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Original Article

Dosimetric study of three-dimensional conformal radiotherapy, electronic compensator technique, intensity-modulated radiation therapy and volumetric-modulated arc therapy in whole breast irradiation†

Chonnipa Nantavithya, Kitwadee Saksornchai, Puntiwa Oonsiri, Kanjana Shotelersuk

Department of Radiology, Division of Radiation Oncology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

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Abstract

Background: Whole breast irradiation is an essential treatment after breast-conserving surgery (BCS). However, there are some adverse effects from inhomogeneity and dose to adjacent normal tissues.

Objective: Aim of this study was to compare dosimetry among standard technique, three-dimensional conformal radiotherapy (3D-CRT), and advanced techniques, electronic compensator (ECOMP), inverse intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT).

Methods: Whole breast irradiation treatment plans of patients who had underwent BCS and whole breast irradiation were re-planned with all four techniques. Clinical target volume was contoured according to the Radiation Therapy Oncology Group atlas for breast only in patients who had negative node or ductal carcinoma in situ and breast with chest wall for patients with positive node. Planning target volume was non-uniformly expanded. Dose prescription was 50 Gy in 25 fractions with 6 MV photon energy.

Results: In total, 25 patients underwent whole breast irradiation with computed tomography simulation from November 2013 to November 2014 were included. Six patients with positive nodes were re-planned for breast with chest wall irradiation and 19 patients with negative nodes were re-planned for breast only irradiation. Primary outcome, radical dose homogeneity index (HI) of 3D-CRT, ECOMP, IMRT and VMAT were 0·865, 0·889, 0·890 and 0·866, respectively. ECOMP and IMRT showed significant higher HI than 3D-CRT (p-value $< 0{\cdot}001$). Secondary outcome, conformity index (CI) of advanced technique were significantly better than 3D-CRT. Lung V20, mean ipsilateral lung dose (MILD), mean heart dose (MHD), heart V25, heart V30 of advanced techniques were also lower than 3D-CRT. ECOMP had better mean lung dose (MLD), mean contralateral lung dose (MCLD) and mean contralateral breast dose (MCBD) when compared with 3D-CRT. Monitor units of advanced techniques were significantly higher than 3D-CRT.

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Correspondence to: Kanjana Shotelersuk, Associate Professor, Department of Radiology, Division of Radiation Oncology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital (KCMH), 1873 Rama 4 Road, Patumwan, Bangkok 10330, Thailand. Tel: +66 256 4334; E-mail: kanjanash@yahoo.co.th

Conclusions: HI of ECOMP and IMRT were significantly higher than 3D-CRT technique. All advanced techniques showed statistically better in CI. Lung V20, MILD, heart V25 and heart V30 of advanced techniques were lower than 3D-CRT. However, only ECOMP showed decreased MLD, MHD, MCLD and MCBD when compared with 3D-CRT.

Keywords: electronic compensator; intensity-modulated radiation therapy; three-dimensional conformal radiotherapy; volumetric-modulated arc therapy; whole breast irradiation

INTRODUCTION

At present, radiation therapy is an essential part for the treatment of localised breast cancer. Breast conservation therapy (BCT), or also known as lumpectomy followed by radiotherapy, is widely accepted as the standard of treatment for patients with localised breast cancer and ductal carcinoma in situ (DCIS).[1–4] Aside from that, patients tend to feel more confident about their body images and are more satisfied with BCT compared with mastectomy.[5]

Adjuvant radiotherapy in BCT has been proven to be effective in reducing local recurrence.[1–4] Standard radiation treatment of the whole breast irradiation is three-dimensional conformal radiotherapy technique (3D-CRT) with images set from a computed tomography (CT) simulator to deliver 45–50 Gy in 25 fractions. However, there are still some acute and long-term toxicities, especially to the skin[6–10] and adjacent organs, such as the heart,[11–15] lung[16–18] and contralateral breast.[19] Several studies showed that toxicities were associated with inhomogeneous dose at the target volume and unwanted dose to adjacent organs. For these reasons, several advanced whole breast irradiation techniques have been developed to increase dose homogeneity, improve target volume coverage and reduce dose to organs at risk (OAR).[7,20–24] However, there are few studies of these advanced techniques in Asians,[25,26] who have different size and shape of breasts compared with participants reported in previous studies. Moreover, there is no standardisation of the definition of the target volume. Therefore, this could result in unreliable outcomes.

The purpose of this study was to compare the dose distribution of the standard of treatment for whole breast irradiation, 3D-CRT, to the other three advanced techniques such as electronic tissue compensation (ECOMP), inverse intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) that were available at the King Chulalongkorn Memorial Hospital (KCMH).

MATERIALS AND METHODS

Records of Thai women diagnosed with locally advanced breast cancer or DCIS who had already underwent breast-conserving surgery and whole breast irradiation treatment at the Division of Therapeutic Radiation and Oncology of KCMH from November 2013 to November 2014 were retrospectively reviewed. The authors excluded patients who previously underwent mastectomy or breast augmentation of the ipsilateral or contralateral breast. The number of patients in this study (sample size) was calculated based on a pilot study in order to achieve the adequate number for statistical analysis. We used the quota technique for the sampling method. The images from the GE Lightspeed RT CT (LightSpeed RT GE Medical system, Waukesha, WI, USA) simulation that had been used for whole breast irradiation of each patient were used for contouring target volumes, OAR and re-planning the whole breast irradiation by four techniques. The review of medical records in this study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (approval no. 349/56).

