

# A Dosimetric and Radiobiological Comparison of Intensity Modulated Radiotherapy, Volumetric Modulated Arc Therapy and Helical Tomotherapy Planning Techniques in Synchronous Bilateral Breast Cancer

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## Abstract

**Objective:** The present investigation intends to identify the optimal radiotherapy treatment plan for synchronous bilateral breast cancer (SBBC) using dosimetric and radiobiological indexes for three techniques, namely, helical tomotherapy (HT), volumetric modulated arc therapy (VMAT), and intensity-modulated radiotherapy (IMRT). **Methods:** Twenty SBBC treated female patients treatment planning data (average age of 52.5 years) were used as the sample for the present study. Three different plans were created using 50 Gy in a 25 fraction dose regime. Poisson, Niemierko, and LKB models were applied for calculating normal tissue complication probability (NTCP) and tumour control probability (TCP). **Result:** The target average dose comparison between IMRT with HT and VMAT with HT was highly substantial ( $P=0.001$ ). The percentage of TCP for IMRT, VMAT, and HT in the Poisson model were  $93.70\pm 0.28$ ,  $94.68\pm 0.30$ , and  $94.34\pm 0.57$ , respectively ( $p<0.05$ ). The dose maximum was lower for the whole lung in the HT plan, with an average dose of  $49.31\text{Gy}\pm 3.9$  ( $p<0.009$ ). The NTCP values of both Niemierko and LKB models were lower for the heart, lungs, and liver for the IMRT plan. **Conclusion:** The sparing of organs at risk was higher in the HT plan dosimetrically, and the TCP was higher in the three techniques. The comparison between the three techniques shows that the IMRT and HT techniques could be considered for treating SBBC.

**Keywords:** Bilateral breast cancer- radiobiology- TCP- NTCP

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## Introduction

Breast cancer is the most common cancer among women and one of the leading causes of death worldwide. The incidence of bilateral breast cancer is around 2% to 5% and is not a common occurrence (Wadasadawala et al., 2017). Synchronous breast cancer (SBC) is widely defined as two tumors diagnosed more or less simultaneously (Padmanabhan et al., 2015). Patients with unilateral breast cancer could be treated by applying a tangential field, either two-dimensional (2D) radiotherapy or three-dimensional conformal radiotherapy (3DCRT). Nevertheless, during the application of the traditional field to the bilateral breast, the junction in the mediastinal could be inevitable due to the overlapping radiotherapy (RT) field. This could lead to high dose deposition in the mediastinal. The target dose coverage will be compromised while reducing the junction dose (Mani et al., 2017). The bias dose planning method can also be used to reduce the junction dose without compromising the junction dose for the complex radiotherapy treatment planning (Sharma et al., 2009).

Treating synchronous bilateral breast cancer (SBBC) requires complex treatment planning with several isocentres and field matching to achieve acceptable treatment plans (Farooqi et al., 2017). Modern radiotherapy techniques, such as helical tomotherapy (HT), volumetric modulated arc therapy (VMAT), and intensity-modulated radiotherapy (IMRT) used for treating SBBC.

This research aims to identify the optimum radiotherapy treatment plan for SBBC, including the nodal areas, using dosimetric indexes, such as conformity index (CI), homogeneity index (HI), and prescription dose to the planning target volume (PTV). In addition, radiobiological indexes, such as equivalent uniform dose (EUD)-based NTCP and TCP, are computed and utilized for justification in planning techniques of HT, VMAT, and IMRT.

Matlab (Mathworks) is used to create in-house software for analyzing the NTCP and TCP that originated from differential dose-volume histograms (dDVH). Various model predictions were compared and analyzed by estimating competing treatment plans using the application and integrating associated current knowledge of the

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radiobiological framework (Gay et al., 2007; Warkentin et al., 2004).

## Materials and Methods

### Selection of patients and contouring

The treatment data of twenty female patients (aged between 30 and 72 years, with an average of 52.5 years) who received bilateral breast treatment was used in this research. All patients were simulated with all-in-one (AIO) breast solutions in the headfirst supine position with both arms raised upwards. A thermoplastic mask was prepared for the patients. Contouring and planning were done by acquiring a computed tomography (CT) scan with a slice thickness of 2.5 mm. All CT images were obtained during free-breathing, and it was ensured that the entire volume of the liver and lungs were included in the scan by maintaining its range from the mandible to the second lumbar vertebra.

