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Dosimetric comparison between three-dimensional conformal radiation therapy versus intensity-modulated radiation therapy in non-metastatic esophageal carcinoma patients receiving definitive radiation with concurrent chemotherapy: a prospective single institutional study

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ABSTRACT

Background: Esophageal cancer, a highly aggressive and often fatal gastrointestinal disease, frequently reaches advanced unresectable stages. The standard treatment involves definitive chemoradiation due to concerns about regional failure. To address this, intensified radiation dosages and advanced techniques like Intensity-Modulated Radiation Therapy (IMRT) and Three-Dimensional Conformal Radiation Therapy (3D-CRT) are being explored. This study aimed to compare dosimetric factors in patients with esophageal carcinoma undergoing IMRT versus 3D-CRT treatments.
Methods: Twenty patients were alternately assigned to receive either treatment. Each patient's alternate virtual plan resulted in a total of forty plans. Dosimetric evaluations included coverage of the Planning Target Volume (PTV) and dose-volumes of lungs, heart, and spinal cord. Treatment consisted of 50.4 Gy radiation with concurrent weekly paclitaxel and carboplatin chemotherapy. Statistical analysis was conducted using the two-tailed Paired t-Test.
Results: Dosimetric evaluations revealed no significant distinctions in PTV parameters such as maximum dose, minimum dose, mean dose, D2%, D50%, and V95% between IMRT and 3D-CRT plans. However, IMRT exhibited improvements in D98% and Homogeneity Index. While Conformity Index did not differ significantly, IMRT displayed reduced lung irradiation in various aspects such as Dmean, V20, and V30, while 3D-CRT showed lower irradiation in V5 and V10. IMRT effectively spared the heart with lowered heart irradiation in V30. Spinal cord Dmax remained consistent across both techniques.
Conclusions: IMRT demonstrated better dose homogeneity and superior lung and heart sparing capabilities compared to 3D-CRT in treating esophageal carcinoma. While both techniques had similar dose conformity, IMRT's potential to reduce long-term radiation-induced lung and heart complications through improved sparing of these organs is noteworthy.

Keywords: Esophageal carcinoma, Dosimetry, 3D-CRT & IMRT

INTRODUCTION:

Esophageal cancer is a global health concern with varying incidence rates worldwide, particularly affecting low- and middle-income countries.[1] In 2018, it ranked seventh in new diagnoses and sixth in cancer-related deaths globally, with squamous cell carcinoma (SCC) prevalent in Asia and Eastern Europe, while adenocarcinoma is more common in North America and Western Europe.[2,3] The so-called "Asian Esophageal Cancer Belt" encompasses areas such as Turkey, Iran, Kazakhstan and northern and central China, with an estimated esophageal squamous carcinoma of more than 100 cases /100000 person-year.[4] Regions with a lower Human Development Index, like India, bear a substantial burden, especially in the North-East, part of an esophageal cancer belt with high SCC incidence rates.[5]

In light of the challenging prognosis and limited treatment options for non-metastatic unresectable esophageal carcinoma, understanding the dosimetric nuances between Intensity-Modulated Radiation Therapy (IMRT) and Three-Dimensional Conformal Radiation Therapy (3D-CRT) becomes imperative. This investigation delves into the intricate details of Planning Target Volume (PTV) coverage and the impact on organs at risk (OAR), providing crucial insights to guide clinicians in selecting the most effective treatment modality for this specific patient cohort.

Methods and Materials:

This study employs a single-institutional, prospective, open-label, comparative design for dosimetric comparison conducted at the Department of Radiotherapy, R. G. Kar Medical College and Hospital, Kolkata, India. The study period spans 2 years, from January 2021 to December 2022.

The study population comprises biopsy-proven unresectable non-metastatic esophageal carcinoma patients attending the outpatient department. Twenty patients were selected for the study and alternately allocated to the 3D-CRT and IMRT treatment arms. Alternate virtual plans were generated for each patient, resulting in a total of 40 plans—20 for 3D-CRT and 20 for IMRT. Inclusion criteria specify an age range of >18 to <70 years, Eastern Cooperative Oncology Group (ECOG) Performance Status score 0-2. Exclusion criteria encompass prior chemotherapy or thoracic radiation, refusal of chemo-radiation, contraindication to external beam radiotherapy, and pregnancy/lactation.

