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Benefits and Limitations of Volumetric Modulated Arc Therapy in Treating Bilateral Breast Cancer with Regional Lymph Nodes

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Abstract

Purpose: The study was performed comparing dosimetric characteristics of volumetric modulated arc therapy (VMAT) and field-in-field (FiF) techniques on a patient with synchronous bilateral breast carcinoma. **Methods:** The patients with bilateral breast cancer treatment were included in this study. A total dose of 40.05 Gy in 15 fractions was prescribed to the Planning Target Volume (PTV) of the whole bilateral breast cancer with the supraclavicular and infraclavicular nodes, with a complementary boost of 10 Gy in 4 fractions to the surgical bed (PTV_{boost}). For both radiotherapy techniques, several V_{xGy} parameters were analyzed for the PTVs, together with the Conformity index (CI), the Homogeneity index (HI) and the critical organs at risk (OARs), lungs and heart. **Results:** The patient was treated by the VMAT technique and the daily treatment time was less than 20 minutes with daily CBCT imaging. In the VMAT plan, the PTV 95% dose covered 38.89 ± 0.81 Gy, compared to 37.26 ± 1.02 Gy in the FiF technique. The VMAT plan improved the dose homogeneity index and lower dose in lung towards high dose region. **Conclusion:** The study demonstrates the viability of the VMAT technique in the treatment of bilateral breast cancer. The introduced single isocentric VMAT technique is fast to deliver and it increases the dose homogeneity of the target volume with some limitations. The treatment was well tolerated, without interruption of the treatment courses caused by treatment-related toxicities.

Keywords

Bilateral Breast Cancer (BCC), Volumetric Modulated Arc Therapy (VMAT), Field in Field (FiF), Planning Target Volume (PTV), Organ's Volume That Receives x Gy of Dose (V_{xGy})

1. Introduction

Breast cancer is the most common cancer in women, constituting 24.2% according to GLOBOCAN 2018 [1]. Synchronous bilateral breast cancer (BBC) is defined as two or more malignant tumors occurring simultaneously in both breasts. Synchronous bilateral breast cancer is an uncommon finding in women, presenting multiple breast lumps with an estimated incidence of 2.1% [2]. Bilateral breast cancers are classified depending on the time of occurrence into synchronous (detected simultaneously or within a 6 months gap) or metachronous [3] (detected in an interval longer than 6 months).

Risk factors are familial breast cancer, young age, lobular invasive carcinoma, multicentricity, BRCA 1 & 2 gene mutations and radiation exposure [4]. Patients with breast carcinoma are treated with either modified radical mastectomy or breast conservative surgery (BCS), followed by breast irradiation in appropriately selected women. Adjuvant radiotherapy for breast cancer is classically given using medial and lateral tangential fields.

In patients diagnosed with early synchronous bilateral breast cancer, breast conservation therapy is feasible [5]. Planning for bilateral breast cancer radiotherapy is a challenging task. The radiotherapy planning and dose delivery are more complex in bilateral breast cancer.

The use of classical tangential fields in the treatment of bilateral breast cancer has many disadvantages, including significant inhomogeneity in dose distribution, high dose to critical structures and lack of conformity to planning target volume (PTV) even after using the field-in-field (FiF) technique [6]. These can lead to acute side effects, such as skin toxicity, and late effects, for instance, soft tissue fibrosis, pneumonitis and cardiotoxicity, which affect the quality of life. Modern techniques of radiation, Rapid Arc (Volumetric Modulated Arc Therapy—VMAT) and Intensity Modulated Radiotherapy (IMRT) have been utilized to overcome these problems. The purpose of this report is to share the perceived dosimetric benefits and drawbacks of VMAT over FiF for bilateral breast cancer radiotherapy.

