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Original Research Article

Evaluation of Xerostomia and Dysphagia in Cases of Well Lateralized Carcinoma Oral Cavity Treated with IMRT or VMAT: Comparison of Dosimetry and Toxicity Outcome

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Abstract:

Introduction: Radiotherapy plays a pivotal role in the treatment of carcinoma of the oral cavity. However, associated toxicities like xerostomia and dysphagia significantly affect patient quality of life. Advancements in radiotherapy techniques, including Intensity-Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT), have aimed to improve dosimetric outcomes and reduce toxicity to organs at risk (OARs).

Aims: To compare acute and late toxicity in patients of well lateralized carcinoma of oral cavity treated with two different radiotherapy techniques: Intensity modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) with special interest in xerostomia and dysphagia

Materials and Methods: It was a Prospective Observational Study this study was conducted 2 years at the Department of Radiotherapy, Medical College Kolkata. 36 Patients were included in this study

Results: Target coverage was comparable in both groups with no significant differences in D95%, D50%, D2%, or D98%. VMAT demonstrated a significantly better conformity index ($p < 0.002$) and reduced doses to the parotid glands and pharyngeal constrictors ($p < 0.001$). Treatment time and MUs were significantly lower in the VMAT group ($p < 0.0001$). Although not statistically significant, VMAT showed a trend toward lower incidences of Grade 2 dysphagia and xerostomia at all-time points. No Grade 3 toxicities were reported in either group.

Conclusion: VMAT provides superior conformity and reduced dose to critical OARs, along with shorter treatment times and fewer monitor units compared to IMRT. Clinically, VMAT is associated with a trend toward lower rates of xerostomia and dysphagia, supporting its potential as the preferred technique in well-lateralized oral cavity cancers.

Keywords: Oral cavity carcinoma, IMRT, VMAT, xerostomia, dysphagia, dosimetry, toxicity, radiotherapy planning.

Introduction

As per GLOBOCAN 2022 data, lip & oral cavity cancer ranks the 16th in incidence (389,846 cases) and 15th in mortality (188,438 deaths) among all cancers worldwide [1]. More than 500,000 cases of Oral cavity cancers are diagnosed worldwide, and 40,000 to 60,000 cases occur in the India annually [2]. In India the scenario is worse where Lip & oral cavity cancers rank 2nd in both overall incidence (143,789 cases) and mortality (79,979 deaths) [3]. About 57.5% of global oral cavity cancers occur in Asia with India contributing a large proportion to the global burden where it accounts for 30% of all cancers in men and approximately 14% in females [4]. It is the most common cancer of males in India and fourth most common cancer in females. Majority of patients in India present in locally advanced stage. The cause of late presentation might be ignorance towards healthcare, patient preference to alternative medicines as initial treatment & poor penetration of health education programmes. Most patients are older than 50 years, incidence increases with age, and the male-to-female ratio is 2:1 to 5:1. Death rates have been decreasing since at least 1975, with rates declining more rapidly in the past decade [4]. Human papillomavirus (HPV)–related oral cavity cancers that is increasing in number and is associated with a better prognosis, in part due to better response to treatment.[5,6] Common risk factors include tobacco (smoking tobacco and other forms) and alcohol intake. Heavy alcohol consumption increases the risk of developing oral cavity cancer 2- to 6-fold, whereas smoking increases the risk 5- to 25-fold, depending on gender, race, and the amount of smoking. Both factors together increase the risk 15- to 40-fold. Smokeless/chewing tobacco and snuff are associated with oral cavity cancers. Use of smokeless tobacco, or chewing betel with or without tobacco, and slaked lime (common in many parts of Asia and some parts of Africa), is associated with premalignant lesions and oral squamous cancers. Chronic dental irritation due to ill-fitting dentures, sharp teeth, or inflammatory lesions like oral lichen planus also predispose to oral cavity cancers. [7] To compare acute and late toxicity in patients of well lateralized carcinoma of oral cavity treated with two different radiotherapy techniques: Intensity modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) with special interest in xerostomia and dysphagia

Materials and Methods

Study Design: Prospective Observational Study.

Study Area: Department of Radiotherapy, Medical College Kolkata.