The radiation therapy oncology group (RTOG) 1005 protocol-based breast-contouring has been used as a guideline to define the targets and organs at risk (OARs) in an eclipse treatment planning system (Varian Medical Systems, Palo Alto, USA). The entire breast, and if involved, the supraclavicular node (SCN), was encompassed by the clinical target volumes (CTVs). The planning target volumes (PTVs) have been created from CTVs using a 5 mm isotropic margin, which has limited to the cropping of 3 mm from the skin surface. Fourteen left-side and six right-side SCN were contoured; three patients had both right and left SCN involved, and three patients did not have SCN involved. The defined OARs used for comparison are the heart, lungs, liver, esophagus, and spinal cord.

### Treatment Planning

All the patient's plans have been optimized with an aggregate dose of 50 Gy in 25 fractions using three planning proficiencies (HT, IMRT, and VMAT). The Varian Eclipse treatment planning system (TPS), version 15.6, has data configured for the six MV photon energy Varian TrueBeam accelerator, with an HD 120 Multi-Leaf Collimator (MLC) with 60 leaf pairs (with a spatial resolution of 0.25 cm in the center and 0.5 cm in the periphery), has been used to create the VMAT and IMRT plans. An Anisotropic Analytical Algorithm (AAA) dose calculation model has been used to calculate the dose after setting the calculation grid size to 2.5 mm.

To achieve maximum tangential coverage with good conformity for both left and right breasts, three anterior and posterior tangent fields with an angle interval of 10-15 degrees each and three oblique fields with an angle interval of 30-40 degrees each have been introduced into IMRT plans (Figure 1a). Also, to achieve the dose coverage in SCN, three RT fields have been utilized with angles of 0, 30, and 330 degrees.

For VMAT plans, three arc fields from 300 to 175 degrees clockwise and counter clockwise (CW and CCW) for the left breast and three arc fields from 60 to 185 degrees CW and CCW direction for the right breast have been introduced (Figure 1b). Also, to get the dose coverage

of SCN, one arc field has been used with an angle of 300 to 175 degrees CW for the left side and 60 to 185 degrees CCW direction for the right side SCN, if required.

The Radixact (Accuray, Version X9) with six MV photon energy is equipped with a dynamic jaw (Tomo edge), 0.625cm resolution binary MLC and parameters such as field width of 2.5cm, modulation factor of 3, and the pitch value of 0.3 are used for optimization in the treatment planning workstation (Accuray, precision, Version 3.3). The final dose calculation has been performed using the collapsed cone convolution superposition (CCCS) algorithm for HT plans.

The criteria are that the dose coverage of 95% of the target volume needs to receive at least 95% of the prescription dose. Also, the optimization process has been repeated until the OAR dose could be further reduced without increasing hot spots or compromising PTV coverage for all three techniques.

### Treatment plan evaluation

The dose volume histogram (DVH) analysis was utilised to evaluate the plans. D98% and D2% (minimum dose to PTV's 98% and 2%), Dmean (mean dose to PTV), Dmin (minimum dose to PTV), and Dmax (maximum dose to PTV) were reported for PTV (Loic F et al., 2006). The following indices are used in this study.

### Conformity index

$$CI = \frac{\text{Volume}_{95\% \text{ of PD}}}{\text{PTV Vol}} \quad (1)$$

where PD = prescription dose to the PTV; and PTV Vol = total PTV volume.

### Homogeneity index

$$HI = \frac{D2\% - D98\%}{D50\%} \quad (2)$$

where D98%=minimum dose to 98% of PTV; D2%=minimum dose to 2% of PTV; D50%=minimum dose to 50% of PTV.

### Coverage Index

$$Cov I = \frac{Dmin}{PD} \quad (3)$$

where Dmin = minimum dose to PTV; PD = prescription dose to PTV.

### Equivalent Uniform Dose (EUD)

Equivalent uniform dose (EUD) is defined as the dose absorbed with a biological effect similar to non homogeneous irradiation, if applied uniformly to the tumour or normal tissue (Niemierko A, et al., 1999).

$$EUD = \left( \sum_{i=1} V_i EQD_i^a \right)^{1/a} \quad (4)$$

where EQDi = dose delivered to a sub volume Vi; a = unitless model parameter, which is specific to the tumour of interest or normal structure.

$$EQD_i = D_i \frac{\left(\frac{\alpha}{\beta} + \frac{D_i}{n_f}\right)}{\left(\frac{\alpha}{\beta} + 2\right)} \quad (5)$$

where  $D_i$  = total dose received by the bin;  $n_f$  = total number of fraction;  $D_i/n_f$  = dose received by the bin at each fraction;  $\alpha/\beta$  = parameters of the linear-quadratic (LQ) model (for a particular tumour or organ that is generally exposed).

