RESEARCH ARTICLE

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Hybrid Treatment Planning in Breast and Esophageal Cancer: A Feasible Approach for High-Volume Radiotherapy Centers

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Abstract

Objective: To evaluate the feasibility of hybrid intensity-modulated radiotherapy (IMRT) technique in patients with esophageal and breast cancer within a high-patient volume setup. **Materials and methods:** A total of 36 patients with carcinoma of the left breast and esophagus were retrospectively studied with 3D-CRT, IMRT and Hybrid techniques. 3D-CRT plans for esophageal cancer consisted of one anterior-postertior (AP) and two oblique beams, while IMRT consisted of seven beams. The hybrid plan consisted of AP and PA static beams combined with five conformal beams, with a weighting ratio of 5:5 and 4:6. In breast cases, hybrid planning involved two tangential static beams and three conformal beams with a weighting ratio of 7:3. Dosimetric parameters of the hybrid-IMRT plans were then compared with those of the 3D-CRT and IMRT plans. **Results:** In esophageal cancer patients, there was a significant difference found in the PTV coverage and conformity. The V_{20} and D_{mean} of left lung showed significant differences between IMRT and Hybrid IMRT. V25 and D_{mean} for heart showed reduced values in IMRT plan. The maximum dose to the spinal cord was higher in Hybrid IMRT compared to IMRT and 3D-CRT. In breast cancer patients, V_{20} and D_{mean} for the left lung were 23.77±4.28% and 11.09±1.70 Gy in hybrid plans; 26.50±5.06 % and 12.44±1.62 Gy in IMRT; and 25.47±5.07% and 11.52±1.54 Gy in 3D-CRT. The dose to the contralateral breast was higher in the IMRT plans. **Conclusion:** Considering its comparable planning time to IMRT and the added benefit of reduced OAR doses, hybrid planning could be a valuable option in high-patient-volume settings.

Keywords: Breast cancer- Conformal Radiotherapy- Esophageal cancer- Hybrid planning

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Introduction

Breast and esophageal cancers represent significant clinical challenges due to their high incidence and the complexity of their treatment. Breast cancer in women ranks as the top most common cancer while esophageal cancer is the tenth most common malignancy across the globe [1]. Radiotherapy plays a pivotal role in the management of both types of cancer, with advancements in technology continually enhancing treatment efficacy and reducing side effects. Among these advancements, Intensity-Modulated Radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT) have been extensively studied and implemented. 3D-CRT shapes the radiation beams to match the tumor's three-dimensional structure, offering improved targeting over traditional techniques. However, with 3D-CRT, the dose to the critical structures surrounding the target is higher compared to IMRT [2, 3]. IMRT, with its ability to modulate the intensity of the radiation beam, allows for precise targeting of the tumor while sparing surrounding healthy tissue. IMRT has advantages in terms of improved target coverage, better dose homogeneity and reduced normal tissue toxicity [4, 5]. However, in IMRT, there is a possibility of dose spillage in the vicinity of critical structures and chances of setup errors with changes in the shape of tumor volume [6-8].

Recently, hybrid techniques, which combine the strengths of both IMRT and 3D-CRT have emerged as a promising approach. Hybrid technique derives the benefits from both techniques. It aims to optimize tumor coverage and minimize exposure to surrounding organs at risk (OARs) by integrating the capabilities of IMRT with that of conformal radiotherapy. Hybrid technique helps to minimize low-dose region around the target volume while increasing conformity and homogeneity [9]. In breast cancer, this is particularly crucial due to the proximity of critical structures such as the heart and lungs. Similarly,

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for esophageal cancer, the challenge lies in delivering effective doses to the tumor while protecting the spinal cord and other adjacent organs.

In this study we evaluated the efficacy, safety, and dosimetric advantages of hybrid techniques in contrast to IMRT and 3D-CRT for the treatment of breast and esophageal cancer. Since our department has a high patient load, by evaluating the dosimetric parameters and delivery efficiency of three techniques viz. IMRT, Hybrid-IMRT and 3D-CRT, we investigated if hybrid planning is helpful in improving the target coverage and minimizing the dose to OARs in breast and esophageal cancer.

