arm raised above the head. The scan was extended from the jugular notch to 5 cm below the lower edge of the breast with a scan interval of 5 mm. Target volume, heart and lungs were manually contoured on each CT slice by a single radiation oncologist (LC) following the RTOG guidelines. The clinical target volume (CTV) was defined as the remaining breast excluding the outer 5 mm. The planning target volume (PTV) was defined as CTV + 8 mm in the direction of the chest wall.

Treatment planning techniques

Oncentra Masterplan version 4.0 treatment planning system (Nucletron B.V., Veenendaal, and The Netherlands) was used to generate 4 different treatment techniques that are described below. For all plans, a fractionation schedule of 50 Gy in 2 Gy/fraction to the PTV was used. All plans were optimized according to the following constraint for the PTV: $V_{95\%} > 95\%$ (the volume receiving 95% of the

prescription dose or more) must be greater than 95% of the PTV volume). This was considered as the primary constraint. As a secondary constraint, we considered the following: Maximum dose ($D_{2\%}$) to the PTV < 107% of the prescribed dose. All plans were performed with the tangential technique and slight beam orientation (gantry angles optimized to match divergence of the posterior edges of the beam) to avoid contralateral breast irradiation and minimize the ipsilateral lung area in the beam's eye view (BEV).

Cobalt-based treatment plans

For all patients, a standard tangential wedged plan (Co60-WF) and a plan based on the FinF technique (Co60-FinF) were carried out. In the standard wedged treatment, irradiation of the PTV was planned with 2 tangential beams produced by a cobalt-60 source, with 15° or 30° wedge filters used to compensate the dose inhomogeneity. In the FinF treatment, the dose on each of the 2 tangential beams was split into 2 different segments. The first segment was designed to encompass the entire breast without the use of filters [Figure 1a]. This configuration in the absence of filters generally produces a volume of under-dosing in the central and deep region of the breast being the region with greater thickness. A second segment was then directed to this area of under-dosing, in order to compensate for the drop in dose [Figure 1b]. The weights of the 2 segments were determined with an iterative process repeated until optimal results are achieved. The weight of these segments is typically in the range of 15-20%. The 2 segments have a rectangular shape without shielding. For comparison purposes, a standard treatment plan using only open fields (Co60-OF) without wedge filters was generated. All cobalt plans were generated with the beam parameters of a Theratron machine (Best Theratronics Ltd, Canada).

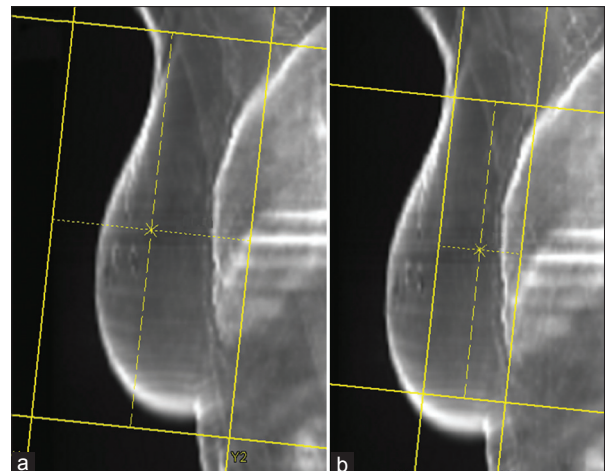


Figure 1: Medial beam's-eye view of (a) main field and (b) subfield used in FinF technique for a representative patient

3D-CRT technique

For each patient, the 6-MV photon standard wedged tangential treatment plan (6MV-CRT) used for clinical irradiation was also considered for comparison purposes. In this last technique, MLC were used in order to minimize normal tissue (lung and heart) dose without compromising the target coverage. The shape of the MLC was defined in the BEV with a distance of 7 mm from the PTV in the lung region to take into account for beam penumbra. These plans were generated with the 6 MV beam parameters of an Elekta Precise linac (Elekta, Crawley, UK). The dose specification was performed according to ICRU 62. In all techniques, the dose calculation was carried out using the pencil beam algorithm with inhomogeneity correction and a dose grid resolution of 0.2 cm.