*TCP and NTCP calculation models*

*Poisson Linear Quadratic model*

The Poisson distribution is used to derive the Poisson linear quadratic model (Wang et al.,2018). from the model of linear quadratic cell survival.

$$TCP = \left[\frac{1}{2}\right]^{\sum_i V_i} \exp\left[\frac{2\gamma\left(1 - \frac{EQD_2}{D_{50}}\right)}{\ln 2}\right] \quad (6)$$

where  $D_{50}$  = dose yields 50% of tumour control;  $\gamma$  = normalized dose-response gradient;  $EQD_2$  = equivalent dose given in 2Gy fraction. The parameters of  $D_{50} = 39.3\text{Gy}$  and  $\gamma_{50} = 1.7$  are used to calculate the tumour control probability (Liang et al., 2019; Okunieff et al., 1995).

*Niemierko's model*

$$TCP = \frac{1}{1 + \left(\frac{TCD_{50}}{EUD}\right)^{4\gamma_{50}}} \quad (7)$$

$$NTCP = \frac{1}{1 + \left(\frac{TD_{50}}{EUD}\right)^{4\gamma_{50}}} \quad (8)$$

A unit less model parameter describing the dose-response curve's slope is  $\gamma_{50}$ , and the tolerance dose needed for controlling 50% of the tumour (if irradiated uniformly) is  $TCD_{50}$ . OARs' tolerance dose for producing 50% of complications (if irradiated uniformly) is  $TD_{50}$  (Marks et al., 2010; Niemierko et al., 1991) Table 1. summarises the parameters utilized for the calculations of Niemierko's EUD model (Emami et al., 1991).

*Lyman-Kutcher-Burman (LKB) NTCP model*

Lyman, Kutcher, and Burman (LKB) established a possible way to estimate the complication probability for the heterogeneously irradiated normal organs (Lyman et al., 1987; Kutcher et al., 1989; Kutcher et al., 1991).

The LKB formalism is denoted as:

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-\frac{x^2}{2}} dx \quad (9)$$

$$t = \frac{D_{eff} - TD_{50}}{m * TD_{50}} \quad (10)$$

$$D_{eff} = \left(\sum_i V_i D_i \frac{1}{n}\right)^n \quad (11)$$

where  $TD_{50}$  = tolerance dose of OARs to produce 50% of complication (if uniformly irradiated);  $V_i$  = volume in a specific dose bin  $i$ ;  $D_i$  = dose given to each bin;  $m$  = dimensionless parameter for determining the slope of complication probability versus dose curve;  $n$  = volume dependence of the complication's probability. Table 2 summarises the parameters' corresponding sets [Seppenwoolde et al., 2003).

*Statistical Analysis*

Data statistics have been demonstrated as mean  $\pm$  standard deviation (SD). Radiobiological metrics and differences in the dosimetric parameters among the three plans have been analyzed through one way ANOVA post hoc (SPSS\_v24). A value of less than 0.05 has regarded as statistically substantial.

**Results**

The case with 95% of the prescription dose to PTV coverage for IMRT, VMAT, and HT plan has shown in Figure 2. Table 3 shows the dosimetric and TCP parameters for the PTV of the three plans. Substantial differences did not found in the mean dose coverage of PTV between VMAT and IMRT plans. The mean dose comparison between IMRT with HT and VMAT with HT was highly significant ( $P = 0.001$ ). Meanwhile, the conformity index (CI) and homogeneity index (HI) has

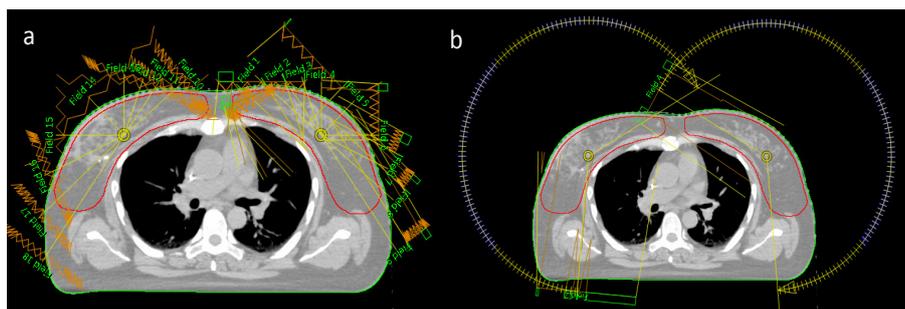


Figure 1. (a) Field arrangement for IMRT plan and (b) Field arrangement for VMAT plan

