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ORIGINAL RESEARCH ARTICLE

Assessment of Radiation-Induced Xerostomia in Patients of Head and Neck Cancers: A Comparative Study of Three-Dimensional Conformal Radiotherapy and Intensity Modulated Radiotherapy

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ABSTRACT

Introduction: Radiotherapy is a cornerstone in the management of head and neck cancers, but radiation-induced xerostomia remains one of the most common and debilitating late toxicities, significantly affecting long-term quality of life. With the advent of conformal radiotherapy techniques, particularly intensity-modulated radiotherapy (IMRT), better sparing of salivary glands has been achieved compared to three-dimensional conformal radiotherapy (3DCRT). This study aimed to compare the incidence, severity, and recovery of radiation-induced xerostomia between 3DCRT and IMRT using objective, subjective, and quantitative assessment tools.

Materials and Methods: This prospective randomized study included 50 previously untreated patients with locally advanced head and neck cancers, randomly assigned to receive either 3DCRT (Group I, n=25) or IMRT (Group II, n=25). All patients received a total dose of 70 Gy in 35 fractions over 7 weeks with concurrent weekly cisplatin (35 mg/m²). Xerostomia was assessed at baseline, at completion of radiotherapy, and at 3 and 6 months post-treatment using RTOG morbidity criteria (objective), EORTC H&N35 quality-of-life questionnaire (subjective), and the Saxon test for quantitative salivary flow measurement. Parotid mean doses were recorded and correlated with xerostomia outcomes. Statistical analysis was performed using the chi-square test, with $p < 0.05$ considered significant.

Results: At completion of radiotherapy, both groups demonstrated a significant reduction in salivary flow rates with no statistically significant difference in acute xerostomia. During follow-up, recovery of salivary function was observed in both groups; however, the IMRT group showed significantly better recovery at 3 months ($p = 0.02$) and 6 months ($p = 0.01$). Quantitative salivary flow rates at 6 months approached baseline values more closely in the IMRT group. Although objective RTOG xerostomia grades did not show a statistically significant difference between the two groups, subjective assessment using EORTC H&N35 revealed significantly better quality-of-life scores in the IMRT group for head and neck pain, swallowing, speech, and sensory domains. Mean parotid doses were substantially lower in the IMRT group, correlating with improved salivary flow recovery.

Conclusion: IMRT offers a significant advantage over 3DCRT in reducing the severity and improving the recovery of radiation-induced xerostomia in patients with head and neck cancers. While acute xerostomia remains comparable between techniques, IMRT demonstrates superior long-term salivary gland function preservation and better quality-of-life outcomes, supporting its preferential use in curative-intent treatment of head and neck malignancies.

Keywords: Xerostomia, IMRT, 3DCRT.

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INTRODUCTION

Radiotherapy is an important therapeutic modality in the treatment of head and neck cancers with curative intent and is used either as a primary or adjuvant treatment modality. The radiation-induced adverse events manifest as either acute reactions or delayed reactions. The acute reaction includes mucositis and difficulty in swallowing. The delayed effects include xerostomia, nocturnal dry mouth, and difficulty in swallowing, speech, dental caries, periodontitis and osteoradionecrosis. This would compromise the outcome of the patient with respect to the long-term physiological functioning and quality of life.[1]

The most common delayed morbidity is xerostomia, which describes both the subjective sensation of oral dryness and objective reduction in salivary function and subjective experience of dry mouth with reduced salivary gland flow. It has a profound negative impact on quality of life as it has a considerable negative global impact, resulting in shame, anxiety, disappointment, and verbal communication difficulties. There should, therefore, be more efforts to decrease this delayed morbidity.

There are various techniques to deliver radiotherapy in head and neck cancer patients. The conventional

techniques of radiotherapy (two-dimensional) treat large volumes of normal tissue, causing more toxicity such as xerostomia, dysphagia and fibrosis of the skin. Newer conformal techniques like three-dimensional conformal radiotherapy (3DCRT) and intensity modulated radiotherapy (IMRT) have improved target coverage and limited the dose to the surrounding organs at risk (OARs). After the advent of IMRT, there is increased sparing of the salivary gland, resulting in a decrease in the incidence of xerostomia. But as xerostomia is a subjective experience, there is still an incidence of dry mouth in patients treated by IMRT.[1]

This study is comparing both the conformal techniques of radiotherapy with assessment tools and assessing the incidence of xerostomia and recovery of salivary flow and the impact of xerostomia on quality of life. The relation of dose delivered to the parotid glands in both the conformal techniques and their impact on xerostomia will also be discussed in further headings.

MATERIAL AND METHODS

For the present study, previously untreated fifty patients of histologically proven locally advanced head and neck malignancies were selected. Patients are allotted to each group based on simple randomization.

Patient Selection

Inclusion criteria

Previously untreated patients of histologically proven malignancies of the head and neck region; age ≥ 18 years; ECOG performance status 0-2; normal haemogram, renal and liver function tests; normal ECHO.

