International Journal of Research in Medical Sciences
Kucha N et al. Int J Res Med Sci. 2026 Aug;14(8):3257-3266
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20262356

Original Research Article

Late dysphagia, xerostomia and submucosal fibrosis following concurrent chemoradiotherapy for locally advanced head and neck squamous cell carcinoma: a prospective comparison of intensity-modulated radiotherapy and three-dimensional conformal radiotherapy

Nileshkumar Kucha[1,2]*, Tej P. Soni[1], Kavita Valiya[3], Dineshkumar Singh[1]

[1]Department of Radiation Oncology, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, Rajasthan, India
[2]GCRI-BCCRI, Bhavnagar, Gujarat, India
[3]Department of Pathology and Laboratory Medicine, Government Medical College, Bhavnagar, Gujarat, India

Received: 23 June 2026
Accepted: 14 July 2026

***Correspondence:**
Dr. Nileshkumar Kucha,
E-mail: nil.kucha@gmail.com

ABSTRACT

Background: Late radiation-induced toxicities remain an important cause of long-term morbidity in survivors of locally advanced head and neck squamous cell carcinoma (LA-HNSCC). Intensity-modulated radiotherapy (IMRT) offers improved dose conformity and normal tissue sparing compared with three-dimensional conformal radiotherapy (3D-CRT). This study compared late toxicity outcomes following definitive concurrent chemoradiotherapy delivered using IMRT versus 3D-CRT.

Methods: This prospective observational study enrolled patients with LA-HNSCC treated with definitive concurrent chemoradiotherapy between September 2017 and December 2018. Seventy-eight evaluable patients (39 IMRT, 39 3D-CRT) were analysed. Late xerostomia, dysphagia, and submucosal fibrosis were graded at 12 months using RTOG/EORTC late radiation morbidity scoring criteria.

Results: Clinically significant xerostomia (grade ≥2) occurred in 23.1% of patients treated with IMRT compared with 51.3% of those treated with 3D-CRT (p=0.019). IMRT was associated with a 55% reduction in the risk of xerostomia (RR 0.45, 95% CI 0.24-0.86). Grade ≥2 dysphagia was observed in 61.5% of patients in the IMRT group and 64.1% in the 3D-CRT group (p=1.000), while grade ≥2 submucosal fibrosis occurred in 30.8% and 43.6%, respectively (p=0.349). Patients treated with IMRT also had fewer treatment interruptions and lower rates of clinically significant weight loss.

Conclusions: IMRT was associated with a significantly lower incidence of late xerostomia than 3D-CRT in patients with LA-HNSCC undergoing definitive concurrent chemoradiotherapy. Although differences in dysphagia and submucosal fibrosis were not statistically significant, the overall toxicity profile favoured IMRT. These findings support IMRT as the preferred radiotherapy technique for reducing long-term treatment-related morbidity in head and neck cancer.

Keywords: 3D-CRT, Concurrent chemoradiotherapy, Dysphagia, Head and neck cancer, IMRT, Xerostomia

INTRODUCTION

Among all malignancies, head and neck squamous cell carcinoma (HNSCC) carries a disproportionately heavy burden in India, where it accounts for approximately 30% of all cancers among men and represents the single largest cancer category treated at most tertiary oncology institutions across the country.[1] Unlike the epidemiological pattern seen in Western nations, where human papillomavirus-associated oropharyngeal cancer

has reshaped disease demographics, the Indian head and neck cancer landscape is overwhelmingly shaped by habitual tobacco exposure in its multiple forms: cigarette and bidi smoking, smokeless tobacco chewing, and areca nut preparations, frequently used in combination with alcohol.[1,2] Compounding this risk profile is a deeply inequitable healthcare landscape, in which inadequate cancer awareness and limited access to diagnostic facilities drive a large proportion of patients, estimated at over 60% in India, to seek treatment only after their disease has progressed to locoregional stage III or IV.[2] At this advanced stage, surgical extirpation is often technically impractical or functionally unacceptable, and concurrent delivery of platinum-based chemotherapy alongside definitive radiotherapy has emerged as the evidence-based standard, validated across multiple randomized controlled trials and confirmed by large-scale meta-analyses to yield superior tumour control and survival outcomes relative to radiotherapy administered without concurrent systemic therapy.[3]

The very improvements in treatment efficacy that have extended survival have simultaneously expanded the population living with the long-term consequences of therapy. In India, where many patients are diagnosed in nutritionally compromised states and carry significant comorbidity burden, the late effects of definitive chemoradiotherapy impose particularly severe functional consequences. Radiation-induced xerostomia, swallowing dysfunction, and progressive submucosal fibrosis rank among the most clinically impactful sequelae, disrupting salivary gland output, deglutition mechanics, and mouth opening in ways that erode dietary intake, phonation, and social function, impairments that characteristically worsen or persist well beyond the conclusion of active treatment.[4] Reducing these late effects is therefore essential not only for improving quality of life but also for optimizing long-term functional outcomes and survivorship.