Materials and Methods

Thirty six post-operative patients with carcinoma of left breast and esophageal carcinoma treated with 3D-CRT were retrospectively studied. 36 patients included 18 patients with locally advanced carcinoma of the esophagus without any metastasis and 18 patients with locally advanced non-metastatic carcinoma of the left breast. This study was approved by our Institutional Ethics Committee. All patients underwent CT scans of slice thickness 3 mm on a CT simulator (Brilliance CT simulator, Philips) in the supine position with suitable immobilization devices. The contouring of target and OARs of both the sites was done. In breast patients, the PTV and OARs including left lung, heart and contralateral breast was delineated. In esophageal cancer patients, PTV and OARs including Ipsilateral and contralateral Lungs, Heart and Spinal cord were contoured. These contoured images were exported to the Monaco treatment planning system version 5.11.03 (Elekta AB, Stockholm, Sweden) for treatment planning.

Treatment planning

Treatment planning of both sites was performed in Monaco TPS. IMRT and hybrid plans were created for already treated 3D-CRT patients of breast and esophageal cancer. The hybrid technique for the esophagus consisted of AP and PA conformal static beams combined with 5 conformal beams with a weightage ratio of 4: 6 and 5:5. 3D-CRT plans consisted of 1 AP and 2 oblique beams while IMRT plans consisted of 7 beams. In breast cases, hybrid planning involved 2 tangential static beams and 3 conformal beams with a weightage ratio of 7:3. The hybrid-IMRT plans were then compared with the 3D-CRT and IMRT plans in terms of target coverage, OAR doses, and planning time.

Esophagus

Three plans were created for each patient with esophageal cancer. These included conventional 3D-CRT, IMRT, and a hybrid plan. The prescribed dose was 50.4 Gy in 28 fractions.

a. 3D-CRT

3D-CRT plan consisted of three static beams, one anterior and two posterior oblique fields to avoid the critical structures like spinal cord and heart. Figure 1a demonstrates the beam placement and dose distribution in a 3D-CRT plan.

b. IMRT

IMRT plans consisted of 7 non-opposing beams at equal angles around the patient. The planning goal was to achieve at least 95% coverage of the Planning Target Volume (PTV) with 95% of the prescribed dose. Plans were optimized to achieve this goal while minimizing the dose to critical structures like the spinal cord and heart. Figure 1b demonstrates the beam placement and dose distribution in IMRT plan.

c. Hybrid plan

The hybrid technique consists of two opposing anteroposterior posteroanterior static beams combined with 5-intensity modulated conformal beams in the weightage ratio of 4:6 for eight patients and 5:5 for the remaining patients. The 4:6 weightage was given to reduce the heart and spinal cord doses in such patients due to their anatomy. For optimizing the hybrid plan, the static beam plan served as a base plan. This meant that the dose distribution of static plan was considered and the dose was then optimized for the combination of static and IMRT beams. Figure 1c demonstrates the beam placement and dose distribution in a hybrid plan.

The hybrid technique involved two phases of radiation delivery: In the initial phase, two opposing anteroposterior posteroanterior fields delivered the dose as per the weightage ratio and in the second phase five intensity-modulated conformal beams delivered the remaining dose as per the weightage allotted.

Breast

For each patient with breast cancer, three plans were created. These included conventional 3D-CRT, IMRT and hybrid plan. The prescribed dose was 42.6 Gy in 16 fractions. The coverage criterion for planning was to achieve a minimum of 95% coverage to the Planning Target Volume (PTV) with 95% of the prescribed dose.

a. 3D-CRT

3D-CRT plan consisted of 2 static beams, one medial tangential (MT) and one lateral tangential (LT) field at a suitable angle to avoid exposure to the contralateral breast (Figure 1d). The angles of collimator and position of jaws for all the fields were adjusted before calculation to minimize the dose to the lungs and heart. The gantry angles ranged from 280° to 320° for MT and 110° to 160° for LT.

b. IMRT plan

IMRT plans consisted of 5 non-opposing beams (3 MT and 2 LT beams) at different angles to reduce exposure to the contralateral breast (Figure 1e).

c. Hybrid plan

The hybrid technique consisted of 2 static MT & LT beams and three IMRT beams. 70 % of the dose was delivered using the static beams, and the remaining 30 % was delivered using the IMRT beams (Figure 1f).