Plan comparison and statistical analysis

Dose-volume histograms were generated for PTV and organs at risk for all plans. For PTV, D_{mean} , $D_{98\%}$, $D_{2\%}$, $V_{95\%}$, $V_{110\%}$ and a homogeneity index (HI) defined as $HI = 100 \times (D_{2\%} - D_{98\%}) / D_p$ (D_p = prescribed dose) were chosen as parameters for comparison. D_{mean} , $D_{98\%}$, $D_{2\%}$ were calculated as percentages of the prescribed dose (50 Gy). $D_{98\%}$ and $D_{2\%}$ were defined as surrogates for maximum and minimum doses. Lower HI values indicate a more homogeneous target dose. $V_{110\%}$ was chose to specify the target volume receiving high doses. In addition, a conformity index CI was defined as $CI = V_{ri} / V_{ptv}$, where V_{ri} is the volume encompassed by the reference isodose for the PTV (95% of the prescribed dose) and V_{ptv} is the PTV volume. For ipsilateral lung and heart, plans were compared in terms of D_{mean} , $D_{2\%}$, $V_{10\text{ Gy}}$, $V_{20\text{ Gy}}$, $V_{30\text{ Gy}}$, $V_{40\text{ Gy}}$ and $V_{50\text{ Gy}}$. One-way analysis of variance was used to compare dosimetric differences among plans using the 4 techniques. *Post-hoc* testing was assessed using the Bonferroni multiple comparison adjustment method; $P < 0.05$ were considered significant. The Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, IL, USA).

Results

Target coverage

Fourteen patients were included in this analysis. Patients’

characteristics are reported in Table 1. The analysis results for target coverage are reported in Table 2 in terms of the mean value and standard deviation. Figure 2 shows the PTV box-and-whisker plot for the 4 techniques.

Median breast volume was 654.5 cc (range 260.0-1365.1 cc). In all patients, as provided for in the study design, the constraint $V_{95\%} > 95\%$ were achieved for all plans. Concerning the PTV, the Co-FinF technique improved the dose homogeneity compared to other Co60 techniques. In particular, Co-FinF reduced maximum doses ($D_{2\%}$) by 2.9 Gy ($P < 0.001$) and 1.8 Gy ($P = 0.027$) compared to Co-OF and Co-WF, respectively. High doses volume ($V_{110\%}$) were reduced to 7.5% with the use of Co-FinF, from 22.1% ($P < 0.001$) to 10.0% ($P = 0.042$) of Co-OF and Co-WF, respectively. Mean homogeneity index was significantly improved with Co-FinF (19.5) as respect to Co-WF (23.0, $P = 0.042$) and Co-OF (25.6, $P < 0.001$). The CI over the 14 patients for all of the four different techniques is shown in Figure 2e. The results show that mean CI is higher for Co-WF than for Co-FinF (2.6 vs. 2.2, $P < 0.001$) and no significant different as respect to Co-OF ($P = 0.289$).

Figure 3 shows the dose distribution for one representative

Table 1: Patients characteristics

	Number
Patients	14
Age, median (range), years	63 (46-75)
Tumor stage	
Tis	2
T1	9
T2	3
Tumor side	
Left breast	7
Right breast	7
Tumor position (in the breast)	
Central	3
Lateral	8
Medial	3
Superior	9
Inferior	2
PTV, median (range), cc	654.5 (260.0-1365.1)

PTV: Planning target volume

Table 2: Comparison of target coverage metrics (mean values±SD)

	6MV-CRT	Co-OF	Co-WF	Co-FinF	P^* (Co-OF vs. Co-FinF)	P^* (Co-WF vs. Co-FinF)	P^* (6MV vs. Co-FinF)
D_{mean} (%)	100.1±0.8	105.5±1.8	103.0±2.1	103.3±1.7	<0.001	1.000	<0.001
$V_{95\%}$ (%)	96.7±1.5	95.9±0.9	96.0±0.9	95.8±0.8	1.000	0.182	0.128
$V_{110\%}$ (%)	0.0±0.0	22.1±11.7	10.0±7.9	7.5±6.7	<0.001	0.042	0.006
$D_{98\%}$ (%)	94.2±1.1	92.1±2.4	92.5±3.0	92.4±2.1	0.819	1.000	0.112
$D_{2\%}$ (%)	105.0±1.3	117.8±5.9	115.5±5.3	111.9±3.7	<0.001	0.027	<0.001
HI	10.7±2.2	25.6±6.5	23.0±7.6	19.5±4.6	<0.001	0.042	<0.001
CI	1.7±0.3	2.2±0.6	2.6±0.7	2.2±0.5	0.289	<0.001	<0.001

*By Bonferroni *post-hoc* analysis, HI: Homogeneity index, CI: Conformity index, CRT: Conformal radiotherapy, SD: Standard deviation

