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ORIGINAL ARTICLE

A Dosimetric Comparative Analysis of TomoDirect and Three-Dimensional Conformal Radiotherapy in Early Breast Cancer

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Purpose: The purpose of this study is to compare dosimetric parameters of intensity-modulated mode of TomoDirect and three-dimensional conformal radiotherapy (3D-CRT) in patients with early breast cancer. **Methods:** TomoDirect and 3D-CRT planning were carried out for 26 patients with early breast cancer who had received breast-conserving surgery. A total of 50.4 Gy in 28 fractions were prescribed to the planning target volume. The organs at risk (OAR) such as lung and heart were contoured. Planning target volume (PTV) dose coverage, radiation conformity index (RCI), radical dose homogeneity index (rDHI), and irradiation dose of organs at risk were compared between TomoDirect and 3D-CRT planning. **Results:** The mean PTV dose (51.65±0.37 Gy) and $V_{47.8}$ (100%) in TomoDirect were significantly higher than the mean PTV dose (50.88±0.65 Gy) and $V_{47.8}$ (89.23%±0.06%) in 3D-CRT (all, $p<0.001$). The RCI value in TomoDirect was significantly better than that in 3D-CRT (1.00 vs. 1.13, $p<0.001$). However, the rDHI value in TomoDirect was not significantly better than that in 3D-CRT (0.72 vs. 0.67, $p=0.056$). The mean lung dose and V_{10}, V_{20}, V_{30}, and V_{40} values of ipsilateral lung in TomoDirect were significantly lower than those in 3D-CRT (all, $p<0.05$). There is no significant difference in the V_{10}, V_{20}, V_{30}, and V_{40} values of heart between TomoDirect and 3D-CRT. And the mean dose for heart in TomoDirect was marginally lower than that in 3D-CRT (1.05 Gy vs. 1.62 Gy, $p=0.085$). The mean dose for left anterior descending coronary artery in left breast cancer was significantly lower in TomoDirect than in 3D-CRT (7.2 Gy vs. 12.1 Gy, $p<0.001$). **Conclusion:** Compared to 3D-CRT, TomoDirect could result in favorable target coverage while reducing the irradiation dose of the ipsilateral lung for patients with early breast cancer.

Key Words: *Breast, Neoplasms, Radiometry, Radiotherapy*

INTRODUCTION

Breast cancer is the second most common cancer in Korean women based on the Korean National Cancer Screening Survey. The incidence of breast cancer has been gradually increasing in Korea [1].

Breast-conserving surgery followed by breast irradiation has become a standard treatment for early breast cancer [2]. Radiotherapy (RT) has a definite role in reducing locoregional recurrence, leading to improved recurrence-free survival in early breast cancer [3]. Conventional radiotherapy consisted of tangential opposed beams to deliver radiation to the entire breast. However, the entire breast irradiation has acute toxicities to organs at risk such as lung and heart [4]. Therefore, clinicians have made great efforts to minimize the dose of irradiation to adjacent normal tissues near the breast to avoid acute and long-term adverse effects in breast cancer patients.

Modern radiotherapy techniques, such as TomoTherapy using image-guided radiotherapy and intensity-modulated radiotherapy (IMRT), are able to improve the accuracy of radiation delivery while reducing the irradiation dose to normal tissues. TomoDirect, a nonrotational treatment option of TomoTherapy Hi-Art System (Accuray, Sunnyvale, USA), allows planning and delivering of RT with a series of highly modulated linear beam paths [5,6]. TomoDirect can yield IMRT which allows highly conformal distributions of radiation dose to the target while minimizing irradiation to the adjacent dose limiting organs. Use of TomoDirect technique for breast cancer can attain optimal planning target volume coverage and

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adequate normal tissue sparing in a pilot study [7].

Moreover, the beam-on time of TomoDirect during breast irradiation is less than helical TomoTherapy and comparable to that of three-dimensional conformal radiotherapy (3D-CRT) [7]. In Lee et al. [8], median beam-on time was just 175 seconds. These considerations could make TomoDirect as a useful option for the radiation oncology department which only equipped with helical TomoTherapy without conventional linear accelerator. However, it has been not clinically determined whether TomoDirect was dosimetrically better than 3D-CRT for Asian patients with early breast cancer. Therefore, the objective of this study was to compare dosimetric parameters of TomoDirect and 3D-CRT in early breast cancer patients of an Asian cohort.

