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ORIGINAL ARTICLE

Comparison of whole breast dosimetry techniques – From 3DCRT to VMAT and the impact on heart and surrounding tissues

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Abstract

Introduction: Various techniques for whole breast radiation therapy (WBRT) have been reported to increase dose to contralateral tissues. Heart dose is of critical importance as there is no apparent dose threshold below which there is no risk. The aim of this study was to compare planning techniques for WBRT that achieves the best target dosimetry and lowest organ at risk (OAR) dose. **Methods:** Thirty early-stage whole breast patient datasets, 15 each left- and right-sided cases, were retrospectively selected. Five techniques were generated for each data set: three-dimensional conformal radiation therapy (3DCRT), hybrid intensity modulated radiation therapy (HYI), hybrid volumetric modulated arc therapy (VMAT) – (HYV), reduced arc VMAT – bowtie (BT), and BT flattening filter free (FFF) – (BTFFF). Plan goals and OARs were evaluated and compared between techniques. **Results:** BT had the highest median conformity index (CI) values (0.82, IQR: 0.80–0.85 left and 0.83, IQR 0.80–0.86 right). BT recorded lower mean heart doses (median value 1.19Gy, IQR: 0.90–1.55), and BTFFF recorded lower heart $V2.5_{Gy}$, $V5_{Gy}$; median 3.96% (IQR: 2.90–6.80) and 0.90% (IQR: 0.50–1.50) respectively for left-sided patients. There was a statistically significant difference in all ipsilateral lung measures, ($p < 0.001$) with BTFFF producing significantly lower doses across all measures: mean, $V5_{Gy}$, $V10_{Gy}$ and $V20_{Gy}$. **Conclusion:** Overall BT and BTFFF techniques produced lower OAR doses and equivalent PTV coverage for WBRT. BT and BTFFF techniques increased contralateral lung and breast doses; however, these were within prescribed tolerances and comparable to results published in the literature.

INTRODUCTION

Whole breast radiation therapy (WBRT) has traditionally utilised three-dimensional conformal radiation therapy (3DCRT). The disadvantages of high-dose gradients in the heart and ipsilateral lung have been widely published,[1] identifying the need for alternatives. An alternative, deep inspiration breath hold (DIBH) is being routinely used in clinical practice to reduce heart dose for left-sided breast patients[2] and increase the lung volume, reducing the ipsilateral lung dose.[3]

There are clinical scenarios where 3DCRT techniques do not adequately control dose within the planning target volume (PTV) and reduce organ at risk (OAR) doses below prescribed tolerances.[4] As a result, 3DCRT is becoming less favourable as a primary radiation therapy

technique, giving rise to alternative planning techniques. Hybrid techniques have been reported to improve dose conformity and limit OAR doses by combining the advantages of 3DCRT and modulated techniques.[5] Intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) techniques have been reported to further improve PTV coverage, homogeneity and conformity and reduce high dose to OARs.[6]

Although IMRT and VMAT techniques may improve PTV coverage and dose conformity, the potential to increase low dose to OARs has been published.[7] VMAT techniques have been reported to increase dose to the contralateral tissues (breast and lung).[4] Heart dose, particularly low-dose wash, is of critical importance as Darby et al. has reported that there is no apparent dose threshold below which there is no risk.[8] This increase in low-dose wash may be attributed to the beam angle position as well as PTV position in relation to surrounding anatomy and OAR location when conforming dose for these structures. An approach using reduced arc VMAT – bowtie (BT) that does not traverse the anterior breast could be considered a viable option, conforming and reducing low dose wash to the heart and ipsilateral lung.[9,10] Further to this, as these patients are frequently treated in DIBH, the faster dose rate offered by flattening filter free (FFF) beams could be considered potentially advantageous to incorporate into VMAT planning.

The aim of this study was to compare planning techniques for WBRT to achieve the best PTV dosimetry and lowest OAR doses, with attention to reducing heart dose.

Methods and materials

Patient selection

Datasets of 30 patients who received radiation therapy from January to September 2019 for early stage (stage 1 and 2) breast cancer were retrospectively selected from the hospital data base. Fifteen left-sided and fifteen right-sided patients were randomly selected across a range of breast sizes. Patients were eligible for inclusion in the study if they were: female, aged between 45 and 75 years and treated with a prescription dose of 42.5 Gy in 16 fractions. Patients were excluded if they received a boost, were unable to position both arms above their head, had a mastectomy or had nodal volumes treated.

Negligible risk ethics approval was granted on the 7th January 2020, through the Metro South Human Research Ethics Committee (HREC number LNR/2019/QMS/60747).

Simulation and Contouring

Patients were scanned on a Posiboard™-2 breast board (CIVCO Medical Solutions, Orange City, IA, USA) angle 12.5° or less, both arms above head and bolster under knees. A T-shape Vac-Lok cushion (Qfix, Avandale, USA) was utilised for arm and shoulder stabilisation where standard arm cuffs did not provide support. Left-sided patients were scanned in DIBH and right-sided patients in free breathing. Where left-sided patients were unable to achieve consistent DIBH, a free breathing scan was performed ($n = 3$).

The radiation oncologist (RO) marked the breast clinically at simulation as a guide for target delineation, adding a 1.5 cm margin to the clinical breast tissue for superior, inferior, medial and lateral field borders. Patients were scanned on either a Toshiba Aquilion large bore CT system (Toshiba Medical Systems Corporation, Tochigi-Ken, Japan) or Philips Brilliance CT big bore (Philips Medical Systems, Cleveland, OH, USA) CT scanners, using 2-mm slice thickness. Scan limits were set to cover 5 cm superior to the superior field border and 7 cm inferior to the breast tissue, ensuring the entire lungs and liver were included.

