



Comparison of VMAT, Field in Field, Inverse IMRT, and Helical Tomotherapy Planning in Bilateral Synchronous Breast Cancer: A Case Study

Zedef DAĞ,¹ Şilem ERTÜRK,² Oguzhan AYRANCIOĞLU,² Fikri KURT,³
 Ayse KUTLUHAN DOĞAN,² N. Deniz ARSLAN¹

¹Department of Radiation Oncology, Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery, İstanbul-Turkey

²Department of Radiation Oncology, Health and Science University, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul-Turkey

³Department of Radiation Oncology, Kocaeli Government Hospital, Kocaeli-Turkey

SUMMARY

This study aims to compare the technical feasibility and benefits of four different planning techniques, VMAT, helical tomotherapy, IMRT and Field in Field, for synchronous bilateral breast cancer patients. In this study, two patients with early bilateral breast cancer after breast conservation surgery were planned for radiotherapy. Three different treatment planning techniques were generated for each patient on the Eclipse treatment planning system, and both patients were planned on the Tomotherapy planning system. For planning target volumes (PTVs), the mean doses, values of D2, D98, conformity index and homogeneity index were reported. For the organs at risk, the analysis included the mean dose and VXGy, depending on the organs (lungs, heart). In all techniques used in this study, there was no difference in D98% tPTV, while the lowest D2% was seen in HT plans. HT was the best in conformity and homogeneity index. For Pat#1 and Pat#2, the mean dose (Dmean) to total lungs were 10.8;10.5, 11;13,5, 10.3;10 and 12.2;14.5 Gy for FinF, IMRT, HT and VMAT, respectively and the mean dose to the heart was 5.6, 5.7, 7.9 and 6.8Gy (Pat#1); 4.6, 8, 8.4 and 6.3Gy (Pat#2), respectively. Heart volume at high doses (V25Gy, V30Gy) was approximately 80% lower for HT and 90% lower for VMAT than for FinF. The highest total motor unit value (14555 MUs) was seen in HT plans. Among the SBBC radiotherapy treatment plans, the HT plans improved the PTV dose coverage and dose homogeneity with improved sparing of lungs and heart.

Keywords: Bilateral synchronous breast cancer; field in field, helical tomotherapy, inverse IMRT, radiation therapy; VMAT.

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Introduction

Bilateral Breast Carcinoma (BBC) is a rare entity with an incidence of synchronous carcinoma being 2-5% of all breast malignancies. Despite the infrequency of cases of synchronous bilateral breast cancer (SBBC),

the numbers of SBBC diagnoses have been showing an upward trend along with the increase in breast cancer cases.[1] Against this background, research on prognosis and treatment is still ongoing. However, to our knowledge, no definite radiation therapy has been reported for SBBC yet.

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Dr. Zedef DAĞ
Yedikule Göğüs Hastalıkları ve Göğüs Cerrahisi,
Radyasyon Onkolojisi Anabilim Dalı,
İstanbul-Turkey
E-mail: ozdemirzedef@hotmail.com

Compared to unilateral breast cancer radiotherapy, the treatment planning and dose delivery of the BBC is very complex and time-consuming. One of the standard treatment techniques for BBC is 2-dimensional radiation therapy (2DRT) or 3-dimensional conformal radiation therapy (3DCRT) with tangential beam irradiation.[2,3] It is rather difficult to protect organs at risk (OARs) that lie in the same direction as the target. For complex treatment volumes, such as SBBC, recent trends have shown that intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) are applied.[3,4] Once IMRT and VMAT have been used for SBBC radiation therapy, the problems associated with isocenter and junction can be addressed. There have been only a few studies of treatment for SBBC, but there have recently been several studies comparing conformal radiation therapy (3DCRT) and IMRT treatment plans in SBBC, [3] as well as a study comparing IMRT with Rapid Arc (RA) treatment plan.[4] Another study was conducted to evaluate treatment plans with complex treatment volumes using helical tomotherapy.[5] Thus, this is the first planning case reported in the literature on all four techniques (FiF, IMRT, VMAT and HT) for synchronous bilateral breast cancer patients.

In this study, we aimed to compare the technical feasibility and benefits of two different helical intensity-modulated RT (RapidArc VMAT and Tomotherapy) with three dimensional conformal (Field-in-field (FiF)) and multi-field dynamic (sliding-window) IMRT for SBBC patients.