Technological advances in radiotherapy delivery have opened meaningful avenues for mitigating this morbidity. The shift from two-dimensional planning to 3D-CRT marked an important early step, as volumetric tumour delineation and beam arrangement optimization permitted tighter dose conformation around target volumes and reduced the bath of high-dose radiation received by uninvolved adjacent tissues.[5] IMRT extended this progress substantially: through computerized inverse optimization algorithms and dynamic multileaf collimator modulation, IMRT generates dose distributions with steep spatial gradients that afford substantially enhanced sparing of the bilateral parotid glands and other neighbouring critical structures, without sacrificing the target dose coverage required for disease control.[6,7]

Evidence from prospective and randomized studies conducted predominantly in high-income settings has established that the dosimetric superiority of IMRT translates into clinically meaningful reductions in salivary toxicity and measurable patient-reported quality-of-life benefits.[6,7] In India, however, access to IMRT remains geographically and institutionally uneven: although metropolitan tertiary cancer centres have progressively incorporated IMRT into routine practice, a considerable number of regional and district-level oncology units continue to rely on 3D-CRT as their primary radiotherapy modality, constrained by the significant technical, financial, and human resource demands that IMRT implementation entails. In this context, prospective clinical data comparing toxicity outcomes between IMRT and 3D-CRT within the Indian patient population are not only scientifically valuable but operationally essential for guiding rational, evidence-informed treatment and infrastructure decisions.

The present study was designed to address this evidence gap directly. The primary objective was to prospectively compare the incidence of clinically significant late xerostomia, dysphagia, and submucosal fibrosis, graded at 12 months post-treatment using the RTOG/EORTC late radiation morbidity scoring criteria, between patients with locally advanced HNSCC undergoing definitive concurrent chemoradiotherapy with IMRT versus 3D-CRT at a tertiary cancer centre in India. Secondary objectives encompassed comparison of overall treatment time, frequency of unplanned treatment interruptions, and rates of clinically significant weight loss between the two treatment groups.

METHODS

Study design and ethical approval

This investigation was designed as a prospective, non-randomized, two-arm comparative observational study carried out within the Department of Radiation Oncology at [Institution masked for review], a dedicated regional tertiary oncology facility. Institutional ethical clearance was secured prior to study initiation (IRB Reference: [masked for review]), and each participant provided written informed consent following a thorough explanation of the study procedures and their voluntary nature.

Patient selection

Consecutive patients between 18 and 70 years of age harbouring biopsy-proven squamous cell carcinoma arising from the oropharynx, hypopharynx, or larynx were recruited prospectively over a 16-month period from September 2017 through December 2018. Eligibility required a Karnofsky performance status score of 70 or above, along with satisfactory pre-treatment haematological indices and adequate renal and hepatic reserve.[8] Individuals were excluded if they had previously received head and neck irradiation, carried a diagnosis of any other active or prior malignancy, presented with histology other than squamous cell carcinoma, demonstrated radiological evidence of distant metastatic spread, or had locoregionally recurrent disease.

Sample size calculation

The target sample size was derived from published data reporting the differential impact of IMRT and 3D-CRT on salivary gland function, as documented by Gupta et al.[6] Formal power calculations indicated that a minimum of 33 evaluable patients per arm would provide 80% power to detect a clinically relevant between-group difference at a two-sided significance threshold of α=0.05. Each arm was expanded to 40 patients to preserve statistical power in the event of protocol deviations or patient withdrawal during follow-up.

Radiotherapy simulation and target delineation

All participants underwent computed tomography simulation in the treatment position using individually fabricated five-point thermoplastic immobilization shells to ensure reproducible positioning throughout the treatment course. Tumour and nodal target volumes were defined in accordance with the volumetric planning framework set out in ICRU Report 83 and established institutional contouring protocols.[9] For each patient, the gross tumour volume (GTV), clinical target volume (CTV) incorporating appropriate anatomical margins for microscopic disease extension, and planning target volume (PTV) accounting for setup uncertainty were systematically delineated on the simulation dataset.

Radiotherapy planning and delivery

Treatment was delivered using megavoltage photon beams of 6 MV energy generated by a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA). Both treatment groups received a curative-intent total dose of 70 Gy administered in 35 daily fractions of 2 Gy each over a seven-week course, with five treatment sessions per week. Patients in one arm received this dose via IMRT, with dose optimization performed using inverse planning; the remaining patients received the equivalent prescription via a conventional 3D-CRT beam arrangement. For all patients, critical normal structures, including the spinal cord, brainstem, mandible, oral cavity mucosa, and bilateral parotid glands, were carefully contoured, and dose-volume constraints were applied in line with the QUANTEC evidence-based tolerance guidelines.[10]

Concurrent chemotherapy

Radiosensitisation was achieved using cisplatin administered intravenously at a weekly dose of 40 mg/m² throughout the radiotherapy course, a regimen well established in the Indian head and neck cancer setting for its tolerability and efficacy. Antiemetic prophylaxis, intravenous hydration, nutritional support, and symptomatic management were delivered in accordance with departmental protocols.