Study Period: Began on the day of approval of synopsis 2Years.

Study Population: Patients attending the Outpatient department (OPD) of the Department of Radiotherapy, Medical College Kolkata during the study period who are biopsy proven cases of oral cavity cancer and who fits the inclusion and exclusion criteria.

Sample Size: Total 36 patients with well-lateralized carcinoma of the oral cavity were evaluated.

Inclusion Criteria: Patients eligible for inclusion in the study were biopsy-proven, well-lateralized cases of squamous cell carcinoma of the oral cavity who required postoperative radiotherapy. Eligible participants were aged between 18 and 70 years, with a Karnofsky Performance Status (KPS) of ≥70, and had undergone a complete preoperative evaluation showing no evidence of contralateral neck node involvement on both clinical and radiological assessment. Only patients classified as AJCC stage I to IVA were included. All participants were required to provide informed consent prior to enrollment. Additionally, patients underwent comprehensive clinical, biochemical, and dental evaluations to confirm their fitness to receive radiotherapy, with or without concurrent chemotherapy.

Exclusion Criteria: Exclusion criteria included tumors arising from subsites of the oral cavity such as the minor salivary glands or histologies other than squamous cell carcinoma, including adenocarcinoma, lymphoma, and others. Patients who had received neoadjuvant chemotherapy or radiotherapy prior to surgery for the primary disease, or those with a history of prior radiotherapy for an earlier oral cavity carcinoma, were excluded. Additionally, individuals found to have metastatic disease at the time of evaluation, as well as pregnant or lactating women, were not considered eligible for the study.

Study Variable

- Sex
- Addiction History
- Primary Site
- AJCC Stage
- KPS Score
- Total Dose
- Target Volume Dosimetry
- Organs at Risk (OARs)
- Treatment Delivery Parameters
- Dysphagia
- Xerostomia

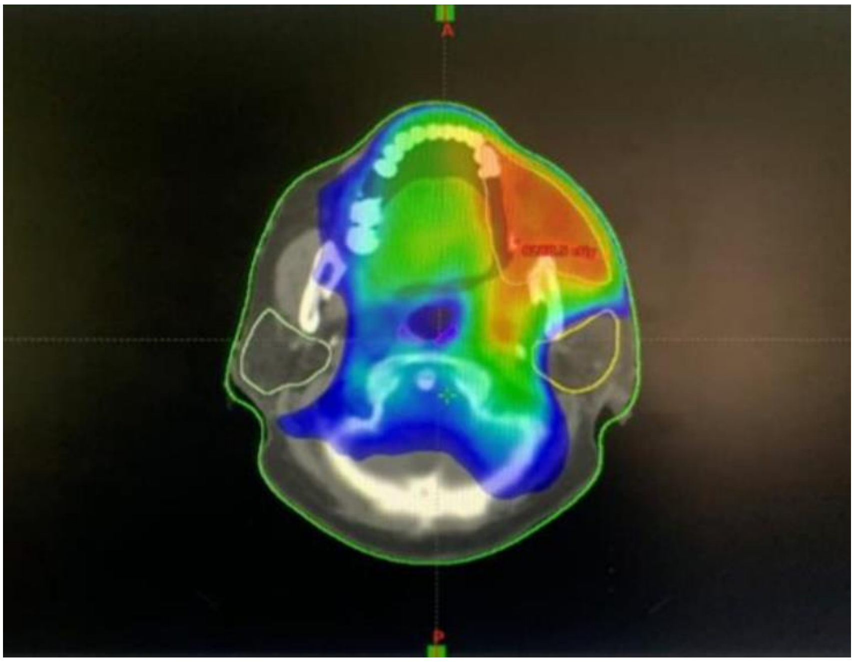

Figure 1: Contouring of PTV sparing the bilateral parotids (yellow) and pharyngeal constrictor (pink)

Methodology

All patients included in the study were biopsy-proven cases of oral cavity carcinoma who met the inclusion and exclusion criteria and provided informed consent. Eligible patients received radiotherapy (RT) to the oral cavity and were assigned to either the IMRT or VMAT group. Patients who did not meet the criteria or refused consent were excluded.