METHODS

Patients

Consecutive 26 patients diagnosed with early breast cancer with negative axillary node or carcinoma *in situ* between November 2013 and April 2014 were evaluated in this study. The 26 patients had breast-conserving surgery followed by entire breast irradiation using TomoDirect-IMRT. Patients with metastatic breast cancer or previous radiation history of chest wall due to the thoracic malignancy and patients had resection margin were excluded. This study was approved by the Institutional Review Board of our institution (VC14RISI0064).

Simulation and treatment planning

During simulation, patients were immobilized on wing board with both arms raised. Patients underwent computed tomography (CT) scans from the lower neck to the mid abdomen with 3 mm-slice thickness. Axial images were imported to the Eclipse treatment planning system (Varian Medical System, Palo Alto, USA) for three-dimensional planning and TomoTherapy Hi-Art System.

Planning target volume (PTV) was defined using the contouring guideline of Radiation Therapy Oncology Group [9,10]. PTV included breast palpable tissue and the tumor bed. The heart was contoured according to the Taylor et al. [11]. The cranial limit of the heart included the right atrium and excluded the pulmonary trunk, ascending aorta and superior vena cava. The lowest contour of the heart was the caudal myocardial border. For IMRT-mode of TomoDirect plan, the field width, pitch, and modulation factor need to be selected. Then, the dose distribution for each beamlet that passes through the target is calculated by a convolution/superposition algorithm. Two tangential beams with a jaw size of 2.5 cm, a pitch of 0.25, and a modulation factor of 2.0 was set. A normal calculation grid of 0.356×0.356 cm^2 was used in optimization and calculation processes. Beam angles were selected to minimize the dose to normal tissues and to avoid the irradiation to the contralateral breast (Figure 1A). A total of 50.4 Gy in 28 fractions with 6 MV photon were prescribed to the PTV in TomoDirect. The organ at risk (OAR) such as lung and heart was contoured. The goals of TomoDirect were as follows: (1) at least 95% of PTV received 100% of the prescribed dose; (2) more than 105% of the prescribed dose should be below 10% of PTV; (3) more than 110% of the prescribed dose should be below 5% of PTV; (4) mean irradiation dose of the lung should be under 10 Gy; (5) 20% of the lung was kept under 20 Gy; (6) 10% of the lung was kept under 30 Gy; (7) 10% of the heart was kept under 10 Gy; and (8) 5% of the heart was kept under 20 Gy. For 3D-CRT planning, two tangential fields with en-

