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Research Article

PROSPECTIVE STUDY TO COMPARE THE DOSE DISTRIBUTION AND ACUTE TOXICITY OF THREE-DIMENTIONAL CONFORMAL RADIATION THERAPY WITH INTENSITY-MODULATED RADIATION THERAPY FOR POST-MASTECTOMY RADIOTHERAPY IN CARCINOMA BREAST

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Abstract

Introduction: Adjuvant radiotherapy (RT) substantially reduces recurrence rates of breast cancer (BC), and improves overall survival. However, RT-induced toxicities have been noted, including skin, lung and heart toxicity. Radiation dermatitis is the common clinical problem for BC patients receiving adjuvant RT.

Materials and Methods: It was a double arm, single institutional, prospective, comparative study among post-modified radical mastectomy female patients of locally advanced carcinoma breast aged between 20-70 years having adequate hepatic, renal, haematological parameters and an ECOG score of 0-2. Patients with bilateral, recurrent or metastatic breast carcinoma, previous history of any other malignancy or radiotherapy were excluded. This study was done at radiation oncology department of Great Eastern Medical School and Hospital, Srikakulam, AP during the study period from May 2022 to April 2023.

Results: Baseline characteristics of patients like age, residence, education level, side of the disease, tumour (T) stage, nodal (N) stage at presentation and performance status were comparable between both the arms of the study. The mean of D2 value of IMRT and 3DCRT were 52.92 Gy and 54.45 Gy respectively. IMRT has statistically significant lower value than arm B (p value <0.0001). The mean of D98 value of IMRT and 3DCRT were 45.46±1.85 Gy and 41.50±3.08 Gy respectively. IMRT has statistically significant higher value than arm B (p value <0.0001). The mean value of Dmean for IMRT and 3DCRT were not significantly different (50.17 Gy vs 50.29 Gy, p value 0.32).

Conclusion: To conclude, it can be said that in case of post mastectomy chest wall irradiation IMRT has better planning target

volume coverage than 3DCRT with more homogenous and conformal plans. To spare the organs at risk, IMRT is more efficient than 3DCRT in high dose volume. But, further studies with large sample size and longer duration of follow up is necessary for defining an ideal radiotherapy technique with special emphasis on long term disease control and treatment related late toxicities.

Key words: Adjuvant radiotherapy, breast cancer, IMRT, 3DCRT.

INTRODUCTION

Adjuvant radiotherapy (RT) substantially reduces recurrence rates of breast cancer (BC), and improves overall survival. However, RT-induced toxicities have been noted, including skin, lung and heart toxicity. Radiation dermatitis is the common clinical problem for BC patients receiving adjuvant RT. [1]

Various RT techniques, such as intensity-modulated RT (IMRT), have been developed to improve dose conformity within the irradiated compared to conventional RT. IMRT delivers a more homogenous dose and may result in a lower rate of moist desquamation than conventional RT technique. We previously reported that an incidence of 23% for moist desquamation induced by three-dimensional conformal radiotherapy (3D-CRT) and the volume of hotspots was a predictor for the risk of moist desquamation.[2]

Patients with locally advanced breast cancer (LABC) require multidisciplinary team approach, that incorporates surgery, chemotherapy, radiation therapy, biologic and hormonal therapies, in varying combination. Large prospective trials and a meta-analysis have shown that adjuvant chest wall radiotherapy improves local control and survival in node positive breast cancer patients. Chest wall irradiation is commonly done with tangential beams which include part of the anterior thoracic cavity, thereby potentially affecting the lung and heart and leading to higher risk of cardiac morbidity. This becomes even more complicated as most of the chemotherapeutic agents used to treat breast cancer like anthracyclines, trastuzumab, possess cardiotoxic potential.[3]

Intensity Modulated Radiation Therapy (IMRT) has proved to be superior than 3-Dimensional Conformal Radiation Therapy (3DCRT) in various sites like head and neck, central nervous system, lung, prostate to prescribe maximum dose to the target with minimum dose to critical organs at risk.[4] IMRT directs radiation at the breast tumour and modulates the intensity of the radiation beams with better accuracy, helping to spare healthy tissue surrounding the breast tumour. But on the other hand, IMRT increases integral dose to normal healthy tissues, increasing concern about second malignancy in long term survivors. our study was carried out to compare the dosimetry and acute toxicity profile of 3DCRT and IMRT in post-mastectomy patients.[5]

MATERIAL AND METHODS

It was a double arm, single institutional, prospective, comparative study among post-modified radical mastectomy female patients of locally advanced carcinoma breast aged

between 20-70 years having adequate hepatic, renal, haematological parameters and an ECOG score of 0-2. Patients with bilateral, recurrent or metastatic breast carcinoma, previous history of any other malignancy or radiotherapy were excluded. This study was done at radiation oncology department of Great Eastern Medical School and Hospital, Srikakulam, AP during the study period from May 2022 to April 2023.