Target volumes and OAR

Clinical target volume (CTV), planning target volume (PTV) and OAR, which were heart, ipsilateral lung, contralateral lung and contralateral breast, were contoured by the author from the

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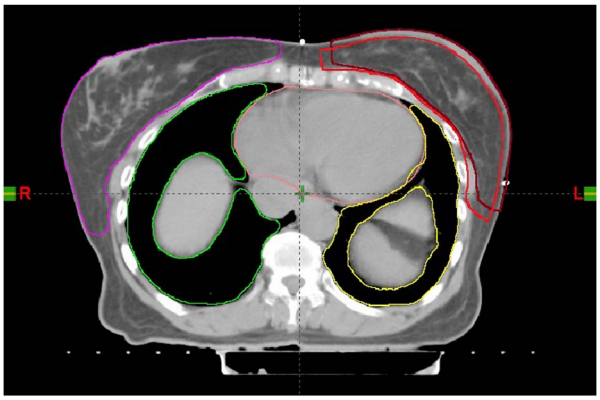

Figure 1. Target volumes and organs at risk for whole left breast irradiation; planning target volume (red line), clinical target volume (brown line), contralateral breast (magenta line), left lung (yellow line), right lung (green line).

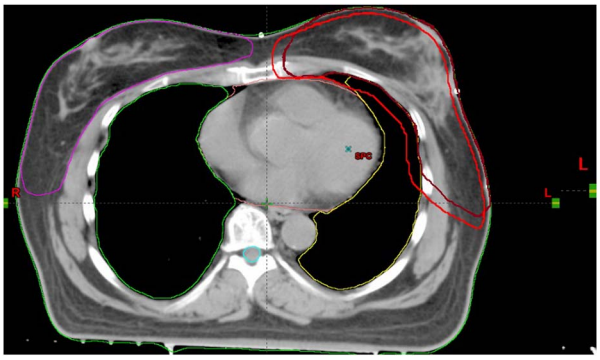

Figure 3. Target volumes and organs at risk for whole left breast and left chest wall irradiation; planning target volume (red line), clinical target volume (brown line), contralateral breast (magenta line), left lung (yellow line).

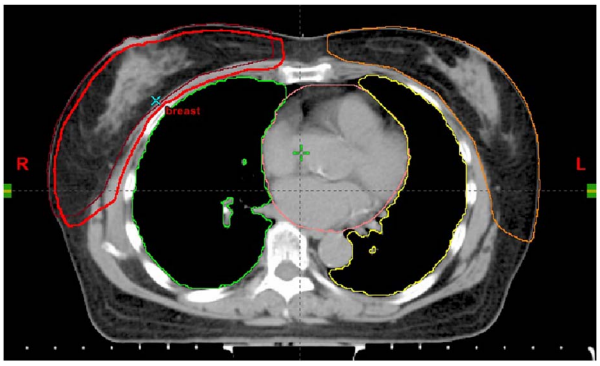

Figure 2. Target volumes and organs at risk for whole right breast irradiation; planning target volume (red line), clinical target volume (brown line), contralateral breast (orange line), left lung (yellow line), right lung (green line).

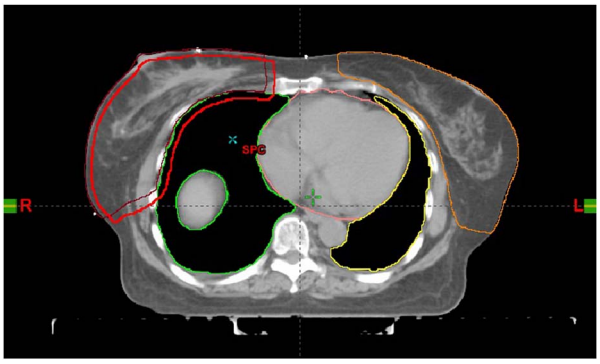

Figure 4. Target volumes and organs at risk for whole right breast and right chest wall irradiation; planning target volume (red line), clinical target volume (brown line), contralateral breast (orange line), left lung (yellow line).

CT simulation images. The definition of the CTV boundaries was based on the Radiation Therapy Oncology Group (RTOG)[27] (see Supplementary Table 1). For DCIS and invasive cases that had negative nodes, the author contoured the CTV for whole breast irradiation. For cases with positive nodes, the author contoured CTV for whole breast and chest wall irradiation. Regional nodes were not contoured in this study. PTV was defined according to the RTOG 1005 protocol[28] for whole breast irradiation, which was CTV +7 mm 3D expansion but excluded the part that extended posteriorly into the anterior surface of the ribs (bony thorax and lung), cross midline, extended anteriorly to the outside of the body and excluded 5 mm of tissue under the skin (Figures 1 and 2). For the whole breast and chest wall irradiation, the authors adapted the PTV from the RTOG 1005 protocol by excluding part of the PTV that extended posteriorly towards the heart but kept the border that extended into chest wall and lung. The other borders were the same as for the whole breast irradiation PTV (Figures 3 and 4).

