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ORIGINAL RESEARCH

Dosimetric Evaluation In Post Operative Carcinoma Breast patients Between Volume Modulated Arc Therapy, Intensity Modulated Radiation Therapy And Conventional Radiotherapy

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Abstract

Introduction: Breast cancer patients have a significant risk of loco-regional recurrence after surgery and hence adjuvant radiation is indicated. Radiation therapy to the chest wall/breast and regional lymphatics is technically challenging. Various different techniques are available for treatment of chest wall / breast with radiation namely: Conventional, MRT and VMAT.

Aim: This study aimed to compare dosimetric evaluation of doses to target volumes by conventional, IMRT and VMAT techniques for post operative radiation the rapy in breast cancer.

Material and method: This prospective, comparative study of patients was conducted in Department of Radiation Oncologyat Max Hospital Saket, New Delhi for post operative radiotherapy after post Modified Radical Mastectomy (MRM) or Breast Conservation Surgery(BCS) included 25 patients in each group.

Result: Comparing the doses to the same CTV volumes, CTV D95% was comparable in IMRT and VMAT plans being 48.74±0.61Gy and 48.66±0.85Gy respectively and was less in conventional planning (45.96±1.27Gy). The coverage of IMRT and VMAT were better and statistically significant when compared with conventional plan

Conclusion: VMAT technique is superior to the IMRT and conventional techniques due to its better chest wall/breast, axilla and SCF coverage. However, further studies are needed to authenticate the dosimetric findings of our study.

Introduction

The incidence of breast cancer has steadily increased in India over the years and as many as 100,000 new patients are being detected every year [(1)].According to the Indian Council of Medical Research (ICMR) Cancer Registry, Cancer of breast with estimated 1.5 lakh (over 10 per cent of all cancers) new cases during 2016, is the number one cancer overall. [(2)] In India, breast cancer is usually seen in stages III and IV. Stage III B is the commonest (35.2%) and lymph node positivity has been observed in 80.2% of patients[(3)]. In Delhi, the incidence of breast canceris 21.3% and age adjusted rate (AAR) is28%[(3)]. Due to the high incidence and morbidity rates of breast cancer, great strides have been made in the early detection and the treatment of breast cancer. Various treatment modalities are available for carcinoma breast:

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surgery, radiotherapy, chemotherapy, hormonal therapy and targeted therapy. The treatment of choice for most of the patients is surgery: Modified radical mastectomy or BCS, followed by adjuvant chemotherapy, external beam radiotherapy and hormonal therapy.[4] This of course is dependent on the stage of presentation and the key prognostic indicators like tumor size, margin status, nodal positivity, LVI, PNI and hormonal status etc.[5] Radiation therapy offers an improvement in overall survival and has been reported to reduce the 15year isolated loco-regional recurrence rate from29% to8%in node positive subjects witha5% reduction in mortality rate.[6]Radiation therapy after breast-conserving surgery substantially reduces the risk of cancer recurring in the breast and moderately reduces the risk of death from the disease, according to updated results from a meta-analysis by the Early Breast Cancer Trialists' Collaborative Group.[7]Radiation therapy offers an improvement in overall survival and has been reported to reduce the 15year isolated loco-regional recurrence ate from29% to8%in node positive subjects witha5% reduction in mortality rate.[6]

Post mastectomy radiation therapy includes treatment to the chest wall and patients who undergo breast-conserving surgery receive whole-breast irradiation. Radiation to draining lymphatics in the axilla, internal mammary and supraclavicular fossa depends onn umber of nodes positive and nodal level positive for disease. Patients undergoing BCS also receive electron/photon boost/interstitial brachy therapy to the lumpectomy cavity.