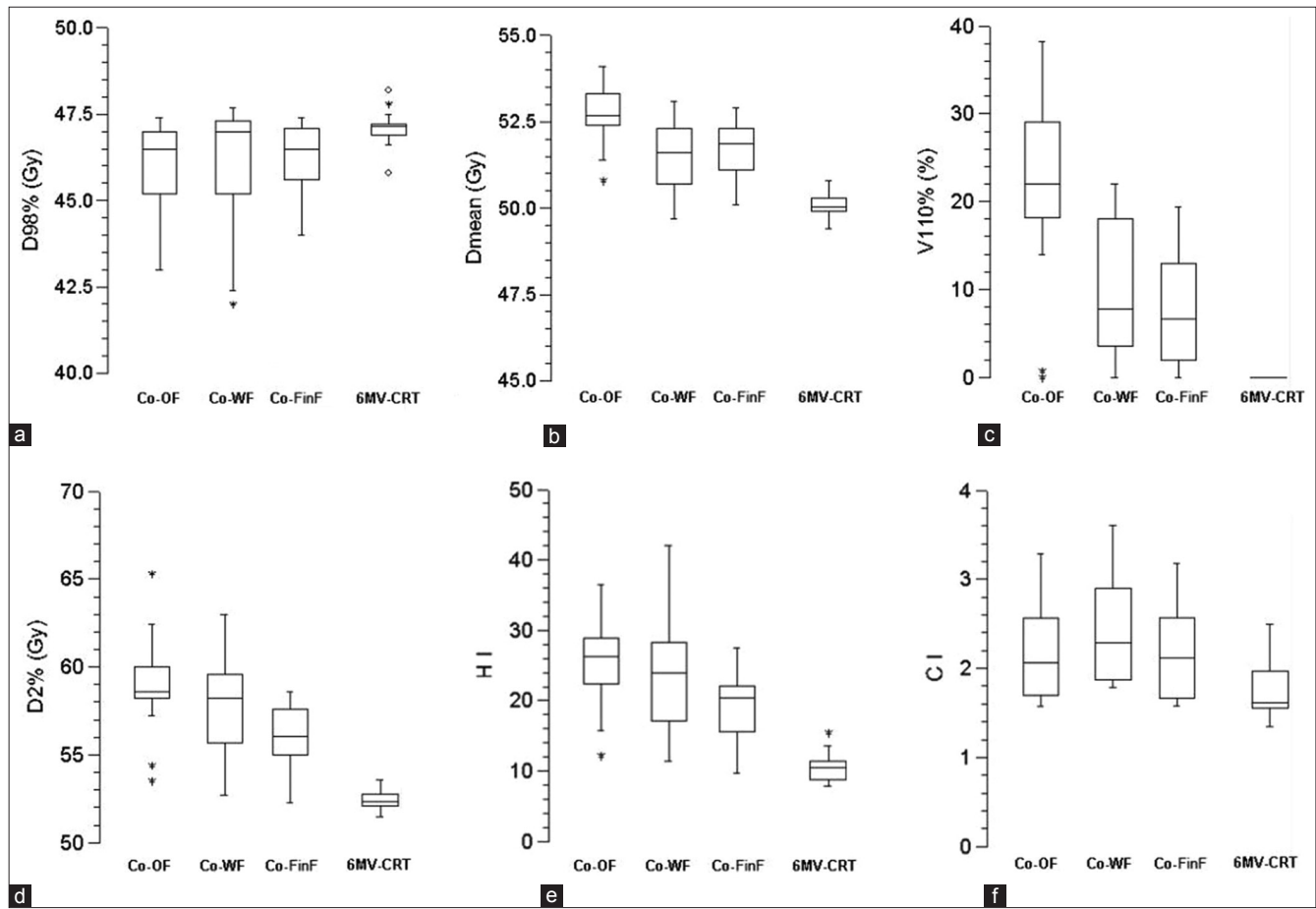


Figure 2: Planning target volume box-and-whisker plot of (a) minimum dose ($D_{98\%}$), (b) mean dose (D_{mean}), (c) percentage volume receiving more than 110% of the prescribed dose ($V_{110\%}$), (d) maximum dose ($D_{2\%}$), (e) homogeneity index, and (f) conformity index for the four techniques

