








Original Research Article

Comparison of Intensity-modulated radiation therapy (IMRT) versus RapidArc technique in head and neck cancers – A dosimetric and clinical research

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Abstract

Introduction: Head and neck cancers (HNC) result in significant morbidity and mortality throughout the world, with an expected 900,000 cases and 400,000 deaths annually. In India, head and neck cancer accounts for 30% of all cancer cases, with >65% of patients presenting with locally advanced disease.

Objectives: To compare the dosimetric (target volume coverage, dose to organs at risk (OARs), and monitor units (MUs) and clinical (mucositis and dermatitis) parameters in patients receiving IMRT versus RapidArc in HNC.

Materials and Methods: This cross-sectional, prospective study of locally advanced head and neck cancer patients (oral cavity, oropharynx, larynx, hypopharynx) was conducted on those planned for treatment with definitive concurrent chemoradiation therapy from 01.06.2023 to 31.05.2024 at Capitol Hospital, Jalandhar. These patients were randomly allocated to the IMRT or RapidArc group. The patients with previous irradiation for HNC, metastatic disease, and those who underwent surgery were excluded from the study. The target volume coverage, OARs doses, and MUs with weekly radiation-induced mucositis and dermatitis were assessed in the IMRT and RapidArc arm.

Results: A total of 26 patients were randomized into the IMRT and RapidArc group. There was no statistically significant difference between IMRT and RapidArc techniques in terms of target dose coverage for PTV70 and PTV59.4 Gy. The dose to OARs including mandible, lips, unilateral parotid, bilateral parotid, and spinal cord was similar for both IMRT and RapidArc techniques. The average MU to deliver a dose of 2Gy per fraction in the RapidArc technique was fewer as compared to those with the IMRT technique ($p < 0.001$). Our results showed that a higher percentage of patients treated with the IMRT technique had grade 3 mucositis. There was no difference noted between the two groups in terms of RT-induced dermatitis.

Conclusion: Our study concluded that the only significant benefit with RapidArc was much smaller total MUs required than with IMRT. Both techniques were comparable concerning target coverage and dose to OARs. However, we noticed that IMRT resulted in higher grade 3 mucositis though not statistically significant.

Keywords: Dermatitis, Head and neck neoplasms, Intensity-modulated radiotherapy, Mucositis, Organs at risk

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1. Introduction

HNC are the most common type of malignancy in the world. According to GLOBOCAN estimates of cancer incidence and mortality represented by the International Agency for Research on Cancer, an estimated 9,31,931 newly diagnosed and 4,67,125 cancer-related deaths occurred in 2020 worldwide.¹ For loco-regionally advanced head and neck carcinoma (LAHNC), the preferred treatment is surgery followed by adjuvant RT or definitive concurrent chemoradiation therapy (CCRT), if surgery is not feasible.²

Significant advancements in RT have been demonstrated mainly because of the technological advancements to achieve the aim of RT which means to deliver the maximum dose of radiation to the tumor while sparing the surrounding normal structures. IMRT is an evolution of 3D-CRT, the current standard treatment modality for OARs sparing, target coverage, and dose conformity.³ RapidArc is a newer radiation technique that delivers highly conformal dose distributions through 360° gantry rotation and varying speeds of the gantry.⁴ RapidArc technique has demonstrated various advantages over IMRT such as significantly reducing the

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treatment time, the number of MUs, and better sparing of normal tissues while keeping the target coverage optimal.⁵

We planned to conduct this study, to fill the gap in the existing knowledge by comparing IMRT and RapidArc techniques in terms of clinical and dosimetric parameters in HNC.

2. Materials and Methods

2.1. Study design

This was a cross-sectional, prospective study, conducted in the Department of Radiation Oncology on LAHNC patients (oral cavity, oropharynx, larynx, hypopharynx) from 01.06.2023 to 31.05.2024 planned for treatment with definitive CRT. Written informed consent was obtained from all the patients. However, the patients with previous irradiation for HNC, metastatic disease, and those who underwent surgery were excluded from the study.

2.2. Study population

This study was approved by the Institutional Research Committee with CAP/SRC/2023-01 number and Ethics Committee approval no: IEC/23/15. The patients fulfilling the inclusion criteria were allocated based on a computerized randomization list by simple randomization to the IMRT or RapidArc group. All patients underwent a pre-treatment evaluation, including a complete history and general physical examination, magnetic resonance imaging of the head and neck region, and blood investigations including a complete blood count and renal function tests. These patients underwent a CT chest and ultrasound abdomen to rule out metastasis. All patients were staged by physical examination and radiological evaluation according to the American Joint Committee on Cancer Staging System- 8th edition.