Irradiation techniques, calculation and dose prescription

Each patient was re-planned by using all four techniques: standard 3D-CRT, ECOMP, inverse IMRT and VMAT. The total dose of radiation was 50 Gy in 25 fractions with 6 MV photon energy which was prescribed to PTV. The skin flash was

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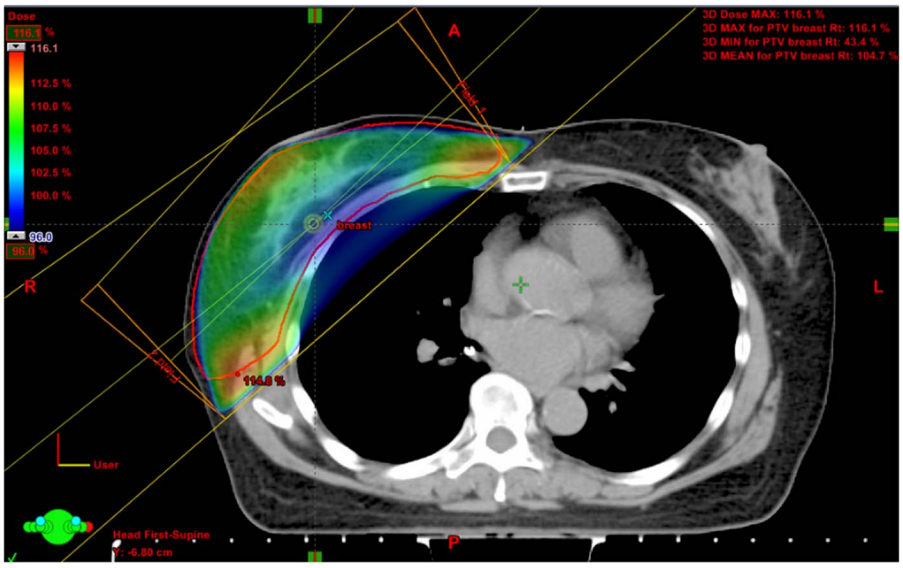

Figure 5. The dose colour wash representing 95% of the prescribed dose and beam alignment of three-dimensional conformal radiotherapy technique.

used in ECOMP technique. All treatment plans were calculated with Eclipse treatment planning software (version 11.0.31; Varian Medical Systems, Palo Alto, CA, USA). The radiation fields for each technique are described as follows:

(1) Standard 3D-CRT was planned by the same author that contoured target volumes and OAR. The plans consisted of two tangential fields. The angles between these beams were chosen in such a way that the posterior border of the lateral and medial fields were non-divergent. The optimal wedge angles and multileaf collimators (MLC) were chosen based on the dose distribution and calculated with inhomogeneity correction according to the standard protocol (Figure 5).

(2) ECOMP was planned by the same author as 3D-CRT technique. The plans consisted of two tangential fields. Tissue compensation was used to correct the dose inhomogeneity which could occur from an irregular surface of the patient's breast. The fluent distribution was calculated by ray tracing and determining the amount of missing tissue along each ray line. The fluent maps were converted to leaf sequences for dynamic MLC (DMLC) delivery (Figure 6).

(3) Inverse IMRT was planned by a physicist. The plans composed of five co-planar fields. The first two out of five fields were tangent, but not opposing. Gantry angles were adjusted as appropriate to cover PTV and avoid unnecessary normal tissue. Dose–volume constraints were inputted according to RTOG 1005 protocol (Table 1). The plan was optimised by The Eclipse Planning System, using inverse planning with DMLC (Figure 7).

(4) VMAT was planned by the same physicist who planned IMRT technique. Two co-planar arcs were inserted and adjusted as they needed to cover the PTV and avoid dose to the normal tissues. The VMAT plans were generated with a gantry angle sampling frequency of 2°, maximum MLC leaf motion between gantry samples of 2·5 cm and the gantry speed of 4·8°/second. Dose–volume constraint was inputted according to the RTOG 1005 protocol (Table 1) and then optimised by The Eclipse Planning System (Figure 8).

Data analysis

Dose–volume histograms (DVHs) were generated and recorded for PTV size, volume enclosed by the 95% isodose (V95%), PTV maximum dose (Dmax, PTV2%), PTV minimum dose (Dmin, PTV98%),

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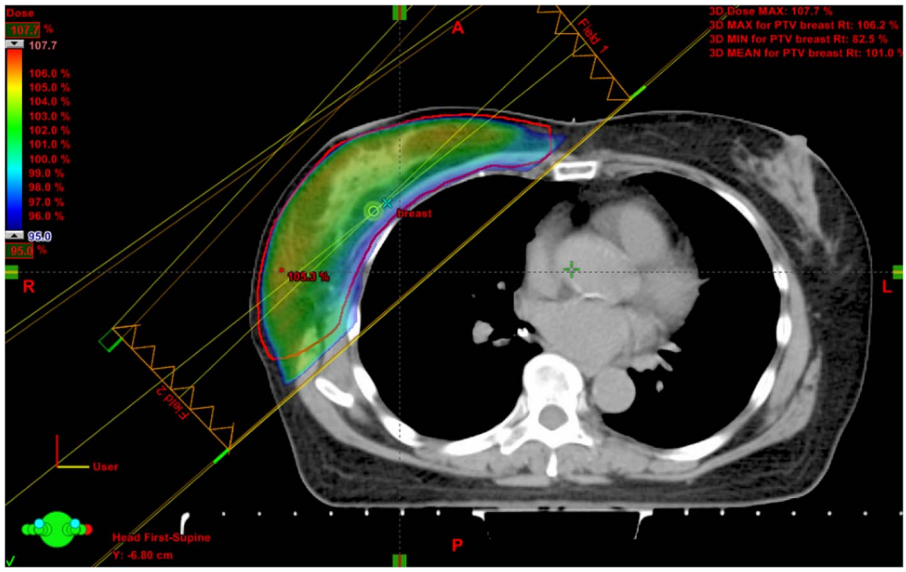