Plans were generated on the Pinnacle treatment planning system (TPS) version 16.2 (Philips Radiation Oncology Systems, Fitchburg, WI, USA). Supporting information 1 outlines the structures contoured and Supporting information 2 displays contours created for beam optimisation. All structures were taken from clinically used plans excluding beam optimisation contours, liver, skin and contralateral breast structure (CLBS) which were prospectively generated for the purpose of this study.

Plan Construction

The prescribed dose was 42.5 Gy in 16 fractions for all cases; plans were calculated using a collapsed cone convolution (CCC) algorithm with a 0.25 cm × 0.25 cm × 0.25 cm grid size. The grid encompassed all PTV and OAR volumes with a 1 cm margin. Dose to PTV, CTV, lungs, heart, CLBS, liver, maximum point dose (Dmax), HI and CI were recorded and assessed according to departmental planning goals outlined in Table 1. Plans were normalised or optimised to ensure PTV, and OARs met planning goals according to the priorities set in Table 1 and in accordance with the departmental protocol. Total fractional monitor units (MU) and segments were recorded to assess plan deliverability and complexity. For the purpose of this study segments referred to open fields, wedged fields and/

Table 1. Plan objectives and tolerance doses.

Structure	Priority	Constraint	
PTV Eval	1	D2	<107% PD
		D50	~ PD
		D98	>95/98/99% PD
		Conformity Index (CI)	
		Homogeneity Index (HI)	
		Constraint (Gy)	Optimal Result
Minor Variation			
Heart - Right sided lesions VMAT	2	Maximum	≤2 Gy
		N/A	
Mean	≤1 Gy		N/A
Heart – Left sided lesions VMAT	2	V2.5	<40%
		V5	<10%
		V10	<5%
V20	<3		
Mean	<2-3 Gy		<4 Gy
Ipsilateral Lung	3	V5	<40%
		V10	<35%
<40%			
V20	<15%		<20%
Contralateral Lung	4	V5	<10%
Mean	ALARA		
Contralateral breast structure (CLBS)	4	Maximum	ALARA
Liver	5	V15	ALARA
Non-target tissue (NTT)	5	cc>PD	ALARA
Skin	5	V35	<85cc

PD – prescription dose, ALARA – as low as reasonably achievable, VMAT – Volumetric Modulated Arc Therapy.
Highest priority =1, lowest priority=5.

or control points. A wedged tangent field was considered as two segments (one open field and one wedged field).

Four chest team specialist radiation therapists (RTs) with a minimum six years' experience were randomly assigned techniques to be planned on each data set. Five techniques were generated for each dataset, described in the following paragraphs.

3DCRT

3DCRT employed medial and lateral opposing tangential 6MV fields. A zero posterior field jaw was used with the field entering and exiting to cover the entire PTV (Fig 1a). The isocentre was placed mid separation along the posterior field edge. A minimum anterior overshoot of 2 cm was set for the tangential fields. Wedges were used to improve target dose homogeneity. Fields were collimated and shielded as required to minimise dose to heart and lungs without compromising PTV coverage. Dose was prescribed to a reference point or a maximum percentage. A field-in-field approach was used to achieve chest wall coverage and/or to reduce the maximum dose.[11]

Hybrid IMRT (HYI)

HYI plans comprised 4–5 fields, combining 3DCRT and IMRT beams using the same isocentre. The posterior tangential border abutted the PTV, without encroaching on the CTV. As in 3DCRT, tangential 6MV fields overshot the anterior skin surface by 2 cm. The tangential fields were copied and converted to 6MV IMRT 'step and shoot' fields and additional fields were added or adjusted, similar to that reported by Peulen et al. (Fig 1b).[12] Fields were collimated to improve PTV coverage and minimise OAR doses.

Two prescriptions were required. 3DCRT beams were prescribed to a maximum dose of between 98 and 110%. The IMRT beams prescription was set to 16 fractions, with the optimiser driving dose to an objective PTV structure, limiting dose to avoidance and OAR structures. IMRT fields had a minimum segment area set to 10 cm^2, minimum 5 MU per segment and maximum segments initially set between 12 and 18 for the IMRT component of the plan.

Hybrid VMAT (HYV)

HYV used the same conformal tangents as the HYI plans, with the hybrid component consisting of two 40° arcs, angled 20° above and below the gantry angle of the tangential fields (Fig 1c). VMAT fields were collimated to 5° or 355°. The prescription and optimisation used was the same for the HYI technique. Arcs had a minimum segment area of 2 cm^2 with a minimum 3 MU per segment.

Reduced arc VMAT– Bowtie (BT)

Plans started with one medial and one lateral arc to keep the total arcs to a minimum. The number of arcs

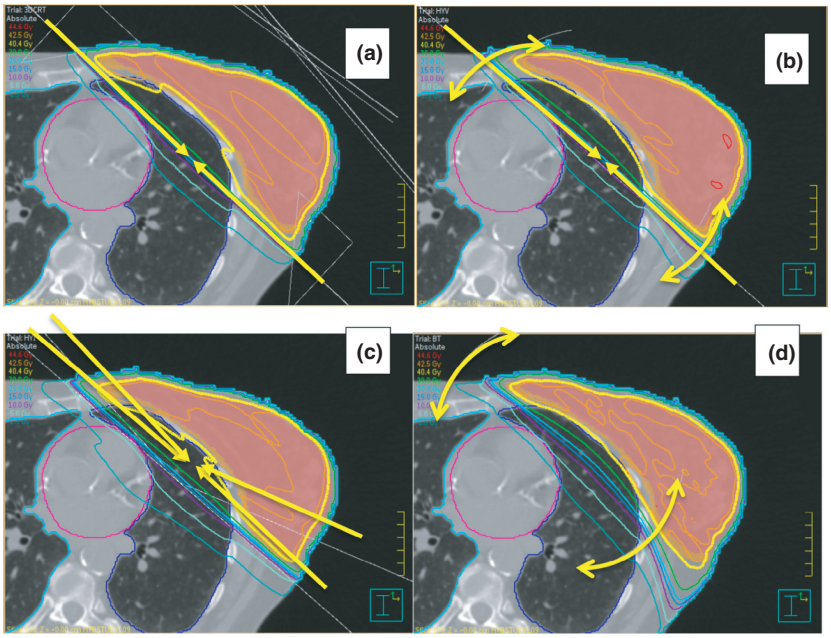

Figure 1. Planning technique representation (a) Conformal plan - 3DCRT; (b) Hybrid IMRT – HYI. (c) Hybrid VMAT -HYV. (d) Bowtie -BT. The yellow straight arrowed lines indicate beam incidence, and the yellow curved arrows indicate the arc rotation.