2.3. Radiotherapy planning

All the patients had undergone simulation in supine position with neck rest and shoulder traction using the 5-point thermoplastic cast. All patients had undergone planning computed tomography (pCT) imaging (Philips Brilliance 64) at a slice thickness of 3 mm from the forehead to the xiphisternum. All patients were given intravenous contrast to better visualise the enlarged lymph nodes and the vasculature. These pCT images were transferred to the treatment planning system (TPS, Eclipse version 13.5) thereafter. Direct aperture optimization i.e. DAO algorithm was used for IMRT and progressive resolution optimization i.e. PRO algorithm was used for RapidArc optimization.

2.3.1. Target volume definition

Gross tumor volume (GTV) was contoured as the gross primary disease including all enlarged lymph nodes detected by clinical examination or radiological imaging. Clinical target volume (CTV) was composed of GTV with a 10-mm margin. The CTV subclinical disease was composed of CTV

gross disease including areas at high risk of microscopic disease.

2.3.2. CTV coverage

The representative dose distribution and Dose-volume histograms (DVHs) were generated to evaluate the dose to the CTV for IMRT and RapidArc treatment plans according to the ICRU 83 (Hodapp N., 2012). The CTV coverage was analyzed as per the following parameters:

1. D2% and D98% parameters were representative markers for maximum and minimum doses.
2. The H.I. was defined by the following equation $(D2\% - D98\%) / D50\%$ (ratio of the difference between the dose covering 2% and 98% to the dose received by 50% of the PTV volume). This equation denotes that a lower HI value indicates a more homogeneous target dose⁵.
3. The C.I.95% was defined as the ratio between the patient volume receiving at least 95% of the prescribed dose and the volume of the PTV. This was used as a measure of target conformity of the CTV⁵. Total MUs for each plan were also documented.

These parameters were assessed for both PTV70 and PTV59.4

2.3.3. Dose and fractionation

The dose to the PTV70 was prescribed as 70 Gy in 2 Gy per fraction, and the dose to the PTV59.4 was prescribed as 59.4 Gy in 1.8 Gy per fraction. The prescribed doses were delivered in 35 once-daily fractions, five fractions per week using simultaneous integrated boost.

2.3.4. OARs delineation

For each patient, the following OARs were delineated: spinal cord, mandible, parotids, and lips depending on the primary tumor site.

Table 1: Planning dose objectives for the OARs as per quantitative analysis of normal tissue effects in the clinic (QUANTEC) guidelines

OARs	Parameter	Plan objective
Spinal cord	Dmax	<45Gy
Mandible	Dmax	< 70 Gy
Lips	Dmean	<30 Gy
Unilateral Parotid	Dmean	<20 Gy
Bilateral Parotid	Dmean	<25 Gy

2.3.5. Treatment plan evaluation

All the patients were treated with linear accelerator (6MV) Truebeam with millennium MLC. The plans were created in the Eclipse Treatment Planning System (version 13.5) provided by Varian. Inverse planning with one or multiple optimizations and running was done to achieve the target dose distribution and OARs sparing. AAA algorithm was used for dose calculation after the optimization process.

There were 7-9 beams used in the IMRT plan while 2 arcs in RapidArc. In the RapidArc plan, 2 full arcs were used (ARC-I 181.1° to 179.9° and ARC-II 179.9° to 181.1° clockwise and counter-clockwise arcs respectively).

2.3.6. Concurrent chemotherapy

Irrespective of the technique used, all patients received chemotherapy with weekly cisplatin (40mg/m²) concurrently with RT either IMRT or RapidArc technique. All patients were monitored weekly for RT-induced mucositis and dermatitis as per the Radiation Therapy Oncology Group (RTOG) criteria. All patients were given symptomatic treatment and supportive care if acute reactions occurred.

2.3.7. Sample size calculation

The formula used for sample size calculation was as follows:

$n = (\sigma_1^2 + \sigma_2^2) (Z_\alpha + Z_\beta)^2 / (m_1 - m_2)^2$ where, Z_α = value of standard normal variate corresponding to a level of significance (1.96), Z_β = The standard normal deviate for desired power (1.282), m = average, σ = Standard deviation.