There are two categories of complications that occur after radiation treatments, acuteand late effects. Acute effects occur around till 3 months after the radiation treatments. Common acute effects that occur after loco-regional radiation include skin irritation, erythema, hyper pigmentation, desquamation of skin, sore throat andf atigue. [8]

Breast cancer spreads loco-regionally through lymphatics. Irradiation of nodal areas is still a complex challenge in external radiotherapy for breast cancer. Acceptable target coverage is always desired but at the same time protection of organs at risk is to be taken careof.Uniquetechnicalproblemsareposedinconventionalmethodsofirradiationtothedifferentregionallymphnodedrainageareas,namelysupraclavicularnodes,internal mammary nodes and axillary nodes, as they are present at different sites at varying depth. For example, supra clavicular nodes usually lies at mean depth of 3.9cm, axillary nodes at 4cmdepth, internal mammary nodes at 5-6 cm depth [9]. Developments have been mainly driven by the need to reduce the dose to normal tissue structures and there by minimize the risk of toxicity and morbidity. Various new treatment techniques like 3DCRT, IMRT, IGRT, VMAT have beendevelopedtoachievedosedistributionsthatcanprovidehighdegreesoftargetdoseconformityand homogeneity.

This study had been proposed to carry systematic comparative dosimetric evaluation of doses to target volumes by conventional, IMRT and VMAT techniques for post operative radiation therapy in breast cancer.

Materials and methods

This prospective, comparative study of patients was conducted in Department of Radiation Oncologyat Max Hospital Saket, New Delhi for postoperative radiotherapy after post Modified Radical Mastectomy (MRM) or Breast Conservation Surgery (BCS) included 25 patients in each group. This study included Female Patients between 18-80Years with histopathologically confirmed cases carcinoma breast. All patients had Stage I-III (TNMstaging-AJCC7th edition) and had no other malignancy in the rest of the body. Patients treated by radiation as palliativeintent, any Recurrent disease, Re-irradiation, any other Metastaticdisease were excluded from the study.

All patients underwent detailed history and physical examination, post surgery health of the scar, complete blood counts and biochemistry, biopsy, histopathology, Mammogram ,Chest

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X-ray PA view, Ultrasound abdomen, ECG,ECHO,Bonescan (ifindicated),PET Scan(if indicated).

Target contouring and Treatment Planning

The CT data sets were transferred to Eclipse treatment planning system (Version 10.0 of Varian Medica Systes, Palo, Alto, CA). The clinical target volumes (CTV) and the critical structures were contoured by the Radiation Oncologists. All the contours of CTV, Supra clavicular, axilla and Internal Mammary chain were done as per RTOG consensus guidelines for Breast Cancer. The Planning Target Volume (PTV) was a combination of the chest wall expanded by 5mm in all direction but zero towards skin. Bolus of 0.5 cm was used for half of the treatment to ensure adequate dose to the skin. Same targets and OAR's were planned by conventional, IMRT, VMAT methods.

Plan Evaluation

Each Plan was evaluated individually and compared the coverage of D95%, Dmean, D2% and D5% of prescription dose, V95%,V107%,V110%andVprescription were used as parameters to judge the hot spot and dose heterogeneity for CTV,PTV and nodal volumes.
Data was collected as detailed history and physical examination, post surgery health of the scar, complete blood counts and biochemistry, biopsy, histopathology, Radiological examination, Type of plan, Dose to target volumes and surrounding critical structures.

Statistical Analysis

Statistical analysis was performed to compare doses of conventional therapy, IMRT and VMAT by using Analysis of Variance (ANOVA) for comparison of means between all the parameter of the 3 treatment techniques. All statistical analysis were done usingSPSS 16 software.

Table1: Comparison of clinical target volume (CTV) for chest wall (CW)/ breast

Volumes of the targets												
										PVALUE		
	CONVENTIONAL			IMRT			VMAT			ConvVsIMRT	ConvVsVMAT	IMRT VsVMAT
	N	Mean	Std. Deviation	N	Mean	Std. Deviation	N	Mean	Std. Deviation			
CTV(CW/BREAST)_D95%Gy	25	45.962	1.266	25	48.748	0.610	25	48.668	0.853	0.000	0.000	0.449
CTV(CW/BREAST)_D2%Gy	25	55.254	1.399	25	55.434	0.938	25	53.785	0.419	0.604	0.000	0.000
CTV(CW/BREAST)_D5%Gy	25	54.241	1.110	25	54.650	0.838	25	53.316	0.355	0.155	0.000	0.000
CTV(CW/BREAST)_V95%	25	83.574	17.628	25	97.996	1.604	25	97.609	1.825	0.000	0.000	0.250
CTV(CW/BREAST)_V107%	25	11.557	10.809	25	15.475	8.635	25	3.848	2.398	0.157	0.001	0.000