For optimizing the hybrid plan, the static beam plan served as a base plan. This meant that the dose distribution of static plan was considered and the dose was then optimized for the combination of static and IMRT beams.

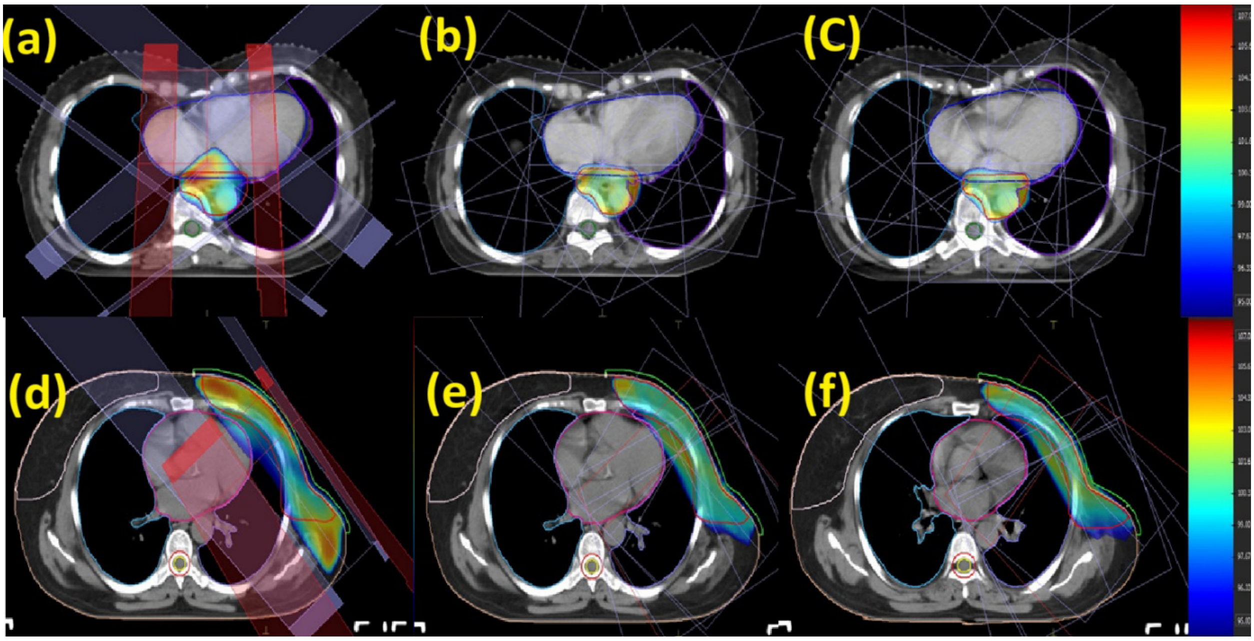

Figure 1. Beam Placement and Dose Distribution in Esophageal Cancer Patient Planned with (a) 3D-CRT (b) IMRT and (c) Hybrid IMRT and a breast cancer patient planned with (d) 3D-CRT (e) IMRT and (f) Hybrid IMRT

Treatment Plan Evaluation

The Dose-Volume Histogram (DVH) of all of the plans were evaluated. All the three types of plans viz. 3D-CRT, IMRT and hybrid plans were compared in terms of target coverage, OAR doses, Homogeneity Index (HI) and conformity index (CI). Dose constraints and tolerance values used for the plan evaluation followed the QUANTEC Guidelines.

For breast case, parameter compared for the PTV was V95%. For OARs, the volume of lung receiving 20 Gy (V_{20}), 5 Gy (V_5), mean dose (D_{mean}) to both lungs; mean dose to the contralateral breast; volume of heart receiving 25Gy (V_{25}) and mean dose (D_{mean}) to heart were compared. The conformity index (CI) and homogeneity index (HI) were also compared in all three types of plans.