2.4. Statistical analysis

Data were described in terms of range; mean \pm standard deviation (\pm SD), frequencies (number of cases), and relative frequencies (percentages) as appropriate. A comparison of quantitative variables between the study groups was done using Mann Whitney *U* test for non-parametric data. For comparing categorical data, Chi-square (χ^2) test was performed and Fisher exact test was used when the expected frequency was less than 5. A probability value (*p-value*) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

3. Results

A total of 52 patients were included in this study after fulfilling the inclusion criteria. IMRT and RapidArc were the two arms of the study into which eligible patients were put after randomization. Analysis was conducted for 26 patients in each group.

The most common age group was 51-60 years in both the groups (42.31% vs. 38.46%). Oropharynx was the commonest site in IMRT and RapidArc group (34.62% vs. 46.15). Majority of the patients (61.54% vs. 57.73%) had Stage IV disease in IMRT and RapidArc group respectively. All patients in both the groups had ECOG performance status 2 (**Table 2**).

There was no statistically significant difference between IMRT and RapidArc techniques in terms of target dose coverage for PTV70 and PTV59.4 Gy (**Table 3**).

Table 2: Baseline characteristics

Baseline characteristics	IMRT (26)	RapidArc (26)
	No. of patients (%)	No. of patients (%)
Age (years)		
31-40	0	1 (3.85)
41-50	4 (15.38)	3 (11.54)
51-60	11 (42.31)	10 (38.46)
61-70	10 (38.46)	7 (26.92)
71-80	1 (3.85)	5 (19.23)
Primary tumor site		
Oral cavity	4 (15.38)	2 (7.69)
Oropharynx	9 (34.62)	12 (46.15)
Larynx	7 (26.92)	7 (26.92)
Hypopharynx	6 (23.08)	5 (19.23)
T-staging		
T1	4 (15.38)	1 (3.85)
T2	6 (23.08)	5 (19.23)
T3	9 (34.62)	12 (46.15)
T4	7 (26.92)	8 (30.77)
N-staging		
N0	9 (34.62)	8 (30.77)
N1	3 (11.53)	8 (30.77)
N2	13 (50)	8 (30.77)
N3	1 (3.85)	2 (7.69)
Group staging		
Stage III	10 (38.46)	11 (42.31)
Stage IV	16 (61.54)	15 (57.73)
ECOG Performance status		
1	3 (11.54)	5 (19.23)
2	22 (84.62)	21 (80.77)
3	1 (3.85)	-

The dose to OARs including mandible, lips, unilateral parotid, bilateral parotid, and spinal cord was similar for both IMRT and RapidArc techniques (**Table 4**). The average MU to deliver a dose of 2Gy per fraction in the RapidArc technique was 422.03 \pm 44.84 compared to 1000.65 \pm 150.20 with the IMRT technique ($p < 0.001$).

Our results showed that a higher percentage of patients treated with IMRT technique had grade 3 mucositis as compared to those treated with RapidArc, mainly in weeks 4 and 5 of RT, although not statistically significant. There was no difference noted between the two groups in terms of RT-induced dermatitis. In the IMRT group, a higher percentage of patients required treatment interruptions as compared to those in the RapidArc group (23.1% vs. 11.5%, $p = 0.09$).

