

Rapid ARC Radiotherapy in a Patient with Bilateral Breast Carcinoma - 10 Year Follow UP

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ABSTRACT

Introduction: A patient with synchronous bilateral breast cancer was treated with Rapid arc (Volumetric Modulated Arc therapy - VMAT) radiotherapy following breast conservation surgery. She is alive and without radiotherapy complications in the 10 year follow up period.

Case report: A 51 year old lady presented with synchronous bilateral breast cancer. She underwent wide excision of both breast lumps with bilateral axillary lymph node sampling (Invasive Ductal Carcinoma, pT1N1 in left breast and pT2N0 in right breast). She was treated with adjuvant chemotherapy and post-operative radiotherapy to both breasts with rapid arc (VMAT) technique in August 2009. The radiotherapy planning was compared among Three Dimensional Conformal Radiotherapy, Intensity Modulated Radiotherapy and Rapid arc techniques. Details of dose homogeneity and sparing of Organs at risk are discussed. She tolerated the treatment well without major toxicity. She has been on regular follow up till her last visit in June 2019. She was also treated for surgery followed by radiotherapy for Carcinoma of cervix 12 years ago.

Conclusion: This case is presented for the novel radiotherapy technique in treating bilateral breast cancer resulting in good quality of life and long term survival.

Keywords: Synchronous Bilateral Breast Cancer, Rapid Arc Technique, Radiotherapy, 10 Year Follow Up

INTRODUCTION

Breast cancer is the most common cancer in women constituting 24.2% according to GLOBOCAN 2018.¹ Synchronous bilateral breast cancer(BBC) has an incidence of 0.7% to 3.0% in women with primary breast cancer.² Risk factors include familial breast cancer, young age, lobular invasive carcinoma, multicentricity, BRCA 1&2 gene mutations and radiation exposure.³ Bilateral breast cancers are classified depending on the time of occurrence into synchronous (detected simultaneously or within 6 months gap) or metachronous (detected with more than 6 months).⁴ Patients with breast carcinoma are treated with either modified radical mastectomy (MRM) or breast conservative surgery (BCS) followed by breast irradiation in appropriately selected women.

Adjuvant radiotherapy for breast cancer is given postoperatively with medial and lateral tangential fields. Radiotherapy planning and dose delivery are more complex in BBC. The use of tangential fields in the treatment of BBC has numerous drawbacks with significant inhomogeneity in dose distribution, high dose to critical structures especially heart and lack of conformity to planning target volume

(PTV) even after using 'Field in Fields'.⁵ These can lead to acute side effects like skin toxicity and late effects like soft tissue fibrosis, pneumonitis and cardiotoxicity which affect quality of life. Modern techniques of radiation, Rapid arc (VMAT – Volumetric Modulated Arc Therapy) and Intensity Modulated Radiotherapy (IMRT) have been utilized to overcome these drawbacks. We are reporting a case of synchronous BBC treated with Rapid arc radiation technique.

CASE REPORT

A 51 year old lady, school teacher by profession, with comorbidities of hypertension, diabetes, obesity and past history of carcinoma cervix had presented with lump in her right breast in 2009. She had no history of white discharge or bleeding from vagina.

On Physical examination, she was weighing 103kg with a good performance status. Locoregional examination revealed a well defined, mobile lump of 2 x 2cm in the upper outer quadrant of the right breast. Examination of the left breast and both axillae were unremarkable. Her vaginal vault was healthy with no evidence of recurrence of carcinoma cervix. She was treated in December 1997 for carcinoma of the cervix (Moderately differentiated Squamous cell carcinoma) with Wertheim's hysterectomy. She received adjuvant postoperative radiotherapy to pelvis to a dose of 50 Gy in 25 fractions with 4 field technique on cobalt machine followed by 3 applications of Iridium 192 HDR brachytherapy with vaginal cylinder till February 1998.