Exclusion criteria

Pre-existing salivary gland disease; patients with prior or synchronous malignancy; tumor involving the parotid gland; distant metastasis; previously radiotherapy or chemotherapy treated patients.

Patients were randomized into two groups (25 each) as follows:

- Group I was planned by 3-dimensional radiotherapy (70 Gy/35 fractions) over weeks with concurrent cisplatin 35 mg/m^2 given every week.
- Group II was planned by intensity modulated radiotherapy (70 Gy/35 fractions) over 7 weeks with concurrent cisplatin 35 mg/m^2 given every week.

Radiotherapy Planning and Technique

Immobilization

The patients who were planned for radiotherapy were immobilized using a fixed 5-point thermoplastic cast system.

Simulation

All patients underwent a contrast-enhanced CT (CECT) scan and radiotherapy planning (RTP).

- Contrast-enhanced CT neck was performed with a flat table insert.
- CT images of the simulation were acquired with the patient in the supine and treatment position, along with fiducial markers.
- The axial images were obtained with a 3 mm slice thickness.

These images were transferred through Digital Imaging and Communications in Medicine (DICOM-CT) into the eclipse treatment planning system (Version 8.6.17, Varian Medical System, Inc., Palo Alto, CA, US).

Organ	*Whole organ*	*Dose constraints*	*Criteria*
PRV spine	Partial organ	Dmax≤ 50	QUANTEC
Mandible	Whole organ	Point Dose<70	Emami 20133
		1cc<75	RTOG
Brainstem	Whole organ	Dmax<54	QUANTEC
		D1-10cc ≤ 59	QUANTEC
		Dmax<64(Pointdose<1cc)	QUANTEC
Parotid gland	Unilateral Whole gland	Mean Dose<20	QUANTEC
	Bilateral Whole gland	Mean Dose<25	QUANTEC
	Bilateral Whole gland	Mean Dose<26	QUANTEC
Cochlea	Whole organ	Mean Dose ≤45	QUANTEC
Lips		Dmean<30	RTOG
Optic nerve/optic chiasma	Whole organ	Dmax<55	RTOG
		52 Gy when target is oropharynx	QUANTEC

Delineation of structures

A gross tumor volume (GTV), including the gross tumor and positive regional lymph nodes, was contoured. The clinical target volume (CTV) was defined as per RTOG Guidelines.[2] The OARs were also contoured. A margin of 7 mm was taken for PTV. All the patients were planned for 3DCRT or IMRT techniques. The total prescription dose was 70 Gy in 35 Fractions to the target Mean.

Dosimetric parameters

All plans were aimed to achieve a minimum dose of >95% and a maximum dose <107% of the prescribed dose.

Field 3D CRT technique

- Five fields were created for five different gantry angles.
- Plans were normalised for PTV.
- The completed plan was evaluated by isodose coverage and DVH. If the coverage of PTV and tolerance to OAR were not achieved, the beam angles and weightage were adjusted to achieve the goal.

IMRT technique

- Coplanar 7 to 9 fields around the isocenter using isotropic gantry angles were used.
- In the next step of fluence optimization, the parameters of PTV and OARs were defined as follows.
- Plans were evaluated by DVH and isodose distributions.

Chemotherapy administration

- Patients received Inj. cisplatin 35 mg/m^2 weekly
- Patients were adequately hydrated with 2 to 2.5 litres of I.V fluids and supplemented with Inj.KCL, Inj. $MgSo_4$.
- Radiotherapy was delivered within 1 hour of the administration of cisplatin.
- Proper antiemetic therapy with 5-HT_3 antagonist, dexamethasone, and ranitidine was given prior to chemotherapy administration.

Assessment of xerostomia

Assessment was done pre-radiotherapy and post-radiotherapy at completion of radiotherapy, at 3 months, and at 6 months of follow-up.

- *Subjective*

EORTC head and neck 35 quality of life questionnaire for analysis of data. (Annexure I).[4]

- *Objective*

RTOG radiation morbidity scoring schema.

Grade	Description
Grade 0	None
Grade 1	Slight dryness of the mouth and good response to stimulation
Grade 2	Moderate dryness of the mouth, poor response to stimulation
Grade 3	Complete dryness of the mouth, no response to stimulation
Grade 4	Fibrosis
Grade 5	Death directly related to radiation effects

- *Quantitative*

The Saxon test (a quantitative test for Xerostomia) - A simple, reproducible, and low-cost test for Xerostomia. A sterile 10 x 10 cm gauze was first folded twice at *90"* angles (final size 5 x *5* cm) and placed in a sterile, screw-topped 60 mL plastic tube, and the dry gauze and tube were weighed. After swallowing to remove any preexisting oral fluid, saliva was collected by having the individual vigorously chew on the gauze for exactly *2* minutes. After chewing the gauze, the patient replaced it in the same tube, and the amount of saliva produced in 2 minutes was determined by subtracting the original weight from the weight obtained after chewing. Weights were measured on a Mettler laboratory balance (pan weighing machine), which is accurate to gm.