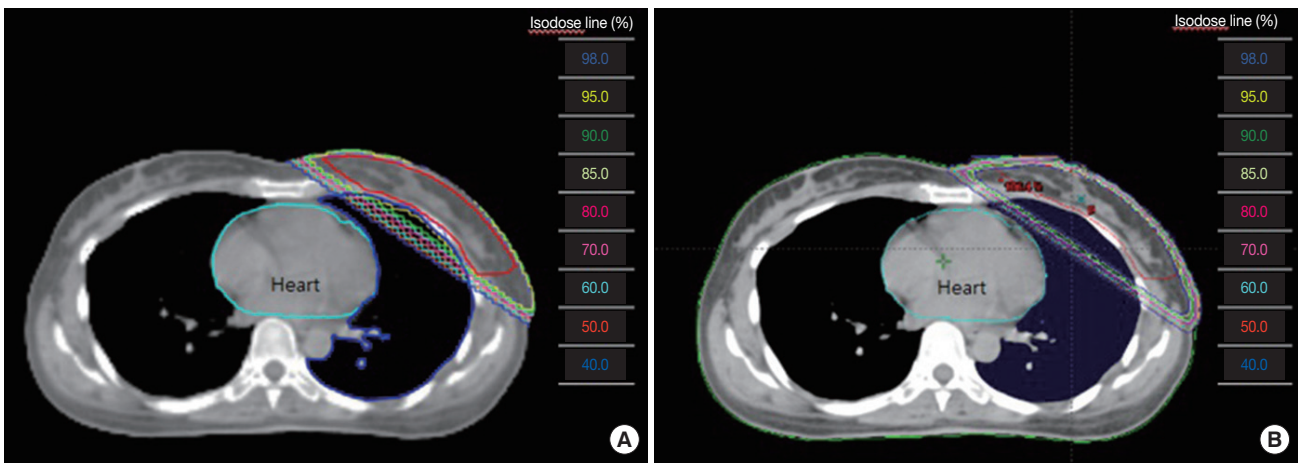

Figure 1. Dose distribution for TomoDirect plan (A) and three-dimensional conformal radiotherapy plan (B). Red contour means the planning target volume which contains lumpectomy site with clips and normal breast tissue.

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hanced dynamic wedge were used. The same gantry angles were used for TomoDirect and 3D-CRT planning. Dynamic wedge and beam weighting were applied to optimize the coverage of the PTV while minimizing the exposure to the normal tissue. A total of 50.4 Gy in 28 fractions delivered with 6 to 15 MV photon was prescribed for the PTV in 3D-CRT. The isocenter was set at the half point between the mid-axilla and the anterior chest wall in the middle CT-slice of the PTV. The superior, inferior, and lateral border of the field was 1.5 cm apart from the contoured PTV without block. Medial border of the field was 1 cm apart from the PTV with a conventional block margin (Figure 1B).

Dosimetric comparison between TomoDirect and 3D-CRT

Dosimetric parameters between TomoDirect and 3D-CRT for the same patient were compared. The mean dose, percentage of the volume receiving radiation ≥ n Gy (V_{nGy}), minimum dose (D_{min}), maximum dose (D_{max}), radiation conformity index (RCI), and radical dose homogeneity index (rDHI) were analyzed for the PTV. RCI and rDHI were defined as follows: RCI = PTV/V_{95} (volume enclosed by the 95% of isodose line); rDHI = D_{min}/D_{max} in the PTV [12,13].

The avoidance of irradiation to the heart and lung was evaluated using the values such as mean dose and V_{nGy}. Paired t-test was performed to compare the dosimetric parameters between TomoDirect and 3D-CRT. Difference was considered statistically significant when *p*-value was less than 0.05. Data analysis was performed with R software version 2.15 (Alcatel-Lucent, Murray Hill, USA).

Table 1. Patient characteristics (n = 26)

Characteristic	No. (%)
Age (yr)*	51 (37–70)
Body mass index (kg/m^2)*	23 (19–29)
Site	
Right	11 (42.3)
Left	15 (57.7)
pT stage	
Tis	12 (46.2)
T1	10 (38.4)
T2	4 (15.4)
Tumor location	
Upper	24 (92.3)
Lower	2 (7.7)
Axillary staging	
None	9 (34.7)
Sentinal node biopsy	3 (11.5)
Axillary node dissection	14 (53.8)
Presence of seroma ≥ 15 mL	
Negative	20 (77.0)
Positive	6 (23.0)
Adjuvant chemotherapy	
No	13 (50.0)
Yes	13 (50.0)

*Median (range).

RESULTS

Patient characteristics were summarized in Table 1. A total of 10 patients (38.5%) had ductal carcinoma *in situ*. Twelve (46.2%) with T1 tumors and four (15.3%) patients with T2 tumors were enrolled for this study. All patients had pathologically negative node. Of the 26 patients, 11 had right-sided breast tumors, and 15 had left-sided breast tumors. The median age of the 26 patients was 51 years (range, 37–70 years).