Table 1. Set of Parameters Used for Niemierko’s Model

Organ	a	$\gamma_{50}$	TCD <sub>50</sub> (Gy)	TD <sub>50</sub> (Gy)	$\alpha/\beta$	End point
PTV	-7.2	2	28	-	4	-
Heart	3	3	-	50	3	Pericarditis
Lungs (R&L) *	1	2	-	24.5	3	Pneumonitis
Liver	2	3	-	40	1.5	Liver failure
Esophagus	19	4	-	68	3	Perforation
Spinal cord	13	4	-	66.5	2	Paralysis

\*Right and left side lungs both combined

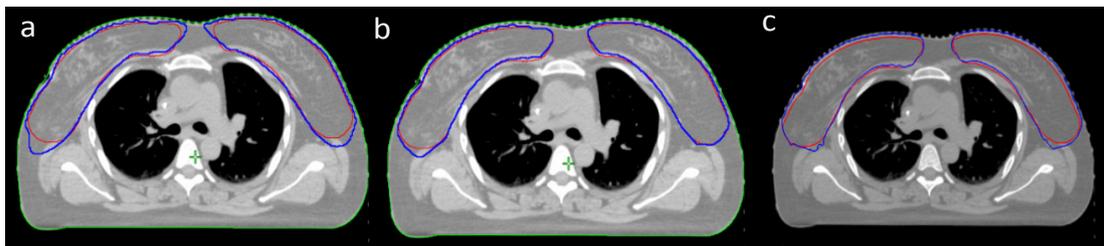


Figure 2. Dose Coverage for Plan IMRT (a), plan VMAT (b) and plan HT (c)

nearly identical results for all three regimens.

The average and standard deviations for TCP for IMRT, VMAT, and HT were 93.70%±0.28, 94.68%±0.30, and 94.34%±0.57, respectively, with the Poisson model and 99.07%±0.05, 99.26%±0.05, and 99.18%±0.12, respectively, with the Niemierko model. Consequently, a statistically substantial level ( $p < 0.05$ ) was identified.

Figure 3 demonstrates the EUD variation for OARs for the three different plans. The HT plan showed a lower average EUD value for the heart, lungs, liver, and esophagus. At the same time, the spinal cord received a higher EUD value in the HT plan. The IMRT plan showed an intermediate EUD value between the VMAT and HT plans. Barring the spinal cord, the VMAT plan showed a

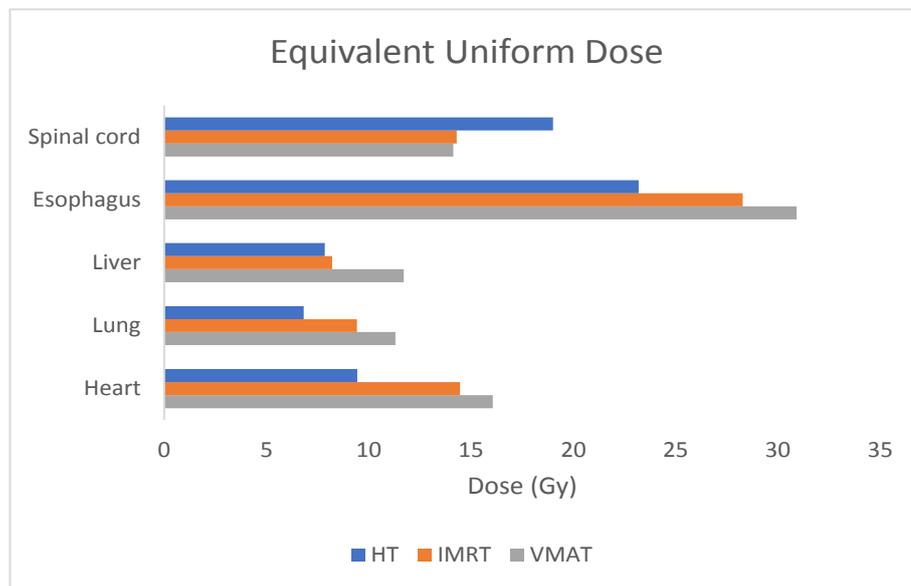


Figure 3. Equivalent Uniform Dose for Plan HT, IMRT, and VMAT of Organ at Risk

Table 2. Set of Parameters Used for LKB Model

Organ	n	m	TD <sub>50</sub> (Gy)	$\alpha/\beta$	End point
Heart	0.35	0.1	48	3	Pericarditis
Lungs (R&L) *	0.87	0.18	30.8	3	Pneumonitis
Liver	0.32	0.15	40	1.5	Liver failure
Esophagus	0.69	0.36	47	3	Perforation
Spinal cord	0.05	0.175	66.5	2	Paralysis