The study includes patients with tumors at various sites, including cervical, upper, middle, and lower thoracic, as well as gastro-esophageal junction, regardless of size and without distant metastases. All patients underwent simulation using the Siemens Somatom Definition AS 20-slice flat couch CT simulator. Target volumes and organs at risk (OARs) were contoured by two radiation oncologists, and treatment planning was performed using Eclipse version 15.1 treatment planning system with the assistance of a physicist. Treatment was delivered using 6 MV external beam photon energy with both seven-field dynamic IMRT and 3D-CRT techniques on the Varian TrueBeam version 2.7 linear accelerator.

Different variables were analyzed, including Gross Tumor Volume (GTV), Clinical Target Volume (CTV), Planning Target Volume (PTV), minimum, maximum, and mean dose, V95%, D2, D50, D98, Homogeneity Index (HI) [Homogeneity index = (D2%-D98%) / D50% (ICRU 83)] Conformity Index (CI) [Conformity Index =Treated Volume (TV) / PTV (ICRU 62)]. Organs at Risk (OARs) dose constraints were assessed for lungs (Dmean, V5, V10, V20, V30), heart (Dmean, V30, V50), and spinal cord (Dmax).

As per the International Commission on Radiation Units (ICRU) guidelines, GTV represents the visible or palpable tumor, CTV encompasses GTV and potential microscopic disease, PTV expands from CTV, accounting for setup uncertainties, and OARs are normal tissues vulnerable to radiation.V5, V10, V20, V30, V50 represent the percentage volume of the organ receiving a specific dose, and D2, D50, D98 refer to specific dose values at certain percentages of the organ volume. V95 represents the volume receiving at least 95% of the prescribed dose. Data were summarized using Microsoft Excel, and statistical analysis employed Online Statistics Calculator-DA-

TAtab and SPSS software (version 21). Dose prescription was 50.4 Gy in 28 fractions, 1.8 Gy per fraction, [6] with concurrent chemotherapy included Paclitaxel 50 mg/m2 and Carboplatin, area under the curve (AUC) 2. [7]

Results:

SThe study revealed a median patient age of 61 years, demonstrating a relatively balanced gender distribution with approximately 70% males and 30% females. Furthermore, the predominant histological type of esophageal cancer was squamous cell carcinoma, and the most frequently observed site was the mid thoracic region, followed by the lower thoracic region. (Table 1)

The median GTV was 34.45 cc and the median PTV was 374.8 cc in both treatment planning arms. The prescription dose was 5040 cGy, with 98.80% and 97.42% of the dose delivered to V95% of the PTV in the IMRT and 3D-CRT arms, respectively. The mean minimum dose was 4395.7 cGy in the IMRT arm and 4485.89 cGy in the 3D-CRT arm. The mean maximum dose was 5222.84 cGy in the IMRT arm and 5606.78 cGy in the 3D-CRT arm.

The homogeneity index (HI) was 0.06 with a standard deviation of 0.04 in the IMRT arm and 0.1 with a standard deviation of 0.04 in the 3D-CRT arm (p=0.008). The conformity index (CI) was 0.98 with a standard deviation of 0.02 in the IMRT arm and 0.97 with a standard deviation of 0.03 in the 3D-CRT arm (p=0.074). (Table 2)

The mean dose to the lungs was significantly lower in the IMRT arm than in the 3D-CRT arm (1525.82 cGy vs. 1746.6 cGy, p<0.001). The IMRT arm also achieved a higher V5 (77.04%), V10 (63.63%) and lower V20 (28.62%), V30 (9.37%) than the 3D-CRT arm (69.53%, 59.71%, 41.44%, and 22.88%, respectively, all p<0.001). The mean dose to the heart was not significantly different between the two arms (1771.23 cGy vs. 1781.72 cGy, p=0.899). However, the IMRT arm achieved a lower V30 (19.12%) and V50 (6.56%) than the 3D-CRT arm (21.88% and 8.0%, respectively, p=0.039 and p=0.69). The mean maximum dose of spinal cord was not significantly different between the two arms (3859.56 cGy vs. 3946.2 cGy, p=0.74). (Table 3)