For esophagus case, parameter compared for the PTV were V95%. For OARs, the volume of lung receiving 20 Gy (V_{20}), 5Gy (V_5), mean dose (D_{mean}) to both lungs; volume of heart receiving 25 Gy (V_{25}), 30 Gy (V_{30}), mean dose (D_{mean}); maximum dose (Dmax) received by spinal cord was compared. The conformity index (CI) and homogeneity index (HI) were also compared in all three types of plans

The Homogeneity Index (HI) values were calculated using the following equation [10]

$$HI= \frac{D_{2\%}-D_{98\%}}{D_{50\%}} \quad (1)$$

Where, $D_{2\%}$=Dose received by 2% of target volume (minimum dose received by target)

$D_{98\%}$=Dose received by 98% of the target volume (maximum dose received by target)

$D_{50\%}$= Dose received by 50% of the target volume.

The conformity index (CI) was calculated using the following equation [11]:

$$CI = \frac{V_{RI}}{TV} \quad (2)$$

Where, V_{RI}=Reference isodose volume

TV= Target volume

Statistical analysis

For statistical analysis, SPSS Statistics 20.0 (IBM Corp., Armonk, NY, USA) was used. The dosimteric parameters of 3D-CRT, IMRT and hybrid plans were compared statistically using a paired p-test. A p-value of less than 0.05 was considered to be statistically significant.

Results

The mean volume of PTV in breast cases was 548.73 cc and for esophagus was 300.76 cc. The dosimetric parameters comparing the three techniques viz 3D-CRT, IMRT and hybrid planning have been summarized in Table 1.

PTV coverage and OAR dose in breast patients

The PTV coverage in 3D-CRT, IMRT and hybrid plans was 95.68±2.99%, 98.54±0.99% and 98.60±0.82% (Figure 2a). A significant difference was found in the Conformity index between the IMRT and hybrid plan (Figure 2b). At the same time, there was no difference in the HI values between IMRT and hybrid IMRT (Figure 2c). There was significant difference found in the coverage with 3D-CRT and Hybrid technique (Table 1). However, there was no significant difference in the PTV coverage between IMRT and hybrid IMRT. The V_{20}, V_5 and D_{mean} for left lung were lower in hybrid plans (Figure 2d, Figure 2e, Figure 2f). A significant difference was found in the V_5 and D_{mean} values between IMRT and hybrid IMRT. V_{25} and D_{mean} of heart were higher in IMRT than hybrid and 3D-CRT plans (Figure 2g, Figure 2h). However, there was no significant difference in V_{25} and D_{mean} of heart found between IMRT