increased if plan goals were not being met, up to a maximum of two medial and two lateral arcs. All arcs used 6MV. Initially medial and lateral arc angles were set at 300°–0° and 60°–0° and 170°–100° and 190°–260° for left- and right-sided plans, respectively (Fig 1d). Arc angles were then adjusted for patient-specific anatomy or OARs as required.

Isocentre placement was based on isocentre distance from the couch top, arc angles and contralateral arm clearance. Using a single prescription, plans were optimised using the same parameters and similar optimisation structures as the HYV plans, with an additional medial avoid optimisation structure to reduce low dose wash to the contralateral breast and lung.

Reduced arc VMAT - Bowtie flattening filter free (BTFFF)

BTFFF plans were a duplication of the BT technique, utilising a 6 MV FFF beam model.

Plan Evaluation

Treatment plans were independently assessed by a quality assurance (QA)–competent RT. CTV and PTV eval coverage, HI, CI, OAR, non-target tissue (NTT) dose, total fractional MU and segments were evaluated, recorded and assessed. Qualitative visual assessment of the plans was performed by the QA RT and RO for clinical acceptability in conjunction with quantitative evaluation of the dose-volume histogram (DVH) constraints (Table 1).

HI and CI were used to assess the dose homogeneity and conformity within the PTV eval respectively. HI and CI formulas used in this study were described by Yin et al. and shown inTable 2.[13]

Dosimetry data were recorded using Microsoft Excel (Microsoft Excel 2019, Microsoft corporation, USA) and reviewed by a QA RT.

Statistical analysis

Statistical descriptions of continuous variables were presented as a mean and standard deviation (SD) or

Table 2. Homogeneity and conformity formulas.

Homogeneity Index (HI)	D_2-D_{98}/D_P
Conformity Index (CI)	(TV_{95}/TV) x (TV_{95}/V_{95})

D_2 represents the dose corresponding to 2% target volume as shown in the Dose Volume Histogram (DVH), D_{98} represents the dose corresponding to 98% of the target volume as shown in the DVH and D_P represents the prescription dose. TV_{95} refers to the volume of the target covered by the 95% isodose line. TV refers the target volume and V_{95} refers to the volume of tissue covered by the 95% isodose line.

median and inter-quartile range (IQR) depending on the distribution of the data. Normality was assessed using the Shapiro-Wilk test.

Comparison between techniques were conducted using linear mixed model (LMM) analysis with technique as fixed effect and patient as random effect (random intercept). When overall significance was found, a post-hoc test with adjustment for multiple testing was performed.

When the assumptions of the LMM model were not met, a Friedman test was performed. When overall significance difference was found between techniques, the test was followed by a Conover's test of a two-way balanced complete block design for pairwise comparisons.

All analyses were performed using the R statistical software,[14] and *P*-values were two-tailed with $P < 0.05$ considered statistically significant.

RESULTS

Patient volume characteristics for the PTV, heart and lungs are displayed in Table 3. Dosimetry results for left-sided plans are displayed in Table 4 and right-sided plans in Table 5.

Table 3. Patient volume characteristics.

Volume (cc)	Left (n = 15)		Right (n = 15)	
	Mean (SD)	Range	Mean (SD)	Range
PTV	978.76 (±390.13)	444.96–1652.52	1156.14(±528.38)	410.63–2424.03
Heart	563.93 (±70.84)	464.13–670.10	594.04 (±112.46)	402.88–770.53
Left Lung	1970.93 (±453.09)	1208.20–2706.80	1567.78 (±317.61)	953.13–1858.79
Right Lung	2279.78 (±504.94)	1342.77–3050.30	1272.83 (±248.28)	1075.14–2268.05

PTV- Planning target volume.

Table 4. Left side dosimetry results for the plans 3DCRT, HYI, HYV, BT and BTFFF.