Investigations

Mammogram on 28.1.2009 revealed two spiculated hypoechoic lesions of size 1.35 x 1.43cm and 1.89 x 1.36cm adjacent to each other in upper medial quadrant of right breast, a lesion of 0.77 x 0.78cm in lower outer quadrant of left breast and small bilateral axillary lymph nodes (figure 1). Whole body PET CT (19.1.2009) showed irregular necrotic

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Parameter	3DCRT	IMRT	VMAT
V _{95%} (%)*	95	96	96
PTV Dmean (cGy)	4840	4658	4503
Dmax (cGy)	9577	5018	4727
CI	1.65	1.99	1.45
HI	0.99	0.13	0.10
Treatment time (minutes)	7	12	3

*V_{95%} - percentage of volume (PTV) receiving 95% of dose
 Dmax - maximum dose received by 1cc volume
 CI is defined as ratio of the volume to 95% of the prescribed dose to the PTV. $CI = V_{95} / PTV$ [6,7]
 PTV = target volume, V₉₅ = volume of the reference isodose (reference isodose = 95%).
 The ideal CI value is 1 (optimal conformal coverage).
 HI is defined as the ratio of the dose difference of 2% and 98% to the PTV to dose to 50%, $HI = D2\% - D98\% / D50\%$ [6]
 D2% = minimum dose to 2% of PTV, D98% = minimum dose to 98% of PTV, D50% = minimum dose to 50% of PTV.
 HI optimal value is zero (ideal dose homogeneity).

Table-1: Comparison of dose-volume parameters and treatment time of 3D CRT, IMRT and VMAT

		3DCRT	IMRT	VMAT
RT lung	V _{40Gy} § (%)	20.1	10.8	4.8
	V _{20Gy} § (%)	29.0	37.8	29.3
	V _{10Gy} § (%)	34.1	60.1	61
	V _{5Gy} § (%)	44.0	100	100
LT lung	V _{40Gy} § (%)	11.9	22.9	6.2
	V _{20Gy} § (%)	41.8	58.4	28.2
	V _{10Gy} § (%)	50.5	87.8	59.9
	V _{5Gy} § (%)	56.8	100	99.76
Total lung	D _{Mean} (cGy)	1629	2227	1683
Heart	D _{Mean} (cGy)	1734	3200	1629
	V _{40Gy} § (%)	10.2	7.04	0.03
	V _{30Gy} § (%)	33	67.8	5.6

§VxGy - Volume irradiated to xGy
 DMean - Mean dose to OAR

Table-2: Comparison of dose-volume parameters to OARs in 3D CRT, IMRT and VMAT

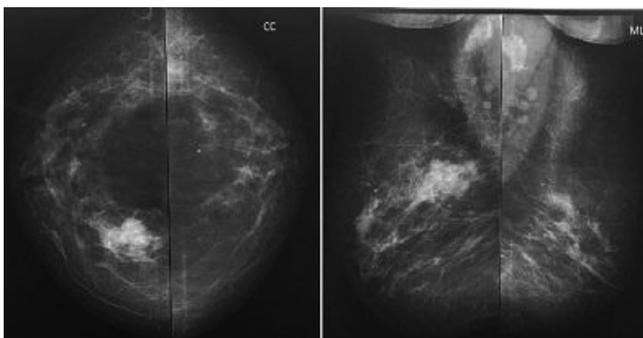


Figure-1: Bilateral Mammogram with Cranio-caudal (CC) and medio-lateral (ML) views showing two spiculated hypoechoic lesions of size 1.35 x 1.43cm and 1.89 x 1.36 cm adjacent to each other in upper medial quadrant of right breast and a lesion of 0.77 x 0.78cms in lower outer quadrant of left breast with bilateral axillary lymph nodes.

mass of 3.5cm (SUV max 9) in upper medial quadrant of right breast and 2.8cm (SUV max-5.6) lesion in lower lateral quadrant of Left breast with an enlarged 2.3cm left inguinal

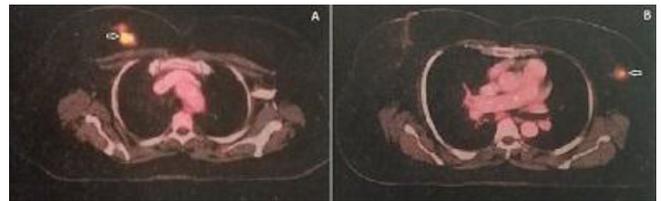


Figure-2: Whole body PET CT. A: Arrow showing irregular necrotic mass of 3.5cm (SUV max 9) in upper medial quadrant of right breast. B: Arrow showing 2.8cm (SUV max-5.6) lesion in lower lateral quadrant of Left breast.