Grade	Flow rate per Min
Grade 1	Flow > 0.2 mL/Min
Grade 2	Flow 0.1–0.2 mL/Min
Grade 3	Flow < 0.1 mL/Min

- *Follow-up*

The patients were followed up at least for a period of 6 months from the day of completion of treatment.

- *Statistical analysis*

Collected data was analyzed using standard statistical methods and software to calculate the level of significance using the *p-value* by using the chi-square test.

RESULTS

A total of 50 patients with locally advanced head and neck cancers were recruited from October 2016 to January 2018 for this study. The patients were selected according to the inclusion and exclusion criteria as mentioned earlier. Treatment consisted of radiotherapy [70 Gy/35 fractions, 2 Gy/fraction over 7weeks] with concurrent cisplatin (35 mg/m^2/week) in both groups. Patients were treated by either the 3DCRT technique (Group I) and IMRT technique (Group II).

Table 1: Patient characteristics

	Group I N (%)	Group II N (%)
Sex distribution		
Male	20 (80)	23 (92)
Female	05 (20)	02 (08)
Age		
18–30	01 (4)	0
30–40	0	0
41–50	05 (20)	04 (16)
51–60	08 (28)	09 (36)
61–70	07 (24)	07 (28)
71 and above	04 (12)	05 (20)
Stage		
Stage I	0	0
Stage II	7 (28)	7 (28)
Stage III	17 (68)	15 (60)
Stage IV	1 (4)	3 (12)
Primary tumor site-wise distribution		
Oral Cavity	1 (4)	2 (8)
Oropharynx	16 (64)	12 (48)
Hypopharynx	02 (08)	04 (32)
Larynx	06 (24)	06 (24)
Others	0	01 (04)

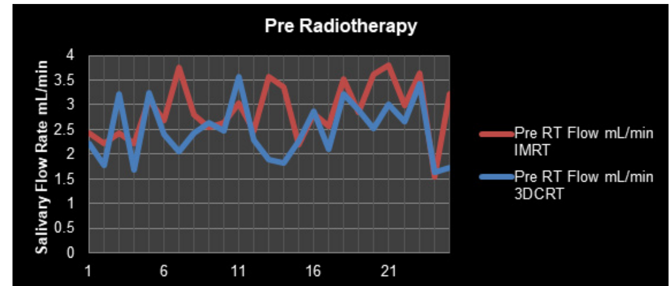

Figure 1: Pre-radiotherapy salivary flow rates (3DCRT vs IMRT)

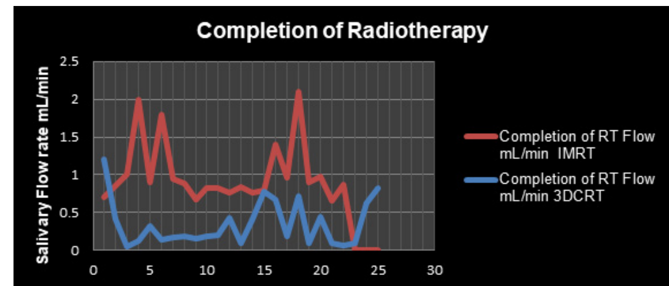

Figure 2: Completion of radiotherapy salivary flow rates (3DCRT VS IMRT)

Table 2: Quantitative salivary flow rates of group I (3DCRT)

Patient No	*Pre-RT flow (mL/min)*	*Flow at completion (mL/min)*	*Flow at 3 months (mL/min)*	*Flow at 6 months (mL/min)*
1	2.21	1.21	2.02	2.0
2	1.78	0.42	0.53	0.64
3	3.21	0.05	0.1	0.23
4	1.68	0.12	0.08	0.16
5	3.25	0.32	0.78	1.22
6	2.41	0.14	0.54	0.87
7	2.05	0.17	0.38	0.56
8	2.44	0.19	0.29	0.69
9	2.64	0.16	0.29	0.49
10	2.47	0.18	0.23	0.43
11	3.57	0.2	0.22	0.44
12	2.3	0.43	0.63	0.83
13	1.89	0.1	0.3	0.53
14	1.83	0.42	0.54	0.74
15	2.26	0.78	1.23	1.43
16	2.86	0.67	0.87	1.87
17	2.11	0.18	0.23	0.45
18	3.21	0.72	1.08	1.21
19	2.9	0.09	0.18	0.2
20	2.53	0.45	0.75	0.83
21	3.02	0.1	0.3	0.67
22	2.67	0.06	0.12	0.2
23	3.43	0.09	0.18	0.23
24	1.63	0.62	1.34	1.45
25	1.73	0.83	1.65	1.78

Table 3: Quantitative salivary flow rates of group II (IMRT)