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CTV(CW/BREAST)_V110%	25	4.068	6.352	25	4.329	4.002	25	0.156	0.274	0.863	0.005	0.000
CTV(CW/BREAST)_VPdosecc(50 Gy)	25	612.298	537.859	25	703.457	215.94		721.113	230.783	0.417	0.339	0.096

Comparing the doses to the same CTV volumes, CTV D95% was comparable in IMRT and VMAT plans being 48.74±0.61Gy and 48.66±0.85Gy respectively and was less in conventional planning (45.96±1.27Gy). The coverage of IMRT and VMAT were better and statistically significant when compared with conventional plan.

D2% was found to be less in VMAT plans (53.7±0.42Gy) as compared to the same in IMRT (55.43±0.94Gy) or conventional plans(55.24±1.4Gy) . Hence VMAT plans were less found to be better than IMRT and conventional plans and the results were statistically significant.

D5% was compared among the three plans. It was 54.24±1.11Gy for conventional plan, 54.47±0.84Gy for IMRT plans, 53.31±0.36Gy for VMAT. VMAT was better and statistically significant when compared with both conventional and IMRTplans.

V95% which defined the volume(in %) receiving 95%(47.5Gy) of the dose was foundto be 83.57±17.63% with conventional planning, 97.99±1.6% in IMRT and 97.7±1.83% inVMAT. IMRT was better than VMAT and conventional. The result was statistically significant when IMRT or VMAT plans were compared with conventional plans but IMRT and VMAT plans were found to be comparable.

V107% was 11.55±10.81% in conventional plan, 15.4±8.64% in IMRT plan and3.85±2.4% in VMAT .As expected the volume receiving 107% (53.5Gy) of total dose was least in VMAT plans and maximum in IMRT. The result was found to be statistically significant with VMAT better than both conventional and IMRT.

V110% followed the same pattern and was statically significant better for VMAT plans as compared to conventional (p=0.005) and IMRT (0.0002). However conventional and IMRT plans were found to be comparable.

Volume receiving prescription dose which was 50 Gy was least in conventional 612.29cc whereas it was 703.4cc in IMRT and 721.11cc in VMAT plans.The results were not statistically significant.

Table2: Comparison of planning target volume (PTV) for chest wall (CW)/breast

	CONVENTIONAL			**IMRT**			**VMAT**			**Conv VsIMRT**	**ConvVsVMAT**	**IMRT VsVMAT**
	N	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**			
PTV(CW/BREAST)_D95%	25	45.238	1.282	25	46.806	1.224	25	47.180	0.846	0.000	0.050	0.050
PTV(CW/BREAST)_D2%	25	55.452	1.616	25	55.292	0.880	25	53.788	0.382	0.000	0.043	0.000
PTV(CW/BREAST)_D5%	25	54.268	1.095	25	54.484	0.778	25	53.280	0.323	0.000	0.044	0.442
PTV(CW/BREAST)_V95%	25	83.486	9.072	25	93.208	3.107	25	93.942	2.583	0.000	0.000	0.143

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PTV(CW/BREAST)_V107%	25	10.822	8.857	25	12.878	6.744	25	3.643	2.010	0.350	0.000	0.000
PTV(CW/BREAST)_V110%	25	3.833	4.871	25	3.513	3.101	25	0.156	0.290	0.789	0.001	0.000
PTV(CW/BREAST)_V Pdosecc (50 Gy)	25	707.513	189.33	25	821.18	230.68	25	855.560	223.40	0.000	0.000	0.000

D95% coverage of PTV was better in VMAT as compared to IMRT and conventional plans and was statistically significant. Even when IMRT plans were compared with conventional plans the PTVD 95% was seen to be significantly better for IMRT.