Follow-up and toxicity assessment

All patients entered a structured post-treatment surveillance programme with clinical review at regular intervals. Formal late toxicity evaluation was conducted at the 12-month post-radiotherapy time point. Three endpoints, xerostomia, dysphagia, and submucosal fibrosis, were independently graded by the treating clinician using the RTOG/EORTC late radiation morbidity scoring schema (Table 7).[11] For the purpose of this analysis, toxicity scores of grade 2 or above were designated as clinically significant, reflecting the threshold at which symptoms begin to meaningfully interfere with daily functioning.

Outcome measures

The three primary endpoints were the rates of clinically significant (grade ≥2) late xerostomia, dysphagia, and submucosal fibrosis at 12 months post-treatment. Secondary endpoints captured aspects of treatment delivery and nutritional status: overall treatment time (OTT) from the first to the last radiotherapy fraction, the number and duration of unplanned treatment interruptions, the proportion of patients sustaining weight loss exceeding 10% of their pre-treatment body weight, and the distribution of late toxicities stratified by primary tumour subsite.

Statistical analysis

All statistical computations were carried out using MedCalc statistical software version 16.4 (MedCalc Software Ltd., Ostend, Belgium). Normally distributed continuous variables are reported as mean±standard deviation and were compared between groups using the unpaired Student's t-test. Categorical and dichotomous variables were evaluated using Pearson's chi-square test or Fisher's exact test, the latter applied when expected cell frequencies fell below five. For the primary xerostomia endpoint, the magnitude of between-group difference was quantified using relative risk (RR) and odds ratio (OR) with their respective 95% confidence intervals (CI). Throughout, statistical significance was defined as a two-tailed p value of less than 0.05.

RESULTS

Patient characteristics

Of the 83 patients with locally advanced HNSCC who were initially registered into the study between September 2017 and December 2018, five were unable to complete the protocol, either through voluntary discontinuation of treatment or loss to scheduled follow-up, and were consequently excluded from all analyses. The final evaluable cohort comprised 78 patients, distributed equally between the two treatment arms: 39 allocated to intensity-modulated radiotherapy and 39 to three-dimensional conformal radiotherapy.

Pre-treatment demographic and clinicopathological characteristics were well matched across both groups. Independent statistical testing revealed no meaningful between-group disparity in age, sex distribution, primary tumour subsite, T classification, N classification, or functional status as measured by the Karnofsky performance score (all p>0.05). Full baseline data for both cohorts are presented in Table 1.

Treatment compliance and nutritional outcomes

Every enrolled patient who reached the analysis stage successfully completed their prescribed radiotherapy course, yielding a treatment completion rate of 100% in both arms. The mean overall treatment time was 53.5±4.7 days in the intensity-modulated radiotherapy cohort versus 55.6±6.5 days among those receiving three-dimensional conformal radiotherapy (p=0.110). Unplanned gaps in treatment delivery were less frequent and shorter in duration in the intensity-modulated radiotherapy group, with a mean treatment gap of 3.5 days recorded, compared with 5.8 days in the three-dimensional conformal radiotherapy group. With regard to nutritional status, body weight loss exceeding 10% of the pre-treatment baseline was documented in seven of 39 intensity-modulated radiotherapy patients (17.9%) and in 14 of 39 patients in the three-dimensional conformal radiotherapy arm (35.9%; p=0.126). The weight loss distribution between groups is illustrated in Figure 1. Full compliance and nutritional data are tabulated in Table 2.

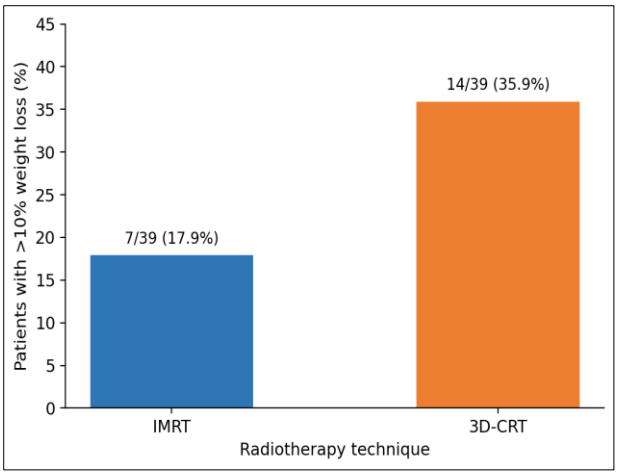

Figure 1: Incidence of clinically significant weight loss.