Materials and Methods

Patients and Planning Objectives

Two different patient cases were reported in this study and patients' consent was obtained for this report. The first patient (Pat#1) was a 48-year-old premenopausal female with bilateral ductal breast carcinoma. She underwent bilateral breast-conserving surgery and sentinel lymph node biopsy (SLNB) (right breast:T2N0M0 stage IIA, left breast:T1bN0M0 stage IA). The Pat#2 was a 54-year-old postmenopausal female with early-stage SBBC. She underwent bilateral breast-conserving surgery and SLNB (right breast:T1bN0M0 stage IIA, left breast: T1cN0M0 stage IA). With both patients, chemotherapy consisted of four cycles of doxorubicin and cyclophosphamide (AC). They also received hormone therapy for five years.

Both patients were imaged supine with a CT scanner (Siemens Somatom Spirit) in the treatment posi-

tion (both arms up). CT was performed at 3-mm slice spacing. For patients, the clinical and planning target volumes (CTV and PTV) of the right and left were delineated on the CT data. The CTV included visible breast parenchyma, excluding the muscles and ribs, retracted 5 mm from the skin into the body. The PTV comprised the CTV with a 10-mm circumferential margin to allow for daily set-up variations and potential intrafraction thoracic wall motion, also retracted by 5 mm from the skin into the body.

The critical structures delineated were both lungs, heart, spinal cord. The heart was contoured from below the level of the great vessels up to the diaphragm. The lungs were contoured in the appropriate lung window setting (width 1600, level 400). The volumes of the PTVs and lungs were shown in Table 1. The goal of all plans was to cover 95% of PTVs with 100% of the prescribed dose.

Planning Techniques

Three different treatment planning techniques were generated by medical physicists on the Eclipse treatment planning system (TPS) (Version 11) for Varian Trilogy linear accelerator with Millennium MLC. 6 MV photon energy and Anisotropic Analytical Algorithm (AAA) were used for all planning techniques. The dose calculation grid was set to 2.5 mm.

Patients were also planned on the Tomotherapy planning system Hi art (Version 4.2.3). There was no overlapping of treatment fields in any of the plans. Neither bolus nor other techniques were used for skin doses.

Field in Field

Two fixed main tangential fields which have sub-fields were used for both breasts separately to achieve more homogeneous dose distribution in PTVs. All fields were shaped to cover their PTVs with fall offs to the surfaces of the breasts of both patients. Single isocenter was used for both breasts; we used 310°-130° and 50°-230° beam angles for left and right breasts, respectively.

Table 1 The volumes of the PTVs and lungs in cases

	Pat 1		Pat 2	
	Right	Left	Right	Left
PTV _{volume}	598.2 cm ³	524.2 cm ³	1443.2 cm ³	1294 cm ³
LUNG _{volume}	1240.8 cm ³	1054.4 cm ³	1475.6 cm ³	1150.2 cm ³

PTVs: Planning target volumes

Intensity-modulated Radiation Therapy (IMRT)

The dynamic sliding window method with fixed gantry beams was used for left and right breasts with angles 310°, 325°, 300°, 100°, 115°, 130° and 55°, 40°, 25°, 260°, 245°, 230°, respectively. Two isocenters were used for both patients. Fluence transmission factors for each field were optimised using the fluence editor.

Volumetric Modulated Arc Therapy (VMAT)

Single isocenter method was used for VMAT plans. Two arcs for each breast were generated in the planning of both patients. For the first patient, clockwise (CW) and counterclockwise (CCW) 190° arc (40° to 210° and 320° to 150°), for the second patient 241° arc (300° to 179° and 60° to 181°) were used. Collimator angle was set to 30° for CW and 330° for CCW.

Helical Tomotherapy

In HT planning 2.5 cm field width, 3.0 modulation factor and 0.215 pitch value were used. To reduce the bilateral lung and heart doses, a directional and complete block was used. In addition, to prevent high doses out of the breast wall, we used ring contour around the breast wall.

Treatment Delivery with Image-Guidance

Image-guided radiation therapy (IGRT) significantly improves the accuracy of radiotherapy. IGRT plays an essential role in the accurately delivery of a highly confirmed dose to target. Varian Trilogy's On-Board Imager (OBI) kV imaging system provides a wide array of imaging modalities, including kV, MV, cone-beam CT (CBCT) and fluoroscopy. For the reported patient cases, daily kV-CBCT images were taken to set up the

patients. 3 mm slice distance and 512x512 reconstruction volume were used for CBCT imaging. After doing necessary corrections on the images, patients were treated.