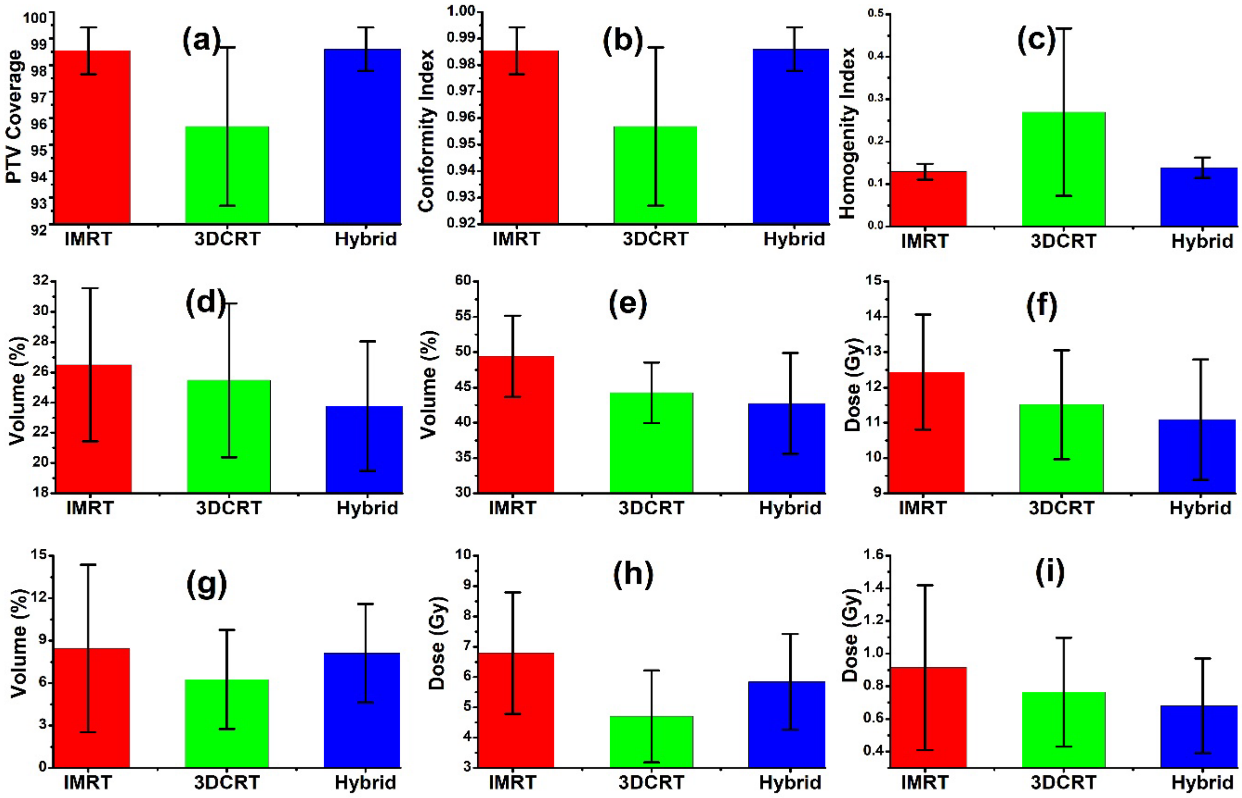

Figure 2. Comparison of Dosimetric Parameters in Breast Patients among 3D-CRT, IMRT and Hybrid Technique (a) PTV coverage (b) CI (c) HI (d) V_{20} for left lung (e) V_5 for left lung (f) D_{mean} for left lung (g)V_{25} of heart and (h) D_{mean} of heart (i) D_{mean} of contralateral breast

and hybrid IMRT. Mean dose to contralateral breast was also lesser in hybrid plans (Figure 2i).

PTV coverage and OAR dose in esophagus patients

The PTV coverage in 3D-CRT, IMRT and hybrid plans was 97.86±1.17 %, 99.39±0.87 % and 98.59±0.90 % respectively. There was a significant difference found in the PTV coverage between the 3D-CRT Vs. IMRT and between IMRT Vs. hybrid technique. The dose conformity and homogeneity in PTV was better in hybrid and IMRT plans (Figure 3a, Figure 3b). There was a significant difference in the HI values between 3D-CRT Vs. IMRT and between 3D-CRT and Hybrid IMRT. The V_{20}, V_5 and D_{mean} for both left and right lungs were reduced in hybrid planning (Figure 3c, Figure 3d, Figure 3e, Figure 3f, Figure 3g, Figure 3h). There was a significant difference in the V_{20} and D_{mean} values between IMRT Vs. Hybrid technique and 3D-CRT Vs. Hybrid IMRT in both lungs. The dose to the spinal cord was relatively higher but within tolerance in hybrid plans (Figure 3i). Additionally, the difference in dose to spinal cord among the three techniques wasn't significant. The V_{30}, V_{25} and D_{mean} for heart were found to be higher in hybrid plans compared to IMRT and 3D-CRT (Figure 3j, Figure 3k, Figure 3l). However, only V_{25} showed significant difference between IMRT and hybrid plans.

Discussion

We investigated the feasibility of using a hybrid planning technique in busy radiotherapy settings such as our department in the treatment of esophageal and breast cancer. Since the patient load in our department is huge, there was a need to investigate the techniques that could provide an optimal solution in terms of time taken for treatment planning, treatment delivery and dosimetric outcome.

In case of breast, we found that hybrid planning gave better results in terms of improved PTV coverage and reduction of OAR doses. Although PTV coverage, homogeneity and conformity was similar in IMRT and hybrid techniques, there was a great advantage of using hybrid technique in reducing OAR doses.

Our findings were similar to the study done by Bi et al. [12] who compared the three techniques IMRT, hybrid IMRT and hybrid VMAT in right breast cancer patients. They found that the hybrid IMRT gave better target coverage and lesser OAR doses than full IMRT and hybrid VMAT.

