RESEARCH ARTICLE

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Assessment of Anatomic Surface Contour Variations During Radiation Therapy in Oral Cavity Cancer Patients with Flap Reconstruction by Co-Registering Planning CT and Cone Beam CT Scan

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Abstract

Background: Oral cavity cancer (OCC) patients undergoing flap reconstruction during surgery present unique anatomical challenges during postoperative radiation therapy (PORT). Variations in body contour and internal anatomy can affect dose distribution and necessitate adaptive radiotherapy (ART). However, limited data is available regarding the frequency, timing, and causes of re-planning. **Objective:** To evaluate anatomical surface contour variations and the need for adaptive re-planning in OCC patients with flap reconstruction (OCCwFR) receiving PORT using co-registration of planning CT and cone-beam CT (CBCT). **Methods:** This prospective observational study included adult OCCwFR patients treated with curative-intent PORT. Daily portal imaging and weekly CBCTs were analyzed. Variations greater than 1 cm across three or more consecutive CBCTs were considered significant. Changes were categorized as progression, regression, internal target motion, or setup error. Factors associated with adaptive re-planning were recorded. **Results:** Among 111 patients, 39 (35%) required re-planning. Regression was the predominant change (92%), mainly due to weight loss (80%), followed by edema resolution and tumor response. Re-planning occurred mostly around the 20th fraction. Progression-related changes were rare (5%) and occurred earlier (3rd week). No association was found between flap type and re-planning (p= 0.21). Weight loss strongly correlated with re-planning (χ^2= 45.5, p< 0.0001) and mean volume reduction of 50 cc. **Conclusion:** Anatomical changes during PORT in OCCwFR patients are frequent, predominantly due to weight loss. Mid-treatment ART around the 5th week and proactive nutritional support are essential to maintain dosimetric accuracy and treatment efficacy.

Keywords: adaptive radiation therapy- cone beam CT-scan- weight loss

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Introduction

Oral cavity cancer (OCC) is a major public health concern. It ranks as the 16th most common cancer worldwide, with an estimated 390,000 new cases and 150,000 deaths each year [1, 2]. The incidence is particularly higher in lower middle-income countries (LMICs), where it reaches 6.5 per 100,000 population, making it the sixth most common cancer in these regions. The standard of care treatment for OCC is surgical resection often followed by the adjuvant treatment when indicated [3]. Chemo-radiation therapy as an adjuvant treatment has been shown to improve loco-regional control, disease free-survival and overall survival [4].

Radiation therapy (RT) for head and neck cancers is challenging considering the anatomic variations that occur during treatment [5]. Advanced tumors can shrink considerably during RT, altering the position and shape of adjacent structures and external surface contour of the body. Patients may also experience variations such as reduction in nodal masses, weight loss or resolving postoperative edema which can significantly affect treatment accuracy [6]. Apart from changes in the initial target volume, normal tissue delineation and anatomic surface variation these changes also include external daily setup variations and internal geometric and volumetric changes occurring throughout the 6–7-week RT course [7-10]. Considering these challenges,

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Radiation Oncologists (RO) now rely on deformable image registration techniques, i.e. co-registering cone beam computed tomography scan (CBCT) and planning CT scan, to track variations over time. Onboard CBCT and off-board portal image verification are widely being used by ROs during treatment to monitor these changes and support adaptive planning [11-13].

Despite these advancements, the impact of adaptive re-planning in postoperative radiation therapy (PORT) for OCC in patients who have undergone flap reconstruction (OCCwFR) during primary surgery to restore oral cavity form and function, remains poorly defined, largely due to limited data availability [14-17]. Our study aimed to evaluate these anatomical variations in OCCwFR undergoing PORT. We also aimed to evaluate the frequency and trend of re-planning, and to determine whether different types of reconstruction flaps influence the need and pattern of replanning.

Materials and Methods

A prospective, cross-sectional observational study was carried out between January 2023 and December 2024. Ethical approval for the study was obtained from the Institutional Review Board. Eligible participants included all biopsy-confirmed cases of stage I–IV oral cavity squamous cell carcinoma aged 18 years and above who had undergone surgery with flap reconstruction and were receiving curative-intent PORT with adaptive re-planning. The study included routine clinical patients scheduled for PORT.