Table 3: Dosimetric comparison between IMRT and RapidArc for PTV 70Gy, PTV59.4

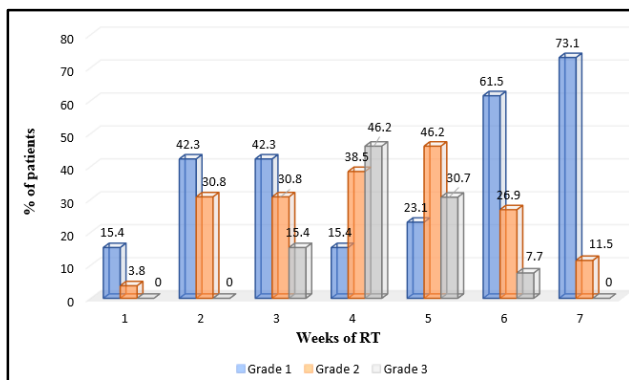
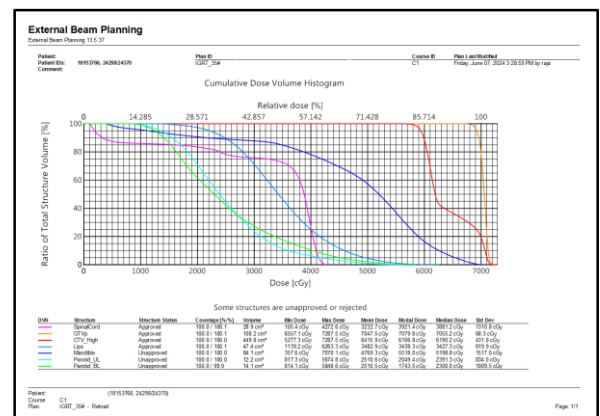
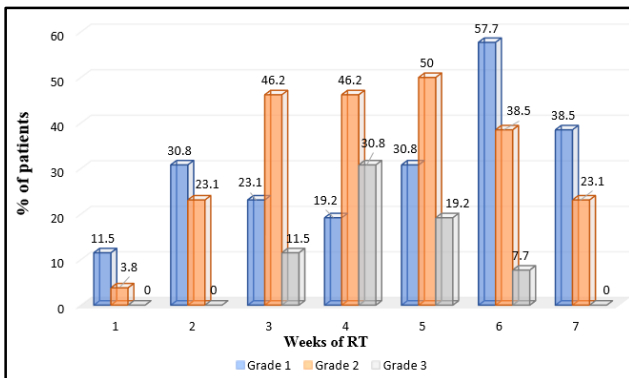
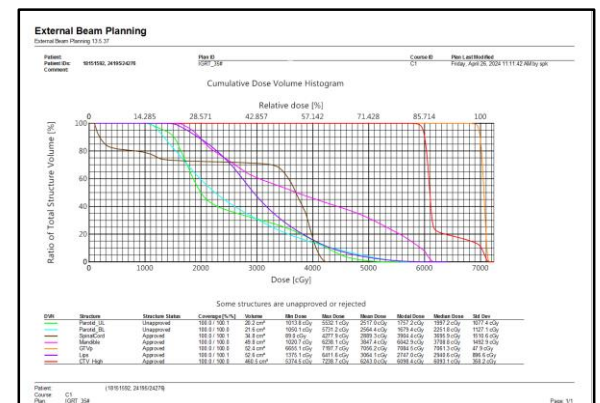
Parameters	IMRT	RapidArc	Chi-square value	p-value
PTV70				
HI	0.037 ± 0.01	0.038 ± 0.01	-1.28	0.20
CI	0.99 ± 0.03	0.99 ± 0.001	-0.65	0.51
D2%	71.48 ± 0.28	71.49 ± 0.18	-0.87	0.38
D98%	68.84 ± 0.42	68.80 ± 0.33	-1.16	0.24
PTV59.4				
HI	0.19 ± 0.04	0.20 ± 0.06	-0.38	0.70
CI	0.99 ± 0.03	0.96 ± 0.001	-0.65	0.51
D2%	71.21 ± 0.23	71.44 ± 1.17	-1.20	0.23
D98%	59.36 ± 2.83	58.22 ± 4.15	-1.94	0.05

IMRT: Intensity-Modulated Radiation Therapy, **HI:** Homogeneity Index

Table 4: Dosimetric comparison of doses to OARs between IMRT and RapidArc

OARs	IMRT	RapidArc	Chi-square test	p- value
Mandible	58.45 ± 14.11	66.53 ± 9.39	-1.56	0.11
Lips	20.18 ± 10.07	23.64 ± 11.49	-0.82	0.41
Unilateral parotid	21.17 ± 5.25	19.81 ± 4.88	-1.35	0.17
Bilateral Parotid	20.47 ± 4.94	18.87 ± 5.57	-1.02	0.30
Spinal cord	37.08 ± 7.31	40.12 ± 7.54	-2.34	0.01

OARs: Organs at Risk

**Figure 1:** Weekly grading of mucositis in the IMRT group**Figure 3:** Dose-volume histograms for a patient treated with the IMRT plan**Figure 2:** Weekly grading of mucositis in the RapidArc group**Figure 4:** Dose-volume histogram for a patient treated with the RapidArc plan

4. Discussion

IMRT technique with dynamic MLCs shapes the beams differently when emerging from different angles. The precision of IMRT not only allows the sparing of OARs but makes it possible to deliver inhomogeneous doses, facilitating simultaneous boost to the tumor and dose escalation in certain regions of the tumor.⁶ RapidArc is a specific type of IMRT that uses dynamic MLCs to achieve continuous adjustments, ensuring accurate target volume irradiation.