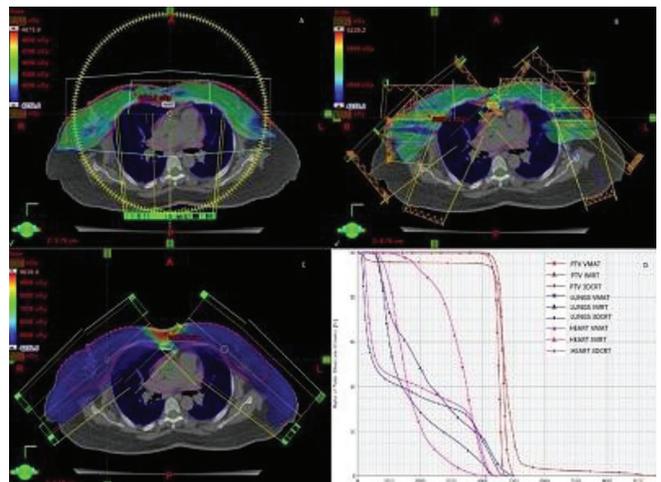


Figure-3: Comparison of 3 radiotherapy plans. A: VMAT (Rapid arc) with best dose conformity. B: IMRT with multiple beams. C: 3D CRT technique with hot spot in the middle of the front of chest. PTV is red line, 95% isodose wash in blue color. D: Dose Volume Histograms depicting dose distribution with all three techniques. Red- Combined PTV, Pink-Heart, Royal Blue-Total lung.



Figure-4: Dose distribution in 3D CRT Plan showing intense hotspot in the middle of the front of chest due to overlapping of tangential fields. A: Axial B: Coronal C: Sagittal and D: Beams eye view.

lymph node (figure 2).

Treatment

She underwent wide local excision of lumps in both breasts with bilateral axillary lymph node sampling in January 2009. Her left inguinal lymph node was also excised and sent for frozen section which was negative for malignancy.

HPE of the left breast specimen showed 1.3x1x1 cm Invasive ductal carcinoma, grade III with lymphovascular invasion (LVI), negative margins and 2 of 4 lymph nodes (LN) with metastatic deposits - pT1c N1. The right breast specimen showed 2.8x2x2cm Invasive ductal carcinoma grade III with LVI, negative margins and foci of intermediate to high grade ductal carcinoma in situ. None of the 5 dissected LN showed metastatic deposits - pT2N0. Immunohistochemistry of both tumours was negative for Estrogen receptor(ER), Progesterone receptor(PR) and HER 2 Neu (Triple negative). She received adjuvant chemotherapy with 4 cycles with Adriamycin and Cyclophosphamide followed by 4 cycles of Paclitaxel. In view of BCS, she was advised adjuvant radiotherapy to both the breasts. 3 radiotherapy plans were generated with 3 Dimensional Conformal Radiotherapy (3D CRT), Intensity Modulated Radiotherapy (IMRT) and Rapid Arc (VMAT) techniques (figure 3).

Radiotherapy

Patient was immobilised with thermoplastic mask, Vac-loc and breast board in supine position with both hands raised above the head. CT data was acquired from mandible to 5th lumbar vertebra with slice thickness of 5mm. These CT images were then transferred online to the Treatment Planning System (TPS). Planning Target volume (PTV) was contoured according to RTOG breast contouring guidelines. Organs at risk including heart, lungs and spinal cord were delineated. 3 plans were generated with 3 techniques i.e. 3D CRT, single isocentre IMRT and single isocentre Rapid Arc (VMAT). After comparison of the 3 plans and weighing pros and cons for each plan, it was decided to treat her according to plan generated in RapidArc technique.

She was treated from 20.8.2009 to 9.10.2009 using Clinac CD 2100 linear accelerator with three arcs to a total dose of 4500cGy in 25 fractions to both breasts and left supraclavicular area (as 2 of the 4 axillary LN were positive) at 180cGy/fraction (single fraction per day, 5 fractions in a week) with 6MV photons. She received radiation boost to the tumor bed areas in both breasts with 9 MeV electrons to a dose of 1400cGy to the right and 1200cGy to the left at 200cGy/fraction (single fraction a day, 5 fractions in a week). Treatment verification was done with daily KV X ray and once weekly cone beam CT imaging.

Outcome and follow up

She tolerated treatment well except for Grade I skin reaction in the entire irradiated area and Grade III skin reaction in the inframammary fold of left breast. Later she was on regular follow up.