For treatment planning, patients were immobilized using a custom five-point thermoplastic face and neck mask during simulation. A planning-CT scan was acquired and registered in the ARIA system for contouring and treatment planning. Once the treatment plan was finalized and approved, patients commenced RT.

Throughout the treatment, daily kV, mV imaging and weekly CBCT scans were performed as part of routine monitoring, along with weekly physical examinations. Daily portal imaging was used to verify bony alignment and soft tissue reconstruction. Any gaps noted in the mask during treatment were correlated with clinical examination and reviewed against CBCT or portal imaging.

Anatomical changes more or less than 1 cm in external body contour observed and quantified using rigid body displacement of bony anatomy or a single point of a soft organ, on three or more consecutive CBCT scans were considered significant (Figure 1.A-F). These changes were further confirmed clinically by noting either looseness or tightness in the mask. All variations were categorized as progression, regression, internal target motion, setup error, or other. Progression was further subclassified as disease progression, edema-related progression, or weight gain, while regression included treatment response, resolution of postoperative changes, or weight loss. Internal target motion was classified into occipito-cervical, cervical, or mandibular movements.

Initial assessments were performed by radiation therapy technologists (RTTs) during CBCT acquisition or patient setup, who alerted the RO if changes were

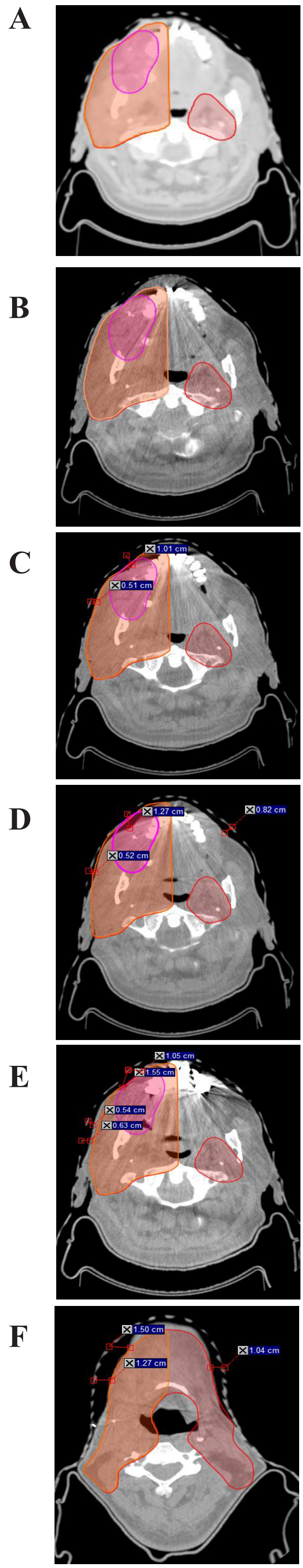

Figure 1. A-F, Gradual Decrease in Cheek Contour at Flap Site and Appearance of Gaps through Subsequent Fractions (A-E). Significant gap observed later at hyoid bone level also (F).

G

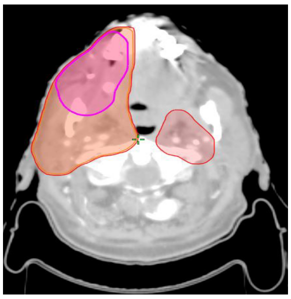

Figure 1. G, Patient re-planned and Mask adjusted to Cover the Gap

observed, or vice versa if changes were detected during portal image review by RO to RTTs. Decisions regarding adaptive re-planning (Figure 1.A-F). were made after detailed analysis and discussion with the clinical medical physicist. The specific reason for re-planning was documented along with the number of fractions, changes in patient weight and target volume (in cubic centimeters) across all treatment phases.

