e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(1); 907-912

Original Research Article

An Investigation of the Feasibility of Using Adaptive Radiotherapy: A Real-World Experience

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Received: 01-11-2025 / Revised: 16-12-2025 / Accepted: 16-01-2026

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Conflict of interest: Nil

Abstract

Objective: Using predetermined relative thresholds as benchmarks, the study aims to quantify the anatomical and dosimetric changes that patients with head and neck cancer undergoing intensity-modulated radiation treatment experience and assess the necessity of adaptive radiotherapy.

Methods: 31 consecutive participants participated in this trial. For preliminary treatment planning and a halfway evaluation, two computed tomography (CT) scans were used. In order to apply primary dose calculation to midpoint CT, the study used rigid registration and contour transfer techniques. This resulted in a hybrid plan and an adaptive plan on the midpoint CT.

Results: The PTV70, PTV60, and PTV54 volumes showed statistically significant volume reductions, according to the results. In the majority of patients, the parotid glands' volume showed volumetric reductions. Comparisons between hybrid and adaptive plans revealed notable differences in the maximal doses, while hybrid plans showed poorer dose coverage of the tumor regions.

Conclusion: Replanning was mostly justified by anatomical variations that required a second CT scan and the use of a new immobilization mask. Before a replan is implemented, indicators such as a breach of 95% dose coverage for 95% of the tumor volume, maximum doses exceeding 50 Gy in the spinal cord and 59 Gy in the brainstem, and lateral neck displacement exceeding 1 cm from the initial position serve as benchmarks.

DOI: 10.25258/ijcpr.18.1.151

Introduction

In the head and neck (HnN) region, the proximity of organs at risk (OAR) to the tumour raises concerns about overdosage or underdosage in specific regions [1]. During HnN cancer radiotherapy (RT), monitoring of possible changes during treatment is crucial for the accuracy and preservation of therapeutic outcomes [2,3]. Tumour coverage and sparing of surrounding normal tissues leads to the best therapeutic outcome especially when high-precision RT techniques are implemented. Image-guided radiotherapy (IGRT) has significantly enhanced treatment precision by minimizing setup errors.4,5 Both offline and online IGRT correction strategies are applied to optimize treatment reproducibility, aiming to reduce the margins between the clinical target volume (CTV) and the planning target volume (PTV) as much as possible, while still achieving the desired clinical outcome. In clinical practice, patient imaging is used before and during treatment, to preserve the accuracy and efficacy of radiation treatment. Several studies noted that anatomical changes occur around the third or fourth week of treatment [6,7]. Adaptive radiotherapy (ART) is the result of incorporating anatomical and dosimetric variables into the treatment plan. The goal of ART improved by IGRT is to detect anatomical alterations. Potential discrepancies between the intended and actual dosages administered to the tumor and the OARs are the focus of this strategy.8–10 As a result, ART entails modifying and carrying out the treatment plan in accordance with the tumor's response and the morphological alterations in normal structures, which becomes crucial.11 A new treatment plan based on the repeat-midpoint computed tomography (CT) scan must be adopted and compared with the original treatment plan that is currently being given to the patient in cases where significant anatomic differences occur during treatment therapy. The first dose calculation on the original CT and the initial dose calculation transferred and calculated on the repeat CT, which is typically referred to as the hybrid plan, are compared.Twelve It should be possible to recalculate the initial treatment plan to account for the updated anatomy, allowing the plan to be adjusted to these anatomical changes, according to the hypothesis, which is based on the analysis of registered images and structures. There are many advantages to starting ART for patients with HnN cancer, especially in terms of limiting overexposure in vital organs to improve future quality of life.

In order to assess whether a replan is necessary, the current study intends to describe an implementation of ART for HnN patients using a hybrid plan and midway CT. Analysis has been done on volumetric and dosimetric variations over the course of treatment. There have also been given anatomic and dosimetric trigger points that may indicate the necessity for a replan.