All patients were monitored for acute toxicities throughout the treatment course and up to three months post-treatment. Subsequently, they were assessed for late toxicities such as dysphagia and xerostomia.

Treatment response was evaluated six weeks after completion of therapy through detailed history-taking, clinical examination, and radiological imaging, with follow-up assessments conducted every three months. Local recurrence and distant metastasis were identified based on clinical findings and confirmed with radiological imaging, including MRI, CT, or PET-CT scans, and histopathological confirmation when necessary.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Association between two groups with all parameters

	Particulars	IMRT Group (n = 18)	VMAT Group (n = 18)	P Value
	Age (Median)	50 years	52 years	
Sex	Male	14 (77.8%)	13 (72.2%)	0.7003
	Female	4 (22.2%)	5 (27.8%)	
Addiction History	Tobacco	3 (16.7%)	7 (38.9%)	0.4929
	Alcohol	2 (11.1%)	2 (11.1%)	
	Tobacco + Alcohol	5 (27.8%)	4 (22.2%)	
	None	8 (44.4%)	5 (27.8%)	
Primary Site	Buccal mucosa	9 (50.0%)	10 (55.6%)	0.99965
	Floor of mouth	4 (22.2%)	5 (27.8%)	
	Gingiva	2 (11.1%)	2 (11.1%)	
	Hard palate	1 (5.6%)	1 (5.6%)	

	RMT	1 (5.6%)	1 (5.6%)	
AJCC Stage	Stage I	1 (5.6%)	1 (5.6%)	0.9832
	Stage II	3 (16.7%)	3 (16.7%)	
	Stage III	4 (22.2%)	5 (27.8%)	
	Stage IV	10 (55.6%)	9 (50.0%)	
KPS Score	90–100	12 (66.7%)	13 (72.2%)	0.7174
	70–90	6 (33.3%)	5 (27.8%)	
Total Dose	60 Gy	10 (55.6%)	10 (55.6%)	1.0000
	66 Gy	8 (44.4%)	8 (44.4%)	

Table 2: Distributions of mean with all parameters

	Parameters	**IMRT Plan (Mean ± SD)**	**VMAT Plan (Mean ± SD)**	**P Value (Unpaired T-Test)**
Target Volume Dosimetry	D95%	58.59 ± 0.68	58.68 ± 0.66	0.773
	D50%	60.50 ± 0.44	60.69 ± 0.34	0.093
	D2% (Dnear max)	61.71 ± 0.68	62.02 ± 0.27	0.126
	D98% (Dnear min)	57.71 ± 0.85	57.47 ± 0.99	0.569
	Conformity Index (CI)	1.29 ± 0.13	1.14 ± 0.09	<0.002
	Homogeneity Index (HI)	0.06 ± 0.01	0.07 ± 0.01	0.147
Organs at Risk (OARs)	Parotid mean dose (Gy)	24.20 ± 2.28	22.42 ± 2.18	<0.001
	Pharyngeal constrictor (Gy)	43.52 ± 1.86	42.17 ± 1.39	<0.001
	Brainstem (Gy)	38.59 ± 5.82	39.05 ± 4.32	0.07
	Mandible (Gy)	62.48 ± 1.05	63.10 ± 0.49	0.076
	PRV Spine (Gy)	39.54 ± 2.65	40.18 ± 2.35	0.525
	Right Cochlea (Gy)	12.19 ± 5.53	13.49 ± 5.87	0.652
	Left Cochlea (Gy)	20.32 ± 12.04	20.30 ± 9.36	0.994
Treatment Delivery Parameters	Treatment Time per Fraction (minutes)	3.95 ± 0.85	1.21 ± 0.34	<0.0001
	Monitor Units (MUs)	1581.6 ± 341.78	486.9 ± 136.23	<0.0001

Table: 3 Comparison of Dysphagia (Late Toxicity) and xerostomia Between Two Treatment Groups