Structure	Dosimetry	3DCRT	HYI	HYV	BT	BTFFF	*P*-value
PTV eval	$D_{95\%}$ (%)[Ǫ]	97.61 (96.90-98.60)	97.98(97.25-98.30)	97.49 (96.70-97.75)	97.71 (96.85-98.40)	97.29 (97.25-98.30)	0.57
	$D_{2\ Gy}$ (Gy)[Ǫ]	44.89 (44.65-45.10)	44.40 (44.30-44.45)	44.14 (43.90-44.35)	43.97 (43.80-44.15)	44.22 (44.10-44.40)	N/A
	$D_{98\ Gy}$ (Gy)[Ǫ]	40.24 (39.85-40.50)	40.21 (39.65-40.50)	40.13 (39.70-40.25)	40.12 (39.60-40.55)	39.92 (39.65-40.55)	N/A
	D_{max} (Gy)[Ǫ]	45.60 (45.55-45.75)	45.33 (40.05-45.40)	45.18 (45.10-45.45)	45.40 (45.13-45.40)	45.49 (45.40-45.50)	<0.001
	$CI_{95\%}$[Ǫ]	0.69 (0.65-0.72)	0.75 (0.72-0.78)	0.76 (0.71-0.78)	0.83 (0.80-0.85)	0.81 (0.78-0.84)	<0.001
	HI[Ǫ]	0.11 (0.11-0.12)	0.10 (0.09-0.11)	0.10 (0.09-0.11)	0.09 (0.08-0.10)	0.10 (0.08-0.11)	<0.001
CTV	$D_{95\%}$ (%)[Ǫ]	98.49 (97.85-99.10)	98.84 (98.60-99.15)	98.28 (98.10-98.50)	98.94 (98.35-99.40)	98.69 (97.70-99.00)	0.01
NTT	$V_{42.5\ Gy}$ (cc)[Ǫ]	96.24 (46.90-121.90)	30.89 (20.90-41.15)	14.36 (7.25-30.40)	7.95 (2.40-15.50)	6.78 (5.15-12.80)	<0.001
Heart	D_{mean} (Gy)[Ǫ]	1.57 (0.95-2.15)	1.70 (1.15-1.90)	1.29 (1.10-1.80)	1.19 (0.90-1.55)	1.22 (1.00-1.45)	<0.001
	$V_{2.5\ Gy}$ (%)[Ǫ]	10.98 (5.05-14.50)	11.34 (6.55-18.65)	8.04 (5.40-14.45)	6.90 (2.70-10.20)	3.96 (2.90-6.80)	<0.001
	$V_{5\ Gy}$ (%)[Þ]	4.33 (±4.15)	4.22 (±2.91)	2.67 (±2.18)	1.65 (±1.71)	1.23 (±1.17)	<0.001
	$V_{10\ Gy}$ (%)[Ǫ]	1.41 (0.60-3.85)	0.79 (0.60-2.20)	0.57 (0.20-2.10)	0.32 (0.00-0.95)	0.20 (0.04-0.45)	<0.001
	$V_{20\ Gy}$ (%)[Ǫ]	0.79 (0.20-2.40)	0.19 (0.00-0.85)	0.19 (0.01-1.05)	0.00 (0.00-0.06)	0.00 (0.00-0.03)	<0.001
	D_{max} (Gy)[Ǫ]	39.66 (36.83-41.62)	32.83 (28.05-40.74)	30.30 (19.00-39.39)	17.76 (10.69-27.91)	20.36 (16.70-28.86)	<0.001
Left Lung	D_{mean} (Gy)[Ǫ]	5.94 (4.60-7.10)	5.69 (4.95-6.40)	5.31 (5.05-6.40)	4.93 (4.00-5.60)	4.60 (4.00-5.30)	<0.001
	$V_{5\ Gy}$ (%)[Ǫ]	21.79 (16.75-25.80)	22.69 (20.35-26.15)	20.74 (20.20-25.45)	20.66 (17.45-24.35)	16.78 (15.55-21.80)	<0.001
	$V_{10\ Gy}$ (%)[Ǫ]	16.03 (12.25-19.20)	16.34 (14.40-18.45)	14.39 (13.55-18.30)	12.66 (10.50-16.20)	11.66 (10.65-14.65)	<0.001
	$V_{20\ Gy}$ (%)[Ǫ]	12.40 (8.90-14.95)	10.78 (8.60-12.95)	10.15 (9.15-12.70)	8.31 (5.90-10.05)	7.76 (6.25-9.15)	<0.001
Right Lung	D_{mean} (Gy)[Þ]	0.19 (±0.06)	0.22 (±0.07)	0.22 (±0.04)	0.28 (±0.10)	0.34 (±0.08)	<0.001
CLBS	D_{mean} (Gy)[Ǫ]	0.31 (0.20-0.40)	0.29 (0.30-0.50)	0.32 (0.30-0.60)	0.42 (0.30-0.75)	0.41 (0.35-0.70)	<0.001
	D_{max} (Gy)[Ǫ]	2.19 (1.55-11.20)	3.80 (2.25-9.00)	4.37 (2.90-7.50)	3.19 (2.35-9.50)	4.13 (2.45-7.70)	0.14
Skin	$V_{35\ Gy}$ (cc)[Ǫ]	21.17 (19.35-25.50)	30.19 (22.15-33.40)	18.59 (16.85-28.85)	17.53 (13.95-20.05)	15.40 (12.45-22.50)	<0.001

PTV eval - planning target volume evaluation, CTV - clinical target volume, NTT - non target tissue, CI - conformity index, HI - homogeneity index, CLBS - contralateral breast structure, 3DCRT – three dimensional conformal radiation therapy, HYI - Hybrid intensity modulated radiation therapy, HYV- Hybrid volumetric arc therapy, BT- Bowtie, BTFFF-Bowtie flattening filter free. Bold text is indicative of the best metric value for the structure.

[Þ]Descriptive statistics presented as mean and standard deviation and Linear mixed model performed.

[Ǫ]Descriptive statistics presented as median and inter-quartile range and Friedman test performed.

Table 5. Right side dosimetry results for the plans 3DCRT, HYI, HYV, BT and BTFFF.