Patients were randomized into two groups-

Arm A (Study arm): Received radiotherapy with IMRT technique at a dose of 50 Gy in 25 fractions, 2 Gy/fraction, 5 days per week for total 5 weeks.

Arm B (Control arm): Received radiotherapy with 3DCRT technique at a dose of 50 Gy in 25 fractions, 2Gy/fraction, 5 days per week for total 5 weeks.

Radiotherapy technique

Patient positioning: Supine position on breast board (10º - 30º) to get longitudinal axis of sternum parallel to the radiation couch. Arms are in the abducted and externally rotated position above their head with holding the hand grips. Neck is extended on a suitable head-rest.

Immobilisation: After proper positioning of the patient, a 1cm wax bolus is kept over the chest wall followed by a thermoplastic mask customised to individual patient's chest wall.

Simulation- A non-contrast CT simulation was done with proper positioning. Radio-opaque wires used to mark the mastectomy scar and the clinical boundaries.

Contouring and planning: Delineation of target volumes and organ at risk (OAR) was done on the basis of planning CT scan as per contouring guideline. Clinical

Target Volume (CTV) included ipsilateral chest wall and supraclavicular and axillary lymph nodes as clinically indicated.

PTV was created adding5mm margin to CTV. Lung, heart, spinal cord, thyroid gland, esophagus and contralateral breast were contoured as organs at risk.

IMRT planning was done by five to seven non-coplanar beams to adequately cover the planning target volume (PTV), while minimizing the dose to ipsilateral lung, heart, contralateral breast.

3DCRT planning was done by two tangential semi-opposed beams (to avoid divergence), physical wedges (usually 15° or 30°) and multi-leaf collimator. The beam angles, wedge angles, and beam weighting (usually minimal) were chosen to optimize coverage of the PTV, while minimizing exposure to OARs.

Treatment delivery: Treatment plans were generated using Eclipse treatment planning system. Treatment was delivered using TRUE BEAM machine (VARIAN, Version 15.6) with 10MV energy beam.

Dosimetric evaluation: Data collection included the volume of PTV receiving greater than 95% to 107% of prescribed dose (V95 and V107); the dose delivered to 98% (Dnear-min, D98) and 2% (Dnear-max, D2) of the volume of PTV; and mean dose of the PTV (Dmean) from the dose-volume histogram (DVH).

Dose homogeneity index (HI) and Conformity Index (CI) were calculated according to definition proposed by the

International Commission on Radiation Units and Measurements (ICRU) Report 83.

Evaluation of organ at-risk

Lung: Percentage volume of ipsilateral lung receiving 5Gy (V5), 20 Gy (V20), and the mean lung dose (Dmean) was calculated.

Data was analysed and compared according to appropriate statistical tests using SPSS V.24 software and Microsoft word-excel and GraphPad prism. Significance of dose distribution was statistically evaluated using non-parametric statistical methods. Any p value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of patients like age, residence, education level, side of the disease, tumour (T) stage, nodal (N) stage at presentation and performance status were comparable between both the arms of the study. The mean of D2 value of IMRT and 3DCRT were 52.92 Gy and 54.45 Gy respectively. IMRT has statistically significant lower value than arm B (p value <0.0001). The mean of D98 value of IMRT and 3DCRT were 45.46±1.85 Gy and 41.50±3.08 Gy respectively. IMRT has statistically significant higher value than arm B (p value <0.0001). The mean value of Dmean for IMRT and 3DCRT were not significantly different (50.17 Gy vs 50.29 Gy, p value 0.32).