Lin et al. [13] studied the dosimetric comparison of hybrid volumetric-modulated arc therapy (hybrid-VMAT), only VMAT, and fixed-field intensity-modulated radiotherapy for left breast cancer patients (F-IMRT). They concluded that hybrid VMAT resulted in good target coverage and better homogeneity and conformity. The dose to ipsilateral lung, heart and contralateral breast

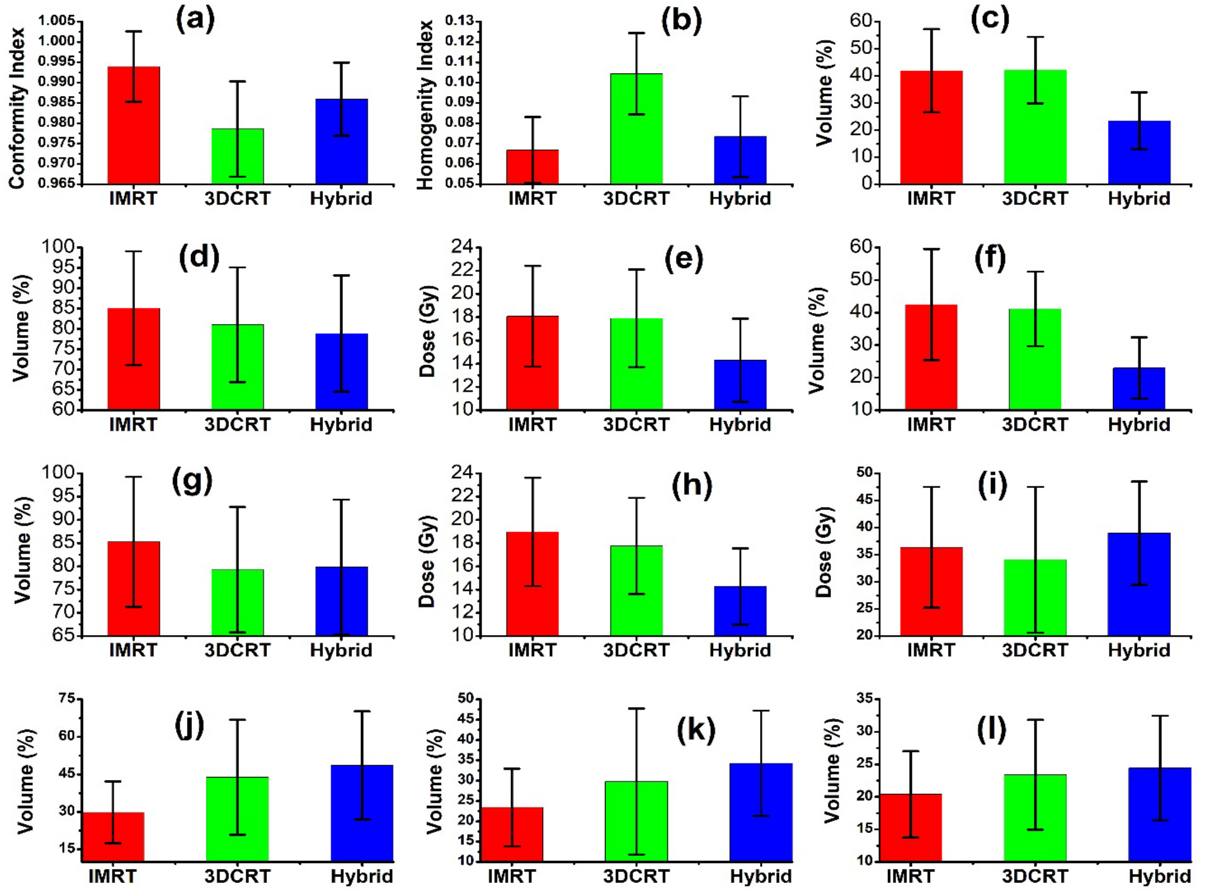

Figure 3. Comparison of Dosimetric Parameters in Esophagus Patients among 3D-CRT, IMRT and Hybrid technique (a) CI (b) HI (c) V_{20} for left lung (d) V_5 for left lung (e) D_{mean} for left lung (f) V_{20} for right lung (g)V_5 for right lung and (h) D_{mean} for right lung (i) D_{max} for spinal cord (j) V_{25} for heart (k) V_{30} for heart and (l) D_{mean} for heart

Table 1. Dosimetric Analysis of 3D-CRT, IMRT and Hybrid Plans of Ca Breast and Esophageal Cancer