\*Right and left side lungs both combined

Table 3. Dosimetric and TCP Outcomes for Planning Target Volume

Parameters	IMRT <sup>(a)</sup>	VMAT <sup>(b)</sup>	HT <sup>(c)</sup>	P Value		
	Mean (SD)	Mean (SD)	Mean (SD)	a Vs b	a Vs c	b Vs c
D <sub>min</sub> (Gy)	33.35 (5.56)	33.85 (6.99)	33.36 (4.28)	0.959	1.000	0.961
D <sub>max</sub> (Gy)	54.21 (0.72)	54.81 (0.78)	53.77 (0.83)	0.047	0.190	0.000
D <sub>mean</sub> (Gy)	51.50 (0.35)	51.27 (0.58)	50.47 (0.33)	0.205	0.000	0.000
CI	0.99 (0.02)	0.96 (0.05)	0.96 (0.02)	0.013	0.009	0.988
HI	0.10 (0.02)	0.14 (0.03)	0.12 (0.03)	0.000	0.029	0.047
Cov I	0.70 (0.12)	0.71 (0.15)	0.70 (0.09)	0.967	1.000	0.967
TCP <sub>poisson</sub> (%)	93.70 (0.27)	94.68(0.30)	94.34 (0.57)	0.034	0.000	0.000
TCP <sub>Niemierko</sub> (%)	99.07 (0.05)	99.26 (0.05)	99.18 (0.12)	0.015	0.000	0.000

IMRT, Intensity modulated radiotherapy; VMAT, Volumetric modulated arc therapy; HT, Helical tomotherapy; TCP, Tumour control probability; D<sub>max</sub>, maximum dose to the PTV; D<sub>min</sub>, minimum dose to the PTV; D<sub>mean</sub>, mean dose to the PTV; CI, Conformity Index; HI, Homogeneity index; Cov I, Coverage Index

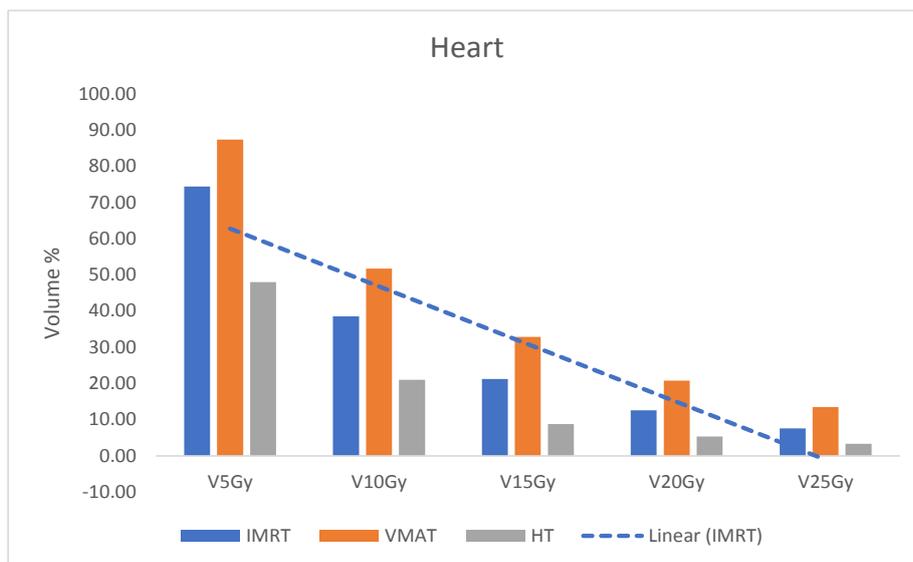


Figure 4. Dosimetric Values of Heart for IMRT, VMAT, and HT Plan

higher EUD for all OARs.