Results

A total of 111 patients with OCC with reconstructed flaps were treated with PORT and 39 of them underwent re-planning. The median age was 43 years (27-73). There was a strong male predominance (97%) Table.1. The most common tumor subsite was buccal mucosa (82%) with stage IV (77%) and grade-II disease (54%). All patients received VMAT-based radiation therapy with concurrent chemotherapy and had PEG tubes in place. The most frequently used flaps were the anterolateral thigh flaps (ALTF, 49%). Anatomic variations observed during treatment were predominantly regression (92%), with progression and setup errors each accounting for 5% and 3%, respectively. Within progression, disease progression and edema each comprised 50% of cases. Among regression cases, weight loss was the leading subtype (80%), with resolution of edema (11%) and treatment response (3%) being less common. The median number of fractions for re-planning was 21st fraction (4-28) at 5th week of treatment. ALTF was re-planned at 20th fraction, Pectoralis major flap at 18th fraction, radial forearm at 20th fraction, nasolabial at 20th and free fibular at 25th (Figure.2). However, there was no statistically significant association between type of flap and type of anatomic variation ($p= 0.21$). Treatment dose was via conventional fractionation for 7000 cGy in 35 fractions (72%). The mean difference in weight from the start of treatment to re-planning was 3 kilograms. It was observed that there was a mean difference of 50 cc volume in phase-II and 7 cc volume in phase-III at the time of re-planning (Table 2). Statistical analysis confirmed that weight loss was the predominant cause of anatomical regression among patients undergoing PORT with adaptive planning. This was supported by a highly significant Chi-square test result ($\chi^2 = 45.5$, $p < 0.0001$).

Table.2 Compares patients with “Progression” vs. “Regression” anatomic variation in terms of several variables measured at re-planning. Patients with

Table 1. Patient Characteristics

Characteristics	No. (%)
Gender	
Male	38 (97.4%)
Female	1 (2.6%)
Site	
Oral Cavity Primary	39 (100%)
Sub-Sites	
Alveolar Ridge	3 (7.7%)
Buccal Mucosa	32 (82.1%)
Retromolar Trigone	1 (2.6%)
Tongue	3 (7.7%)
Histopathology	
Squamous Cell Carcinoma	39 (100%)
Grade	
I	13 (33.3%)
II	21 (53.8%)
III	5 (12.8%)
Stage of The Disease	
I	1 (2.6%)
II	1 (2.6%)
III	7 (17.9%)
IV	30 (76.9%)
Intent of Therapy	
Curative	39 (100%)
Definitive Surgery	
Yes	39 (100%)
Presence of Flap	
Yes	39 (100%)
Type of Flap	
ALTF	19 (48.7%)
Free Fibular	4 (10.3%)
Nasolabial	1 (2.6%)
Pectoralis Major	9 (23.1%)
Radial Forearm	5 (12.8%)
Supraclavicular Flap	1 (2.6%)
Presence Of Peg Tube	
Yes	39 (100%)
Concurrent Chemo	
Yes	39 (100%)
RT Technique	
VMAT	39 (100%)
Total Dose (cGY)	
6600	10 (25.6%)
7000	28 (71.8%)
7475	1 (2.6%)
Type of Anatomic Variation	
Progression	2 (5.1%)
Regression	36 (92.3%)
Internal Target Motion	-
Setup Error	1 (2.6%)

Table 1. Continued

Characteristics	No. (%)
Sub-Types of Progression	
Disease Progression	1 (2.6%)
Edema	1 (2.6%)
Weight Gain	-
Sub-Types Of Regression	
Treatment Response	1 (2.6%)
Resolution Of Edema	4 (10.3%)
Weight Loss	31 (79.5%)
Sub-Types of Internal Target Motion	-
Occipito-Cervical	
Cervical Alone	
Mandibular	
Setup Error	
Misalignment	1 (2.6%)

Abbreviations. ALTF, Anterolateral Thigh Flap; VMAT, Volumetric Modulated Arc Therapy

regression needed significantly more fractions at the time of replanning (5th week). Possibly, regression (weight loss) accumulates over a longer RT course, necessitating replanning later. While progression cases triggered replanning earlier (3rd week). Patients who had regression had significantly greater difference in volume (cc) at Phase-2. This suggests regression is associated with bigger mid-treatment anatomical shifts requiring dose adaptation.