D2% was 55.4±1.61Gy in conventional plan, 55.29±0.90Gy in IMRT and 53.78±0.38Gy in VMAT plans. The result was statistically significant with VMAT better than IMRT and conventional plans. D5% or dose received by 5% volume was least for VMAT (53.28±0.32Gy) as compared to IMRT (54.48±0.78Gy) and conventional (54.27±1.1Gy). But did not show any statistical significance when VMAT was compared with IMRT.

PTVV 95% is the % of volume receiving 95% of prescribed dose (47.5Gy). It was 83.4±9.1% in conventional plan, 93.2±3.1% in IMRT and 93.9±2.6% in VMAT plans. The difference was not significant between IMRT and VMAT planning, but IMRT and VMAT were better than conventional and the difference was statistically significant. V107% and V110% were comparatively better for VMAT plans as compared to IMRT and conventional plans and the difference was statistically significant.

Volume getting the prescription dose (50Gy) was 707.5cc in conventional plan, 821.18cc in IMRT and 855.5 cc in VMAT. Thus, VMAT was better than IMRT and Conventional plans as volume which received the prescribed dose was significantly higher for VMAT. When IMRT was compared with conventional it was also significantly better for IMRT as compared to conventional plans.

Table3: Comparison of clinical target volume (CTV) for SCF+AXILLA

	Conventional			**IMRT**			**VMAT**			**PV ALUE**	**ConvVs IMRT**	**ConvVs VMAT**	**IMRT VsVMAT**
	N	**Mean**	**Std. Deviation**	**N**	**Mean**	**Std. Deviation**	**N**	**Mean**	**Std. Deviation**				
CTV(SCF+AXILLA)_D95%	23	45.675	1.915	23	48.507	0.574	23	49.070	0.360	0.324	0.000	0.000	0.001
CTV(SCF+AXILLA)_D2%	23	56.883	3.087	23	52.951	1.092	23	53.093	0.427	0.000	0.000	0.000	0.568
CTV(SCF+AXILLA)_D5%	23	56.339	2.945	23	52.367	0.849	23	52.624	0.479	0.000	0.000	0.000	0.233
CTV(SCF+AXILLA)_V95%	23	82.555	11.998	23	97.518	1.392	23	96.258	10.675	0.000	0.000	0.000	0.558
CTV(SCF+AXILLA)_V107%	23	28.691	21.423	23	1.680	3.518	23	1.193	1.238	0.000	0.000	0.000	0.531
CTV(SCF+AXI	23	17.0	19.74	2	0.4	1.455	2	0.00	0.023	0.000	0.001	0.000	0.192

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LLA)_V110%		24	3	3	13		3	5					
CTV(SCF+AXILLA)_VPdosecc	23	102.380	32.34	23	103.42	30.882	23	106.357	38.244	0.442	0.487	0.874	0.000

VP dose: Prescription dose (50Gy) SCF: Supraclavicular Fossa

D95% or dose received by 95% of the volume was found to be 45.67±1.9Gy in conventional plan, 48.5±0.57Gy in IMRT and 49.07±0.36Gy in VMAT plans. VMAT was better than IMRT and conventional plan and the results were significant. The IMRT plans when compared with conventional plans were also found to be significantly better.

D2% was 56.8±3.1Gy in conventional planning technique, 52.9±1.1Gy in IMRT and53.09±0.43Gy for VMAT. IMRT and VMAT were better than conventional plan and the difference was statistically significant. Although IMRT and VMAT were comparable.

D5% was 56.34±2.9Gy in conventional planning, 52.36±0.84Gy in IMRT and 52.6±0.48Gy in VMAT plans. Dose received by 5% of total CTV (axilla + SCF) was less in IMRT and VMAT.