2. Material and Methods

***Clinical history*:**

Five patients with a bilateral breast cancer, who underwent treatment with the VMAT technique in our institute during April 2019-August 2020, were included into this study. A 68-year-old patient with a bilateral breast cancer underwent left mastectomy and sentinel node dissection for a pT1c bifocal pN0(sn) and right-side lumpectomy with axillar dissection for pT2pN1a (2/12). Bilateral radiotherapy was specified before the prescription of hormonal therapy. The dose prescription was 15 times 2.67 Gy by the START scheme to the thoracic wall and 15 times 2.67 Gy to the left and to the right breast and regional lymph nodes (axillar-susclavicular level 2 to 4 and the nodes of the internal mammary chain). There was a boost dose prescribed to the original tumor bed of the right breast

of 4 times 2.5 Gy.

***Treatment simulation*:**

The patients were imaged with a CT scanner (Toshiba Aquilion LB, Toshiba Medical Systems Co., Tochigi, Japan) in the treatment position on the breast board—in supine position with both hands raised above the head. CT data was acquired from the mandible to the 4th lumbar vertebra, with a slice thickness of 3 mm during normal breathing. These CT images were then transferred online to the Eclipse (v15.4, Varian Medical Systems, Palo Alto, CA) Treatment Planning System (TPS). In the first step, Planning Target volumes (PTV) of (right and left breasts) were delineated on the CT data according to the department guidelines. The organs at risk (OAR) were contoured, including the heart and both lungs. The plans were generated by two techniques, *i.e.* field-in-field (FiF) and VMAT, to a total dose of 40.05 Gy in 15 fractions to both breast, thoracic wall and supraclavicular areas.

***Treatment planning*:**

FiF is a radiation therapy technique that uses several less-weighted fields with a small treatment field size to optimize dose distributions. The initial calculation of the FiF plan was performed with two equally weighted, open, tangential photon beams without wedges.

Two cm leaf margins have been added towards the skin side. Two or three subfields were determined for hot spot volumes blocking to improve dose homogeneity, while decreasing overdoses in the PTV. The beam weight of the subfield was 2% to 3% of the main field. The minimum monitor unit (MU) of each subfield was 8 and the main field and the subfields were merged into one portal.

The VMAT plan was generated in the Eclipse TPS, having Acuros XB algorithm, in the dose-to-medium dose reporting mode, with 2.5 mm calculation grid size. The plan was completed using four continuous arcs (arc length: 179˚ - 181˚), with 6 MV photon beams on Varian Clinac iX accelerators equipped with a Millennium 120 multileaf collimator (MLC) (Varian Medical Systems, Palo Alto, CA, USA). A single isocenter placed medially under the sternum was used for optimization. The collimator angle was set to a value of ±15˚. For optimization purposes, a breast PTV was defined as the combination of the left and right breast PTVs cropped 5 mm inwards from the skin edge. PTVs were cropped to achieve plan objectives without forcing the optimizer to increase skin dose excessively to compensate for the lack of scatter in this region. To create robust radiotherapy planning by reducing positioning uncertainties, we used the pseudo skin flash method described by Giorgia [7].

***Treatment evaluation*:**

Conformity Index (CI) and Homogeneity Index (HI) are defined according to the ICRU 83 report. CI is defined as the ratio of the volume to 95% of the prescribed dose to the PTV (CI = $V_{95\%}$ PTV). HI is defined as the ratio of the dose difference of 2% and 98% to the PTV to the dose to 50% (HI = $D_{2\%}$ – $D_{98\%}/D_{50}$%). V95% is the percentage of volume (PTV) receiving 95% of dose.

Quality Assurance (QA) of the treatment plan was performed on a Varian

EPID (Electronic Portal Imaging Devices). The differences between calculated and measured dose distributions were evaluated by the gamma parameter [8].

3. Results

We compared the two treatment plans to determine which one would offer the best coverage of our target areas, while at the same time minimizing the dose to OARs. After comparison of both plans and weighing the pros and cons for each plan, it was decided to treat the patient according to the plan generated in VMAT.