S.No	*Pre-RT flow (mL/min)*	*Flow at completion (mL/min)*	*Flow at 3 months (mL/min)*	*Flow at 6 months (mL/min)*
1	2.43	0.80	2.00	2.11
2	2.23	0.70	1.20	1.52
3	3.11	0.85	2.20	3.00
4	2.68	1.00	1.40	2.50
5	3.75	2.00	2.50	3.00
6	2.81	0.90	1.82	2.33
7	2.55	1.80	2.00	2.00
8	2.64	0.94	1.40	2.20
9	3.04	0.88	1.56	2.60
10	2.47	0.67	0.77	1.0
11	3.57	0.82	0.90	0.94
12	3.36	0.83	1.80	2.20
13	2.19	0.77	1.33	2.09
14	2.83	0.84	1.56	2.11
15	2.58	0.76	0.77	2.10
16	3.53	0.80	2.11	2.67
17	2.84	1.40	1.84	2.10
18	3.61	0.96	1.33	3.12
19	3.80	2.10	2.43	2.64
20	2.98	0.90	1.35	2.43
21	3.63	0.97	1.86	2.82
22	1.54	0.66	0.92	0.74
23	3.23	0.87	0.93	0.82
24	2.73	0.72	1.24	1.55
25	2.53	0.70	0.84	1.62

Patient characteristics are shown in Table 1**.** Twenty patients in group I and 23 patients in group II are males and 5 patients in group I and 2 patients in group II are females. Male sex predominance is seen in both groups. The mean age in group I is 52 years and in group II is 50 years, and the median age in both groups is 56 and 55 years, respectively. The most common age group of incidence in both groups is the sixth decade. Neck Swellings are present in 28% patients and 40% patients in group I and II, respectively. Hoarseness is present in 28 and 36% patients in group I and II, respectively.

Pain is the dominant symptom of presentation in group I in more than half of patients. The symptoms in both groups are related to the site of primary disease. Smoking history is seen 84% patients in each group and is the most common addiction seen. Both smoking and chewing of tobacco are seen in 68 and 72% patients in group I and II, respectively. Alcohol is also a common addiction seen in patients of both groups. One patient of CLUP is present in group II. T2 primary tumor staging is the most common in both groups. More than 75% patients in both groups have T-Staging of T2 and above. No patients with T4b staging are present in either of the groups. About 64% in group I and 72% in group II have clinically positive neck nodes. In group II, about 60% patients have clinically positive neck nodes. Three patients in group I have clinically palpable N3 lymph nodes. But as such, there is no statistical difference between the groups. Seven patients in both groups had stage II, 68% patients in group I and 60% patients in group II were of stage III, showing the increased dominance of stage III tumors in both groups. However, there is no significant difference between the groups. The most common site is Oropharynx that is 16 patients in group I and 12 patients in group II. There is a site predilection of Oropharyngeal tumors in both groups. There is one patient of CLUP present in group II.

Table 2 shows that salivary flow rates show that at the completion of radiotherapy, there is a decrease in flow rates, and after which there is a salivary flow rate increase at 3 and 6 months follow-up, indicating a significant repair of the salivary gland. The amount of recovery

Table 4: Quantitative Saxons- pre-radiotherapy, post-radiotherapy (3 and 6 months)

	Group I N (%)			*Group II N (%)*		
	Pre RT	*Post RT (3months)*	*Post RT (6months)*	*Pre RT*	*Post RT (3months)*	*Post RT (6months)*
NORMAL	16 (64)	0	0	15 (60)	0	0
GRADE I	09 (36)	07 (28)	09 (36)	10 (40)	18 (72)	18 (72)
GRADE II	0	18(72)	14 (56)	0	7 (28)	7 (28)
GRADE III	0	0	2 (8)	0	0	0

of the salivary function is dose-dependent, which is discussed in the dose and salivary function relation.

Table 3 demonstrates salivary flow rates, which show that at the completion of radiotherapy, there is a decrease in flow rates and after which there is a salivary flow rate increase at 3 and 6 months follow-up, indicating a significant repair of the salivary gland. There is a better salivary flow rate recovery, almost becoming close to baselines at the end of 6 months follow up. Figures 1 and 2 suggest that there is not much difference between Pre RT flow rates and flow rates at completion of radiotherapy. After radiotherapy, the salivary flow rates in both groups are similarly affected. Figures 3 and 4 suggest that there is a significant difference between the salivary flow rates of 3DCRT and IMRT, suggesting better flow rates in the IMRT group. There is an obvious observation of the widening gap between the lines (red and blue). Table 4 shows the quantitative saxons pre radiotherapy and at 3 and 6 months after completion of radiotherapy. The salivary flow rate recovery is seen in both groups, but there is better improvement in IMRT compared to the 3DCRT group, suggesting IMRT patients recovered better than their 3DCRT counterparts with a significant *p-value* of 0.01 at 6 months and 0.02 at 3 months.