Discussion

This study highlights the role of adaptive radiation therapy (ART) in adjuvant setting in OCCwFR. Image guided ART has become an important tool in the management of head and neck cancers, addressing the significant anatomical changes that occur during radiation treatment [18-23]. These anatomical variations can lead to dosimetric deviations, affecting both target coverage and sparing of organ-at-risk [12, 17]. Studies evaluating CTV shrinkage and organ at risk doses in definitive radiation therapy demonstrated that CTV shrinkage occurs gradually, with a 5% reduction by the 18th fraction and a 14% reduction by the 22nd fraction. Furthermore, a mean reduction of 76.44 cm^3 in PTV low-risk volume and 47.10 cm^3 in PTV high-risk volume have been reported [8, 11]. Similarly, the volumes of parotid glands shrink

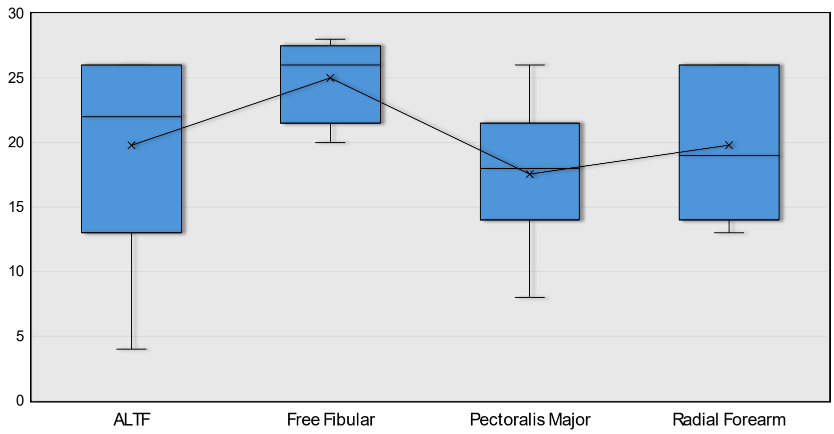

Figure 2. Box-and-Whisker Plot Illustrates the Distribution of the Number of Fractions at which re-Planning was Required According to Flap Type. Median (IQR; range): ALTF 22 (13–26; 4–26), Free Fibular 26 (21.5–27.5; 20–28), Pectoralis Major 18 (14–21.5; 8–26), Radial Forearm 19 (14–26; 13–26). The overlaid line indicates the mean: ALTF 19.8, Free Fibular 25.0, Pectoralis Major 17.6, and Radial Forearm 19.9 fractions. Data for Supraclavicular and Nasolabial flaps were excluded from the graph due to limited sample size (n=1 each).

Table. 2. Replanning was Predominantly Performed for Tumor Regression and Occurred at a Significantly Later Number of Treatment Fractions Compared to Progression ($p = 0.026$). Dose variation during Phase 2 was significantly greater in the regression group ($p = 0.034$), indicating a stronger impact of anatomical changes on dose distribution. No significant differences were observed in the week of CBCT at replanning or Phase 3 dose variation between the two groups.

	Variation	Frequency (n)	Mean Value	Standard Deviation	P-Value
Fractions at replanning	Progression	2	11.5	0.7071	0.026
	Regression	36	20.806	5.8	
Week of CBCT at replanning	Progression	2	3	0	0.071
	Regression	36	4.75	1.339	
Difference of Dose (Phase 2)	Progression	2	2.4	1.555	0.034
	Regression	36	54.4333	46.549	
Difference of Dose (Phase 3)	Progression	2	8.3	10.74	0.922
	Regression	36	7.7083	26.17978	

by 16–24%, requiring adaptation to prevent over dosage to these structures [12, 13, 23]. In addition, setup errors contribute to treatment uncertainties. Attachment of the rigid skull to the semi-rigid cervical spine and mandible leads to rotational (pitch, roll, yaw) and translational shifts along the x, y, and z axes resulting in dose differences between the planned dose and the delivered dose [10, 24, 25]. Such variations may compromise local tumor control, increasing the risk of radiation-related toxicity and disease recurrence [26].