Materials & Methods

According to the American Joint Committee on Cancer and Eastern Cooperative Oncology Group criteria, 31 consecutive patients with HnN cancer who were 15 years of age or older and diagnosed with different forms of HnN cancer at stages I to IV and performance status 0 to 2 were included in this study. Multimodal scans (CT, MRI, and PET-CT) were used for radiological diagnosis, which were verified by a multidisciplinary team consensus. Over the course of 30–33 fractions (6–7 weeks), patients received either definitive or postoperative concurrent step-and-shoot IMRT. OARs and tumor volumes were defined in accordance with ICRU guidelines.13–15 Using visible tumors, suspicious lymph nodes, and imaging methods such CT, MRI, and FDG-PET, gross tumor volume (GTV) was determined. Anatomical boundaries were used to define CTV; the primary tumor's CTV expanded from its GTV, and the CTV of the affected lymph nodes extended three Multimodal scans (CT, MRI, and PET-CT) were used for radiological diagnosis, which were verified by a multidisciplinary team consensus. Over the course of 30–33 fractions (6–7 weeks), patients received either definitive or postoperative concurrent step-and-shoot IMRT. OARs and tumor volumes were defined in accordance with ICRU guidelines. The daily doses were 2–2·12 Gy for the tumor bed, 1·8 Gy for high-risk lymph nodes and microscopic tumor regions, and 1·64 Gy for low-risk lymph nodes.16–21 In order to fulfil the suggested dose limitations during treatment planning, doses to the OARs have been compromised.22 The prescribed doses varied; in the macroscopic disease, 16 patients received 70 Gy, whereas 14 received 66 Gy. At high-risk lymph nodes, the majority (25/31) got 60 Gy. Furthermore, two patients received 50 Gy in low-risk lymph nodes and 25 patients received 54 Gy. PTV50 data were not included since there were not enough patients (2/31). Any obvious anatomical changes or shifts in the patient's position were observed and assessed.

Cubic centimeters (cc) were used to measure the volumetric changes of targets and OARs between CT1 and CT2. To evaluate potential alterations, neck separation at the levels of the C2 and T1 spinal vertebrae was assessed in both CT1 and CT2.23 Different plan quality criteria, including as D95, D50, D2, Dmean, and Dmax, were used to assess dosimetric changes. The statistical study was conducted using IBM's SPSS program, version 21.00. Variables were described using descriptive statistics, and the normality of quantitative variables was verified by the Kolmogorov-Smirnov test. CT1 and CT2 volumes as well as the effect of replanning were evaluated using a paired samples t-test. The threshold for significance was fixed at $p < 0.05$.

Results

Volumetric changes: Tumor and parotid volumes showed notable morphological and volumetric changes following RT (Table 1, Figure 1). In particular, 15/16 patients who received 70 Gy to the tumor bed showed a significant 15% decrease in PTV70 volume ($p < 0·005$). PTV66 showed a 16% volume reduction in 11/14 patients who received 60 Gy, although this was not statistically significant. Furthermore, 22 out of 25 patients showed an 11% decrease in volume for PTV60, while 20 out of 25 patients showed a 15% decrease in volume for PTV54 ($p < 0·005$).

Table 1: Volume variations of tumour regions and OARs

PTV	Parameters	Mean Volume (cc)	P Value
PTV-70	CT1,vol	196,36± 63,73	<0·005
	CT2,vol	177,31± 55,91	
PTV-66	CT1,vol	200,40±126,46	0·067
	CT2,vol	173,34±109,93	
PTV-60	CT1,vol	302,03±232,97	<0·005
	CT2,vol	269,80±195,01	
PTV-54	CT1,vol	287,97±202,56	<0·005
	CT2,vol	264·92±190·22	
Parotid R	CT1,vol	25,28±11,48	<0·005
	CT2,vol	20,15±9,05	
Parotid L	CT1,vol	25,02±10,63	<0·005
	CT2,vol	19,98±8,20	

In 27 cases, the right parotid gland's capacity was reportedly reduced by 18%. Similarly, 25 patients showed a 20% reduction in the left parotid gland. All patients showed significant decreases in lateral height at the C2 and T1 vertebral levels (p < 0.001), with an average loss of 2.6 cm at T1 and 1.1 cm at C2. When compared to their baseline weight, a 12% weight decrease was noted at the time of the midpoint CT scan.