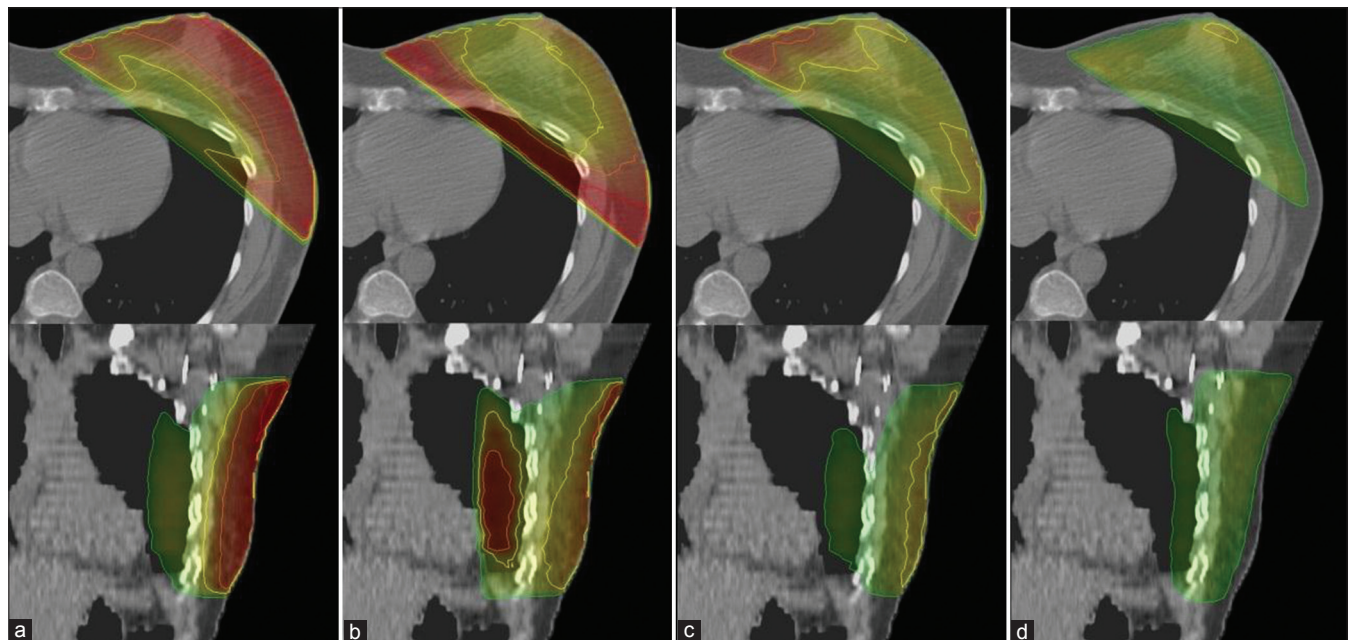


Figure 3: Dose distribution ($V_{95\%}$, green; $V_{105\%}$, yellow; $V_{110\%}$, orange and $V_{115\%}$, red) for (a) Co-OF, (b) Co-WF, (c) Co-FinF and (d) 6MV-conformal radiotherapy on the axial and coronal plane containing isocenter

patient in terms of isodoses equal to 95%, 105%, 110%, and 115% of the prescribed dose on the axial slice and coronal view containing isocenter. The advantages of Co-FinF are clearly evident in terms of reduction of areas irradiated at high doses, which are mainly present in the breast anterior region for Co-OF technique and in the breast portion close to the lung for the Co-WF technique.

Normal tissue irradiation

Normal tissue dosimetric results are displayed in Table 3 in terms of the mean value and standard deviation.

For ipsilateral lung, all parameters used to analyze the lung irradiation showed that significant improvements are obtained with Co-FinF technique with respect to Co-WF technique [Table 3]. Mean lung dose reduced from 12.1 Gy for the Co-WF plans to 9.8 Gy for the Co-FinF technique ($P < 0.001$). Similarly, D_2 dropped from 52.3 Gy for the Co-WF plans to 46.9 Gy for the Co-FinF plans ($P < 0.001$). In addition, lung irradiation reduced at all dose levels [Table 3]. For the seven patients whose left breast was considered, Co-FinF technique shows a slightly improvements in all dosimetric considered parameters for the heart irradiation [Table 3]. Both for the ipsilateral lung and heart, Co-FinF show no significant differences respect to Co-OF technique. Contralateral breast maximum dose (D_2) was lower for Co-FinF compared to Co-WF ($P = 0.009$).

Discussion

A preliminary assessment on the feasibility of FinF technique with a cobalt source for the post-operative treatment of breast cancer has been performed. The results

of this analysis showed that FinF technique can replace the use of filters to optimize the dose distribution despite the limitations of cobalt machine. It was also found out that the dose distribution with the FinF technique is slightly superior to that obtained with wedge filters. In fact, compared to the wedge filters technique, FinF technique is able to reduce the hot-spot areas and dose to lung and heart. Therefore, FinF may be useful as an optimization possibility compared to standard treatment. Particularly, it may be more useful in centers with the unfiltered cobalt equipment.