Figure 6. The dose colour wash representing 95% of the prescribed dose and beam alignment of electronic compensator (ECOMP) technique.

irradiated breast size, mean heart dose (MHD), heart V30 (percentage of the volume receiving >30 Gy), heart V25, mean lung dose (MLD), lung V20, mean ipsilateral lung dose (MILD), mean contralateral lung dose (MCLD), mean contralateral breast dose (MCBD), body volume enclosed by 95% isodose and monitor units (MU).

The primary outcome of this study was the radical dose homogeneity index (HI), which was defined as the ratio of Dmin to Dmax of the PTV (HI = Dmin/Dmax). The secondary outcomes were conformity index (CI), MHD, heart V30, heart V25, MLD, lung V20, MILD, MCLD, MCBD and MU. The CI was defined as the fraction of the PTV that is enclosed by the reference dose (95%) multiplied by the fraction of the total body volume (from the CT simulation) which included the 95% isodose (CI = PTV95%/PTV × PTV95%/V95%).

All results were analysed by IBM SPSS statistics 20 program, using repeated-measures analysis of variance test with a significance level of 0·05.

RESULTS

There were 25 patients in this study. The age of the participants ranged from 40 to 74 years. Mean irradiation of the breast size was 804·57 cm^3 and ranged from 423 to 1,744 cm^3. Median breast size was 646 cm^3. Number of patients were classified according to TNM (primary tumor, nodes, metastasis) stage and PTV as described in Tables 2 and 3, respectively. The primary and secondary outcomes are shown in Table 4.

HI and CI

The HI outcome for the ECOMP and IMRT techniques were significantly higher than the 3D-CRT technique ($p < 0{\cdot}001$ for both comparisons). The HI of VMAT and 3D-CRT were hardly different ($p = 0{\cdot}807$) and also observed this in comparing IMRT and ECOMP ($p = 0{\cdot}858$). However, the ECOMP and IMRT techniques had significantly higher HI when compared with the VMAT technique ($p < 0{\cdot}001$ and $p = 0{\cdot}001$, respectively).

For the CI outcome, the ECOMP, IMRT and VMAT techniques were significantly higher than the 3D-CRT technique ($p < 0{\cdot}001$ for all comparisons). IMRT and VMAT techniques had significantly higher CI compared with the ECOMP technique ($p < 0{\cdot}001$). When comparing between VMAT and IMRT, the CI was hardly different ($p = 0{\cdot}89$).

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Table 1. *Dose–volume histogram constraint for optimisation*

Description	Goal	Volume	Dose
PTV	Per protocol	At least 95% of the PTV receives	At least 95% of whole breast dose (47·5 Gy)
	Variation acceptable	At least 90% of the PTV receives	At least 90% of whole breast dose (45 Gy)
PTV maximum dose	Per protocol		Does not exceed 115% of prescription dose (57·5 Gy)
	Variation acceptable		Does not exceed 120% of prescription (60 Gy)
Heart dose constraint 1	Per protocol	No more than 5% of the heart for left-sided cancer 0% of the heart of right-sided exceeds	20 Gy
	Variation acceptable	No more than 5% of the heart for left-sided cancer 0% of the heart for right-sided exceeds	25 Gy
Heart dose constraint 2	Per protocol	No more than 30% of the heart for left-sided cancer No more than 10% of the heart for right-sided exceeds	10 Gy
	Variation acceptable	No more than 35% of the heart for left-sided cancer No more than 15% of the heart for right-sided exceeds	10 Gy
Heart dose constraint 3	Per protocol	Mean dose does not exceed	400 cGy
	Variation acceptable	Mean dose does not exceed	500 cGy
Ipsilateral lung dose	Per protocol	No more than 15% of the ipsilateral lung exceeds	20 Gy
	Variation acceptable	No more than 20% of the ipsilateral lung exceeds	20 Gy
Ipsilateral lung dose constraint 1	Per protocol	No more than 35% of the ipsilateral lung exceeds	10 Gy
	Variation acceptable	No more than 40% of the ipsilateral lung exceeds	10 Gy
Ipsilateral lung dose constraint 2	Per protocol	No more than 50% of the ipsilateral lung exceeds	5 Gy
	Variation acceptable	No more than 55% of the ipsilateral lung exceeds	5 Gy
Contralateral lung	Per protocol	No more than 10% exceeds	5 Gy
	Variation acceptable	No more than 15% exceeds	5 Gy
Contralateral breast	Per protocol	Dmax does not exceed/no more than 5% exceeds	310/186 cGy
	Variation acceptable	Dmax does not exceed/no more than 5% exceeds	496/310 cGy

Abbreviations: PTV, planning target volume; Dmax, maximum dose.