She developed a recurrence in her right breast, inferior and medial to postoperative scar for which she underwent right mastectomy on 19.05.2011. HPE showed 1.7x 1.5x1.5cm Triple negative Invasive ductal carcinoma with negative resected margins. She refused further chemotherapy and was also not willing for BRCA testing.

Her Mammogram on 16.11.2018 showed no evidence of disease and PET- CT scan on the same day did not detect any metabolically active disease but showed mild sub pleural

fibrotic changes in right lung. Her 2D Echocardiogram showed left ventricular ejection fraction of 54% (pre-treatment value 60%). All of which suggest acceptable long term side effects. Till date in June 2019, there is no dyspnoea or lymphedema in either of her arms, no clinical evidence of disease and good cosmesis of left breast. Thus the primary aim of radiation therapy of cure with good disease control and good quality of life is achieved.

DISCUSSION

The reasons to consider VMAT plan as acceptable and superior to the IMRT and 3D CRT plan are many.

PTV coverage (95% isodose line was chosen as reference)- Table 1 shows that VMAT plan has better PTV coverage with good conformity index(CI) of 1.45 and homogeneity index(HI) of 0.10 when compared to IMRT and 3D CRT techniques.⁶⁻⁷ PTV 95% dose in Rapid Arc was covering 96.1% volume. It is comparable to results of Kim et al, Jan Seppala et al and Fiorentino et al.^{5,8,9}

While VMAT plan showed a hotspot of 107.8% to a volume of 1 cc and IMRT showed a hot spot of 110% to a volume of 12.8cc, the 3D CRT plan had a hot spot of 214 % to a volume of 47.9cc in the middle of front of the chest which was unacceptable (figure 4). This was caused mainly by the overlapping of the two tangential fields.

Organs at risk namely, lung and heart received less dose in VMAT plan compared to IMRT and 3D CRT except for lung V5Gy (Table 2).

Comparing our VMAT plan with Kim et al study, mean heart dose in our patient was 16.29Gy while it was 14.5±2.39Gy in their study. Similarly heart dose of V25Gy in our plan was 11.6% vs 11.7±5.35% in theirs.⁵

Mean total lung dose of 11.8±2.3Gy was reported with VMAT in Fiorentino series while in our plan it was 16.8 Gy.⁹ Kim et al reported in their series right lung V20Gy of about 36.67±4.42% and V5Gy of 86.34 ± 6.93%. Their left lung V20Gy was 27.79 ± 6.28% and V5Gy was 84.85 ± 6.74%.⁵ Our values for right lung V20Gy and V5Gy are 29.3% and 100% and left lung V20Gy and V5Gy are 28.2% and 99.6%. But Jan Seppala had better lung V5Gy of 43% and heart mean dose of 6.6Gy.⁸

The overall treatment time including patient positioning, image verification and 'beam on time' was compared. Our patient was treated with VMAT comprising 3 arcs each delivering 275 to 290 MU at 200 MU per second with 'beam on' time of 3 minutes. On the contrary, IMRT had 12 beams with each beam delivering 120MU to 290MU with 'beam on' time of approximately 12 minutes. In addition, patient positioning, treatment verification and application of corrections/ shifts will make the total treatment time for IMRT about 30 minutes as compared to 15 minutes in VMAT technique. Maintaining the treatment position for such a long time for 25 sittings would be very difficult for the patient. Kim et al and Jan Seppala et al had also reported reduction in treatment time with VMAT.^{5,8}

Thus VMAT helped in reduction of doses to heart and lung, increased dose homogeneity in the target volume and also

considerably decreased treatment delivery time.

The disadvantage of VMAT planning is slightly increased low radiation dose spillage volume. Theoretically this may have a small increased risk of second malignancy.^{8,10} Though our patient is at higher risk for the developing second malignancy with her past history of cervical cancer and bilateral breast cancer, her follow up period of 10 years is uneventful.

CONCLUSION

This case is reported to highlight that the novel radiotherapy technique of Rapid Arc (VMAT) radiotherapy is feasible in bilateral breast cancer with good radiation dose homogeneity and shorter treatment time resulting in better patient compliance and good quality of life. This is also to show that there is no long term toxicity in the follow up duration of 10 years with Rapid arc radiotherapy in this patient with bilateral breast cancer.

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