Dose distribution of the target

The median of PTVs in the 26 patients was 356.5 cc (range, 216.2–525.5 cc). The prescription goal of TomoDirect plan was completely met for PTVs in all cases. The dose parameters for PTV in the TomoDirect and 3D-CRT were compared and summarized in Table 2. The mean PTV dose in TomoDirect was significantly higher than that in 3D-CRT (51.65 Gy vs. 50.88 Gy, $p < 0.001$). The dosimetric value of $V_{47.8}$ for TomoDirect was significantly higher than that for 3D-CRT (100% vs. 89.2%, $p < 0.001$) (Figure 2). However, there was no significant difference in the $V_{52.9}$ and $V_{55.4}$ values between the two radiation techniques. The D_{min} (39.96 Gy) and D_{max} (55.40 Gy) values in TomoDirect were significantly higher than those (D_{min} 36.61 Gy; D_{max} 54.26 Gy) in 3D-CRT (all, $p < 0.05$). The RCI values of TomoDirect and 3D-CRT were 1.00 and 1.13, respectively. The RCI value of TomoDirect was significantly better than that of 3D-CRT ($p < 0.001$). The rDHI value in TomoDirect was not significantly better than that in 3D-CRT plan (0.72 vs. 0.67, $p = 0.056$).

Table 2. Comparison of dosimetric parameters for the planning target volume between TomoDirect and three-dimensional conformal radiotherapy

Parameter	TomoDirect	3D-CRT	*p*-value
Mean dose (Gy)	51.65 ± 0.37	50.88 ± 0.65	< 0.001
$V_{47.8}$ (%)	100 ± 0.00	89.23 ± 6.33	< 0.001
$V_{52.9}$ (%)	5.23 ± 10.02	4.46 ± 4.94	0.727
$V_{55.4}$ (%)	0.13 ± 0.52	0.00 ± 0.00	0.193
D_{min} (Gy)	39.96 ± 5.96	36.61 ± 2.37	0.011
D_{max} (Gy)	55.40 ± 1.45	54.26 ± 0.92	0.001
RCI	1 ± 0.00	1.13 ± 0.10	< 0.001
rDHI	0.72 ± 0.11	0.67 ± 0.04	0.056

3D-CRT = three-dimensional conformal radiotherapy; V_{nGy} = percentage of the volume receiving radiation ≥ n Gy; D_{min} = minimum dose irradiated to the planning target volume; D_{max} = maximum dose irradiated to the planning target volume; RCI = radiation conformality index; rDHI = radical dose homogeneity index.

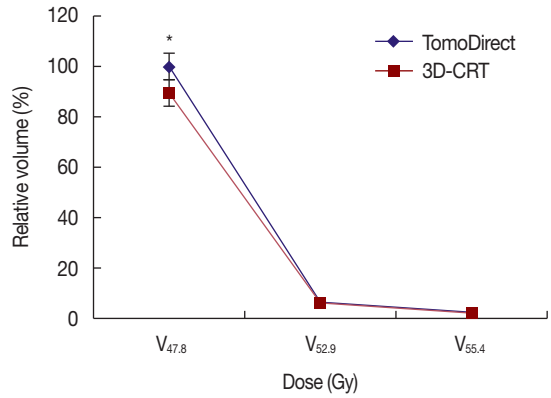

Figure 2. Dose-volume histogram of the planning target volume in TomoDirect and three-dimensional conformal radiotherapy (3D-CRT) planning. The mean value of $V_{47.8}$ was significantly higher in TomoDirect than in 3D-CRT (100% vs. 89.2%, *$p<0.001$).
V_{nGy} = percentage of the volume receiving radiation ≥n Gy.

Table 3. Comparison of dosimetric parameters for the ipsilateral lung and heart between TomoDirect and three-dimensional conformal radiotherapy

Parameter		TomoDirect	3D-CRT	*p*-value
Lung	Mean (Gy)	5.07±1.81	6.94±2.25	0.002
	V_{40} (%)	4.73±2.86	9.71±4.12	<0.001
	V_{30} (%)	6.83±3.51	11.5±4.42	<0.001
	V_{20} (%)	8.98±4.01	13.19±4.70	0.001
	V_{10} (%)	12.32±4.28	15.28±4.99	0.026
Heart	Mean (Gy)	1.05±0.82	1.62±1.44	0.085
	V_{40} (%)	0.24±0.80	0.53±1.53	0.395
	V_{30} (%)	0.47±1.17	0.96±1.98	0.290
	V_{20} (%)	0.73±1.48	1.53±2.53	0.169
	V_{10} (%)	1.16±2.02	2.19±3.26	0.780
Coronary artery*	Mean (Gy)	7.24±2.11	12.13±2.84	<0.001

3D-CRT = three-dimensional conformal radiotherapy; V_{nGy} = percentage of the volume receiving radiation ≥n Gy.
*Irradiated doses of left anterior descending coronary artery were compared in left breast cancer patients.