Discussion:

The study found that the median GTV (gross tumor volume) was 34.45 cc and the median PTV (planning target volume) was 374.8 cc in both IMRT and 3D-CRT techniques. The prescription dose was 5040 cGy, with 98.80%

Table 1. Patient demographics and Tumor characteristics

Features	values
Age (years)	Median: 61, Minimum: 38, Maximum: 70
Gender	Male: 14 (70%), Female: 6 (30%)
Histopathology	Squamous cell carcinoma: 18 (90%), Adenocarcinoma: 2 (10%)
Site	Mid Thoracic: 8 (40%), Lower Thoracic: 5 (25%), Upper Thoracic: 4 (20%), Cervical: 2 (10%), GEJ: 1 (5%)
Stage	I: 7 (35%), II: 6 (30%), IIIA: 3 (15%), IIIB: 2 (10%), IVA: 2 (10%)

Table 2. Comparison of IMRT and 3DCRT for PTV Dose Parameters

Parameters	IMRT	3DCRT	P Value
Minimum Dose (cGy)	4395.7 ± 250.56	4485.89 ± 1,077.53	0.711
Maximum Dose (cGy)	5222.84 ± 188.49	5606.78 ± 922.42	0.077
V95% (%)	98.80 ± 1.85	97.42 ± 3.15	0.074
Homogeneity Index (HI)	0.06 ± 0.04	0.1 ± 0.04	0.008
Conformity Index (CI)	0.98 ± 0.02	0.97 ± 0.03	0.074

Table 3. Comparison of IMRT and 3DCRT for Organs at Risk

Organs	Parameters	IMRT	3DCRT	P Value
Lungs	Mean Dose (cGy)	1525.82 ± 376.98	1746.6 ± 405.28	<0.001
Lungs	V10 (%)	63.63 ± 16.78	59.71 ± 14.29	0.011
Lungs	V20 (%)	28.62 ± 11.21	41.44 ± 11.67	<0.001
Heart	Mean Dose (cGy)	1771.23 ± 995.23	1781.72 ± 993.54	0.899
Heart	V30 (%)	19.12 ± 17.48	21.88 ± 18.25	0.039
Heart	V50 (%)	6.56 ± 13	8 ± 15.11	0.69
Spinal Cord	Maximum Dose (cGy)	3859.56 ± 885.65	3946.2 ± 1033.7	0.74

and 97.42% of the dose delivered to V95% of the PTV in the IMRT and 3D-CRT arms, respectively. This means that the IMRT arm was able to deliver a higher percentage of the prescribed dose to the target volume while also sparing the surrounding tissues.

The mean minimum dose was 4395.7 cGy in the IMRT arm and 4485.89 cGy in the 3D-CRT arm. This means that the IMRT arm was able to deliver a lower minimum dose to the surrounding tissues while still delivering the prescribed dose to the target volume. The mean maximum dose was 5222.84 cGy in the IMRT arm and 5606.78 cGy in the 3D-CRT arm. This means that the IMRT arm was able to deliver a lower maximum dose to the surrounding tissues while still delivering the prescribed dose to the target volume.

The homogeneity index (HI) was 0.06 with a standard deviation of 0.04 in the IMRT arm and 0.1 with a standard deviation of 0.04 in the 3D-CRT arm (p=0.008). This means that the IMRT arm was able to achieve a more homogeneous dose distribution in the target volume. The conformity index (CI) was 0.98 with a standard deviation of 0.02 in the IMRT arm and 0.97 with a standard deviation of 0.03 in the 3D-CRT arm (p=0.074). This means that the IMRT arm was able to achieve a better conformity of the dose to the target volume.

IMRT was able to reduce the mean dose to the lungs while maintaining the prescribed dose to the tumor.