Incidence of clinically significant weight loss (>10% of baseline body weight) stratified by radiotherapy technique. Patients treated with IMRT experienced a lower rate of significant weight loss compared with those receiving 3D-CRT (17.9% versus 35.9%, p=0.126)

Late toxicity outcomes

Formal grading of late radiation morbidity was undertaken at the 12-month post-treatment assessment using the RTOG/EORTC late radiation morbidity scoring schema.[11]

The comparative toxicity data are displayed in Table 3 and Figure 2.

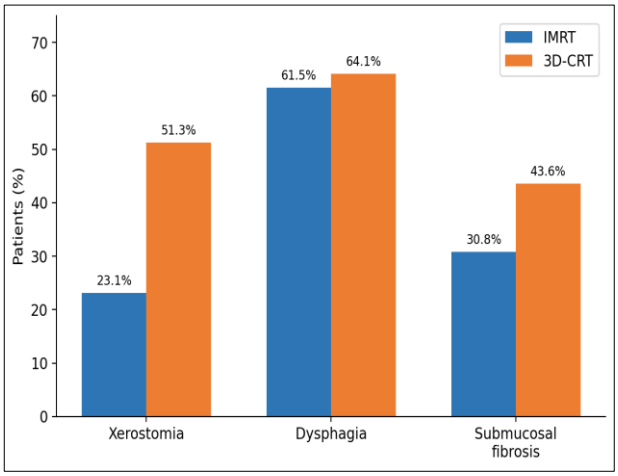

Figure 2: Clinically significant late toxicities at 12 months.

Comparative prevalence of grade ≥2 xerostomia, dysphagia, and submucosal fibrosis between patients receiving intensity-modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT) at 12 months post-treatment. IMRT was associated with a statistically significant reduction in xerostomia (23.1% versus 51.3%, p=0.019). Between-group differences in dysphagia (61.5% versus 64.1%, p=1.000) and submucosal fibrosis (30.8% versus 43.6%, p=0.349) did not reach statistical significance

Regarding salivary toxicity, grade ≥2 xerostomia was identified in nine of 39 patients (23.1%) in the intensity-modulated radiotherapy arm, compared with 20 of 39 patients (51.3%) in the three-dimensional conformal radiotherapy arm, a between-group difference that reached conventional statistical significance (χ^2=5.49, p=0.019).

Swallowing dysfunction of grade ≥2 severity was recorded in 24 intensity-modulated radiotherapy patients (61.5%) and 25 three-dimensional conformal radiotherapy patients (64.1%). This marginal numerical difference carried no statistical weight (p=1.000, Fisher's exact test).

Grade ≥2 submucosal fibrosis was documented in 12 patients (30.8%) treated with intensity-modulated radiotherapy and 17 patients (43.6%) receiving three-dimensional conformal radiotherapy. Although this represented a numerically lower rate in the intensity-modulated radiotherapy arm, the difference did not attain statistical significance (χ^2=0.88, p=0.349).

Risk analysis for xerostomia

Formal risk modelling for the xerostomia endpoint confirmed a statistically significant protective association with intensity-modulated radiotherapy. Relative to patients managed with three-dimensional conformal radiotherapy, those receiving intensity-modulated radiotherapy faced a 55% lower probability of developing grade ≥2 xerostomia

(RR 0.45, 95% CI 0.24-0.86). The odds of grade ≥2 xerostomia were reduced by approximately 71% with intensity-modulated radiotherapy compared with three-dimensional conformal radiotherapy (OR 0.29, 95% CI 0.11-0.76, p=0.019). These estimates are presented in Table 4 and visualized as a forest plot in Figure 3.

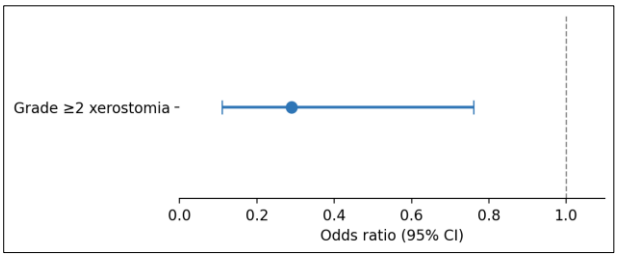

Figure 3: Forest plot for grade ≥2 xerostomia.
Forest plot illustrating the association between radiotherapy technique and clinically significant xerostomia. IMRT was associated with significantly lower odds of grade ≥2 xerostomia relative to 3D-CRT (OR 0.29, 95% CI 0.11–0.76, p=0.019), corresponding to an approximately 71% reduction in the odds of developing late salivary toxicity

Site-wise toxicity analysis

Stratification of toxicity outcomes by primary tumour subsite revealed distinct site-specific patterns. Among patients with hypopharyngeal primaries, xerostomia was the predominant late effect, occurring in six of 11 patients (54.5%). Swallowing impairment was most prevalent in the oropharyngeal subgroup, affecting 35 of 48 patients (72.9%). Submucosal fibrosis was most burdensome among patients with laryngeal cancers, documented in nine of 19 patients (47.4%). The complete subsite breakdown is provided in Table 5.