Structure	Dosimetry	3DCRT	HYI	HYV	BT	BTFFF	*P*-value
PTV eval	$D_{95\%}$ (%)[Ǫ]	97.31 (96.65-98.10)	98.01 (97.10-98.55)	97.86 (97.55-98.15)	97.61 (97.35-98.3)	98.50 (97.55-98.70)	0.09
	$D_{2\ Gy}$ (Gy)[Ǫ]	44.98 (44.75-45.20)	44.30 (44.20-44.30)	44.12 (43.68-44.25)	43.83 (43.70-44.10)	44.19 (43.95-44.20)	N/A
	$D_{98\ Gy}$ (Gy)[Ǫ]	40.15 (39.85-40.50)	40.44 (40.00-40.60)	40.29 (40.20-40.55)	40.21 (40.10-40.50)	40.59 (40.20-40.60)	N/A
	D_{max} (Gy)$_{Ǫ}$	45.66 (45.45-45.80)	44.86 (44.80-45.10)	45.48 (44.80-45.50)	45.33 (45.10-45.50)	45.35 (45.10-45.50)	<0.001
	$CI_{95\%}$[Ǫ]	0.71 (0.67-0.75)	0.78 (0.74-0.80)	0.78 (0.75-0.81)	0.83 (0.80-0.86)	0.81 (0.80-0.86)	<0.001
	HI[Ǫ]	0.11 (0.11-0.12)	0.10 (0.09-0.10)	0.08 (0.08-0.10)	0.08 (0.08-0.09)	0.08 (0.08-0.10)	<0.001
CTV	$D_{95\%}$ (%)[Þ]	98.35 (±0.79)	98.16 (±1.96)	98.37 (±0.61)	98.39 (±1.37)	98.84 (±0.73)	0.33
NTT	$V_{42.5\ Gy}$ (cc)[Ǫ]	70.98 (53.00-139.70)	19.58 (10.9-33.25)	10.48 (8.75-19.70)	4.59 (2.30-10.90)	6.74 (4.90-12.80)	<0.001
Heart	D_{mean} (Gy)[Ǫ]	0.51 (0.40-0.70)	0.61 (0.50-0.80)	0.60 (0.55-0.70)	0.61 (0.50-0.75)	0.71 (0.70-0.80)	<0.001
	$V_{2.5\ Gy}$ (%)[Ǫ]	0.47 (0.17-2.00)	0.17 (0.00-2.65)	0.00 (0.00-0.50)	0.00 (0.00-0.02)	0.00 (0.00-0.00)	N/A
	D_{max} (Gy)[Ǫ]	3.51 (2.92-3.75)	3.39 (2.73-4.05)	2.95 (2.31-4.29)	2.39 (2.22-2.79)	2.13 (1.97-2.56)	<0.001
Right Lung	D_{mean} (Gy)[Ǫ]	6.47 (5.40-7.60)	6.24 (5.65-7.10)	6.34 (5.60-6.85)	5.47 (5.20-6.20)	5.61 (4.65-5.90)	<0.001
	$V_{5\ Gy}$ (%)[Ǫ]	25.01 (19.75-27.35)	23.62 (22.20-27.95)	25.14 (21.25-26.95)	23.11 (20.00-24.60)	21.09 (17.35-23.40)	<0.001
	$V_{10\ Gy}$ (%)[Ǫ]	17.80 (13.45-20.10)	17.36 (15.30-19.60)	17.22 (14.70-18.75)	16.04 (14.05-17.05)	14.97 (12.10-16.05	<0.001
	$V_{20\ Gy}$ (%)[Ǫ]	13.62 (10.10-16.00)	12.30 (10.05-14.20)	12.21 (9.30-13.65)	10.80 (9.30-11.55)	9.48 (8.25-10.55)	<0.001
Left Lung	D_{mean} (Gy)[Ǫ]	0.19 (0.19-0.20)	0.20 (0.19-0.20)	0.20 (0.20-0.20)	0.20 (0.20-0.25)	0.31 (0.30-0.35)	<0.001
CLBS	D_{mean} (Gy)[Ǫ]	0.27 (0.20-0.50)	0.40 (0.20-0.55)	0.26 (0.25-0.40)	0.41 (0.25-0.45)	0.40 (0.30-0.55)	0.01
	D_{max} (Gy)[Ǫ]	2.86 (1.85-16.80)	4.52 (3.00-14.55)	3.72 (2.50-15.60)	3.61 (1.95-13.70)	5.02 (1.80-9.80)	0.09
Skin	$V_{35\ Gy}$ (cc)[Þ]	22.08 (17.00-27.30)	16.73 (15.40-25.60)	16.80 (14.70-25.15)	13.50 (11.75-24.50)	12.51 (11.50-21.70)	0.01
Liver	$V_{15\ Gy}$ (cc)[Ǫ]	41.79 (21.15-51.75)	25.01 (16.20-63.05)	48.14 (19.00-59.70)	41.48 (18.95-68.60)	26.92 (15.40-52.55)	0.04

PTV eval - planning target volume evaluation, CTV - clinical target volume, NTT - non target tissue, CI - conformity index, HI - homogeneity index, CLBS - contralateral breast structure, 3DCRT – three dimensional conformal radiation therapy, HYI - Hybrid intensity modulated radiation therapy, HYV- Hybrid volumetric arc therapy, BT- Bowtie, BTFFF-Bowtie flattening filter free. Bold text is indicative of the best metric value for the structure.

[Þ]Descriptive statistics presented as mean and standard deviation and Linear mixed model performed.

[Ǫ]Descriptive statistics presented as median and inter-quartile range and Friedman test performed.

Target volume and NTT comparison

Target volumes

Left-sided plans showed no significant difference in PTV eval dosimetry between techniques ($P = 0.57$). CTV D95 was statistically significantly lower for HYV than HYI techniques ($P = 0.01$); however on visual inspection, the difference was not considered to be clinically meaningful (median = 98.84%, IQR: 98.60–99.15 for HYI and 98.28%, IQR: 98.10–98.50 for HYV). Right-sided plans showed no significant difference in PTV eval ($P = 0.09$) or CTV ($P = 0.33$).

There was a statistically significant difference in CI and HI between the techniques (left and right $P < 0.001$). BT techniques recorded the highest median CI values (0.83, IQR: 0.80–0.85 left and 0.83, IQR: 0.80–0.86 right). BT recorded the lowest median HI values of 0.09, IQR: 0.08–0.10 and 0.08, IQR 0.08–0.09 for left and right plans, respectively.

Dmax results showed a significant difference between techniques for left- and right-sided plans ($P < 0.001$). The lowest Dmax median value was 45.18 Gy (IQR: 45.10–45.45) in HYV left-sided plans, while HYI techniques recorded the lowest Dmax of 44.86 Gy (IQR: 44.80–45.10) in right-sided plans.