The patient was treated using the VMAT technique with four arcs with 6MV photons. For the 15 VMAT sessions, a single daily cone-beam CT (CBCT) imaging was performed for patient setup. Image reconstruction and automatic image registration were performed. The shifts to cranio-caudal, left-right and anterior-posterior directions from the daily CBCT images ranged between −0.4 to 1.9 cm (average 2 mm), −1.2 to 0.4 cm (average 10 mm) and −0.5 to 1.2 (average 5 mm), respectively.

Figure 1 shows a comparison of dose distribution by FiF and VMAT techniques in the axial, coronal and sagittal planes. On the left side (a) is the clinical FiF plan and on the right side (b) is the full arc VMAT plan in the axial, coronal and sagittal planes. PTV is indicated in red color for both breasts. The color wash represents 95% of dose prescription. The total number of monitor units (MU) was 1546 for the VMAT technique, while it was 910 for the FiF technique. The overall treatment time with daily CBCT matching was less than 20 minutes, with an average beam-on time of 330 s.

Figure 2 shows the dose volume histogram for the FiF and VMAT techniques. The color blue, cyan, magenta and pink curves represent coverage of left lung, right lung, total lung and heart contours, respectively, for FiF (square line) and VMAT (triangle line). The PTV coverage 95% isodose line was chosen as a reference. **Table 1** shows that VMAT plan has better PTV coverage, with good conformity index (CI) of 1.13 and homogeneity index (HI) of 0.10, when compared to the FiF technique. According to the VMAT plan, the PTV 95% dose covered 38.89 ± 0.81 Gy, while it reached 37.26 ± 1.02 Gy by the FiF.

The VMAT technique improved sparing of the surrounding critical structures in the high dose region, however FiF is superior in the low dose region. Beyond 13 Gy, FiF delivered a higher dose, compared to VMAT, for total lung. **Table 2** presents the dosimetric parameter as a point dose and mean to OARs.

Comparing our VMAT plan with the data reported by Kim *et al.*, [7], the mean heart dose obtained for our patient was 3.22 ± 0.65 Gy, while it was 14.5 ± 2.39 Gy in their study. In the QA verification, the gamma parameter (3%, 3 mm) value was 96.5% (tolerance 95%).

Treatment planning for BBC is arduous and, in most cases, the field overlapping cannot be avoided with traditional tangential field arrangements. To minimize damage to the skin, the overlapping areas with large hotspots should be