Regarding the mean dose to the heart among the three plans, the VMAT plan showed the highest mean dose with an average of 13.9Gy±2.9, followed by the IMRT plan showed 10.95Gy±1.44, and the HT plan showed the lowest mean dose with an average of 7.2Gy±1.42, which was statistically substantial (p<0.001). Figure 4 shows that in comparison to IMRT and VMAT plans, the HT plan had significantly lower doses of V5 Gy, V10 Gy, V15 Gy, V20 Gy, and V25 Gy (p<0.006). All the plans exhibited the minimum NTCP values with both LKB and Niemierko models for the heart. The differences in NTCP values between VMAT and HT plans reached statistical significance (p=0.02) (Table 4).

Regarding the maximum dose to the whole lung among the three plans, the dose maximum was higher with an average of 52.02Gy±1.56 for IMRT, followed by the VMAT plan, which showed 50.57Gy±2.3, and the HT plan had a less dose maximum with an average of 49.31Gy±3.9 (p<0.009). The HT plan had less volume involvement of V5 and V20 Gy when compared to VMAT and IMRT plans (p<0.016), and the mean dose was less in the HT plan, which was statistically significant (p<0.07).

The HT plan exhibited the maximum NTCP values with both the LKB and Niemierko models for the whole lung, compared with the VMAT and IMRT plans. The difference between NTCP values for IMRT and VMAT plans not to have any statistical significance(p=0.37).

The liver's mean dose for the IMRT plan was lower with a dose average of 7.71Gy±4.9, and a marginally similar mean dose had observed for the HT plan with a dose average of 7.85 Gy±3.53. The VMAT plan had an average mean dose of 10.74Gy±5.12 is higher than the other plans. All plans exhibited the minimum NTCP values with both models for the liver, and the differences in NTCP values for HT and VMAT plans reached statistical significance (p<0.046) (Table 4).

The mean dose to the esophagus was marginally equal for the three plans, and the mean dose of the esophagus is 9.52Gy±3.02, 10.65Gy±3.66, and 10.67Gy±2.35 for IMRT,VMAT, and HT, respectively (Table 4). The LKB model showed a higher NTCP value for the HT plan when compared with IMRT and VMAT plans. The dose maximum was higher for the spinal cord by the HT plan, and the NTCP value was lower with the LKB and Niemierko models for all of the plans.