Toxicity	**Time Point**	**Grade**	**IMRT Group (n = 18)**	**VMAT Group (n = 18)**	**P-value (Chi-square)**
Dysphagia	Month 3	Grade 1	8 (44.44%)	10 (55.55%)	0.64
		Grade 2	10 (55.55%)	8 (44.44%)	
	Month 6	Grade 1	12 (66.66%)	15 (83.33%)	0.32
		Grade 2	6 (33.33%)	3 (16.66%)	
	Month 9	Grade 1	14 (77.77%)	16 (88.88%)	0.09
		Grade 2	4 (22.22%)	2 (11.11%)	
Xerostomia	Month 3	Grade 1	6 (33.33%)	8 (44.44%)	0.35
		Grade 2	12 (66.66%)	10 (55.55%)	
		Grade 3	0 (0%)	0 (0%)	
	Month 6	Grade 1	7 (38.88%)	9 (50.00%)	0.22
		Grade 2	11 (61.11%)	9 (50.00%)	
		Grade 3	0 (0%)	0 (0%)	
	Month 9	Grade 1	9 (50.00%)	13 (72.22%)	0.07
		Grade 2	9 (50.00%)	5 (27.77%)	
		Grade 3	0 (0%)	0 (0%)	

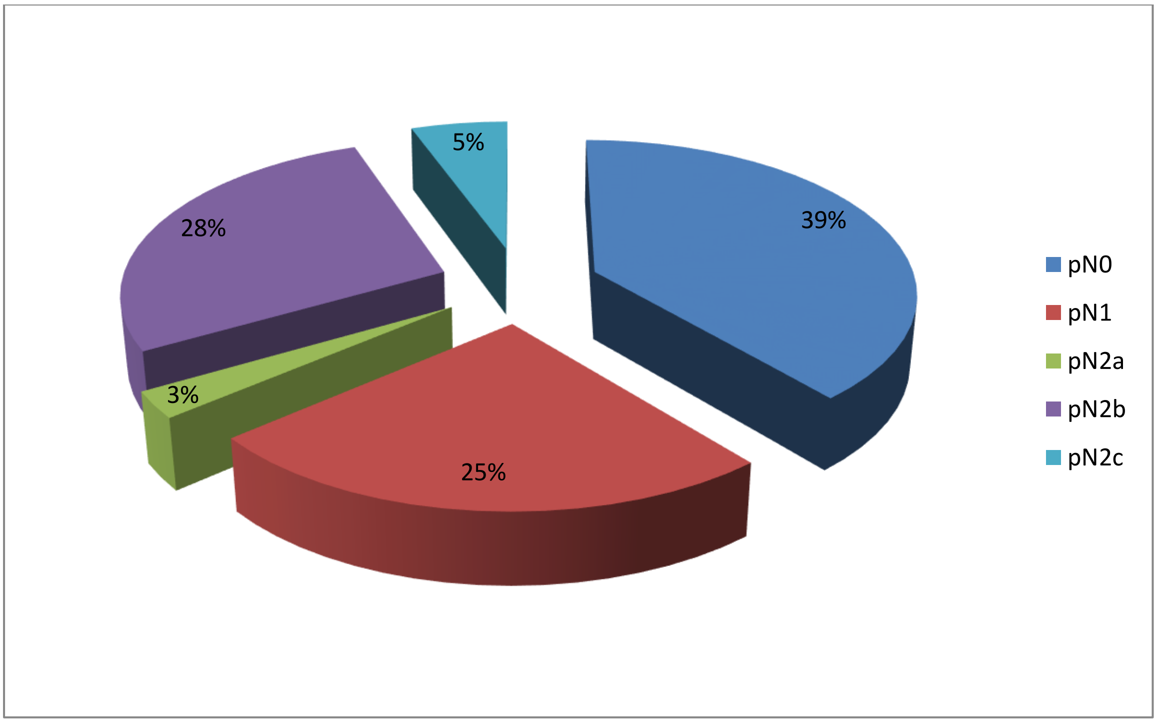

Figure 1: Distribution of N stage

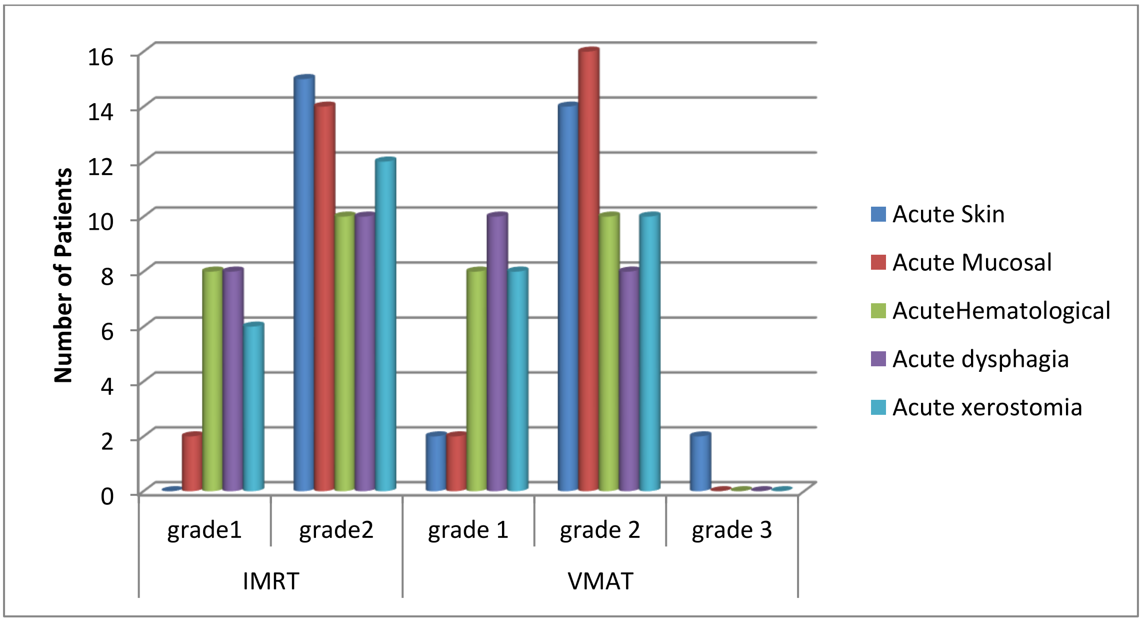

Figure 2: Acute toxicity between the IMRT treatment and VMAT treatment groups

A total of 36 patients with well-lateralized carcinoma of the oral cavity were included in the study, with 18 patients each in the IMRT and VMAT groups. The median age was comparable between the two groups (50 years for IMRT vs. 52 years for VMAT). Males predominated in both groups, comprising 77.8% of the IMRT group and 72.2% of the VMAT group (p = 0.7003). Addiction history showed no significant difference, with tobacco use noted in 16.7% (IMRT) and 38.9% (VMAT), alcohol use alone in 11.1% of both groups, and combined tobacco and alcohol use in 27.8% (IMRT) and 22.2% (VMAT). Patients with no addiction history were slightly more common in the IMRT group (44.4% vs. 27.8%). The primary tumor site was most commonly the buccal mucosa in both groups (50.0% in IMRT vs. 55.6% in VMAT), followed by the floor of the mouth, gingiva, hard palate, and retromolar trigone, with no significant intergroup difference (p = 0.99965). Disease staging based on AJCC classification revealed a similar distribution, with Stage IV being most common (55.6% in IMRT vs. 50.0% in VMAT), followed by Stage III, II, and I (p = 0.9832). Karnofsky Performance Status (KPS) scores were also comparable, with 66.7% of patients in the IMRT group and

72.2% in the VMAT group scoring between 90–100 (p = 0.7174). Regarding radiation dose, both groups had identical distributions, with 55.6% receiving 60 Gy and 44.4% receiving 66 Gy (p = 1.0000).