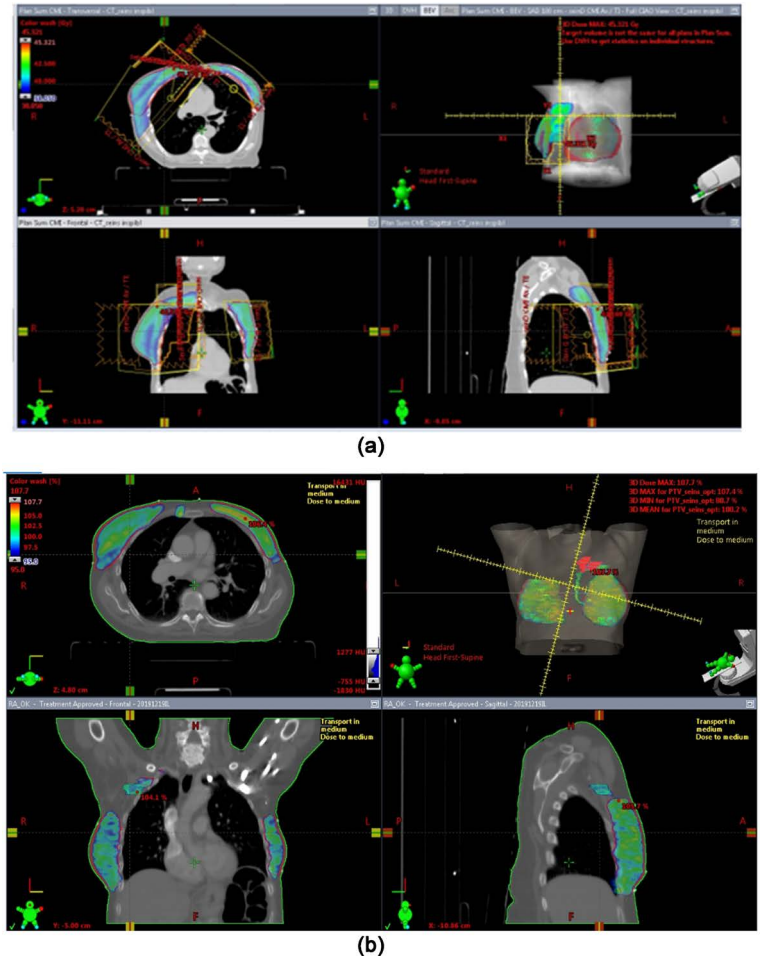

Figure 1. Comparison of isodose distributions seen for left and right breast with IM (internal mammary), SC (supraclavicular region) and AX (axillary lymph) nodes.

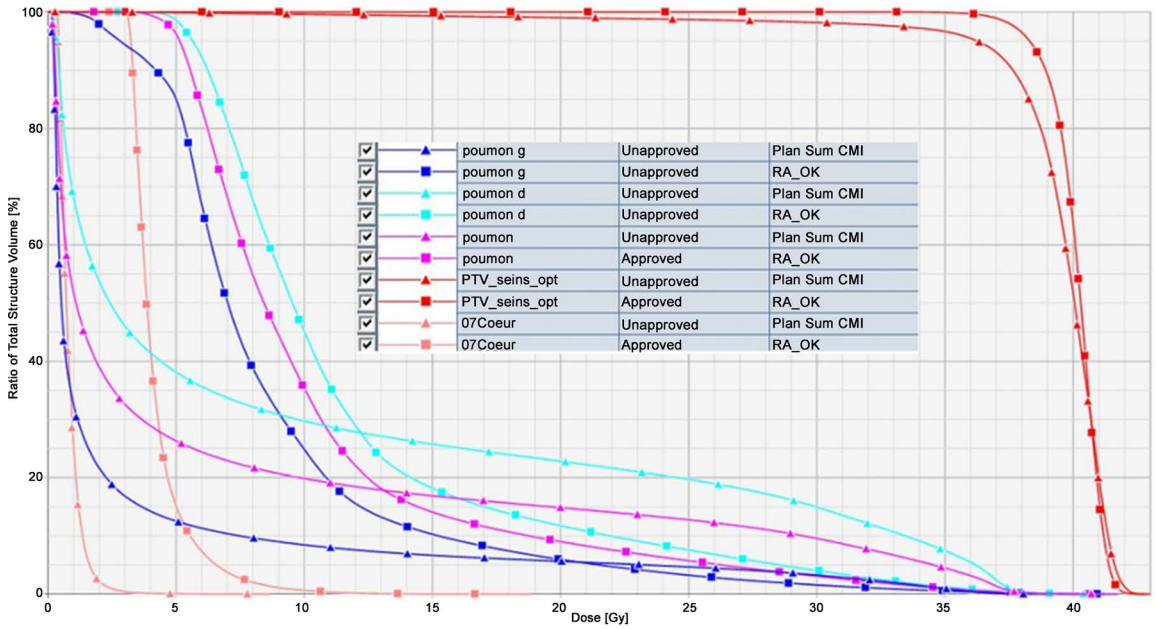

Figure 2. Dose volume histogram for FiF (square line red color) and VMAT (triangle line red color) treatment plans.

Table 1. Dosimetric parameters for PTV for FiF and VMAT. Indicated statistical error uncertainty is standard deviation.