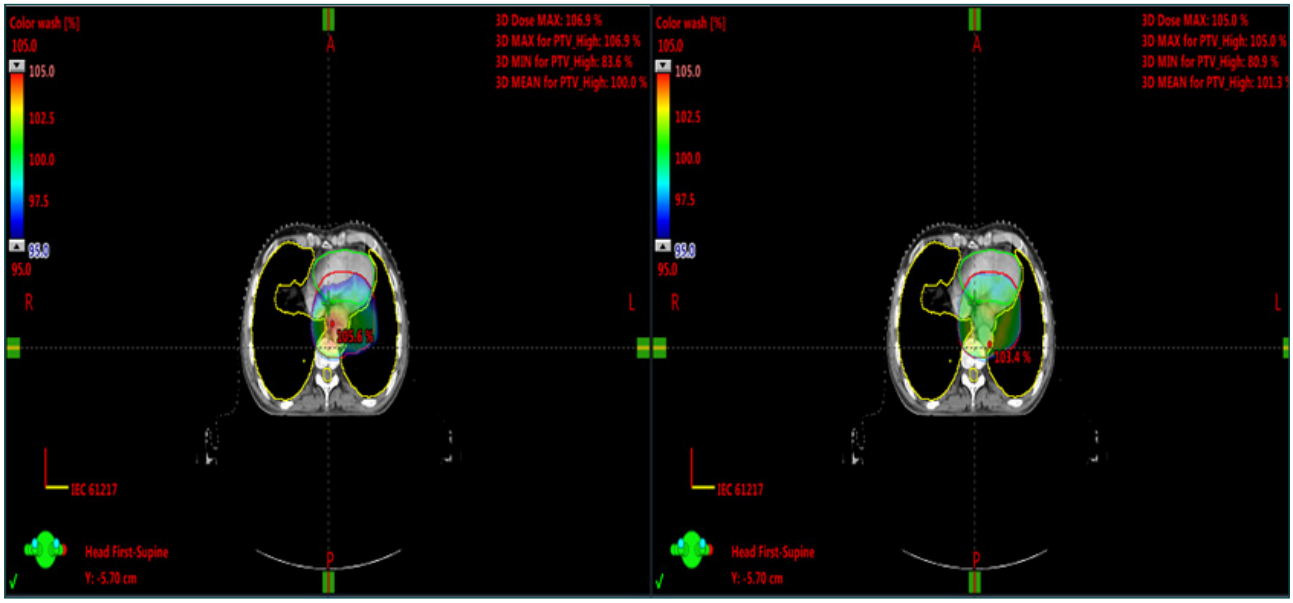

Figure 1. Color wash view of V95% distribution in one patient of our study between 3D-CRT plan (left) and IMRT plan (right)