We found that the majority of patients in both groups were 51-60 years. Chauhan R et al.⁷ demonstrated the prevalence of HNC in North-Eastern India. The authors reported that the most common age group in their study was from 51 to 60 years followed by 61 to 70 years, 41 to 50 years, and 31 to 40 years constituting 26.60%, 21.60%, 21.40%, and 18.40% of the patients, respectively.

Our findings revealed that both IMRT and RapidArc techniques were comparable regarding homogeneity and conformity indexes. The study by Mashhour K et al⁵ illustrated that the PTV coverage was calculated using the ratio of target volume covered by 95% of the prescribed isodose line divided by the volume of PTV. The minimum and maximum doses within the PTV, the D98% and D2% values respectively were recorded. PTV coverage was nearly similar in both techniques.

Our study showed a similar possibility of sparing OARs including the mandible, lips, unilateral parotid, and bilateral parotids with both techniques. These findings enrich the existing data by favoring the various studies suggesting that IMRT and the RapidArc technique offer equivalent dose constraints to OARs. Jaiswal I et al⁷ demonstrated no statistical difference between the Dmax of the spinal cord, brainstem, and Dmean of parotids in the IMRT and RapidArc group. However, we found that the IMRT technique showed statistically significant better spinal cord sparing as compared to the RapidArc technique ($p=0.019$). Contrary to this, various studies by Studenski et al,⁸ Fung-Kee-Fung et al,⁹ and Leung et al¹⁰ demonstrated that only VMAT plans can achieve a higher value of maximum dose (Dmax) for the spinal cord.

Based on treatment compliance, we found that in the IMRT group, 92.31% of patients completed the prescribed treatment while 7.69% defaulted. In the RapidArc group, 88.46% of patients could complete the treatment while 11.54% did not. The reasons for non-compliance being generalized weakness, intolerability, and poor performance status. Our study showed the RapidArc plans required fewer MUs in comparison to the IMRT technique ($Z = -6.186$, $p = 0.001$). Infusino E⁴ demonstrated that the most significant observation in their study was the difference in terms of MUs and treatment time required to deliver the prescription dose daily between VMAT and IMRT. VMAT technique

delivered significantly fewer MUs per treatment session compared with the IMRT technique. Treatment time (including mode-up time) was significantly less with VMAT as compared to IMRT. Several studies have supported similar findings that the mean MU for the VMAT arm was significantly less than IMRT arm.^{4,5,7} Broggi et al¹¹ demonstrated 73% reduction of MUs for Rapid arc than IMRT technique. Higher MUs result in more exposure of healthy tissues to scattered radiation, and lower MUs proportionate to lower scattered radiation.¹²

We assessed the clinical difference in terms of toxicities such as radiation-induced mucositis, and dermatitis between IMRT and RapidArc techniques. However, patients treated with IMRT developed higher grade 3 mucositis with no difference in dermatitis compared to the RapidArc technique. The incidence of severe oral mucositis after IMRT has been reported to be 62.5% and 98.6% of patients developing some degree of oral mucositis following CRT.¹³ It has been reported that nearly 40% of patients developed grade 3 or more mucositis after CRT irrespective of the technique used. Several studies have demonstrated that the trajectory of oral mucositis in HNC patients undergoing radiotherapy such as the grade of mucositis increased from the initial days with a peak after the 4th week (26.9% of patients having grade ≥ 3 mucositis).¹⁴⁻¹⁶

To the best of our knowledge, none of the studies comparing IMRT with RapidArc in HNC have compared the two techniques with clinical toxicities. The merit of this study is that it favours RapidArc in terms of being more efficient in delivering the treatment than IMRT as it required fewer MUs. A limitation of this study is the small number of cases.

5. Conclusion

We found that IMRT and RapidArc techniques showed comparable target coverage and sparing of surrounding normal structures in head and neck cancer patients. RapidArc should be considered as a promising technique to reduce the daily radiation treatment time of head and neck cancers. IMRT could be expected to result in higher grade 3 mucositis and treatment interruptions as compared to RapidArc. However, our results require validation with further studies on the effects of IMRT and RapidArc to confirm these findings in an attempt to improve the outcomes in head and neck cancer patients.

6. Source of Funding

None.

7. Conflict of Interest

None.

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