PTV parameter	FiF	VMAT
$V_{95\%}$ Gy	37.26 ± 1.02	38.89 ± 0.81
D_{max} (Gy)	42.64 ± 0.91	42.45 ± 1.75
D_{mean} (Gy)	39.40 ± 0.5	40.14 ± 0.2
CI	1.25 ± 0.8	1.13 ± 0.4
HI	0.26 ± 0.1	0.10 ± 0.07
Total MU	910 ± 120	1546 ± 227

Table 2. Dosimetric parameters for organs-at-risk by FiF and VMAT. Indicated statistical error uncertainty is standard deviation.

OAR		FiF	VMAT
LT Lung	V_{17Gy}	6.21% ± 5.02%	8.18% ± 6.32%
	V_{10Gy}	8.47% ± 4.02%	24.69% ± 3.55%
Rt Lung	V_{17Gy}	24.54% ± 1.18%	15.04% ± 2.21%
	V_{10Gy}	29.71% ± 3.22%	44.98% ± 4.25%
Total Lung	D_{mean} (Gy)	6.64 ± 2.08	10.48 ± 1.95
Heart	D_{mean} (Gy)	0.89 ± 0.55	3.22 ± 0.65

avoided. On the other hand, the PTV area should receive the prescription dose without cold spots to minimize the risk of tumor recurrence.

4. Discussion

The overall VMAT treatment time, including patient positioning, image verification and application of corrections/shifts and beam-on time, was 20 minutes, which is less than that required by the IMRT and FiF techniques. This finding is in agreement with the results of Seppälä [9].

The intrafractional motion during normal breathing was studied for breast cancer patients [10]. Helical Tomotherapy treatment showed increased treatment duration, which may cause intrafractional uncertainties. Ricotti [10] observed that the baseline deviation of the body triggered more noticeable uncertainties, compared to the respiratory motion. In our study, the mean an average beam-on time is 330 seconds.

Fiorentino A. [11] reported the mean total lung dose of 11.8 ± 2.3 Gy with VMAT, while in our plan it was 10.48 Gy. Galecki J. [12] also found the mean dose of 16.6 Gy to total lung with the VMAT technique. Thus, VMAT increases dose homogeneity in the target volume and considerably decreases the treatment delivery time. The drawback of the VMAT treatment of BBC is the increased low radiation dose volume. Although the risk of cancer recurrence among patients treated with radiotherapy is small [13], it cannot be neglected. The low dose volume must be considered when selecting the patients to be treated with VMAT,

bearing in mind the increased possibility of second cancers, especially for patients with younger age. It should also be recognized that, with the introduced VMAT dose delivery technique, the treatment planning complexity is increased, thus escalating the potential for error and thus increasing the importance of the quality assurance processes [14]. Several studies in the literature have compared the radiotherapy techniques biologically. Lee B. [15] calculated the secondary cancer risk of different organs after radiation treatment of breast cancer based on a biological model. The 3D-CRT resulted in lower radiation-induced cancer risk in breast radiation therapy than IMRT, but dose homogeneity of IMRT was better than those of 3D-CRT.

Our study confined 0.64% volume (V25%) of the heart, while with the reported Helical Tomotherapy treatment deliveries the respective volume was 15% [16]. A population-based case control study was conducted to assess the risk of ischemic heart disease for breast cancer women patients after radiotherapy [17]. The cardiac complications are linearly associated with the mean heart dose. Increasing the mean dose with 1 Gy causes an estimated 7.4% rise in the heart disease risk.

5. Conclusion

This study confirmed that the single isocenter VMAT technique is feasible in bilateral breast cancer, achieving good radiation dose homogeneity. The PTV coverage is better by VMAT. Considering the VMAT planning, the main drawback observed in the present analysis was a slight increase in the low dose volume to the lung and the heart. Our report describes the process of planning synchronous BBC radiotherapy with the single isocenter VMAT technique. Overall, the VMAT technique increases the dose coverage and is easy to deliver.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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