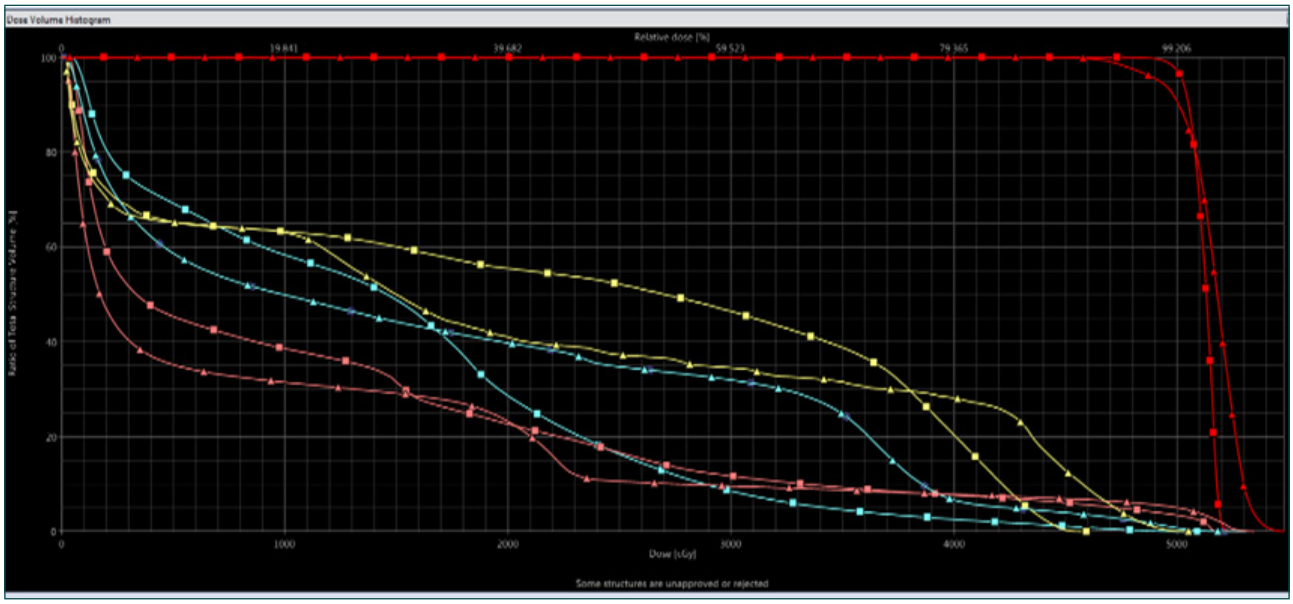

Figure 2. DVH of PTV (red), Lungs(cyan), Heart(pink) and Spinal Cord(yellow) in one patient of our study between 3D-CRT plan(triangle) and IMRT plan(square)

This is because IMRT can deliver more precise radiation beams that conform to the tumor volume while sparing the surrounding tissues. IMRT also achieved a higher V5 and V10, meaning that a higher percentage of the lungs received at least 5 Gy and 10 Gy of radiation, respectively. This reduces the risk of radiation pneumonitis.

The mean dose to the heart was not significantly different between the two arms, but the IMRT arm did achieve a lower V30 and V50. This means that a lower percentage of the heart received at least 30 Gy and 50 Gy of radiation, respectively. This is important because it reduces the risk of cardiac toxicity, a side effect of radiation therapy that can damage the heart.

The mean maximum dose of spinal cord was not significantly different between the two arms. This is good news because it means that IMRT does not appear to increase the risk of radiation-induced myelopathy, a side effect of radiation therapy that can damage the spinal cord.

These results are consistent with the findings of other studies that have compared IMRT and 3D-CRT for the treatment of esophageal cancer. A meta-analysis of 11 randomized controlled trials found that IMRT was associated with a significantly lower mean dose to the lungs and a higher V5 and V10. The meta-analysis also found that IMRT was associated with a lower risk of grade 3 or 4 esophagitis, but there was no difference in the risk of overall survival or progression-free survival. [8, 9, 10] Overall, the results of this study and other studies suggest that IMRT is a more effective way to spare the lungs and heart while still delivering the prescribed dose to the tumor for the treatment of esophageal cancer. However, more research is needed to determine whether IMRT is associated with a better overall survival or progression-free survival.

Conclusions:

TThe study concludes that IMRT can deliver more radiation to the tumor and less to the surrounding tissues. IMRT is able to achieve a more homogeneous dose distribution in the target volume and is also able to achieve a better conformity of the dose to the target volume. IMRT is associated with a lower risk of radiation pneumonitis and cardiac toxicity.

Overall, the study finds that IMRT is a more effective way to deliver radiation therapy to tumors in the esophagus while sparing the surrounding tissues. However, more research is needed to determine whether IMRT is asso-

ciated with a better overall survival or progression-free survival for esophageal cancer.

Limitations:

1. The study's narrow focus on a specific patient group and single institution limits the generalizability of its findings.
2. The modest number of participants compromises the study's robustness and its relevance to a broader population.
3. Results may be influenced by institutional biases, given the study's confinement to a single medical facility.

Declarations:

1. Funding: No funding was used to support this study
2. Disclosure: The authors report no conflict of interest in this work.
3.Ethical clearance was obtained following meticulous review by the appropriate ethical oversight body, ensuring adherence to ethical standards throughout the study.

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