Comparison with published literature

The principal findings of this study were contextualized against comparable prospective and randomized investigations of IMRT in head and neck cancer. The reduction in xerostomia observed with IMRT in the current dataset aligns with outcomes reported across the selected reference studies, as summarized in Table 6.

IMRT demonstrated a statistically significant advantage over 3D-CRT in reducing late salivary toxicity, while consistently showing more favourable, though not statistically significant, trends in submucosal fibrosis, treatment gap duration, and nutritionally significant weight loss.

For reference, the RTOG/EORTC late radiation morbidity scoring schema used to grade the three study endpoints is reproduced in Table 7.[11]

Table 1: Baseline demographic and clinical characteristics.

Characteristic	IMRT (n=39)	3D-CRT (n=39)	P value (χ^2 or t)
Age, mean±SD (years)	58.6±9.2	58.9±8.3	0.887 (t=0.14)
Sex, N (%)			χ^2=0.00, p=1.000
Male	31 (79.5)	31 (79.5)	
Female	8 (20.5)	8 (20.5)	
KPS, median	90	90	0.161
Primary site, N (%)			χ^2=2.14, p=0.340
Oropharynx	27 (69.2)	21 (53.8)	
Hypopharynx	5 (12.8)	6 (15.4)	
Larynx	7 (17.9)	12 (30.8)	
T stage, N (%)			χ^2=1.29, p=0.519
T2	3 (7.7)	5 (12.8)	
T3	18 (46.2)	21 (53.8)	
T4a	17 (43.6)	13 (33.3)	
T4b	1 (2.6)	0 (0.0)	
N stage, N (%)			χ^2=5.10, p=0.088
N1	1 (2.6)	3 (7.7)	
N2	24 (61.5)	30 (76.9)	
N3	14 (35.9)	6 (15.4)	

No statistically significant intergroup differences were identified with respect to age, sex, primary tumour site, T stage, N stage, or Karnofsky performance status (all p>0.05). Test statistics: independent-samples t-test for age (t=0.14); chi-square (χ^2) for all categorical variables (sex: χ^2=0.00; primary site: χ^2=2.14; T stage: χ^2=1.29; N stage: χ^2=5.10). IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy; SD: standard deviation; KPS: Karnofsky performance status

Table 2: Treatment compliance and nutritional outcomes.

Parameter	IMRT (n=39)	3D-CRT (n=39)	P value (statistic)
Mean OTT, days (mean±SD)	53.5±4.7	55.6±6.5	0.110 (t=1.62)
Mean treatment gap, days	3.5	5.8	—
Weight loss >10%, N (%)	7 (17.9)	14 (35.9)	0.126 (χ^2=3.55)
Treatment completion, N (%)	39 (100)	39 (100)	—

OTT: Overall treatment time; SD: standard deviation; IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy. Test statistics: independent-samples t-test for OTT (t=1.62); chi-square (χ^2=3.55) for weight loss. All patients in both groups completed the prescribed radiotherapy course

Table 3: Late toxicity outcomes at 12 months.

Toxicity (grade ≥2)	IMRT (n=39)	3D-CRT (n=39)	P value
Xerostomia	9 (23.1)	20 (51.3)	0.019*
Dysphagia	24 (61.5)	25 (64.1)	1.000
Submucosal fibrosis	12 (30.8)	17 (43.6)	0.349

*Statistically significant. Toxicities graded using the RTOG/EORTC late radiation morbidity scoring criteria.11 Xerostomia assessed using chi-square test (χ^2=5.49); dysphagia using Fisher's exact test; submucosal fibrosis using chi-square test (χ^2=0.88). Grade ≥2 defined as clinically significant. IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy. p<0.05 considered statistically significant

Table 4: Risk estimates for clinically significant xerostomia.

Outcome	RR	95% CI	OR	95% CI	P value
Grade ≥2 xerostomia (IMRT versus 3D-CRT)	0.45	0.24–0.86	0.29	0.11–0.76	0.019

Relative risk (RR), odds ratio (OR), and corresponding 95% confidence intervals (CI) were calculated for grade ≥2 xerostomia (IMRT versus 3D-CRT as reference group). RR: relative risk; OR: odds ratio; CI: confidence interval; IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy

Table 5: Site-wise distribution of toxicities.

Primary site	Xerostomia ≥2, N (%)	Dysphagia ≥2, N (%)	Fibrosis ≥2, N (%)
Oropharynx (n=48)	17 (35.4)	35 (72.9)	16 (33.3)
Larynx (n=19)	6 (31.6)	10 (52.6)	9 (47.4)
Hypopharynx (n=11)	6 (54.5)	4 (36.4)	4 (36.4)

Grade ≥2 toxicities were considered clinically significant per RTOG/EORTC scoring criteria.[11] IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy

Table 6: Comparison of present study findings with major published studies.