NTT

A significant difference in NTT values was noted between techniques for left- and right-sided plans ($P < 0.001$). Median NTT values for left-sided plans were lowest in the BTFFF technique (6.78 cc, IQR 5.15-12.80) compared with the highest in 3DCRT technique (96.24 cc, IQR: 46.90–121.90). Right-sided NTT median values were lowest in the BT technique 4.59 cc (IQR: 2.30–10.90) compared to the highest in the 3DCRT technique 70.98 cc (IQR: 53.00–139.70).

OAR comparison

Heart

Left-sided results showed a significant difference for all measured heart values; mean, V2.5 $_{Gy}$, V5 $_{Gy}$, V10 $_{Gy}$, V20 $_{Gy}$ and maximum dose ($P < 0.001$) between various techniques. The lowest mean heart dose was recorded for the BT technique with the highest value recorded in the HYI technique (median value: 1.19 Gy, IQR: 0.90–1.55 and 1.70 Gy, IQR: 1.15–1.90 respectively). BTFFF recorded the lowest V2.5 $_{Gy}$, V5 $_{Gy}$, V10 $_{Gy}$ and V20 $_{Gy}$ measures with median values of 3.96% (IQR: 2.90–6.80), 0.9% (IQR: 0.50–1.50), 0.20% (IQR: 0.04–0.45) and

<0.01% (IQR: 0.00–0.03) respectively. BT recorded the lowest median Dmax values (17.76 Gy, IQR: 10.69–27.91). HYI plans recorded the highest heart V2.5 $_{Gy}$ (11.34%, IQR: 6.55–18.65).

Right-sided plans showed a significant difference in heart mean dose between techniques ($P < 0.001$); median values were highest in BTFFF (0.68 Gy, IQR: 0.70–0.80) and lowest in 3DCRT (0.51 Gy, IQR: 0.40–0.70). Dmax to heart was higher in 3DCRT techniques and lowest in BTFFF techniques (3.51 Gy, IQR: 2.92–3.75 and 2.13 Gy, IQR: 1.97–2.56 respectively).

Lungs

There was a statistically significant difference in all ipsilateral lung measures for left- and right-sided plans, ($P < 0.001$). BTFFF produced significantly low doses across all measures: mean, V5 $_{Gy}$, V10 $_{Gy}$ and V20 $_{Gy}$ compared with 3DCRT in both left- and right-sided plans.

Ipsilateral left lung mean dose was highest in 3DCRT techniques and the lowest in BTFFF techniques; median values 5.94 Gy (IQR: 4.60–7.10) and 4.60 Gy (IQR: 4.00–5.30) respectively. BTFFF techniques recorded the lowest median V5 $_{Gy}$ and V10 $_{Gy}$ values of 16.78% (IQR: 15.55–21.80) and 11.66% (IQR: 10.65–14.65) respectively. V20 $_{Gy}$ was highest for 3DCRT and lowest in BTFFF with median values of 12.40% (IQR: 8.90–14.95) and 7.76% (IQR: 6.25–9.15) respectively.

Ipsilateral right lung mean dose recorded high values in 3DCRT techniques compared with the lowest in BT techniques; median values 6.47 Gy (IQR: 5.40–7.60) and 5.47 Gy (IQR: 5.20–6.20) respectively. BTFFF recorded the lowest V5 $_{Gy}$, V10 $_{Gy}$ and V20 $_{Gy}$ doses with median values of 21.09% (IQR: 17.35–23.40), 14.97% (IQR: 12.10–16.05) and 9.48% (IQR: 8.25–10.55) respectively.

Contralateral lung mean doses were significantly higher in the BTFFF techniques than all other techniques ($P < 0.001$).

CLBS

CLBS mean dose results for left-sided plans were significantly high ($P < 0.02$) in the BT technique compared with all other techniques excluding the BTFFF technique ($P = 0.6$). 3DCRT results provided the lowest mean CLBS dose. A significant difference in CLBS mean dose was found in right-sided plans $P = 0.01$. After adjustment for multiple testing, none of the comparisons were significant.

Total fractional MU and segments

Mean total fractional MU and segments are displayed in Table 6. Total mean fractional MU ranged from 302.95MU for HYV techniques in left-sided plans to 626.91MU for BTFFF techniques in right-sided plans. Lowest mean segments were recorded in left-sided 3DCRT techniques (6.00) and right-sided BT techniques recorded the highest mean segments (58.00).

DISCUSSION

BT and BTFFF techniques produced low heart doses in left-sided plans and low heart V2.5 $_{Gy}$ in right-sided plans compared to the HYI, HYV and 3DCRT techniques. Across all plans, BT and BTFFF techniques produced lower ipsilateral lung and NTT dose while improving HI and CI values without compromising PTV coverage. Contralateral lung and left-sided CLBS doses were high in BT and BTFFF techniques compared with HYI, HYV and 3DCRT techniques; however these were within prescribed tolerances.

Modulated techniques have been shown to improve dose homogeneity and conformity within the PTV compared with 3DCRT in whole breast cancer planning.[1,15] Haciislamoglu et al. states an additional benefit of VMAT is the reduction of high doses to nearby OARs such as the heart and ipsilateral lung.[16] However,

Table 6. Plan total fractional MU and segments.