RTOG grades are affected after the completion of radiotherapy. One patients in group I and no patients in

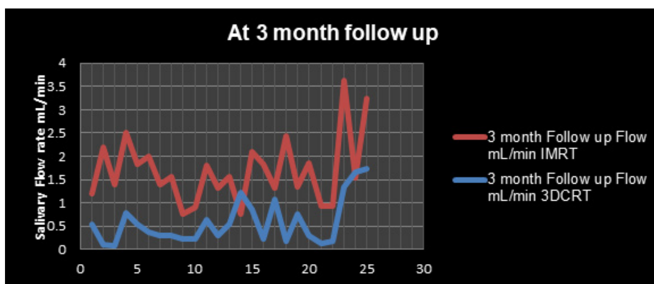

Figure 3: At 3 month follow up post radiotherapy salivary flow rates (3DCRT VS IMRT)

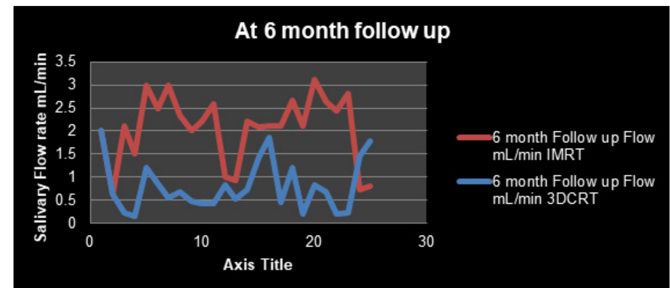

Figure 4: At 6-month follow-up post radiotherapy, salivary flow rates (3DCRT vs IMRT)

Table 5: EORTC H&N35 QoL – Subjective assessment

EORTC H&N35 QoL questions	*At baseline Mean scores in group I and II*			*At 3 months Mean scores in group I and II*			*At 6 months Mean scores in group I and II*		
	I	II	p	I	II	p	I	II	p
Head & neck pain	15	14	ns	12	10	0.02	10.0	7.0	0.01
Swallowing	15	15.4		13.4	11.2	0.05	10.3	8.8	0.03
Teeth	1.2	1.0		1.0	1.0	ns	1.0	1.0	ns
Mouth opening	3.0	2.6		1.6	1.4		1.4	1.2	
Dry mouth	4.0	3.6		3.2	2.8		2.5	1.7	
Sticky saliva	4.0	4.0		3.4	3.0		3.0	2.3	
Cough	3.6	3.0		2.4	2.0		2.2	1.7	
Felt ill	3.6	3.0		2.2	2.0		1.8	1.2	
Senses	7.8	7.6		5.4	4.0	0.05	4.0	2.1	0.03
Social eating	10	10		8.4	8.0	ns	2.6	2.0	ns
Sexuality	1.0	1.1		1.0	1.1		1.0	1.0	
Speech	7.8	7.8		6.0	4.8	0.05	5.2	1.7	0.01

Table 6: Parotid mean doses (Gy) chart of 3DCRT & IMRT

	3DCRT		*IMRT*	
	Right parotid mean dose	*Left parotid mean dose*	*Right parotid mean dose*	*Left parotid mean dose*
1	54.7	58.9	29.3	29.6
2	64.7	63.3	59.2	39.74
3	52.6	53.3	35.8	27.4
4	64.07	67.83	25.1	25.5
5	61.68	63.55	29.2	26.77
6	58.7	53.4	28.2	32
7	61.7	60.3	0	19.1
8	62.25	60.09	27.1	24.1
9	54.54	56.36	29.05	35.77
10	66.08	60.4	23.5	23.55
11	43.78	42.7	39.6	39.8
12	42.16	45	22.9	23.9
13	50.21	50.55	22.5	22.03
14	64.22	62.89	26.6	28.1
15	45.88	43.77	61.5	43.8
16	64.07	67.83	37.5	39.1
17	57.72	54.76	40.5	41.7
18	53.4	52.01	44.6	50.2
19	12.74	7.69	35.6	33.6
20	3.86	4.36	25.16	27.6
21	50.28	49.89	23.05	20
22	57.84	57.87	27.6	28
23	64.17	66.9	38.6	31.8
24	39.3	40.3	35.2	37.3
25	53.4	51.02	27.03	28.11

Table 7: Correlation between quantitative grading and parotid mean doses

Mean Dose of parotid (Gy)	*Grade II or worse Xerostomia*		*p-value*
	Present n(%)	Absent n(%)	0.67
More than 26 Gy	5 (20)	12 (48)	
Less than 26 Gy	2 (08)	6 (24)	

group II had grade I. Seven in each group had grade II, and grade III was 15 patients of group I and 17 patients of group II. There was no significant difference in the objective RTOG morbidity schema grades in both groups.

Table 5 shows the subjective assessment by EORTC H&N 35 QoL questionnaire is done at base line and at 3 and 6 months follow up there is significant improvement in mean scores of 3DCRT and IMRT showing recovery but when comparing both the groups there is better scores in IMRT than in 3DCRT in domains of head and neck pain (*p-value* 0.01), swallowing (*p-value* 0.03), senses (*p-value* 0.03) and speech (*p-value* 0.01). This indicates a better quality of life for the patient. Tables 6 and 7 show the mean doses of left and right parotid along with their correlation with the degree of xerostomia.

DISCUSSION

Radiotherapy-induced xerostomia in head and neck cancers is a chronic morbidity that affects the quality of life in long-term survivors. Conformal techniques like IMRT have been utilized to decrease xerostomia. The present study has been done to quantify xerostomia objectively and subjectively and try to correlate with doses received by parotid glands.