Evaluation Tools

The evaluation of the plans was based on a dose-volume histogram (DVH) analysis. For PTV, the mean dose, near-max dose D2 and near-min dose D98 were reported. The conformity index (CI) is defined as the ratio of the volume to 95% of the prescribed dose to the PTV.[6,7] The homogeneity index (HI) is defined as the ratio of the dose difference of 2% and 98% to the PTV to the prescribed dose.[8] Lower HI values indicate more homogeneous target doses. The Dmean, V20Gy, and V5Gy for the lungs and V35Gy, V25Gy, and Dmean for the heart were compared. To evaluate objectively the efficiency of the treatment plans, the beam times, the treatment times (including setup time), and the monitor units (MUs) for each plan were compared.

Results and Discussion

The prescribed dose for SBB RT was 50 Gy in 2 Gy fractions to the PTVs. The goal of all plans was to cover %95 of PTVs with %100 of the prescribed dose (Fig. 1). Table 2 shows the dosimetric results achieved in all four techniques for these two patients' CT dataset. In this case of SBBC, HT appeared to be more suitable than the other techniques, providing better conformity and homogeneity index (HI) (Table 3). FinF did not have as good conformity, or homogeneity as HT, IMRT and VMAT.

Table 2 Dose distribution in organs at risk and treatment time in all planning techniques

	Patient1				Patient2			
	FinF	iIMRT	VMAT	HT	FinF	iIMRT	VMAT	HT
Total lungs								
Mean (Gy)	10.8	11	12.2	10.3	10.5	13.5	14.5	10
V5 (%)	35	57.1	87.6	45.8	33	65.5	85	45.4
V10 (%)	25.2	35.7	38.7	31.8	23	43.1	56.8	29.1
V20 (%)	20.2	15.7	17.3	15.7	18.4	20.7	23.1	16.9
Heart								
Mean (Gy)	5.6	5.7	7.9	6.8	4.6	8	8.4	6.3
V25 (%)	6.5	4.1	3.1	1.9	5	5.1	2.8	0.6
V35 (%)	4.78	3	0.8	0.5	4.2	4.2	0.2	0
Total MUs	478	1486	781	8462	509	2186	821	14555
Tre.time (minute)	2.36	7.44	5.32	10.3	2.57	10.93	6.66	17.3

FinF: Field in field; iIMRT: Inverse-intensity modulated radiation therapy; VMAT: Volumetric arc therapy; HT: Helical tomotherapy

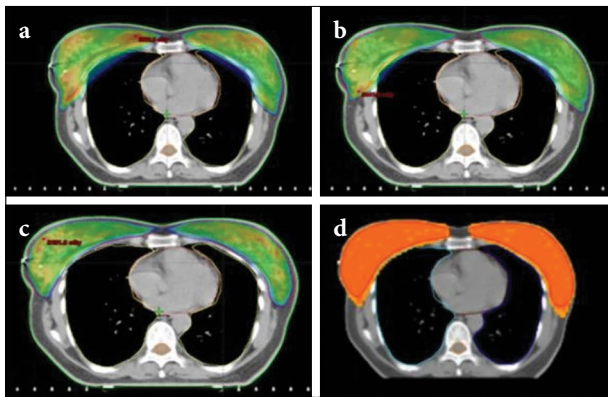


Fig. 1. Axial dose distributions for patient 1 with a dose colour wash of 47,5 Gy for all treatment techniques. (a) FiF (b) IMRT (c) VMAT (d) HT.

Table 3 The comparison of PTV coverage for FinF, IMRT, VMAT and HT using dosimetric parameters

	FinF		IMRT		VMAT		HT	
	Pat1	Pat2	Pat1	Pat2	Pat1	Pat2	Pat1	Pat2
tPTV D _{mean}	52.8	53.2	52.1	52.6	52.3	52.2	50.6	50.3
CI	1.59	1.34	1.14	1.11	1.03	1.01	0.9	0.99
HI	0.1	0.1	0.092	0.093	0.094	0.1	0.03	0.048

D_{mean}: the mean dose for the target (tPTV); CI: Conformity index; HT: Homogeneity index

Lungs

For the first patient, the mean dose (D_{mean}) to total lungs was 10.8 Gy, 11, 10.3 and 12.2 Gy for FinF, inverse IMRT, HT and VMAT, respectively. D_{mean} in the total lung was similar for HT and FinF, but worse for VMAT and IMRT. The D_{mean} to lungs for the Pat#2 was slightly increased using VMAT, from 10 Gy to 14.5 Gy, when compared to the HT technique. In this case, the volume of the lungs covered by the dose of 5 Gy (V5Gy) in VMAT planning was on average 85%, while the respective volume in Helical tomotherapy was only 45,5% (FinF<HT<IMRT<VMAT). Furthermore, V20 is a valid clinical parameter, and helical tomotherapy was the best technique in this study. In contrast to other case studies [9,10], VMAT was related with the most unfavourable dose deposition in the total lung, concerning D_{mean}, V5,V10 in the present study.