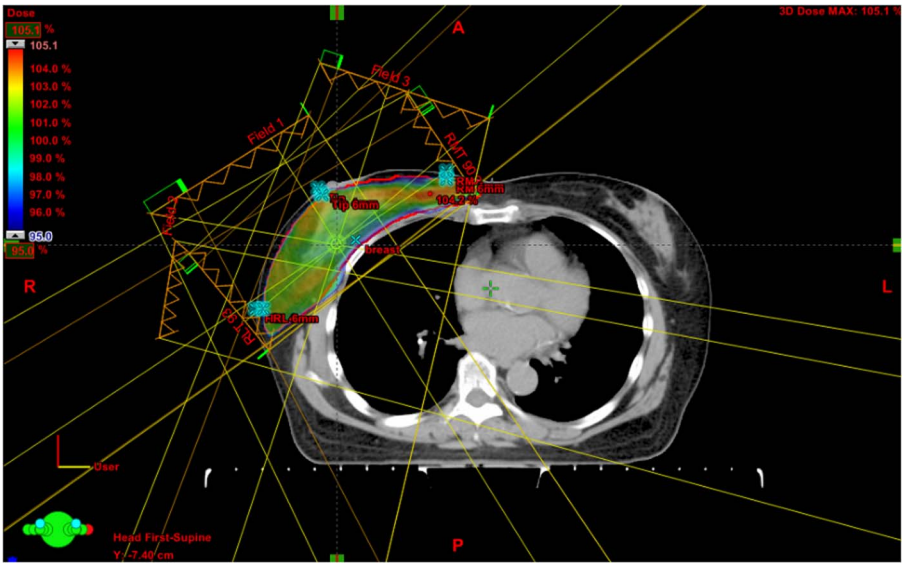

Figure 7. The dose colour wash representing 95% of the prescribed dose and beam alignment of intensity-modulated radiation therapy technique.

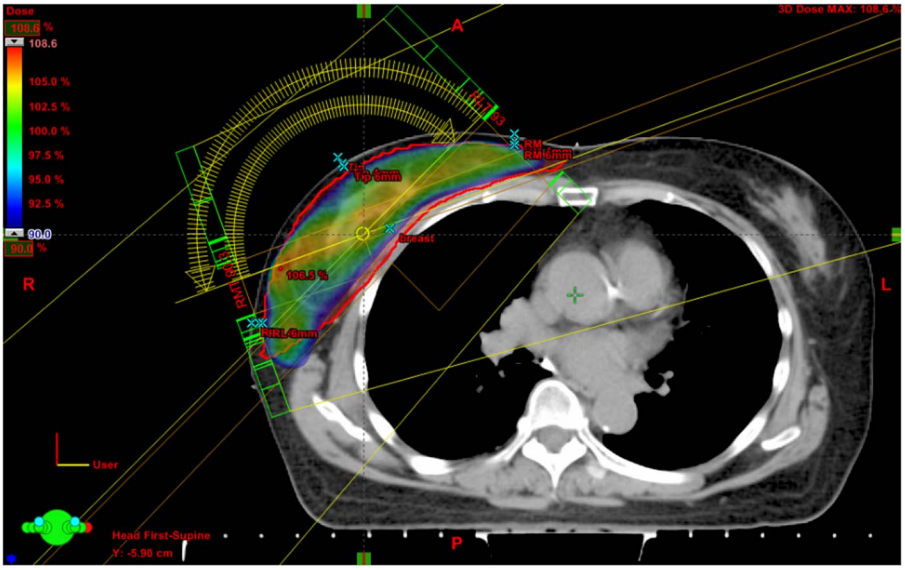

Figure 8. The dose colour wash representing 95% of the prescribed dose and beam alignment of volumetric-modulated arc therapy technique.

Heart dose

For the MHD, this was found to be significantly lower when the ECOMP technique was used compared with the 3D-CRT ($p < 0{\cdot}001$) and VMAT techniques ($p = 0{\cdot}001$). ECOMP also had lower MHD compared with IMRT but not statistically different ($p = 0{\cdot}053$). The 3D-CRT technique had non-significantly lower MHD compared with the VMAT technique ($p = 0{\cdot}202$). The MHD for the IMRT technique was significantly lower than the VMAT ($p = 0{\cdot}001$). But when the MHD for the IMRT was compared with the 3D-CRT, this was found to be comparable ($p = 0{\cdot}715$).

For the heart V25 outcome, this was found to be significantly lower when the ECOMP technique was used compared with the 3D-CRT ($p = 0{\cdot}001$). IMRT technique had statistically significant lower heart V25 compared with the

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3D-CRT, ECOMP and VMAT techniques ($p = 0{\cdot}001$, $0{\cdot}021$ and $0{\cdot}049$, respectively). VMAT technique had statistically significant lower heart V25 compared with the 3D-CRT technique ($p = 0{\cdot}014$). The V25 of the VMAT was non-statistically lower than ECOMP ($p = 0{\cdot}323$).