Table 2: Total statistical results of the paired analysis in tumour regions

Structure Deviation	Parameters	D95		D2		Dmax	
		HYB-INT (Gy)	HYB-ART (Gy)	HYB-INT (Gy)	HYB-ART (Gy)	HYB-INT (Gy)	HYB-ART (Gy)
PTV70	Mean ± SD	−1·03 ± 1·69	0·47 ± 2·12	0·33 ± 1·1	0·37 ± 1·54	0·25 ± 1·68	1·39 ± 2·06
	p-value	0·027	0·389	0·249	0·349	0·562	0·016
PTV66	Mean ± SD	−1·11 ± 1·16	−0·9 ± 1·64	−0·11 ± 1·73	0·7 ± 1·39	−0·02 ± 2·36	1·50 ± 2·15
	p-value	0·05	0·084	0·812	0·082	0·981	0·022
PTV60	Mean ± SD	−0·55 ± 1·85	−0·44 ± 2·13	2·41 ± 2·73	1·76 ± 4·72	2·16 ± 2·33	2·46 ± 4·41
	p-value	0·148	0·312	<0·001	0·074	<0·001	0·01
PTV54	Mean ± SD	−1·53 ± 2·35	−1·29 ± 2·11	0·49 ± 3·74	1·23 ± 2·78	0·47 ± 4·57	1·41 ± 2·86
	p-value	0·03	0·05	0·516	0·036	0·612	0·021

Dosimetric changes

When compared to both INT and ART plans, the HYB plans showed worse total D95 coverage (Table 2). The coverage of D95 in the PTV regions was kept from the original computation in ART plans. There was a substantial difference between HYB and ART plans, and only the PTV54 showed statistically significant results (p < 0·005). When comparing INT and HYB, the dose of Dmax was elevated, and most patients had higher D2. In particular, 70% (22/31) of patients in PTV60 and PTV54 showed a mean increase of 3·5% in the dose coverage of D2.

Compared to both initial and adaptive designs, hybrid plans showed slight changes in D50 coverage (pThe coverage of D95 in the PTV regions was kept from the original computation in ART plans. There was a substantial difference between HYB and ART plans, and only the PTV54 showed statistically significant results (p < 0·005).

Table 3: Total statistical results of paired analysis in OARs

Organ at risk (OAR)	Parameters	Dmean	
		HYB-INT (Gy)	HYB-ART (Gy)
Parotid Right	Mean ± SD	1·54 ± 5·0	2·21 ± 7·19
	p-value	0·102	0·103
Parotid left	Mean ± SD	2·86 ± 7·10	3·45 ± 6·78
	p-value	0·039	0·011

Additionally, dosage variations to OARs were analyzed (Table 3). Due to anatomical alterations that required replanning, the study found higher parotid gland doses in HYB compared to ART designs. In particular, the mean dose to the right parotid increased by 16.5% and the mean dose to the left parotid increased by 13% in 7 out of 31 patients, but the mean dose to both parotids decreased by 13% in other patients receiving ART. Parotid dosages showed non-significant results and similarities between INT and ART programs.

Table 4: Total statistical results of paired analysis in OARs

Organ at risk (OAR)	Parameters	D2 (SD)		Dmax (SD)	
		HYB-INT (Gy)	HYB-ART (Gy)	HYB-INT (Gy)	HYB-ART (Gy)
Brainstem	Mean ± SD	0·86 ± 5·2	2·65 ± 6·69	1·35 ± 4·98	2·19 ± 6·48
	p-value	0·391	0·045	0·162	0·097
Spinal cord	Mean ± SD	0·479 ± 3·27	1·54 ± 5·66	0·36 ± 3·93	2·07 ± 5·33
	p-value	0·422	0·142	0·611	0·039

Because the maximum dose exceeded dose limitations in five out of thirty-one individuals, excess spinal cord radiation in HYB plans required replanning. Twenty out of twenty-eight patients reported a 10% increase in brainstem dosages, even though these were still within HYB plans.