Target volume dosimetry revealed no statistically significant difference between the IMRT and VMAT plans for D95% (58.59 ± 0.68 Gy vs. 58.68 ± 0.66 Gy; p = 0.773), D50% (60.50 ± 0.44 Gy vs. 60.69 ± 0.34 Gy; p = 0.093), D2% (61.71 ± 0.68 Gy vs. 62.02 ± 0.27 Gy; p = 0.126), and D98% (57.71 ± 0.85 Gy vs. 57.47 ± 0.99 Gy; p = 0.569). However, the conformity index (CI) was significantly better in the VMAT group (1.14 ± 0.09) compared to the IMRT group (1.29 ± 0.13; p < 0.002), while the homogeneity index (HI) remained comparable (0.06 ± 0.01 vs. 0.07 ± 0.01; p = 0.147). Among organs at risk (OARs), the VMAT plan demonstrated significantly lower mean doses to the parotid glands (22.42 ± 2.18 Gy vs. 24.20 ± 2.28 Gy; p < 0.001) and pharyngeal constrictors (42.17 ± 1.39 Gy vs. 43.52 ± 1.86 Gy; p < 0.001). No significant differences were observed for brainstem (p = 0.07), mandible (p = 0.076), PRV spine (p = 0.525), or cochlear doses (right: p = 0.652; left: p = 0.994). Regarding treatment delivery, VMAT significantly reduced the treatment time per fraction (1.21 ± 0.34 minutes vs. 3.95 ± 0.85 minutes; p < 0.000) and required fewer monitor units (486.9 ± 136.23 vs. 1581.6 ± 341.78; p < 0.0001), indicating superior efficiency

The incidence and severity of dysphagia and xerostomia were assessed at 3, 6, and 9 months post-treatment in both IMRT and VMAT groups. For dysphagia, no statistically significant differences were observed between groups at any time point. At 3 months, Grade 1 dysphagia was reported in 44.44% of IMRT patients versus 55.55% in VMAT, while Grade 2 was observed in 55.55% vs. 44.44%, respectively (p = 0.64). By 6 months, Grade 1 dysphagia increased to 66.66% (IMRT) and 83.33% (VMAT), and Grade 2 decreased to 33.33% and 16.66%, respectively (p = 0.32). At 9 months, most patients experienced only Grade 1 dysphagia (77.77% IMRT vs. 88.88% VMAT), with a small proportion showing Grade 2 (22.22% vs. 11.11%; p = 0.09).

Similarly, xerostomia showed a gradual reduction in severity over time, with no significant intergroup differences. At 3 months, Grade 1 xerostomia was observed in 33.33% (IMRT) vs. 44.44% (VMAT), and Grade 2 in 66.66% vs. 55.55%, respectively (p = 0.35). No cases of Grade 3 xerostomia were reported at any time point. By 6 months, Grade 1 xerostomia was present in 38.88% (IMRT) vs. 50.00% (VMAT), while Grade 2 occurred in 61.11% vs. 50.00% (p = 0.22). At 9 months, Grade 1 xerostomia improved further to 50.00% (IMRT) and 72.22% (VMAT), while Grade 2 cases dropped to 50.00% and 27.77%, respectively (p = 0.07). These findings suggest a trend toward lower toxicity with VMAT, although the differences were not statistically significant.

The majority of patients had nodal involvement, with pN2b being the most common (29%), followed by pN0 (37%), pN1 (26%), pN2c (6%), and pN2a (3%) Acute toxicities were assessed in both IMRT and VMAT groups, showing a statistically significant overall difference (p = 0.0058). Grade 2 skin toxicity was common in both groups (83.3% IMRT vs. 77.8% VMAT), with slightly more Grade 3 cases in VMAT (11.1%) than IMRT (5.6%). Mucosal toxicity was predominantly Grade 2 in both groups, though Grade 3 was seen only in IMRT (11.1%). Hematological toxicity patterns were identical, with 44.4% Grade 1 and 55.6% Grade 2 in both groups. Dysphagia was more often Grade 1 in VMAT (55.6%) and Grade 2 in IMRT (55.6%), while xerostomia also showed a higher proportion of Grade 1 cases in VMAT (44.4%) compared to IMRT (33.3%). No Grade 3 hematological, dysphagia, or xerostomia toxicities were observed in either group.