Assessment of Xerostomia by a Quantitative Method

Chao *et al.*,[5] assessed the long-term validity of the hypothesis that sparing parotid glands may result in significant benefit from xerostomia. In that study, at 6-month follow-up, there is a significant improvement

in salivary flow rates in IMRT. 3DCRT and IMRT flow rates are 1.3 and 1.4 mL/min, respectively. The mean flow rates in this study are 1.0 and 1.8 mL/min, respectively in 3DCRT and IMRT and quantitative assessment showed that salivary flow rates salivary flow rates show that at the completion of radiotherapy there is a decrease in flow rates and after which there is salivary flow rate increase at 3 and 6 months follow up indicating a significant repair of the salivary gland. There is a better salivary flow rate recovery, almost becoming close to baselines at the end of 6 months follow up. Quantitative salivary flow rates and grades are affected after the completion of radiotherapy. Grade III flow rates are higher in the 3DCRT group compared to IMRT (40 vs 8%) and grade II flow rates are higher in the IMRT group (44 vs 76%), but this difference is not significant. At 3 and 6-months, salivary flow rate recovery is seen in both groups, but there is better improvement in IMRT compared to the 3DCRT group, suggesting IMRT patients recovered better than their 3DCRT counterparts with a significant *p-value* of 0.01at 6 months and 0.02 at 3 months. This can be explained by the fact that dose-dependent recovery of salivary gland function in the parotid gland, which received high mean doses in 3DCRT, when compared to IMRT. The cropped doses of the right parotid received 21 Gy and the left parotid received 21.6Gy in the IMRT group and 3DCRT group parotid doses are 52 Gy in both parotids.

Assessment of Xerostomia by Objective Grading

In studies by Tej Pal Gupta *et al*, Dirix *et al*, Kam *et al*, Lamberchet *et al*,[6-9] which compared 3DCRT and IMRT objectively, they all concluded that grade II or worse RTOG objective grading is less in IMRT groups. Tejpal Gupta *et al*[6] compared 3DCRT with IMRT in curative intent irradiation of head and neck squamous cell carcinoma (HNSCC). In this study, 60 patients randomly allocated to either 3DCRT (n = 28 patients) or IMRT (n = 32) were included and analyzed on an intention-to-treat basis. The assessment at 6 months post radiotherapy The proportion [95% confidence intervals (CI)] of patients with RTOG grade 2 or worse acute salivary gland toxicity was significantly lesser in the IMRT arm [19 of 32 patients (59, 95% CI: 42–75%)] as compared to 3DCRT [25 of 28 patients (89, 95% CI: 72–97%; $p = 0.009$)] and concluded IMRT significantly reduces the incidence and severity of Xerostomia compared to 3DCRT in curative intent irradiation of HNSCC. In our study, grade II or worse which is assessed at completion of radiotherapy showed no significant difference between the two groups (*p-value* 0.67) and dry mouth is seen in about 88% to 96% of the population suggesting the fact that at completion that there is comparable salivary gland damage in both the groups and recovery of salivary function hasn't started in either of the groups. At 3 months, Grade II or worse in the 3DCRT group is 72%, and in the IMRT group is 40% and 6 month follow up its is 60 vs 40% there are better grades in the IMRT group without significance (*p-value* 0.67). In a study done by Dirix *et al*[7], Lambrecht *et al*[9], physicians rated xerostomia done every 2 months for 2 years post radiotherapy, showing they found a significant reduction of toxicity grades in patients treated by IMRT. Objective RTOG morbidity grading explains that a larger pool of population is needed to gain statistical significance and observer-graded toxicity is physician-based grading, which may vary.

Assessment of Xerostomia by Subjective Grading

Xerostomia is defined as a symptom; it is equally important to estimate the subjective appreciation of oral dryness by the patient. Several xerostomia questionnaires have been developed to permit patient self-reporting, most notably the EORTC H&N quality of life Questionnaire 30 and 35. These questionnaires are available in about 18 languages, including Hindi and English.[4]

Various studies by Tribius *et al*., Shrinivas *et al*., verger *et al*.,[10-12] have scored questionnaires and results of Verger *et al* assessed at 6 weeks and 6 months post radiotherapy showed treatment with IMRT also had a positive effect on several general and head and neck cancer–specific HRQoL(Health Related quality of life) dimensions which showed significant scores in head and neck pain (*p-value* 0.03), swallowing (*p-value* 0.01), sticky saliva (*p-value* 0.04), cough and senses (*p-value* 0.02). And concluded that IMRT results in a significant reduction of patient- and observer-rated xerostomia, as well as other head and neck symptoms, compared with standard 3D-CRT. Another study by Shrinivas *et al.* compared quality of life outcomes using the EORTC H&N 35 QoL questionnaire in patients treated by IMRT and 3DCRT and assessed at baseline, 3 months and up to 2 years every 3 months and showed significant score differences at 6 months in head and neck pain score, Dry mouth, and feeling ill (*p-value* 0.04).[11]

In this study, EORTC head and neck quality of life (EORTC H&N 35 QoL)[4] is used and subjectively assessed results showed better mean scores of head and neck pain, swallowing, speech and senses at 3-month and 6-month follow-up in the IMRT group with significant (*p-value* < 0.05). As it is a subjective assessment, there may be differences in the responses of the patients. But these studies show better QoL scores in patients treated by IMRT in different domains, most commonly head and neck pain, swallowing and dry mouth.