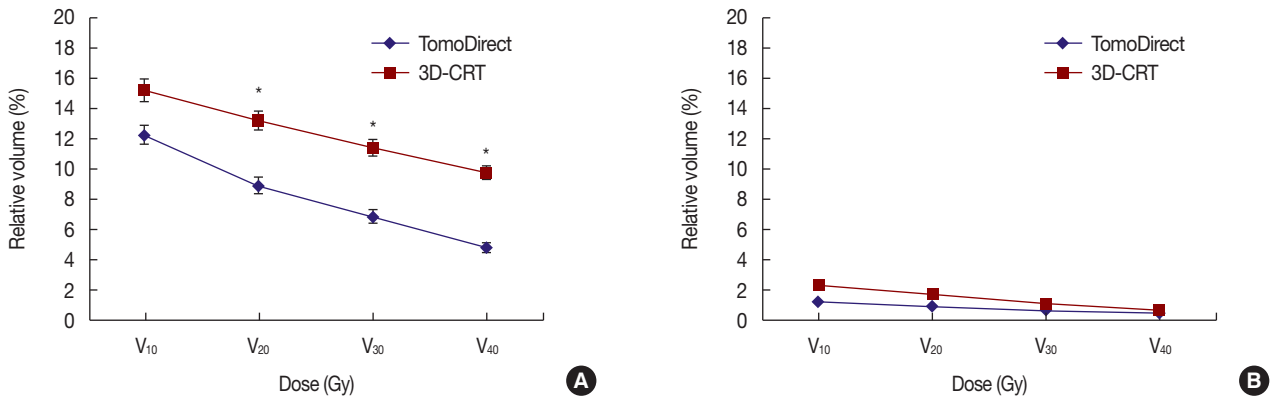

Figure 3. Dose volume histogram of the ipsilateral lung (A) and heart (B) in TomoDirect and three-dimensional conformal radiotherapy (3D-CRT) planning. The mean±SD values of V_{10}, V_{20}, V_{30}, and V_{40} of ipsilateral lung were significantly lower in TomoDirect than in 3D-CRT.
V_{nGy} = percentage of the volume receiving radiation ≥n Gy.
*$p<0.05$.

Dose distribution of OAR

The dosimetric parameters for the ipsilateral lung and heart were summarized in Table 3. The mean dose for the ipsilateral lung in TomoDirect was significantly lower than that in 3D-CRT plan (5.07 Gy vs. 6.94 Gy, $p=0.002$). Values of V_{10}, V_{20}, V_{30}, and V_{40} of the ipsilateral lung in TomoDirect were also significantly lower than those in 3D-CRT (all, $p<0.05$) (Figure 3A). The mean dose for heart in TomoDirect was marginally lower than that in 3D-CRT (1.05 Gy vs. 1.62 Gy, $p=0.085$). There were no significant differences in the V_{10}, V_{20}, V_{30}, V_{40} values of heart between the two arms (Figure 3B). In subgroup analysis of left breast cancer patients, there was not significant heart dose reduction in TomoDirect compared to 3D-CRT planning.

The mean doses for the ipsilateral heart in TomoDirect and 3D-CRT of left breast cancer patients were 1.44 Gy and 2.32 Gy, respectively, and the difference was marginally significant ($p=0.070$). The mean dose for left anterior descending coronary artery in left breast cancer was significantly lower in TomoDirect than in 3D-CRT (7.2 Gy vs. 12.1 Gy, $p<0.001$).