Site	Structures	Dosimetric Parameters	3D-CRT	IMRT	Hybrid plan	3D-CRT Vs. IMRT	IMRT Vs. Hybrid IMRT	3D-CRT Vs. Hybrid IMRT
Breast	PTV	V_{95}% (%)	95.68±2.99	98.54±0.99	98.60±0.82	P<0.01	0.99	P<0.01
		CI	0.75±0.05	0.84± 0.03	0.81±0.03	P<0.01	0.03	P<0.01
		HI	0.27±0.19	0.13±0.02	0.14±0.02	p<0.01	0.92	P<0.01
	Left Lung	V_{20} (%)	25.47±5.07	26.50±5.06	23.77±4.28	0.79	0.22	0.55
		V_5(%)	44.26±4.26	49.41±5.73	42.72±7.15	0.03	0.01	0.71
		D_{mean} (Gy)	11.52±1.54	12.44±1.62	11.09±1.70	0.22	0.04	0.72
	Heart	V_{25} (%)	6.25±3.50	8.44±5.92	8.11±3.49	0.31	0.97	0.32
		D_{mean} (Gy)	4.70±1.51	6.79±2.01	5.84±1.58	0.01	0.23	0.12
	Contralateral breast	D_{mean} (Gy)	0.76±0.33	0.91±0.50	0.68±0.29	0.47	0.17	0.79
Esophagus	PTV	$V_{95\%}$ (%)	97.86±1.17	99.39±0.87	98.59±0.90	P<0.01	0.04	0.07
		CI	0.76±0.03	0.85±0.02	0.84±0.03	P<0.01	0.33	P<0.01
		HI	0.10±0.02	0.07±0.02	0.07±0.02	P<0.01	0.5	P<0.01
	Left Lung	V_{20} (%)	42.13±12.27	41.92±15.34	23.46±10.44	0.99	P<0.01	P<0.01
		V_5(%)	81.01±14.10	85.10±13.98	78.84±14.33	0.66	0.38	0.88
		D_{mean} (Gy)	17.9±14.21	18.09±4.34	14.29±3.57	0.98	0.01	0.02
	Right Lung	V_{20} (%)	41.14±11.46	42.47±14.09	22.97±9.41	0.94	p <0.01	p <0.01
		V_5 (%)	79.27±13.5	85.27±14.02	79.82±14.56	0.41	0.47	0.99
		D_{mean} (Gy)	17.76±4.14	18.96±4.27	14.27±3.29	0.65	0.01	0.03
	Heart	V_{30} (%)	29.80±18.00	23.40±9.56	34.27±12.93	0.35	0.06	0.61
		V_{25} (%)	43.84±22.96	29.77±12.41	48.57±21.60	0.08	0.02	0.74
		D_{mean} (Gy)	23.40±8.44	20.39±6.64	24.44±8.03	0.48	0.26	0.92
	Spinal Cord	D_{max}	34.08±13.45	36.35±11.15	39.00±9.51	0.83	0.77	0.41

were significantly reduced with hybrid-VMAT compared to VMAT and IMRT. Another advantage with hybrid VMAT was the lower number of total MUs delivered with this technique over VMAT and IMRT which made hybrid VMAT feasible for left sided breast cancer patients.

Mayo et al. [14] compared five different techniques in right and left breast cancer patients. These included conventional open tangential beams, field in field technique in 3D-CRT, IMRT, 4 field hybrid IMRT and 6 field hybrid IMRT. They found that field IMRT gave more hot spots than the hybrid techniques. Volume of heart treated to doses of more than 5 Gy was significantly higher in 6 field hybrid technique compared to IMRT and field in field technique. However, in heart volume treated to more than 30 Gy, 6 field hybrid technique and IMRT gave lower dose compared to field in field. This result differed from our study where we found that volume of heart receiving greater than or equal to 25 Gy was higher with hybrid technique. Ipsilateral lung volume receiving greater than or equal to 20 Gy was higher in 6 field hybrid technique compared to IMRT and field in field. These findings were different from our results where we have concluded that hybrid technique reduced the ipsilateral lung doses. Mayo et al. concluded that hybrid technique is a good solution for better dose conformity and normal tissue sparing.