Relation of Xerostomia and Parotid Gland doses

Nowadays, the definition of dose/volume–response relationships for the parotid glands has been well established from the data regarding the correlation of residual salivary function with radiation dose. The consensus has been reached that xerostomia can be substantially reduced by limiting the mean parotid gland dose to <26–30 Gy as a planning criterion.[13] By reducing the mean dose to at least one parotid gland, salivary function can be partially preserved, and it improves gradually over time. Thus, both the prevalence and extent of dry mouth can be greatly reduced over time. This effect has been demonstrated in several clinical studies. However, the improvement in objective parotid function as measured by salivary flow is not always accompanied by improved patient-reported xerostomia.

In a study done by Fang *et al.,*[14] 203 patients were randomized to IMRT and 3DCRT found that doses to the parotids will affect the salivary flow rates. The mean dose to the right parotid is 60.15 Gy and the left parotid is 59.48 Gy in the IMRT group; the right parotid received 47.64 Gy, and the left parotid received 46.84 Gy. They assessed xerostomia by the EORTC H&N35 QoL questionnaire and found a significant correlation between scores and parotid doses with questions of head and pain, swallowing, senses, dry mouth, feeling ill, social contact, social eating, sticky saliva (*p-value* < 0.01). Our dosimetric assessment of parotid mean doses in the case of IMRT is 27.03 and 28.11 Gy for the right and left parotid, respectively. This difference between the mean doses of IMRT groups of both studies is due to the patient population of Fang *et al.,* including nasopharyngeal cancers involving larger volumes of bilateral neck to be treated, whereas in our study, no nasopharyngeal tumors were considered. This also suggests that parotid doses are also related to the site of the primary tumor, along with the technique.

Beetz *et al.,*[15] studied whether the application of quantitative analysis of normal tissue effect in the clinic (QUANTEC) criteria also protected against moderate-to-severe patient-rated xerostomia. In a population consisting of 307 head and neck cancer patients treated with primary (chemo) radiotherapy, either with 3D-CRT (56%) or with IMRT (44%). Patients who met the QUANTEC criteria were classified as low risk and otherwise as high risk. Results were that, in total, 41% of the patients (treated with 3D-CRT and IMRT) were classified as low-risk patients. In the group treated with 3D-CRT and IMRT, it was possible to meet the QUANTEC criteria in 47 and 32% of the patients, respectively. Low-risk patients reported significantly less moderate-to-severe xerostomia than high-risk patients. However, the predicted risk of elderly patients and patients with pre-existing minor patient-rated xerostomia at baseline was about 20%, even when the QUANTEC criteria were met. They concluded that significantly lower rates of radiation-induced patient-rated xerostomia were found among low-risk patients treated according to the QUANTEC criteria, but these criteria do not completely protect against xerostomia. Sparing the parotid glands with IMRT was considerably more difficult in patients with lymph node metastases and in patients with nasopharyngeal and/or oropharyngeal tumours. In this present study, 20% of patients, including both groups, satisfied the criteria, in which 8 (16%) patients are of the IMRT group and 2 (4%) patients of the 3DCRT group. Both patients of 3DCRT are vocal cord cancers who received very low parotid doses and significantly reduced xerostomia in all assessments. This shows dose relation is concerned with the site of primary tumor, even in cases treated by 3DCRT, xerostomia is of lesser grades, whereas criterion I is not achieved in IMRT patients, of about 68% patients treated by IMRT, as there is 72% node positive cases and almost half of the IMRT population are oropharyngeal tumors.

In a study by caroline tram *et al.,*[16] salivary flow rate assessment at 12 months which resulted a lower proportion of patients receiving IMRT there is decreased salivary flow rate (<25% of base line) than those of 3DCRT 59% (p <0.04) fewer patients whose treatment satisfied the QUANTEC guidelines exihibited hyposalivation than patients whose treatment did not fulfill QUANTEC criteria (39 *vs* 71% p <0.02) Upon correlating the xerostomia(Quantitative) between the salivary flow rates and parotid This may be explained by the fact parotids actually received more than 26 Gy.

Van Rij *et al.,*[17] published a study in which patients treated with IMRT reported significantly less difficulty transporting and swallowing their food and needed less water for a dry mouth during the day, night, and meals. They also experienced fewer problems with speech and eating in public. Laryngeal cancer patients in general had fewer complaints than oropharynx cancer patients, but both groups benefited from IMRT. Within the IMRT group, the xerostomia scores were better for those patients with a mean parotid dose to the "spared" parotid below 26 Gy, concluding that Parotid gland sparing IMRT for head and neck cancer patients improves xerostomia-related quality of life compared to conventional radiation, both in rest and during meals.