Study (author)	Design	Patients (N)	Principal finding
Pow et al[12]	RCT	51	Significant reduction in xerostomia with parotid-sparing IMRT compared with conventional radiotherapy in nasopharyngeal carcinoma
Gupta et al[6]	Prospective RCT	60	Superior salivary gland function recovery and improved quality of life with IMRT versus 3D-CRT in head and neck cancer
Nutting et al (PARSPORT)[7]	RCT	94	Parotid-sparing IMRT significantly reduced grade ≥2 xerostomia and improved patient-reported quality of life compared with conventional radiotherapy
Marta et al[13]	Systematic review and meta-analysis	>200	IMRT associated with improved toxicity profile, reduced xerostomia, and superior long-term outcomes compared with conventional radiotherapy techniques

Continued.

Study (author)	Design	Patients (N)	Principal finding
Present study	Prospective observational	78	Significant reduction in grade ≥2 xerostomia with IMRT versus 3D-CRT (23.1% versus 51.3%, p=0.019); RR 0.45 (95% CI 0.24–0.86); OR 0.29 (95% CI 0.11–0.76)

IMRT: intensity-modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy; RCT: randomised controlled trial; QoL: quality of life; RR: relative risk; OR: odds ratio; CI: confidence interval

Table 7: RTOG/EORTC late radiation morbidity scoring schema for study endpoints.

Grade	Xerostomia	Dysphagia	Submucosal fibrosis
0	No symptoms	No symptoms	No fibrosis
1	Mild symptoms	Mild symptoms	Mild fibrosis
2	Moderate symptoms	Moderate symptoms requiring dietary modification	Moderate fibrosis
3	Severe symptoms	Severe symptoms requiring major dietary modification	Severe fibrosis
4	Complete dysfunction	Complete obstruction requiring intervention	Extensive fibrosis

Grading based on the late radiation morbidity scoring criteria of the radiation therapy oncology group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC).[11]

DISCUSSION

This prospective two-arm observational study evaluated late radiation-induced morbidity in patients with locally advanced HNSCC at a tertiary oncology centre in Jaipur, India, comparing outcomes between those treated with IMRT and those who received 3D-CRT as part of definitive concurrent chemoradiotherapy. The foremost finding was a statistically significant and clinically meaningful reduction in grade ≥2 xerostomia in the IMRT-treated cohort. At 12 months post-treatment, the prevalence of grade ≥2 salivary toxicity was 23.1% in the IMRT group versus 51.3% in the 3D-CRT group (p=0.019), with IMRT conferring a 55% reduction in relative risk (RR 0.45, 95% CI 0.24-0.86) and a 71% reduction in the odds of developing clinically significant xerostomia (OR 0.29, 95% CI 0.11-0.76). These findings underscore the real-world clinical value of dose-sculpting technology in protecting salivary gland function while maintaining effective tumour coverage.

Among all late sequelae of head and neck cancer treatment, xerostomia exerts one of the most pervasive and enduring impacts on survivorship. Salivary hypofunction disrupts multiple domains of daily functioning simultaneously: it impairs bolus formation and deglutition, diminishes gustatory acuity, degrades oral mucosal integrity, predisposes to dental caries, and reduces the ease of phonation, collectively imposing a chronic functional burden that undermines nutritional status, social confidence, and overall well-being for years beyond treatment completion.[4] The substantially lower xerostomia rates observed in the IMRT arm of the present study are mechanistically consistent with the superior parotid-sparing capability of inverse-planned IMRT: by generating steep dose gradients around target volumes, IMRT limits the mean dose delivered to the bilateral parotid parenchyma, a parameter that has been shown through formal dose-volume analyses to be a robust and independent predictor of long-term salivary output.[14] These observations are corroborated by landmark evidence from the PARSPORT randomized trial, in which parotid-sparing IMRT was associated with a sustained and statistically significant reduction in xerostomia burden relative to conventional radiotherapy, accompanied by measurable improvements in patient-reported quality of life.[7] Parallel findings were documented by Gupta et al in their prospective Indian randomized trial, which demonstrated superior recovery of salivary gland function among IMRT recipients and provided direct Indian-patient evidence supporting the transferability of these dosimetric benefits.[6] The magnitude of xerostomia reduction achieved in the present study is broadly concordant with published prospective and randomized datasets from diverse patient populations, lending confidence to the generalizability of parotid-sparing radiotherapy benefits across different institutional and epidemiological contexts.[6,7,12]

Swallowing dysfunction of grade ≥2 severity was recorded in 24 IMRT patients (61.5%) and 25 three-dimensional conformal radiotherapy patients (64.1%), a numerically trivial and statistically non-significant difference (p=1.000). Post-chemoradiotherapy dysphagia arises through a multifactorial and anatomically complex cascade involving primary tumour subsite, irradiated volume, pre-treatment swallowing reserve, the additive mucosal toxicity of concurrent cisplatin, and the cumulative radiation dose absorbed by the superior and middle pharyngeal constrictors, the supraglottic larynx, and associated neuromuscular structures.[15-17] The high baseline rates of dysphagia in both arms, reflecting the predominance of oropharyngeal primaries in this cohort, and the relatively modest sample size likely constrained statistical power to detect between-group differences for this inherently complex and multidimensionally determined outcome. It should also be noted that dedicated dysphagia-sparing IMRT optimization, involving explicit

contouring and dose constraint application to swallowing structures, was not mandated in this protocol; this may have attenuated any IMRT advantage for this endpoint.