Our analysis has some limitations. Treatment plans were created using a CT-simulator and a 3D TPS, not necessarily available in centers with limited technology. Furthermore, treatment plans have been performed by an “expert” operator. To overcome these limitations and make available a standardized methodology, a class solution based solely on the traditional simulator and 2D TPS is currently developing.

In this analysis, only 2 segments per field were used. It is possible that the use of a greater number of beams can produce better dosimetric results. In particular, it may be possible to further reduce the dose hotspots, which are still significant (110-115%), by using more and better shaped segments by means of blocking devices or MLCs. Our choice was motivated by the fact that with cobalt machines, the use of this technique requires a double field size change and beam positioning for each field. The use of a greater number of segments in our opinion would prolong the treatment duration considerably to an unacceptable level. However, in case of asymmetric collimators based machine,^[23] the use of a greater number

Table 3: Comparison of organs-at-risk dose volume metrics (mean values±SD)

	6MV-CRT	Co-OF	Co-WF	Co-FinF	P^* (Co-OF vs. Co-FinF)	P^* (Co-WF vs. Co-FinF)	P^* (6MV vs. Co-FinF)
Ipsilateral lung							
D_{mean} (Gy)	5.1±2.4	10.2±3.9	12.1±4.8	9.8±4.1	0.047	<0.001	<0.001
V_{10} (%)	11.2±5.7	23.8±9.4	26.4±10.7	22.9±10.0	0.157	<0.001	<0.001
V_{20} (%)	8.5±5.1	16.7±8.5	18.5±9.3	16.2±8.6	0.059	<0.001	<0.001
V_{30} (%)	6.6±4.5	12.5±7.7	14.5±8.5	12.3±7.6	0.766	<0.001	0.006
V_{40} (%)	4.8±3.8	8.6±6.8	11.2±7.8	8.5±6.5	1.000	<0.001	0.031
V_{50} (%)	0.8±2.1	2.1±3.6	7.0±6.5	2.0±3.2	1.000	0.002	0.540
$D_{2\%}$ (Gy)	41.1±4.4	46.5±5.4	52.3±5.9	46.9±4.8	1.000	<0.001	0.126
Heart							
D_{mean} (Gy)	1.9±0.5	5.5±1.7	6.2±2.6	4.9±2.1	0.331	0.044	0.020
V_{10} (%)	1.6±1.3	9.3±6.0	10.5±8.2	8.3±6.5	0.066	0.047	<0.001
V_{20} (%)	0.6±0.6	4.2±3.7	5.1±4.6	4.0±3.8	1.000	0.023	<0.001
V_{30} (%)	0.2±0.3	2.2±2.3	3.0±3.1	2.1±2.3	1.000	0.026	<0.001
V_{40} (%)	0.1±0.1	0.7±1.0	1.6±1.9	0.7±1.1	1.000	0.044	0.001
V_{50} (%)	0.0±0.0	0.0±0.0	0.3±0.4	0.0±0.0	1.000	0.671	1.000
$D_{2\%}$ (Gy)	8.8±5.5	25.9±12.1	29.4±14.3	24.5±12.5	0.831	0.035	0.001
Contralateral breast							
$D_{2\%}$ (Gy)	2.8±1.2	5.5±2.4	6.9±3.4	5.3±2.6	1.000	0.009	<0.001

*By Bonferroni *post hoc* analysis, CRT: Conformal radiotherapy, SD: Standard deviation

of segments might be feasible without a significant treatment time prolongation.

Some previous studies showed the possibility of performing IMRT treatments with a cobalt machine. In one case, it was a theoretical analysis based on a telecobalt model equipped with MLC.^[24] In another case, a single case of breast cancer patient was reported for whom a mixed conformal-IMRT was suggested.^[25] Therefore, unlike these studies, our analysis was based on a “real” situation and on a simplified technique theoretically feasible in all radiotherapy departments.

There is higher dose homogeneity and reduction of hot-spot regions thus the FinF treatments may encourage the use of accelerated-hypofractionated treatments with the cobalt sources. The Standardization of Breast Radiotherapy Trials studies, in fact, have shown the equivalence between standard and hypofractionated regimes.^[26,27] The adoption of accelerated-hypofractionated schemes would be particularly useful in developing countries, given the lack of facilities and equipment. Hopefully, greater availability of postoperative radiotherapy by the adoption of these accelerated treatments, may promote the spread of conservative treatment in these countries.

Conclusion

A forward-planned IMRT technique, in a field-in-field approach, can be easily implemented in post-operative breast cancer radiotherapy for resource deficient cancer centers world-wide utilizing the cobalt-60 treatment units. Despite cobalt machine limitations, this technique can replace the use of filters to optimize the dose distribution.

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