Characteristics		Arm of the study		P value
		Study arm (n=50)	Control arm (n=50)	
Mean age of patients (In years)		48.09	45.8	0.014
Residence	Urban	14	22	0.24
	Rural	36	28	
Tumour (T) stage	T2	2	4	0.46
	T3	26	32	
	T4	22	14	
Nodal stage	N1	28	28	1.0
	N2	22	22	
Laterality of disease	Right	36	26	0.15
	Left	14	24	
Performance status (ECOG score)	0	16	18	0.59
	1	32	32	
	2	2	0	

Table 1: Distribution of baseline characteristics between two study arms.

Category	Parameter	IMRT (N = 50)	3DCRT (N = 50)	P value
D2	Mean ± SD	52.92 ± 1.13	54.45 ± 0.89	0.0001
	Min-Max	51.1 – 56.4	52.8 – 57.8	
	Median	52.9	54.5	
D98	Mean ± SD	45.46 ± 1.85	41.50 ± 3.08	0.001
	Min-Max	40.75 – 49.54	28.9 – 45.89	

	Median	45.9	42	
D mean	Mean ± SD	50.17 ± 0.67	50.29 ± 0.71	0.32
	Min-Max	49.14 – 51.9	49.7 – 53	
	Median	50	50	

Table 2: Planning target volume (PTV) parameters (D2, D98, Dmean).

Category	Parameter	IMRT (N = 50)	3DCRT (N = 50)	P value
V95	Mean ± SD	92.78 ± 3.36	85.02 ± 4.53	0.0001
	Min-Max	86.54 – 99.97	73.04 – 95	
	Median	93.1	85.9	
V107	Mean ± SD	2.33 ± 2.89	10.26 ± 7.35	0.0001
	Min-Max	0 – 9.33	0.35 – 38.69	
	Median	0.79	10.38	

Table 3: PTV parameters (V95, V107).

Category	Parameter	IMRT (N = 50)	3DCRT (N = 50)	P value
HI	Mean ± SD	0.14 ± 0.04	0.26 ± 0.06	0.0001
	Min-Max	0.06 – 0.24	0.20 - 0.51	
	Median	0.14	0.24	

Table 4: PTV parameters –HI

Category	Parameter	IMRT (N = 50)	3DCRT (N = 50)	P value
CI	Mean ± SD	0.94 ± 0.19	0.74 ± 0.24	0.0038
	Min-Max	0.65 – 1.53	0.32 – 1.17	
	Median	0.9	0.72	

Table 5: Comparison of ci between IMRT and 3DCRT.

DISCUSSION

Several studies demonstrated dosimetric benefit of IMRT compared to 3DCRT for whole breast radiotherapy in early breast cancer patients but for post mastectomy chest wall irradiation, such data is scarce. Fiorentino et al. compared 3DCRT and 4-fields IMRT treatment plans, in term of target dose coverage, integral dose and dose to OARs in early breast cancer and concluded 4-fields IMRT technique significantly reduced the dose to OARs and normal tissue, with a better target coverage compared to 3DCRT. We conducted this study to compare these two techniques in post-mastectomy radiation therapy (PMRT).[6,7]

Comparing the dose distribution parameters of the PTV, near-maximum dose (D2) and near-minimum dose (D98) were better in IMRT than 3DCRT and they were statistically significant with p value of <0.0001. The volume of PTV receiving 95% (V95) and 107% (V107) were also significantly better in IMRT than 3DCRT (p value of <0.0001). But, mean dose (Dmean) was comparable in both the techniques (p value 0.32).[8]

We observed significantly better homogeneity index in IMRT with mean value of 0.14 than 3DCRT with mean value

of 0.26 (p value <0.0001). Similar result has reported by Beckham et al. with p value of <0.05. But no significant difference is noted by Moorthy et al.Rudat et al. and Li et al.[9]

Conformity index is also significantly better in IMRT with mean value of 0.94 compared to 0.74 in 3DCRT (p value 0.003) reflecting more conformal dose distribution in IMRT. Similar result is reported by Beckham et al.,Moorthy et al., and Rudat et al.[10]

CONCLUSION

To conclude, it can be said that in case of post mastectomy chest wall irradiation IMRT has better planning target volume coverage than 3DCRT with more homogenous and conformal plans. To spare the organs at risk, IMRT is more efficient than 3DCRT in high dose volume. But, further studies with large sample size and longer duration of follow up is necessary for defining an ideal radiotherapy technique with special emphasis on long term disease control and treatment related late toxicities.

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