Table 4. Dosimetric and NTCP Results for Organ at Risk

	IMRT <sup>(1)</sup>	VMAT <sup>(v)</sup>	HT <sup>(h)</sup>		P Value	
	Mean	Mean	Mean	I Vs h	I Vs v	v Vs h
<b>Heart</b>						
D <sub>max</sub> (Gy)	47.95	46.58	41.06	0.743	0.001	0.013
D <sub>mean</sub> (Gy)	10.95	13.39	7.2	0.001	0.000	0.000
V5Gy (%)	74.41	87.4	47.99	0.001	0.000	0.000
V10Gy (%)	38.53	51.73	21.05	0.000	0.000	0.000
V15Gy (%)	21.26	32.86	8.78	0.000	0.000	0.000
V20Gy (%)	12.56	20.82	5.32	0.000	0.000	0.000
V25Gy (%)	7.58	13.48	3.31	0.000	0.006	0.000
V40Gy (%)	2.11	1.74	0.21	0.802	0.006	0.031
<b>NTCP (%)</b>						
LKB model	1.00×10 <sup>-10</sup>	4.35×10 <sup>-09</sup>	5.98×10 <sup>-08</sup>	0.315	0.993	0.264
Niemierko Model	1.09×10 <sup>-05</sup>	1.30×10 <sup>-04</sup>	4.79×10 <sup>-04</sup>	0.105	0.757	0.020
<b>Whole Lung</b>						
D <sub>max</sub> (Gy)	52.02	50.57	49.31	0.232	0.009	0.329
D <sub>mean</sub> (Gy)	12.18	14.44	9.18	0.007	0.000	0.000
V5Gy (%)	71.99	81.35	53.96	0.016	0.000	0.000
V20Gy (%)	16.53	24.93	10.75	0.000	0.013	0.000
V45Gy (%)	1.86	1.53	0.56	0.685	0.004	0.037
<b>NTCP (%)</b>						
LKB model	5.77×10 <sup>-03</sup>	2.57×10 <sup>-02</sup>	6.05×10 <sup>-02</sup>	0.055	0.370	0.001
Niemierko Model	3.00×10 <sup>-02</sup>	1.57×10 <sup>-02</sup>	0.37	0.061	0.368	0.001
<b>Liver</b>						
D <sub>max</sub> (Gy)	46.11	48.43	41.91	0.554	0.153	0.014
D <sub>mean</sub> (Gy)	7.71	10.47	7.85	0.115	0.994	0.142
V15Gy (%)	16.27	25.91	18.46	0.092	0.879	0.234
V25Gy (%)	6.5	13.32	7.22	0.013	0.949	0.030
<b>NTCP (%)</b>						
LKB model	2.58×10 <sup>-03</sup>	5.87×10 <sup>-03</sup>	6.69×10 <sup>-02</sup>	0.056	0.991	0.042
Niemierko Model	8.15×10 <sup>-05</sup>	1.78×10 <sup>-04</sup>	2.41×10 <sup>-03</sup>	0.994	0.059	0.046
<b>Esophagus</b>						
D <sub>max</sub> (Gy)	40.78	41.57	36.67	0.981	0.604	0.490
D <sub>mean</sub> (Gy)	9.2	10.65	10.67	0.299	0.288	1.000
V15Gy (%)	16.1	21.36	28.35	0.224	0.001	0.076
V25Gy (%)	7.77	12.47	4.68	0.111	0.378	0.004
V40Gy (%)	2.35	4.54	0.65	0.217	0.395	0.011
<b>NTCP (%)</b>						
LKB model	1.31	1.26	1.74	0.169	0.980	0.238
Niemierko Model	7.23×10 <sup>-04</sup>	1.15×10 <sup>-02</sup>	2.66×10 <sup>-02</sup>	0.425	0.642	0.087
<b>Spinal cord</b>						
D <sub>max</sub> (Gy)	28.738	27.464	33.1685	0.880	0.224	0.088
D0.3cc (Gy)	24.738	23.694	29.413	0.924	0.217	0.105
<b>NTCP (%)</b>						
LKB model	6.08×10 <sup>-02</sup>	2.629×10 <sup>-03</sup>	1.21×10 <sup>-02</sup>	0.977	0.424	0.547
Niemierko Model	4.59×10 <sup>-04</sup>	9.70×10 <sup>-08</sup>	1.55×10 <sup>-05</sup>	0.999	0.443	0.467

IMRT, Intensity modulated radiotherapy; VMAT, Volumetric modulated arc therapy; HT, Helical tomotherapy; NTCP, normal tissue complication probability; LKB model, Lyman-Kutcher-Bruman Model; D<sub>max</sub>, maximum dose to the OAR; D<sub>min</sub>, minimum dose to the OAR; D<sub>mean</sub>, mean dose to the OAR; P value, one way ANOVA Post hoc test

## Discussion

The PTV is large for treating bilateral breast cancer. Hence, radiation exposure to OARs such as lungs, heart, liver, and esophagus increases compared to unilateral breast cancer treatment (Sun et al., 2020). 3DCRT technique has been used to treat unilateral breast cancer patients in many institutions. Nonetheless, the 3DCRT method did not produce better results for patients with SBBC (Kim et al., 2018). The inter-breast overlapping fields create a hotspot in the 3DCRT technique, and trying to reduce the hotspot will lead to PTV dose reduction, whereas the OARs will receive a higher dose.

Evaluation of treatment plans with the integration of radiobiological and dosimetric parameters has been found to be more rational and comprehensive (Wang et al., 2019). As reported in our study, the HT plan provides lower dose levels for OARs compared with VMAT and IMRT plans. The HT plan shows a slightly higher NTCP value for the esophagus and lungs.

Techniques like IMRT and VMAT help in improved target dose uniformity, and significant sparing of healthy normal tissues. This is generally achieved by exposing larger volume of normal tissues to lower doses from scattered and leakage radiation due to the nature of these delivery techniques (Paganetti et al., 2012). Tissues receiving low doses are more prone to developing secondary cancer risk (SCR) because cell mutations are more dominant than cell kill at low doses. Consequently, patients treated with these techniques are at higher risk of radiation-induced SCR compared to conventional radiotherapy; this is due to exposure of larger volumes receiving low doses (Braunstein and Nakamura, 2013).

Sakthivel et al., (2017) evaluated the cohort of 50 early-stage left-sided breast cancer patients with advanced techniques like IMRT and VMAT for SCR using the mechanistic radiobiological model and found higher risks are closer to the target. Also, VMAT plans had a higher SCR in all organs studied compared to IMRT plans, and the increase in risk was higher in both IMRT and VMAT for the left lung and contralateral breast.