DISCUSSION

Several studies have suggested that chemotherapy, hormonal therapy, individual biologic factors, and radiation could induce pneumonitis in breast cancer patients [14-16]. Those therapies could lead to early inflammatory damage and later complications of chronic fibrosis. Radiation induced pneumonitis most commonly occurs as a result of radiation therapy [17]. Many studies have growing concerns that cardiac mortality and mor-

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bidity may be raised by the use of the left sided breast irradiation with cobalt-60 or orthovaltage therapy which often includes some coronary arteries and myocardium [18]. Based on the data from the Ontario Cancer Registry (Ontario, Canada) on breast cancer treated with breast-conserving surgery from 1982 to 1987, 2% of women with left-sided breast irradiation had a fatal myocardiac infarction, which is significantly ($p=0.020$) higher than the 1% of women with right-sided breast irradiation [19].

Although modern radiotherapy technique such as 3D-CRT has been improved, symptomatic radiation induced pneumonitis occured in 1% to 10% of patients irradiated for breast cancer [20]. Therefore, there have been investigational studies to reduce the radiation dose to the lung using IMRT. Several studies have analyzed the dosimetric parameters between IMRT and 3D-CRT for the entire breast irradiation in early breast cancer patients [21-23]. There are obvious dosimetric differences between IMRT and 3D-CRT. IMRT improved the avoidance of radiation to the heart, lung, and axillary region while promoting PTV coverage. There is an investigational report that TomoTherapy could attain fine PTV coverage and OAR sparing compared to 3D-CRT in rectal cancer patients [24]. Thus, this study was conducted to compare the dose distribution of PTV, ipsilateral lung, and heart between TomoDirect and 3D-CRT.

In a pilot study, Borca et al. [7] evaluated plans for 17 breast cancer patients using TomoDirect in 3D-CRT and IMRT mode and field-in field 3D-CRT planning (FIF). They compared in terms of PTV coverage, overdosage, homogeneity, conformality and dose to OARs. In Borca et al. [7], the median PTV volume was 731 cm^3 (range, 425–1,643 cm^3). Unlike their results, the mean PTV volume in our patients was 342.1 ± 101.0 cm^3. This difference meant that Korean women had relatively small breasts, as compared with Western women. They reported that 3D-CRT provided significantly higher values of ipsilateral lung mean volume receiving >20 Gy ($p<0.05$), mean heart volume receiving >25 Gy ($p<0.010$) and mean heart dose ($p<0.010$), while contralateral lung D_{max} and D_{mean} were significantly lower ($p<0.001$) and D_{2cc} was significantly higher for 3D-CRT than TD-IMRT and FIF ($p<0.001$) [7].

Our data showed that, compared to 3D-CRT, TomoDirect plan of the entire breast irradiation reduced the mean ipsilateral lung dose and the V_{10}, V_{20}, V_{30}, V_{40} values of the lung. Similar studies have been published for IMRT of the entire breast in early breast cancer patients [25]. In their data, the dose in 50% of volume of OAR was lower in IMRT than in 3D-CRT. The median dose of the ipsilateral lung was 4.5 to 5 Gy for IMRT and 5.6 Gy for 3D-CRT. Sas-Korczyńska et al. [26] reported that IMRT seemed to reduce the mean heart dose when compared to 3D-CRT. IMRT improved reduction of cardiac high dose area and reduced long-term cardiac complications. In our study, the mean heart dose and the V_{10}, V_{20}, V_{30}, V_{40} values of the heart have no significant difference between TomoDirect and 3D-CRT. In our analysis, the mean heart doses were just 1.05 Gy for TomoDirect and 1.62 Gy for 3D-CRT ($p=0.085$). As compared with 3D-CRT, TomoDirect showed a tendency for reducing the mean heart dose and a significant improvement for reducing the mean left anterior descending coronary artery dose. In the 3D-CRT technique, we applied medial block of 1 cm from the PTV to reduce the heart dose. Heart block could decrease irradiated heart volume. Comparison of RCI values between the two plans showed statistically significant and favorable results for the TomoDirect plan, confirming the findings of Baycan et al. [27] who reported a significant improvement in RCI value with IMRT compared to 3D-CRT.

In conclusion, our study suggests that the use of TomoDirect could result in favorable dose coverage for the target while reducing the radiation dose for the ipsilateral lung in patients with early breast cancer, as compared to 3D-CRT.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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