It is an established fact that stimulated salivary flow rates have a maximum contribution from the parotid glands. Hence, a dose-dependent gradient is seen between parotid doses and salivary gland function. This study has a mean parotid dose of 52 Gy in the whole

parotid of 3DCRT and 31 Gy in the IMRT group. Even in the IMRT group, doses are exceeding 26 Gy (31.7 and 31.14 Gy). The salivary gland dysfunction in IMRT is also affected, but to a lesser extent compared to the 3DCRT group. Hence, there is better recovery of salivary flow rates, which correlates significantly with salivary flow rates (*p-value* 0.03).

CONCLUSION

IMRT significantly reduces the incidence and severity of xerostomia compared to 3D-CRT in curative-intent irradiation of HNSCC. Post-RT patients treated with IMRT and 3DCRT, there is no significant difference between dryness of mouth at completion, but in follow-up of 6 months, IMRT patients recovered better than 3D-CRT.

REFERENCES

1. Bonner JA, Harari PM ,Giralt, *et al* .Radiotherapy plus cetuximab for squamous cell carcinoma of the head and neck. NEngl J Med 2006;354(6)567-78.
2. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995 Mar 30;31(5):1341-6. doi: 10.1016/0360-3016(95)00060-C. PMID: 7713792.
3. Emami, B. (2013) Tolerance of Normal Tissue to Therapeutic Radiation. Reports of Radiotherapy and Oncology, 1, 35-48.
4. Chaukar DA, Das AK, Deshpande MS, Pai PS, Pathak KA, Chaturvedi P, Kakade AC, Hawaldar RW, D'Cruz AK. Quality of life of head and neck cancer patient: validation of the European organization for research and treatment of cancer QLQ-C30 and European organization for research and treatment of cancer QLQ-H&N 35 in Indian patients. Indian J Cancer. 2005 Oct-Dec;42(4):178-84. PMID: 16391435.
5. Chao KS, Deasy JO, Markman J, Haynie J, Perez CA, Purdy JA, Low DA. A prospective study of salivary function sparing in patients with head-and-neck cancers receiving intensity-modulated or three-dimensional radiation therapy: initial results. Int J Radiat Oncol Biol Phys. 2001 Mar 15;49(4):907-16. doi: 10.1016/s0360-3016(00)01441-3. PMID: 11240231.
6. Gupta T Agarwal JP *et al*., Three dimensional conformal radiotherapy (3DCRT), versus intensity modulated radiotherapy (IMRT) J Clin Oncol 2012;104: 343-48.
7. Direx JH: Changes in salivary flow produced by changes in fluid and electrolyte balance, in Sreebny LM, Int J Radiat Oncol Biol Phys 2006;54(1):9-15.
8. Kam A, Homsi U, Kakail AI, *et al*:prospective randomizied study in management of early stage nasopharngeal cancer. Eur J Cancer 2007;37: 2010-14.
9. Lambrchect P, O'Sullivan B, Nuyts J, *et al*. intensity modulated radiotherapy vs. parotid sparing 3D conformal radiotherapy Int J Radiat Oncol Biol Phys 2013;54(1):9-13.
10. Tribius A, Kim HM, Ten Haken R, *et al*: Dose, volume and function relationships in parotid glands following conformal and intensity modulated irradiation of head and neck cancer. Int J Radiat Oncol Biol Phys 2011;45:577-87.
11. Shrinivas R, Gupta T, Laskar SG *et al* Quality of life outcomes in patients with head and neck squamous cell carcinomas treated with intensity modulated radiotherapy and three dimensional confomal radiotherapy(3DCRT): evidence from a prospective randomizied study. Oral Oncology.2013;49(6):634-642.
12. Verger JH, Valdes-Olmos RA, Balm AJS, *et al*: Evidence for early and persistent impairment of salivary gland excretion after irradiation of head and neck tumors. Eur J Nucl Med 2009; 23(3):1485-90.
13. D'Hondt E, Eisbruch A, Ship JA. The infl uence of pre-radiation salivary fl ow rates and radiation dose on parotid salivary gland dysfunction in patients receiving radiotherapy for head and neck cancers. Int J Radiat Oncol Biol Phys 2012; 56(2):292-98.
14. Fang KL, Trodhal JN quality of life in nasopharyngeal patients treated with conformal radiotherapy Int J Radiat Oncol Biol Phys 2008;72(2): 356-64.
15. Beetz ID:validation of three dimensional confomal radiotherapy based NTCP models . Crit Rev Clin Lab Sci 2012;12:321-36
16. Nguyen CT, Lin S, Clark H, Hovan A, Wu J. Salivary flow rate after conventional and intensity-modulated radiation therapy. J Am Dent Assoc. 2018 Jun;149(6):432-441. doi: 10.1016/j.adaj.2018.01.031. Epub 2018 Apr 11. PMID: 29655708.
17. Van Rij CM, Heemsbergen WD, AH Ackerstaff, EA Lamers, AJM Balm, CRN Rasch. Parotid gland sparing IMRT for head and neck cancer improves Xerostomia-related quality of life. 2008; 2(6):763-72.