Discussion

In our study, the dose distribution of the target volume and OAR sparing was comparable amongst both the techniques with significant improvement in conformity was seen with the VMAT technique. A marked difference was a reduction in treatment delivery time (3.95±0.85 mins for IMRT vs 1.21±0.34 mins for VMAT; p<0.0001). This was reduced to nearly one third in the VMAT technique. A similar trend was observed in Monitor Units showing a significant reduction in VMAT technique (1581.6±341.78 vs 486.9±136.23, p<0.0001). As per the findings of our study, VMAT largely reduces the treatment delivery times but did not compromise the planning quality. The reduction in monitor units with the VMAT technique will possibly reduce the total body exposure and the integral dose. Because of the increasing patient load in the radiotherapy department over the period, the waiting time and smooth running become cumbersome. The implementation of the VMAT technique offers an efficient solution to this problem with optimal radiotherapy plans. This is particularly because of the reduction in treatment delivery time by VMAT technique as fewer MUs are required to deliver the prescribed dose with arc beam arrangement. Also chances of intra fraction motion are minimized. The treatment time saved can be utilized in the implementation of more online imaging technologies. But the associated problem is that the VMAT technique is known to have a learning curve and requires a much higher planning time. Studenski M T et al in their study on 20 patients found no significant difference in the dosimetric parameters for both IMRT and VMAT techniques. But there was a significant reduction in treatment delivery times with VMAT plans with an average reduction of 9.2±3.9 min over IMRT plans. Also, there was a significant reduction in monitor units. [8]. In our study also there was a reduction in treatment delivery times by 2.74±0.51 mins in VMAT plans over IMRT plans. This study validated the findings of our study with comparable dosimetry amongst both IMRT and VMAT plans but a significant reduction in the treatment delivery time and MU's [9]. Kryger M et al in a study on 14 patients comparing the dosimetric parameters showed that the VMAT and IMRT plans were comparable in conformity and homogeneity [10].

Although few studies have shown better planning with VMAT over IMRT technique while others have shown comparable dosimetric parameters with both techniques. With a growing incidence of cancer, there is an increase in the patient burden over centres and to have a smooth and efficient running we need to optimize the treatment delivery as well as planning times. Therefore, a validation of the contemporary conformal technique, IMRT and VMAT in terms of dosimetric comparison, and treatment time are needed.

In our study, conformity was significantly better in VMAT treatment group compared to IMRT treatment group (p<0.002). The treatment planning time will play a significant role in VMAT for one accepted plan will take approximately 4-5 hours whereas in IMRT, it will take only half an hour. We could have used the high-definition MLCs, because of the lesser thickness of the MLC, it might play a major role in sparing the OARs. Possibilities of improving the target dose distribution are also there. Holt A et al in a multi-institutional study showed better sparing for almost all OARs with VMAT with no significant difference in the PTV coverage, dose homogeneity and conformity. Similarly, in our study there was a significant reduction in the dose to parotid glands VMAT technique compared to IMRT technique (22.42Gy vs 24.20 Gy for parotids and 42.17 gy vs 43.52 Gy for pharyngeal constrictor, p<0.001) respectively.

On comparison of acute toxicity between the patients treated with IMRT and VMAT, no significant change was noted between the two arms in terms of skin, oral mucosa, pharynx, salivary gland and haematological toxicities. Similar to Studenski M T et al [8], a positive trend was noted for recovery of late salivary gland toxicity/xerostomia and dysphagia on follow up.

At 3 months, here was no statistically significant difference between the both arms. On follow up at 9 months, more patients recovered from grade 2 xerostomia in the VMAT treatment group than the patients in IMRT treatment group which was near significant value (pvalue-0.07). Similar trend was also seen in grade 2 dysphaia though the results were not significant.

Our study has two limitations. Firstly, the sample size is small and secondly, long term clinical outcomes are not known. Most of the studies in the literature have compared dosimetry only and an emphasis on the clinical outcomes and toxicity has not been laid. Large scale studies with clinical outcomes are required to support the widespread implementation of the VMAT technique.

Conclusion

The study suggests that VMAT technology can shorten delivery times and improve recovery from oral cavity cancer patients compared to IMRT. This method is safe for radiation centers with a growing patient load and can reduce the waiting list.

VMAT improves dosimetry parameters and reduces volumetric changes during definitive conformal radiation treatment. However, significant toxicity results and tumor clinical fate information may require randomized research with a larger sample size and longer follow-up.

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