Wang et al., (2019) used existing TCP and NTCP models, such as Poisson, Niemierko, and LKB, for oesophageal cancer patients and found that these models were reliable for planning comparative studies. (Balasubramanian and Shobana, 2021) compared photon and proton planning radiobiologically using LKB and Niemierko NTCP models, and they found that the results were reliable for comparing different planning methods. In our study, we used the Poisson and Niemierko models, and we found that both models achieved more than 90% tumor control. In addition, we used the LKB and Niemierko models to find the probability of normal tissue complications.

Several recent studies on the VMAT and hybrid VMAT plan comparison for unilateral breast or chest wall (CW) irradiation show that hybrid VMAT plans have better results. Zhang et al., (2021) compared the IMRT and VMAT plans dosimetrically and radiobiologically and found that the VMAT plan was good in PTV coverage and dose reduction in the lungs and heart in the medium-dose

region in left-sided CW treatment. Subramanian et al., (2016) compared the VMAT and hybrid VMAT plans in bilateral breast cancer and found that the hybrid plan resulted in fewer doses in low-dose regions in OARs, such as the heart and lungs.

Kang et al., (2019) compared three different VMAT planning techniques for the left-sided breast treatment plan and suggested that the 2pVMAT technique is good for the treatment because of the dose reduction in the ipsilateral lung. Cho et al., (2019) evaluated the optimum treatment planning for SBBC between VMAT only and hybrid VMAT using the dosimetric indices and suggested that the VMAT hybrid plan was the better option for both PTV coverage and OAR dose reduction. At the same time, the treatment plans did not compare with other than VMAT techniques, such as IMRT and HT.

Dosimetrically compared the 3DCRT plan with VMAT and IMRT hybrid plans for hypo-fractionated SBBC. The researchers concluded that a combination of 3DCRT and IMRT techniques provides superior dosimetric parameters. Gaudino et al., (2018) evaluated SBBC only for the VMAT plan dosimetrically between free breath and the deep inspiration breath-hold (DIBH) technique. The investigators suggested that DIBH is possible in SBBC because of its reproducibility. Soujanya et al., (2021) reported that DIBH reduces the OAR dose in left-sided breast cancer patient treatment. In this study, we did not use the DIBH method because this technique is used for left-sided breast cancer treatment to reduce the dose to the lungs and heart. It is a limitation of the present study. Therefore, DIBH needs investigation for SBBC treatment dosimetrically and radiobiologically. The dose calculation algorithm and the radiobiological models are also the limitations of this study.

The observed result shows that the techniques used for comparison had good conformity and homogeneity in the present study and the HT plan had a lower maximum dose for the PTV. As far as the mean dose is concerned, lower doses for all OARs were demonstrated by the HT plan, followed by the IMRT plan. In the VMAT plan, low dose volume, maximum dose, and mean dose had higher values for all OARs.

All plans had a good TCP value in the radiobiological evaluation. The NTCP for the heart, liver, and spinal cord had a negligible value in both models. The whole lung had a marginally higher NTCP value in the Niemierko model, and the esophagus had a marginally higher NTCP value in the LKB model.

In conclusion, in the present comparison of SBBC radiotherapy treatment plans, the sparing of OARs was higher in the HT plan dosimetrically, and the TCP was higher in all three techniques. The TCP and NTCP comparison between the three planning techniques shows that IMRT and HT techniques could be considered for treating SBBC. No standard protocols are defined yet to treat SBBC, and this study provides useful information to create a future treatment guideline. The planning could be ranked and compared based on the anatomical and clinical challenges of each patient, using dosimetric parameters with the TCP and NTCP estimated radiobiological parameters.

## Author Contribution Statement

The authors confirm contribution to the paper as follows: study conception and design: S. Balasubramanian, M.K. Shobana; data collection: S. Balasubramanian; analysis and interpretation of results: S. Balasubramanian; draft manuscript preparation: S. Balasubramanian, M.K. Shobana. All authors reviewed the results and approved the final version of the manuscript.

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### Ethical Approval

Institutional scientific and Ethics Committee has approved this study. This article does not contain any studies with human participants performed by any of the authors.

### Informed Consent

The informed consent has been waived off by the ethics board of the institute considering this as a retrospective study with no human involved. For this type of study formal consent is not required.

### Conflict of interest

The authors declare that they have no conflict of interest with respect to the manuscript.

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