The heart V30 was significantly lower when the ECOMP technique was used compared with the 3D-CRT technique ($p = 0{\cdot}001$). The IMRT technique had statistically significant lower heart V30 compared with the 3D-CRT and ECOMP techniques ($p < 0{\cdot}001$ and $p = 0{\cdot}005$, respectively). The heart V30 was non-statistically higher in VMAT compared with IMRT ($p = 0{\cdot}181$). The VMAT technique had statistically significant lower heart V30 compared with the 3D-CRT technique ($p = 0{\cdot}002$). When the VMAT was compared with the ECOMP, VMAT tended to have statistically lower V30 ($p = 0{\cdot}051$).

Table 2. TNM stage of patients according to AJCC 7th edition

TNM staging	Number
T1N0M0	9
T2N0M0	7
T1N1M0	1
T2N1M0	3
T2N2M0	1
T2N3M0	1
DCIS	3

Abbreviation: TNM, primary tumor, nodes, metastasis stage; DCIS, ductal carcinoma in situ.

Table 3. The target volumes and sides of whole breast irradiation

Side/chest wall	Number
Left breast only	9
Right breast only	10
Left breast with chest wall	3
Right breast with chest wall	3

Lung dose

For MLD, this was found to be significantly lower when the ECOMP technique was used compared with the 3D-CRT, IMRT and VMAT techniques ($p < 0{\cdot}001$ for all comparisons). The MLD of 3D-CRT was comparable with IMRT ($p = 0{\cdot}557$) and non-statistically lower compared with VMAT ($p = 0{\cdot}051$). In addition, the MLD of IMRT was non-statistically lower than VMAT technique ($p = 0{\cdot}058$).

As for the lung V20 outcome, this was found to be significantly lower when the IMRT technique was used compared with the 3D-CRT ($p = 0{\cdot}001$), ECOMP ($p = 0{\cdot}025$) and VMAT ($p = 0{\cdot}006$). ECOMP technique had statistically significant lower lung V20 compared with the 3D-CRT ($p = 0{\cdot}006$). VMAT technique had comparable lung V20 when compared with the 3D-CRT technique ($p = 0{\cdot}890$).

MILD was significantly lower when the ECOMP technique was used compared with the 3D-CRT ($p < 0{\cdot}001$) and the VMAT ($p = 0{\cdot}674$). IMRT technique had statistically significant lower MILD compared with the 3D-CRT

Table 4. Homogeneity index (HI), conformity index (CI) and dose to organs at risk of three-dimensional conformal radiotherapy (3D-CRT), electronic compensator (ECOMP), inverse intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) techniques

Outcomes	3D-CRT	ECOMP	IMRT	VMAT	*p* Value
Mean HI (SD)	0·865 (0·015)	0·889 (0·020)	0·890 (0·025)	0·866 (0·025)	<0·001
Mean CI (SD)	0·457 (0·115)	0·517 (0·130)	0·763 (0·145)	0·765 (0·145)	<0·001
Mean MHD (SD) (Gy)	8·677 (7·525)	6·435 (5·925)	8·245 (3·480)	10·390 (4·530)	0·002
Mean heart V25 (SD) (%)	13·812 (14·660)	9·913 (11·255)	6·179 (6·305)	8·102 (8·835)	<0·001
Mean heart V30 (SD) (%)	13·449 (14·460)	9·415 (10·885)	4·785 (5·440)	5·828 (7·125)	<0·001
Mean MLD (SD) (Gy)	10·427 (2·380)	8·997 (2·350)	10·702 (1·810)	11·580 (2·385)	<0·001
Mean lung V20 (SD) (%)	18·670 (4·695)	17·160 (4·930)	15·198 (4·280)	18·491 (5·645)	0·004
Mean MILD (SD) (Gy)	20·072 (3·720)	17·399 (3·410)	17·010 (2·730)	17·769 (3·530)	<0·001
Mean MCLD (SD) (Gy)	0·511 (0·265)	0·252 (0·130)	3·942 (1·035)	3·942 (1·035)	<0·001
Mean MCBD (SD) (Gy)	1·611 (1·475)	0·986 (0·790)	2·552 (1·135)	5·547 (1·410)	<0·001
Mean MU (SD)	251·96 (3·239)	440·56 (12·959)	1,096·44 (24·445)	528·40 (15·302)	<0·001

Abbreviations: MHD, mean heart dose; MLD, mean lung dose; MILD, mean ipsilateral lung dose; MCLD, mean contralateral lung dose; MCBD, mean contralateral breast dose; MU, monitor units.

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technique ($p = 0{\cdot}001$). The MILD was comparable between the IMRT and the ECOMP ($p = 0{\cdot}587$) and VMAT ($p = 0{\cdot}209$). The VMAT technique had statistically significant lower MILD compared with the 3D-CRT ($p = 0{\cdot}012$).

For MCLD, this was significantly lower when ECOMP technique was used compared with the 3D-CRT, IMRT and VMAT techniques ($p < 0{\cdot}001$ for all comparisons). 3D-CRT technique had statistically significant lower MCLD compared with the IMRT and VMAT techniques ($p < 0{\cdot}001$ for both comparisons). The IMRT technique had statistically significant MCLD compared with the VMAT technique ($p = 0{\cdot}048$).