Discussion

Adynamic strategy in radiation oncology that takes into account the complexity and unpredictability of tumor and normal tissue geometry throughout therapy is demonstrated by the use of ART in the management of HnN cancer. A sophisticated strategy is required to guarantee that the radiation dose administered is both safe and effective because of the intrinsic changes in the patient's anatomy brought on by the tumor's reaction to treatment, weight loss, or tissue oedema. A crucial part of this approach is the mid-treatment CT scan, which provides a current picture of the patient's anatomy that may be used to assess and, if required, modify the treatment plan to improve tumor control while protecting nearby healthy tissues.

Comparisons between HYB and ART plans revealed that HYB plans had greater maximum doses with notable variations throughout the tumor and periphery. There were no discernible changes between ART and HYB plans in terms of tumor dosage coverage. However, HYB plans showed a decline in D95, especially in regressed tumor locations (PTV66, PTV60, and PTV54), which did not meet the suggested D95 ≥ V95 requirement.

A replan was required when the comparison of the INT and HYB plans revealed statistically significant results in the PTV70, PTV66, and PTV54 regions. A mean drop of 65% was seen in target locations that included nodal tissues (PTV60 and PTV54), which correlated with the initial nodal volume deduction. The findings of Bhandari et al. and Aly et al. also led to adaptations since the D95 dosage coverage of tumors decreased [6, 25].

CT scans revealed significant alterations in the neck area, particularly at the C2 and T1 levels. Similar to the findings of the Munich Radiation Oncology Department study, patients in the current trial who had a mean neck separation decrease of more than 1 cm—particularly as a result of severe weight loss—were given a new immobilization mask, which prompted a new CT scan and a replan.Halfway through their RT course, 26 patients lost an average of 12% of their body weight. As a result, the majority of patients showed significant volume decrease at mid-treatment CT, with high consideration for ART, in PTV areas and OARs, particularly in PTV66, PTV60, and PTV54.

Additionally, replanning improved patients' quality of life and increased parotid gland sparing [27, 28]. A mean reduction in parotid volume ($p < 0{\cdot}005$) was observed in this investigation. This outcome is consistent with the decrease in neck separation observed at the level of the C2 vertebral spine, which is home to the parotids. The mean dose of the left parotid gland showed significant variations, increasing by 2·9 Gy in HYB against INT plans and 3·4 Gy in HYB versus ART plans, respectively ($p < 0{\cdot}05$). Comparisons of the right parotid gland did not produce significant results, but hybrid plans showed a mean increase of 2·2 Gy, which is comparable to the findings of Lui et al.'s study [29].

Due to considerable shrinkage (> 31·1%) associated with weight loss and patient age, an 85-patient research highlighted mid-treatment replanning. Thirty The significance of mid-treatment replanning when weight loss variations are more noticeable was underscored by the link between volume loss and an increased mean dose to the parotids. The original dosage calculation of the brainstem and spinal cord was impacted by changes in the surrounding area brought on by things like weight loss, tumor shrinking, and decreased neck separation. Replanning became necessary when the maximum dose surpassed the specified limits (spinal cord Dmax< 45–48 Gy, brainstem Dmax< 59 Gy). However, comparisons of HYB plans between INT and ART plans have not produced statistically significant results.

The fact that CT image registrations were only done at the start and middle of the treatment course was one of the main obstacles to the deployment of ART. As a result, rather of being accurately measured, the dose given to the patient for each fraction was guessed. Relying on dosimetric data from hybrid methodologies as a conservative approach to assessment supported the need for replanning. Furthermore, several forms of HnN cancer were included in the current investigation, and actual dose distributions and intended dose limitations depended on a number of variables. However, setting up replanning trigger points could act as stand-ins before ART is fully implemented.

Conclusion

When patients with HnN cancer experience anatomical and dosimetric changes following radiation therapy, ART has been shown to be required. In addition to calculating a hybrid plan to determine whether a replan is necessary, a mid-treatment CT scan is recommended to offer information on the patient's anatomy. Surrogates for the application of ART include exceeding the maximal dose of vital organs and violating the dose coverage of the tumor volume. The precision needed in radiation is highlighted by the criteria for applying ART, which are based on dose coverage of the tumor volume and adherence to dosage limitations for important organs.

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