	Left (n = 15)		Right (n = 15)	
Technique	MU	Segments	MU	Segments
	Mean (Range)	Mean (Range)	Mean (Range)	Mean (Range)
3DCRT	412.77 (327.00–572.40)	6.00 (5.00–6.00)	420.47 (269.60–533.20)	6.00 (5.00–8.00)
HYI	313.33 (270.50–427.80)	14.00 (8.00–26.00)	316.09 (195.40–500.80)	16.00 (9.00–31.00)
HYV	302.95 (268.80–347.60)	24.00 (24.00–24.00)	328.95 (275.30–417.70)	24.00 (24.00–24.00)
BT	440.56 (362.20–548.20)	58.00 (51.00–60.00)	432.83 (348.50–576.90)	51.00 (35.00–60.00)
BTFFF	622.77 (439.50-835.90)–	56.00 (51.00–60.00)	626.91 (503.00–739.00)	54.00 (35.00–60.00)

MU- Monitor units, 3DCRT – three dimensional conformal radiation therapy, HYI - Hybrid intensity modulated radiation therapy, HYV- Hybrid volumetric arc therapy, BT- Bowtie, BTFFF-Bowtie flattening filter free.

this and similar studies[7,17] report an increase in low-dose wash to ipsilateral and contralateral tissues, indicating the need to be mindful of these dosimetric effects.

Our study reviewed a range of published WBRT techniques in addition to BTFFF, a lesser-reported technique. The focus of this study was to achieve adequate PTV coverage whilst prioritising reduction in heart dose, as there is currently no recognised safe heart dose published in the literature.[8]

In our study heart V2.5 $_{Gy}$ was statistically low in the BT and BTFFF techniques compared to HYI, HYV and 3DCRT techniques. This was shown in both left- and right-sided plans. Numerous studies[9, 10, 16, 18] have reported heart mean dose and heart volume doses and comparatively; we demonstrate equivalent or lower heart doses in left-sided BT and BTFFF techniques. Right-sided plans had high mean heart dose in the BTFFF and BT techniques compared to 3DCRT techniques, consistent with reported studies.[10,18] The range in heart values was small in BT and BTFFF techniques, emphasising improved consistency in these plans compared with 3DCRT techniques. PTV and CTV dosimetry was equivalent in BT and BTFFF techniques with improved CI and HI when compared with the other techniques.

Similar to other studies[9,19] modulated techniques were found to increase conformity and reduce ipsilateral lung dose (V20 $_{Gy}$). Additionally, BT and BTFFF techniques produced lower V10 $_{Gy}$ and V5 $_{Gy}$ ipsilateral lung doses. Our results show reducing heart V2.5 $_{Gy}$ did not increase low dose (V5 $_{Gy}$) to the ipsilateral lung; in fact V5 $_{Gy}$ to ipsilateral lung was lowest for BT and BTFFF techniques. Haciislamoglu et al. reported an increase to lower lung doses using VMAT techniques which was not found in our study.[16] An increase in reported lower lung DVH values using VMAT is likely due to arc angle positioning over optimisation, when using similar optimisation structures. We found that eliminating the anterior portion of the arc angle (left-side arc avoidance 0°–100° and right-side arc avoidance 0°–260°) reduces low dose to the underlying structures (heart and ipsilateral lung). However patient habitus, laterally displaced breast PTVs, contralateral breast positioning, internal anatomical positioning and machine clearances need to be considered and adjusted as appropriate for individual plans.

BT and BTFFF arc angles were designed to avoid the anterior chest wall. By virtue of arc angle placement, dose was reduced to the heart and ipsilateral lung as the optimiser was not required to control low dose in this avoided region. Contralateral tissue doses (breast and lung) were increased in BT and BTFFF techniques compared to HYI, HYV and 3DCRT techniques as a result of adjusted arc angles. This needs to be taken into consideration for technique selection where contralateral dose may be an issue (contralateral breast position, previous radiation treatment or patient age). CLBS mean dose was significantly high in left-sided BT techniques compared to 3DCRT techniques. There was no significant difference noted in right-sided plans. This may be associated to the reduction of heart V2.5 $_{Gy}$ and ipsilateral lung V5 $_{Gy}$. Should CLBS mean dose in left-sided patients be of concern? Relaxing the heart V2.5 $_{Gy}$ and ipsilateral lung V5 $_{Gy}$ may achieve a suitable outcome for all OAR objectives.

BT and BTFFF techniques in this study demonstrated increased segments and MU compared with HYI, HYV and 3DCRT techniques, with significantly lower doses to the heart and ipsilateral lung. In order to achieve the desired dose conformality and reduced OAR dose, an increase in MU and complexity may be required. It has been reported that an increase in MUs can increase the incidence of radiation-induced secondary malignancies.[20] However, the risk of radiation induced secondary malignancies from increased MUs, and plan complexity needs to be balanced against reduced OAR doses. With this taken into consideration, BT WBRT has been implemented in our department. Although not quantified in this study, anecdotal clinical experience has shown that this implementation has not posed a burden on clinical resources including planning, treatment time and patient specific QA within our department.

This study did have its limitations. We did not individually contour the substructures of the heart. Studies[21,22] support individual cardiac structure delineation over whole structure delineation as this may be a better predictor for acute cardiac events. A relatively small sample size was used and the effects of body habitus and breast shape on treatment techniques was not investigated. In addition to these limitations, planning and treatment times were not compared between techniques. Plans were constructed as per departmental protocol to maximise transferability to clinical practice. As such, normalisation practices were different between techniques, and caution should be applied when directly comparing OAR doses. However, there was no statistically significant difference found in PTV coverage between techniques. Increased treatment time may be of concern in HYI techniques that have a large variation in segment, especially for patients treated in DIBH. The number of arcs per plan in BT, BTFFF and HYV techniques were not investigated and potentially may have increased treatment times. Plans were not separated according to patient size, and the effect this may have on plan quality was not investigated. Results may have been affected by multiple planners being involved in the process; however standard methods were followed to minimise any potential impact. A future topic for investigation is separating plans according to size and

evaluating if this affects the number of arcs used in each plan. Further investigations regarding the translation of these results to the treatment of breast/chest wall patients with nodal irradiation using BT and BTFFF techniques is also warranted.