Heart

In the present study, the mean dose to the heart was 5.6, 5.7, 7.9 and 6.8 (Pat#1); 4.6, 8, 8.4 and 6.3 (Pat#2) for

FinF, IMRT, VMAT and HT, respectively, with VMAT providing the poorest outcome. Concerning dose distribution on heart, the percentage of volume at high doses, such as V35Gy and V25Gy, was approximately 70-88% lower for HT and approximately 95-97% lower for VMAT than for FinF and iIMRT.

Monitor Units and Treatment Time

Concerning MUs, HT had the highest total motor units in patient 1 (MUs:8462) and patient 2 (MUs:14555) (FinF<VMAT<IMRT<HT). The overall treatment time was less than 10 min with both patients with the FinF, VMAT and iIMRT techniques (Table 2). Both patients underwent bilateral breast radiotherapy with FinF technique. The cosmetic outcome was good and no breast oedema, erythema, or fibrosis were reported during routine follow-up.

In the literature, dosimetric studies using VMAT and tomotherapy demonstrated the feasibility of delivering radiotherapy in bilateral breast cancer patients.[4,11] The findings showed that h-VMAT and hybrid intensity-modulated radiation therapy (h-IMRT) used for breast cancer patients reduce low dose spillage to the lung and heart.[12] Improved survival in early breast cancer patients has led the radiation oncology fraternity to focus on reducing the dose to the heart and lungs. Quantitative analysis of normal tissue effects in the clinic for lung clearly emphasizes the need to limit the V5Gy to less than <60%, V20Gy less than 30-35% and the mean lung dose (MLD) to <23 Gy.[13]

Darby et al.[14] conducted a study to assess the risk of ischemic heart disease in women after radiotherapy for breast cancer. They cautioned about the potential risk for cardiac injury even at low doses, with a relative risk of 7.4% per Gy increase in adverse cardiac events. Furthermore, to avoid long-term cardiac mortality, extensive blocking of the heart is usually needed with the traditional field arrangements. This will require the acceptance of incomplete dose coverage of the PTV. With the VMAT and HT techniques, the high dose areas in the heart can be avoided without compromising the PTV dose coverage.

Yusoff et al.[3] compared the 3DCRT and IMRT treatment plans for SBBC patients. It was reported that both treatment plans showed similar results for PTV coverage, whereas for OAR dose distributions to the lungs and heart, IMRT was superior. FinF, compared with IMRT and VMAT, it had advantageous concerning OAR low dose distribution and mean dose of heart. HT and FinF provided similar dosimetric results for OARs, but the total lung V20Gy and heart V25Gy/V35Gy were improved with HT.

Kim et al. showed that among the SBBC radiotherapy treatment plans, IMRT was superior to 3DCRT and VMAT concerning PTV dose distribution, whereas VMAT showed the most outstanding treatment efficiency.[15] On the contrary, VMAT was inferior to iIMRT, HT and FinF concerning the dose in organs at risk, especially for low dose levels (V5Gy, V10Gy) and mean dose in the present study.

In a series of 14 patients with SBBC, Ekici et al. reported that HT was well-tolerated, with high HI and CI and low irradiation doses to the lungs and heart.[16] Overall, the HT plans decreased the doses to the lungs and heart and increased the dose homogeneity in the treatment volume in our study, and it is similar to the above reports.

Conclusion

In the present planning case report, all four techniques achieved acceptable target coverage while avoiding the field overlapping issues. The HT achieved better sparing of lungs and heart in the low dose region. It is difficult to suggest a clear guideline or a protocol for bilateral breast cancer plan based on the TPS result from this study alone. This study is expected to provide useful resources for establishing future treatment guidelines for bilateral breast cancer.

Informed consent: Patients provided informed consent for this case report and they were requested a copy of the signed consent to publish.

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