Contralateral breast dose

As for the MCBD, it was significantly lower when the ECOMP technique was used compared with the 3D-CRT ($p = 0{\cdot}001$), IMRT ($p < 0{\cdot}001$) and VMAT ($p < 0{\cdot}001$) techniques. The 3D-CRT technique had statistically significant lower MCBD compared with the IMRT ($p = 0{\cdot}003$) and VMAT ($p < 0{\cdot}001$) techniques. IMRT technique had statistically significant lower MCBD compared with the VMAT technique ($p < 0{\cdot}001$).

MU

The MU of 3D-CRT were statistically lower than other three techniques ($p < 0{\cdot}001$ for all comparisons). The MU of ECOMP were also statistically lower than IMRT and VMAT techniques ($p < 0{\cdot}001$ for both comparisons), whereas the MU of IMRT were statistically higher than other techniques ($p < 0{\cdot}001$ for all comparisons).

DISCUSSION

As whole breast irradiation is the mainstay treatment for localised breast cancer and DCIS, several radiation techniques have been studied to reduce normal organ toxicity. Even though 3D treatment planning has been used widely, inhomogeneity of the target volume, inconformity and dose to adjacent organs are still problematic. As a result of this, many advanced techniques for whole breast irradiation have been developed. However, this study is the first to compare the standard treatment 3D-CRT with the three advanced techniques; ECOMP, IMRT and VMAT.

The results in this study also supported previous reports that IMRT was superior to the 3D-CRT. However, the HI in this study was lower than the results from Rongsriyam et al.[25] and Popescu et al.[24] This discrepancy may be due to the different sizes of the CTV and PTV. The HI of previous studies and this study are shown in Table 5. In addition, only few studies have compared ECOMP or VMAT with the 3D-CRT. A whole breast irradiation study by Caudell et al.[21] compared ECOMP, tomotherapy (TOMO) and IMRT techniques. The results showed that ECOMP was superior in lowering dose to the lung, heart, contralateral breast compared with the IMRT and TOMO techniques which was consistent with the outcomes of comparing ECOMP with IMRT in our study.

When several techniques are compared with each other, interpretation of the data may be difficult because other considerations have to be taken into account. For example, most of the whole breast irradiation studies were conducted

Table 5. *Homogeneity index (HI) of this study and previous studies*

	3D-CRT	ECOMP	iIMRT	VMAT	fIMRT	CR
Our study	0·865	0·889	0·890	0·866	–	–
Rongsriyam et al.[25]	0·879	–	0·908	–	0·903	–
Popescu et al.[24]	0·84	–	0·94	0·96	–	–
Zhang[30] (HI = D5/D9)	1·15	–	1·13	–	–	1·16
Bechham[33]	0·74	–	0·95	–	–	–
Jin[34] [HI = (D2% – D98%)/D50]	0·13	–	0·11	0·14	0·11	–

Abbreviations: 3D-CRT, three-dimensional conformal radiotherapy; ECOMP, electronic compensator; iMRT, inverse intensity modulated radiotherapy; VMAT, volumetric-modulated arc therapy; fIMRT, forward intensity modulated radiotherapy; CR, conventional radiation therapy.

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Table 6. Breast volume, clinical target volume (CTV), planning target volume (PTV) and target delineation of this study and previous studies

	Mean PTV (cm^3)	Mean CTV (cm^3)	Mean breast volume (cm^3)	Target volume delineation
Our study	870·07	–	804·57	RTOG atlas
Popescu et al.[24]	945	–		Medially at the lateral edge of the sternum Inferiorly at the inframammary fold Superiorly at the inferior edge of the medial head of the clavicle Laterally to include all apparent breast tissue
Vicini[7]	<975 975–1,600 >1,600	–	–	Irradiate volume
Hong et al.[22]		Not described		Entire breast delineated on the CT dataset
Rongsriyam et al.[25]	–	–	517	Volume that is conventionally irradiated
Zhang[30]		Not described		Glandular tissue apparent on CT scan
Caudell et al.[21]	–	440	–	Breast tissue encompassed by the original treatment tangents, subtraction 5 mm from skin
Jin[34]	360·8	–	–	Visible breast parenchyma

Abbreviations: RTOG, Radiation Therapy Oncology Group; CT, computed tomography.

in the Western countries. Therefore, results from Caucasians may not be applicable to Asians who have different breast sizes and shapes. Like the study by Popescu et al.,[24] their mean PTV was larger than ours. For a study conducted in China by Zhang and Zheng,[30] the results showed that HI and CI of direct machine parameter optimisation (DMPO) IMRT was the highest compared with conventional radiation therapy and conformal radiation therapy (CRT), consistent with our study. The mean size of the target volumes from previous studies are shown in Table 6.

Another factor that may affect the interpretation of the data is the CTV. The authors noticed that the definition of CTV was different between several whole breast irradiation studies (i.e., glandular breast plus margin, irradiated volume, breast parenchyma, etc.), which could result in high inter-observer variation (Table 6). As a result of this, the RTOG conducted an atlas for contouring breast, chest wall and regional nodes for breast cancer irradiation.[27] The authors decided to use RTOG contouring atlas to standardise the CTV contouring to lower the variabilities among the assessors. However, PTV was not defined in the RTOG atlas, thus the authors adapted the definition of it from the RTOG 1005 protocol.[28] Nevertheless, the target volumes in this study tend to be larger than clinical irradiated volumes from authors' hospital which use 3D anatomical landmarks. Also, in 2013, the Danish Breast Cancer Cooperative Group[29] established a consensus for delineating target volume and OAR for breast cancer. There are some minor differences in cranial, ventral and lateral boundaries, compared with the RTOG atlas, whereas for the other boundaries the definitions used were similar (see Supplementary Table 2).