A numerically lower prevalence of grade ≥2 submucosal fibrosis was recorded among IMRT-treated patients (30.8%) than among those receiving three-dimensional conformal radiotherapy (43.6%), though the difference did not achieve statistical significance (p=0.349). The pathogenesis of radiation-induced mucosal and submucosal fibrosis involves a self-reinforcing cascade initiated by radiation-induced DNA damage, progressing through sustained pro-inflammatory cytokine signalling, TGF-β-mediated myofibroblast recruitment, and ultimately culminating in disordered collagen deposition and irreversible structural remodelling of irradiated tissues.[18] The observed trend toward less fibrosis with IMRT likely reflects the tighter conformity of the high-dose volume around target structures and the consequent reduction in integral dose to the surrounding submucosa and soft tissues. Whether this trend matures into a statistically and clinically significant benefit requires confirmation through longer follow-up and larger cohort studies, particularly relevant in India, where delayed presentations and treatment in nutritionally compromised patients may amplify the burden of fibrosis.

An important secondary observation was the consistently more favourable treatment delivery profile among patients receiving IMRT. The mean treatment gap was 3.5 days in the IMRT arm versus 5.8 days in the three-dimensional conformal radiotherapy arm, and clinically significant weight loss occurred in 17.9% versus 35.9% of patients respectively, with a shorter mean overall treatment time in the IMRT group (53.5 versus 55.6 days). Although none of these secondary differences attained statistical significance, their clinical implications are meaningful: unplanned radiotherapy interruptions are known to promote accelerated tumour repopulation and have been independently linked to inferior locoregional control in head and neck cancer.[3,19] In the Indian healthcare context, where treatment gaps attributable to acute toxicity, transportation barriers, and socioeconomic constraints are particularly common, any reduction in interruption rates carries practical therapeutic value beyond the direct toxicity benefit.

Subsite-specific analysis yielded patterns consistent with anatomical logic. Xerostomia predominated in hypopharyngeal cancers, where larger target volumes encompassing the parapharyngeal space increase parotid irradiation, while dysphagia was most prevalent among oropharyngeal primaries, reflecting their proximity to pharyngeal constrictor muscles and the tongue base. Fibrosis was most common in laryngeal cancers, where circumferential mucosal irradiation is inherent to adequate coverage. These exploratory findings may assist clinicians at Indian centres in pre-treatment patient counselling and in prioritizing which organ-at-risk constraints to emphasize during planning optimization for each tumour subsite.

This study contributes several attributes of methodological value. The prospective design with uniform concurrent chemotherapy, systematic follow-up, and standardized RTOG/EORTC toxicity scoring[11] ensures that outcome assessments are reproducible and directly comparable across the two arms. Importantly, it adds prospective real-world toxicity data from an Indian tertiary cancer centre, a setting characterized by distinct patient demographics, high proportions of tobacco-related disease, late-stage presentations, and resource constraints, where such comparative evidence has been notably sparse. The findings align with contemporary reports from international centres demonstrating that conformal radiotherapy advances translate into improved toxicity profiles without apparent compromise of disease control, suggesting that the biological rationale for IMRT's benefits is not population-dependent.[13]

Limitations

Several limitations of this study warrant acknowledgment. The single-centre design and modest evaluable cohort of 78 patients may limit the external validity and statistical power of the findings, particularly for secondary endpoints. Non-randomized treatment allocation, while reflecting real-world practice and producing well-matched baseline groups, introduces the theoretical possibility of selection bias that cannot be fully excluded. Dosimetric correlations between organ-at-risk dose parameters (mean parotid dose, constrictor muscle dose) and observed toxicity outcomes were not performed, precluding mechanistic validation of the clinical results. The 12-month follow-up horizon, while capturing the majority of clinically established late effects, may be insufficient to detect the full trajectory of fibrosis and salivary recovery, both of which are known to evolve over multi-year timeframes. Future investigations incorporating multicentric patient recruitment, randomized allocation, detailed dosimetric analyses, objective salivary flow measurement, and extended follow-up are needed to build on and validate the observations reported here.