Our work demonstrates the importance of adaptive strategies in the postoperative setting, i.e. that most anatomic changes, prompting replanning, occurred around the 20th fraction (5th week), driven primarily by weight loss. Regression-type anatomical changes dominated (92%), with weight loss accounting for nearly 80% of those cases. Statistical analysis confirmed weight loss as a highly significant factor in regression-related replanning. Since weight loss was the major factor leading to regression, aggressive nutritional intervention including dietitian consultation, close weight monitoring and early feeding tube management should be implemented. Moreover, our analysis of timing highlighted that progression-type variations occurred earlier (mean 3rd week), driven by edema or disease progression, while regression-type variations requiring replanning appeared later (mean 5th week). This aligns with the gradual nature of weight loss–driven anatomical changes. According to a systematic review and meta-analysis, all free flaps show a volume reduction that progresses over time post-surgery, with adjuvant radiotherapy significantly accelerating and increasing the magnitude of volume loss. However, flap type, including anterolateral thigh versus radial forearm free flaps, did not significantly influence the degree of radiation-associated volume reduction [27]. Although flap type was not a significant predictor of progression or regression in our cohort, temporal patterns suggested subtle differences in the timing of these changes. Patients with pectoralis major flaps often required earlier replanning (around the 18th fraction), whereas those with ALTF or free fibular flaps required it closer to the 22nd- 26th fractions. These observations suggest that flap type may influence volumetric stability and timing of anatomical changes, meriting further investigation.

We could not evaluate dosimetric impacts on organs at risk, such as parotid glands, constrictor muscles, and spinal cord. In definitive RT, adaptive planning has shown clear benefits in reducing OAR doses [28-31]. Schwartz et al. showed that adaptive planning led to significant dosimetric impact such as improvement of contralateral parotid sparing by 0.6 Gy and ipsilateral parotid sparing by 1.3 Gy [23]. ART has been shown to achieve a reduction in the mean dose of parotid glands by 0.6-6 Gy, maximum dose to the spinal cord by 0.1-4 Gy, and setup error reductions of 1 to 1.5 mm [5, 18]. Additionally, prior studies have linked setup errors greater than 3 mm with marginal failures as well [23]. However, most of this data comes from definitive settings, with limited evidence for postoperative patients with flap reconstruction.

Prospective trials evaluating adaptive strategies across different flap types, with comprehensive dose assessment for critical OARs, are needed. Such research could help define evidence-based protocols for timing and frequency of imaging, nutritional interventions, and plan adaptation to improve both oncologic and functional outcomes in OCC patients undergoing PORT with flap reconstruction.

In conclusion, our study demonstrates the importance of assessing OCC patients with flap reconstruction, during RT to identify the need for re-planning. Implementing weight monitoring, mid-treatment imaging and flap-specific adaptive strategies would help to optimize treatment accuracy in patients undergoing PORT.

Author Contribution Statement

Mariam Hina: substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; drafting the article and revising it critically for important intellectual content. Muhammad Umer: substantial contributions to analysis and interpretation of data. Bilal Ahmed: revised the draft critically for important intellectual content. Maham Khan: revised the draft critically for important intellectual content. Laraib Khan: revised the draft critically for important intellectual content. Tooba Ali: revised the draft critically for important intellectual content. Tahir Munir: substantial contributions to analysis and interpretation of data. Muhammad Abdul Wasay: substantial contributions to analysis and interpretation of data. Zaka-ur-Rehman Khan: revised the draft critically for important intellectual content. Maria Tariq: revised the draft critically for important intellectual content. Nasir Ali: revised the draft critically for important intellectual content. Asim Hafiz: revised the draft critically for important intellectual content. Ahmed Nadeem Abbasi: revised the draft critically for important intellectual content. Bilal Mazhar Qureshi: substantial contributions to analysis and interpretation of data; drafting the article and reviewing it critically for important intellectual content.

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If it was approved by any scientific Body/ if it is part of an approved student thesis

Approved by Ethical Review Committee of the primary institute.

Any conflict of interest

None.

How the ethical issue was handled (name the ethical committee that approved the research)

Approved by Ethical Review Committee of the primary institute.

Availability of data (if applicable to your research)

The datasets analyzed during the current study are not publicly available due to ethical and privacy restrictions involving patient data but are available from the corresponding author on reasonable request.

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