Doi et al. [15] studied the dosimetric outcome and toxicities of the two techniques 3D-CRT and hybrid VMAT in post-operative breast cancer patients. They found that hybrid VMAT gave better conformity and homogeneity of the dose and was a safe technique to reduce toxicities like dermatitis, esophagitis and pneumonitis. The values of V_{20} and D_{mean} did not differ significantly in hybrid VMAT compared to 3DCRT. V_{20} was 22.9%± 6.8 and 23.7%± 6.4 for 3DCRT and Hybrid VMAT plan respectively. D_{mean} was 11.8 Gy ± 2.8 and 12.0 Gy ± 2.4 for the 3DCRT and the Hybrid VMAT plan. These results were similar to our findings. In their study, mean heart doses were almost similar in 3D-CRT and hybrid VMAT plans. However we found the mean heart dose to be higher in hybrid-IMRT plans compared to 3D-CRT but there was no significant difference.

Cit et al. [16] found that V_5 for ipsilateral was significantly lower in hybrid IMRT compared to complete IMRT. V_{20} was higher in hybrid IMRT. However, the mean dose to ipsilateral lower was similar in both plans. In our findings, the hybrid IMRT showed lower V_5 and D_{mean} doses to the ipsilateral lung. Doses to heart i.e. V_{30} and D_{mean} were significantly reduced in hybrid plans compared to complete IMRT plans in their study which was different from our findings. The mean dose to the contralateral breast was also found to be significantly lower which differed with our results. They concluded that hybrid plans (IMRT+3D-CRT) can reduce the OAR doses without compromising the plan quality.

In our study of esophageal cancer patients, hybrid technique proved beneficial in reducing OAR doses. The lung doses were lowest in hybrid planning. This was similar to our study done by Mayo et al. [8] who compared the hybrid IMRT with 4 and 9 fields IMRT and 3D-CRT in lung and esophageal cancer. They found that the V_5 and V_{20} values for lung were lower in hybrid IMRT compared to 9 field IMRT. They reported a significant difference in the V_{30} heart in IMRT compared to a hybrid technique which was in agreement with our findings.

Takakusagi et al. [17] studied the dose volume parameters of 3D-CRT, VMAT and hybrid plans and compared the dose distribution of these plans with the change in the ratio of 3D-CRT to VMAT in esophageal stage 1 cancer. VMAT proportions with respect to 3D-CRT plans were 0%, 10%, 30%, 50%, 70%, 90%, and 100%. They found that as the proportion of VMAT increased, the V_{30} and mean dose of heart reduced. There was a significant difference in the D_{mean} doses of heart between 3D-CRT and hybrid VMAT in all groups. With the increase in the ratio of VMAT, there was an increase in the values of V_5 and V_{20} for lungs. There was no significant difference between 3D-CRT and hybrid VMAT for different ratios of VMAT except in the V_{50} value. They concluded that VMAT proportion for hybrid VMAT should be 50%-70%. In our study too, we have taken the 3D-CRT to IMRT ratio as 4:6 (IMRT proportion is 60%).

Miyazaki et al. [18] compared the 3D-CRT, VMAT and hybrid VMAT in esophageal cancer patients and found that the Hybrid VMAT reduced the V_{20} and mean doses to lungs and V40 of heart compared to VMAT and 3D-CRT. The maximum dose to spinal cord was lower in VMAT plans comparatively. The PTV coverage did not differ significantly among the three techniques.

In conclusion, we concluded that Hybrid technique is advantageous in improving the target coverage and conformity of the dose for both the site i.e. breast and esophagus. Furthermore, it helped in reducing the dose to OARs and mitigating the low dose contribution to critical structures in esophageal and breast cancer patients. Considering its comparable planning time to IMRT and the added benefit of reduced OAR doses, hybrid planning could be a valuable option in settings with a high patient volume.

Author Contribution Statement

The study was conceived, conceptualized, designed and drafted by Shraddha Srivastava. Data collection was carried out by Shraddha Srivastava and Shyamprasad S. Data analysis and interpretation were performed by Shraddha Srivastava, Atul Mishra, and Nara Moirangthem Singh. The manuscript was edited by Shraddha Srivastava and Nara Moirangthem Singh and the final version was reviewed and approved by all authors.

Acknowledgements

Ethical approval
This study was approved by our Institutional Ethics Committee.

Conflicts of interest
The authors have declared that they have no conflicts of interest.

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