CONCLUSION

BT and BTFFF techniques produced lower OAR doses and equivalent PTV coverage for WBRT. Left-sided plans produced significantly lower heart and ipsilateral lung doses. Right-sided plans produced significantly lower heart V2.5 $_{Gy}$ and ipsilateral lung tolerance doses. BT and BTFFF plans were found to increase contralateral lung and breast doses; however these were within prescribed tolerances and results published in the literature. Further research will be conducted focusing on PTV size and optimal arc/s geometry.

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Conflict of Interest

The authors declare no conflict of interest

REFERENCES

1. Kivanc H, Gultekin M, Gurkaynak M, Ozyigit G, Yildiz F. Dosimetric comparison of three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for left-sided chest wall and lymphatic irradiation. *J Appl Clin Med Phys.* 2019; **20**: 36–44.
2. Karpf D, Sakka M, Metzger M, Grabenbauer G. Left breast irradiation with tangential intensity modulated radiotherapy (t-IMRT) versus tangential (t-VMAT):trade-offs between secondary cancer induction risk and optimal target coverage. *Radiat Oncol.* 2019; **14**: 156–67.
3. Oechsner M, Dusberg M, Borm K J, Combs S E, Wilkens J J, Duma M N. Deep inspiration breath-hold for left-sided breast irradiation: Analysis of dose-mass histograms and the impact of lung expansion. *Radiat Oncol.* 2019; **14**: 109.
4. Byrne M, Archibald-Heeren B, Hu Y, Fong A, Chong L, Teh A. Comparison of semiautomated tangential VMAT with 3DCRT for breast or chest wall and regional nodes. *J Appl Clin Med Phys.* 2018; **19**: 684–93.
5. Ramasubramanian V, Balaji K, Subramanian S, Sathiya K, Thirunavukarasu M, Radha CA. Hybrid volumetric arc therapy for whole breast irradiation: a dosimetric comparison of different arc designs. *Radiol Med (Torino)* 2019; **124**: 546–54.
6. Sudha SP, Seenisamv R, Bharadhwaj K. Comparison of dosimetric parameters of volumetric modulated arc therapy and three-dimensional conformal radiotherapy in postmastectomy patients with carcinoma breast. *J Cancer Res Ther.* 2018; **14**: 1005–9.
7. Haciislamoglu E, Cinar Y, Gurcan F, Canyilmaz E, Gungor G, Yoney A. Secondary cancer risk after whole-breast radiation therapy: field-in-field versus intensity modulated radiation therapy versus volumetric modulated arc therapy. *Br J Radiol.* 2019; **10**: 1102.
8. Darby S, Ewertz M, McGale P, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *N Eng J Med.* 2013; **368**: 987–98.
9. Koivumaki T, Fogliata A, Zeverino M, et al. Dosimetric evaluation of modern radiation therapy techniques for left breast in deep-inspiration breath hold. *Physica Med* 2018; **45**: 82–7.
10. Munshi A, Sarkar B, Anbazhagan S, et al. Short tangential arcs in VMAT based breast and chest wall radiotherapy lead to conformity of the breast dose with lesser cardiac and lung doses: a prospective study of breast conservation and mastectomy patients. *Australas Phys Eng Sci Med.* 2017; **40**: 729–36.
11. Fournier-Bidoz N, Kirova YM, Campana F, Dendale R, Fourquet A. Simplified field-in-field technique for a large scale implementation in breast radiation treatment. *Med Dosim.* 2012; **37**: 131–7.
12. Peulen H, Hanbeukers B, Boersma L, et al. Forward intensity-modulated radiotherapy planning in breast cancer to improve dose homogeneity: feasibility of class solutions. *Int J Radiat Oncol Biol Phys.* 2012; **82**: 394–400.
13. Yin Y, Chen J, Sun T, et al. Dosimetric research on intensity-modulated arc radiotherapy planning for left breast cancer after breast-preservation surgery. *Med Dosim.* 2012; **37**: 287–92.
14. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2013. http://www.R-project.org/.
15. Sudha S, Seenisamy R, Bharadhwaj K. Comparison of parameters of volumetric modulated arc therapy and three-dimensional conformal radiotherapy in postmastectomy patients with carcinoma breast. *J Cancer Res Ther.* 2018; **14**: 1005–8.
16. Haciislamoglu E, Colak FC, Canyilmaz E, et al. The choice of multi-beam IMRT for whole breast radiotherapy in early-stage right breast cancer. *Springerplus.* 2016; **5**(1):688.
17. Aras S, Ikizceli T, Aktan M. Dosimetric comparison of three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy techniques (IMRT) with radiotherapy dose simulation for left-sided mastectomy patients. *Eur J Breast Health.* 2019; **15**: 85–9.
18. Vikstrom J, Hjelstuen M H, Wasbo E, Mjaaland I, Dybvik K I. A comparison of conventional and dynamic

radiotherapy planning techniques for early-stage breast cancer utilizing deep inspiration breath-hold. *Acta Oncologia*. 2018; **57**: 1325–30.
19. Supakalin N, Pesee M, Thamronganantasakul K, Promsensa K, Supaadirek C, Krusun S. Comparison of different radiotherapy planning techniques for breast cancer after breast conserving surgery. *Asian Pac J Cancer Prev* 2018; **19**: 2929–34.
20. Hall E, Wuu C S. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. *Int J Radiat Oncol Biol Phys*. 2003; **56**: 83–8.
21. McWilliam A, Khalifa J, Vasquez Osorio E, et al. Novel methodology to investigate the impact of radiation dose to heart sub-structures on overall survival. *Int J Radiat Oncol Biol Phys*. 2020; **108**: 1073–81.
22. Wennstig A K, Garmo H, Hallstrom P, et al. Inter-observer variation in delineating the coronary arteries as organs at risk. *Radiother Oncol*. 2017; **122**: 72–8.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Supporting Information 1: Structure Naming and Definitions.
Supporting Information 2: Display of drive structures used for beam optimisation described in Supporting information 1.