V95% was found to be 82.5±12%, 97.5±1.4% and 96.2±10.7% in conventional, IMRT and VMAT plans respectively. IMRT planning was better than Conventional plans and the results were statistically significant.V107% and V110% was comparatively better for VMAT plans as compared to IMRT and conventional plans.

Discussion

Breast cancer patients have a significant risk of loco-regional recurrence after surgery and hence adjuvant radiation is indicated. Radiation therapy to the chest wall/breast and regional lymphatics is technically challenging. Various different techniques are available for treatment of chest wall / breast with radiation namely: Conventional, IMRT and VMAT. IMRT can potentially benefit the patient in two ways. First, by improving conformity with target dose it can reduce the probability of in-field recurrence. Second, by reducing irradiation of normal tissue it can minimize the degree of morbidity associated with treatment. IMRT directs radiation at the breast tumor and modulates the intensity of the radiation beams, helping to spare healthy tissue surrounding the breast tumor.[10]. However, the planning and quality assurance (QA) processes required for IMRT are more complex andtime-consuming compared with conventional conformal radiotherapy (CRT) techniques [11]. Volumetric modulated arc therapy (VMAT) is a novel radiation technique, which can achieve highly conformal dose distributions with improved target volume coverage [12]. So present study was carried out to compared osimetric evaluation of IMRT, VMAT conventional planning for patients of breast cancer. Safora Johanson et al compared conventional, IMRT and VMAT plans. D98% and D99% were higher for VMAT (D98%-45.5Gy, D99%-44.8Gy) as compared to IMRT (D98%-43.8Gy, D99%-42.5Gy) and conventional (D98%-43.6Gy, D99%-42.1Gy). D2% and D1% were also least in VMAT (D2%-53Gy; D1%-53.3Gy) when compared with IMRT (D2%-55.5Gy;D1%-56.2Gy) and conventional plans(D2%-55.7Gy;D1%-56.4Gy). V90% was also highest in VMAT(98.5%) as compared with IMRT(97.1%) and conventional plans(96.3%). All these findings corroborated with the findings of our study.[13] Landau D et al showed the volume receiving more than 105% of the prescription dose was reduced by IMRT compared to conventional plans. Volume recieving >105% in conventional was 5.4%andIMRT was 0.9%. [14]

Rongsriyam et al compared conventional and IMRT plans PTV coverage V95% for IMRT and conventional was 96% and87%, hence IMRT was better than conventional ($p<0.05$). Also V107% and V110% was reduced in IMRT as compared to conventional plans which was the same as in our study.[15]

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Zhang et al showed PTVD 2% to be less for VMAT (55.4Gy) as compared to IMRT (55.6Gy). His study also showed V95% of VMAT (99.2%) better than of IMRT (98.1%). V107% was found to be better in VMAT as compared to IMRT. D98% was comparable in between IMRT and VMAT plans. All these finding were similar to our study thus implying that VMAT plans are better than IMRT plans.[16] In our study all the patients were treated with VMAT. However only for dosimetric comparison we planned the IMRT and conventional plans to compare the three different plans in each patient keeping the various target volumes same.

Our dosimetric comparison of VMAT, IMRT and conventional technique in 25patients, suggests that VMAT can be used as a clinical treatment for the treatment of the post-mastectomy and post BCS breast cancer patients to provide homogeneous target coverage while maintaining low doses to normal tissue. VMAT can significantly improve dose distributions for the chest wall/breast and regional nodes while noticeably reducing heart, lung and spinal cord as compared with IMRT and conventional techniques. VMAT significantly reduces number of monitor units and overall treatment time as compared to IMRT.

Conclusion

VMAT technique is superior to the IMRT and conventional techniques due to its better chest wall/breast, axilla and SCF coverage. VMAT seems top rovide the optimum balance between chest wall/breast and regional node coverage and normal tissue sparing. VMAT increased the volume of tissue receiving low doses. VMAT has more homogeneous dose distribution as compared to IMRT and conventional techniques. However, further studies are needed to authenticate the dosimetric findings of our study.

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