Aside from that, the most common adverse effect of the whole breast irradiation is skin toxicity. A randomised clinical trial by Pignol et al.[20] showed that IMRT could significantly improve the dose distribution, resulted in lowering the proportion of moist desquamation which was correlated with the pain score, global health status scale and breast status scale. Besides this, Zaghloul et al.[31] compared the conventional physical wedges or dynamic wedges technique with the multiple fields in field (MFIF) technique, in which the results concurred that MFIF technique had higher HI and also reduced skin toxicity. This correlation of HI and clinical outcome may be applicable to our study which means that IMRT and ECOMP may cause less skin toxicity compared with 3D-CRT.

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Likewise, cardiotoxicity is another serious adverse effect of breast irradiation, especially for the left-sided breast cancer. A large population-based case–control study by Darby et al.,[14] showed an increase of 7·4% in rates of major coronary events when the MHD is increased by 1 Gy of the MHD. This can be rectified by using advanced techniques which could maintain low dose to OAR. A study by Tsai et al.[26] showed that VMAT technique could maintain low dose to OAR, including MHD, heart V5, V10, V15 and V30. Our study showed consistent results. The heart V30 was lower in advanced techniques. However, only the ECOMP technique had statistically significant lower MHD than the 3D-CRT. These discrepancies may be due to the different PTV size which mean PTV from Tsai et al. and our study were 562·1 and 870 cm^3, respectively. As both studies used the RTOG atlas for contouring, the difference in PTV size could have resulted from including the chest wall in our study for patients with positive nodes. These outcomes can be extrapolated to indicate that the IMRT and VMAT could reduce high dose to the heart, regardless of the PTV size, but unable to lower the low dose for the large PTV. On the other hand, ECOMP could reduce both low and high doses in any PTV size.

To avoid cardiotoxicity, several techniques have been proposed. A study conducted by Swanson et al.[32] showed that moderate deep inspiration breath hold (DIBH) could significantly decreased 40% of the cardiac mean dose compared with the free breathing (FB) technique. In this study, only sets of free-breathing CT simulation images were collected. Therefore, we could not evaluate the dosimetry of whole breast irradiation of breath hold technique. However, this technique has been implemented in the authors' hospital for left-sided breast cancer cases with image guide radiation therapy to match the skin surface on the treatment days and skin surface from the CT simulation. As patients who were able to use this technique had to hold deep inspiration for a period, they had to have good performance status and required short treatment time.

Besides the heart injuries, other side effects can include the lung sequelae after breast irradiation. A study by Kahán et al.[16] showed that the radiation dose was positively correlated with the risks of developing pneumonitis or fibrosis. Our study showed that the ECOMP had the lowest MLD compared with other techniques. However, for MILD, IMRT and VMAT had lower dose compared with ECOMP. In addition, the lung V20 was lower when the ECOMP and IMRT techniques were used compared with the 3D-CRT. But for the MCLD, the IMRT and VMAT techniques had higher dose compared with the 3D-CRT. These results corroborates the data reported by Popescu et al.[24] that IMRT and VMAT techniques were able to decrease the lung V20 when compared with the 3D-CRT. Along the similar lines, Rongsriyam et al.[25] reported that the MILD was lower when the IMRT technique was used compared with the 3D-CRT but at the same time it also increased the MCLD.

Moreover, other factors such as the MU are equally important. In clinical practice, the MU are correlated with the treatment time. In this study, ECOMP and IMRT had statistically significant higher primary outcome for HI when compared with the other techniques. However, the mean MU of ECOMP was much less than IMRT. This may imply that the treatment time for ECOMP could be reduced to half of that used in the IMRT technique which was consistent with the findings from our clinical practice. Not only shorter treatment time, but ECOMP also took shorter time for treatment planning comparing with IMRT and VMAT. Therefore, ECOMP may be an optimal option for advanced technique in whole breast irradiation.

The other factor that needs to be considered is the dose intensity. So far, all of the advanced techniques in this study used DMLC to adjust for the dose intensity in a specific area of PTV. As the breast continuously moves, directly related to the respiratory cycle, an accurate dose to the breast tissue is of concern that it may not be the same as the isodose level in the treatment planning. One centimetre-skin flash tool was used for this treatment planning to cover the anterior part beyond the PTV for the inspiration cycle during ECOMP. The opened fields of MLC were significantly larger in ECOMP technique compared with the IMRT and VMAT. Thus, ECOMP

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may be less affected by the free breathing compared with the IMRT and VMAT. The ideal method to solve this problem is probably DIBH. However, for advanced techniques such as IMRT and VMAT, the patients are required to hold their breaths for a long period which may not be practical and achievable.

In conclusion, ECOMP, IMRT and VMAT were superior to the 3D-CRT. The advanced techniques show promising use and maybe preferred over the standard of treatment. However, this research is a dosimetric study, hence the data from the DVH may be different from the clinical situation. Therefore, additional study is warranted to compare between these four techniques in real patients.

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/S1460396917000243

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