CONCLUSION

The results of this prospective non-randomized institutional study provide real-world evidence from an Indian tertiary cancer centre that intensity-modulated radiotherapy achieves a significantly lower rate of late salivary gland toxicity at 12 months compared with three-dimensional conformal radiotherapy when delivered alongside concurrent platinum-based chemotherapy for locoregionally advanced head and neck squamous cell carcinoma. This salivary protection advantage, quantified as a 55% reduction in relative risk and a 71% reduction in the odds of clinically significant xerostomia, reflects the ability of intensity-modulated radiotherapy to concentrate

therapeutic dose within tumour volumes while substantially attenuating radiation exposure to the bilateral parotid glands, with direct consequences for the nutritional and functional recovery of treated patients. Secondary observations pointing toward shorter treatment gaps, reduced weight loss, and a lower prevalence of submucosal fibrosis further strengthen the overall case for intensity-modulated radiotherapy, even where individual differences fell short of statistical significance.

Viewed through the lens of Indian oncology practice, where patients characteristically present with advanced disease, nutritional depletion, and socioeconomic barriers to sustained treatment engagement, the documented reductions in toxicity burden and treatment interruption carry implications that extend well beyond statistical endpoints. Wider institutional access to intensity-modulated radiotherapy planning and delivery should be prioritized as a strategy for improving survivorship outcomes across the heterogeneous spectrum of cancer facilities serving India's head and neck cancer population. Future prospective studies encompassing multiple institutions, longer observational periods, objective parotid function measurement, and detailed dosimetric analyses will be essential for identifying which patient and treatment characteristics most reliably predict late morbidity trajectories following chemoradiotherapy for locally advanced head and neck squamous cell carcinoma.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
2. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers. 2020;6(1):92.
3. Pignon JP, le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomized trials and 17,346 patients. Radiother Oncol. 2009;92(1):4-14.
4. Langendijk JA, Doornaert P, Rietveld DH, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. J Clin Oncol. 2008;26(22):3770-6.
5. Grégoire V, Mackie TR. State of the art on dose prescription, reporting and recording in intensity-modulated radiation therapy (ICRU report no. 83). Cancer Radiother. 2011;15(6-7):555-9.
6. Gupta T, Agarwal JP, Master Z, Murthy V, Budrukkar A, Laskar SG, et al. Randomized trial of parotid-sparing intensity-modulated radiotherapy versus conventional radiotherapy in head and neck cancer: long-term results of salivary function and quality of life. Radiother Oncol. 2012;104(3):343-7.
7. Nutting CM, Morden JP, Harrington KJ. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol. 2011;12(2):127-36.
8. Karnofsky DA, Burchenal JH. The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod CM, ed. Evaluation of Chemotherapeutic Agents. New York: Columbia University Press; 1949:191-205.
9. Grégoire V, Mackie TR, De Neve W, Gospodarowicz M, Purdy JA, van Herk M, et al. Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT): the ICRU report 83. J ICRU. 2010;10(1):1-106.
10. Bentzen SM, Constine LS, Deasy JO. Quantitative analyses of normal tissue effects in the clinic (QUANTEC): an introduction to the scientific issues. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S3-9.
11. 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;31(5):1341-6.
12. Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys. 2006;66(4):981-91.
13. Marta GN, Silva V, de Andrade Carvalho H. Intensity-modulated radiation therapy for head and neck cancer: systematic review and meta-analysis. Radiother Oncol. 2014;110(1):9-15.
14. Deasy JO, Moiseenko V, Marks L, Chao KS, Nam J, Eisbruch A. Radiotherapy dose-volume effects on salivary gland function. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S58-63.
15. Eisbruch A, Schwartz M, Rasch C. Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: which anatomic structures are affected and can they be spared? Int J Radiat Oncol Biol Phys. 2004;60(5):1425-39.
16. Jensen K, Lambertsen K, Grau C. Late swallowing dysfunction and dysphagia after radiotherapy for pharynx cancer: frequency, intensity and correlation with dose and volume parameters. Radiother Oncol. 2007;85(1):74-82.
17. Nguyen NP, Moltz CC, Frank C. Dysphagia following chemoradiation for locally advanced head and neck cancer. Ann Oncol. 2004;15(3):383-8.
18. Delanian S, Lefaix JL. The radiation-induced fibroatrophic process: therapeutic perspective via the

antioxidant pathway. Radiother Oncol. 2004;73(2):119-31.
19. Bese NS, Hendry J, Jeremic B. Effects of prolongation of overall treatment time due to unplanned interruptions during radiotherapy of different tumor sites and practical methods for compensation. Int J Radiat Oncol Biol Phys. 2007;68(3):654-61.

Cite this article as: Kucha N, Soni TP, Valiya K, Singh D. Late dysphagia, xerostomia and submucosal fibrosis following concurrent chemoradiotherapy for locally advanced head and neck squamous cell carcinoma: a prospective comparison of intensity-modulated radiotherapy and three-dimensional conformal radiotherapy. Int J Res Med Sci 2026;14:3257-66.