A Study on Anatomical Changes during Intensity Modulated Radiotherapy for Head and Neck Cancer

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Abstract- The anatomy of a patient's tumor can change significantly during the course of radiotherapy. This study aims to evaluate the impact of anatomical changes on pre-treatment planning during intensity modulated radiotherapy (IMRT) for head and neck cancer. A total of 60 head and neck cancer patients treated with weekly cone beam-computed tomography (CBCT) guidance were included in the study. Digimizer™ software was used for image processing to assess anatomical deviations at the C1 and C5 vertebral levels. CBCT images from the first day, mid-day, and the last day were analyzed. The highest mean slice surface area deviations were 4.8% at the C1 level and 10.1% at the C5 level. The mean highest lateral neck diameter deviations were 4.7% at the C1 level and 7.8% at the C5 level. Significant deviations in both parameters suggest the need for adaptive radiotherapy planning in IMRT to address progressive anatomical changes, ensuring optimal therapeutic outcomes.

Keywords- Cone beam computed tomography, Head and neck cancer, Intensity modulated radiotherapy, Linear accelerator

INTRODUCTION

Squamous cell carcinoma of the head and neck is the seventh most common cancer globally[1]. It accounts for approximately 660,000 cases and more than 325,000 deaths worldwide each year[2]. Lip-oral cavity cancer is one of the most common cancers among males in Sri Lanka[3]. IMRT is the most common type of external beam radiotherapy used for head and neck cancer. Both IMRT and three-dimensional conformal radiotherapy (3D-CRT) are widely practiced in head and neck cancer treatment in Sri Lanka[4].

The IMRT treatment plan is typically developed based on a single computed tomography (CT) scan obtained one or more weeks before treatment. Radiotherapy doses are calculated using this scan, and treatment plans are rarely amended during treatment due to the increased workload caused by a growing number of cancer patients[5]. However, the shape and position of target volumes and organs-at-risk (OARs) can change between radiation treatment planning and delivery, as well as throughout the radiotherapy course. These changes, often caused by weight loss or tumor shrinkage, may result in subtle or significant alterations in the size, shape, and location of the tumor and OARs, potentially affecting the accuracy of radiation dosimetry.

This conventional approach, based on a single planning CT dataset, does not account for anatomical changes or variations in patient positioning during the typical 5-7 weeks of treatment. As a result, even highly conformal IMRT plans may lead to unexpected complications or marginal geographic misses of the target volumes. To mitigate these effects, safety margins are traditionally applied around the clinical target volume to ensure adequate coverage. However, this also exposes surrounding healthy tissue to high radiation doses, increasing the risk of unacceptable side effects.

In IMRT, radiation doses must be delivered precisely to the target volume while ensuring that doses to OARs do not exceed their tolerance levels. Accurate patient positioning is crucial and should replicate the setup during the CT simulation procedure. Verification of patient anatomy is achieved using electronic portal imaging or cone-beam CT (CBCT) before treatment. CBCT images or radiographs can be compared with digitally reconstructed radiographs (DRRs) generated from the treatment planning system[7]. The imaging dose from kV radiographs and kV-CBCT scans is substantially lower than that from conventional MV portal imaging. Using kV imaging improves image quality and reduces patient radiation exposure compared to MV imaging.

Image guided radiotherapy (IGRT) involves acquiring images of the patient's anatomy in the treatment room, comparing the tumor's position during treatment with the planned position, and correcting for deviations. While IGRT is widely used in clinical practice, it assumes that target shapes and OAR doses remain relatively unchanged. However, anatomical changes such as weight loss, posture variations, tumor regression, or differential motion between the primary tumor and involved lymph nodes often challenge these assumptions[6].

The primary goal of Adaptive Radiotherapy (ART) is to deliver radiotherapy precisely and account for anatomical changes during treatment. ART employs an imaging feedback loop to quantify these changes and adjust the treatment plan accordingly. Current ART approaches rely on in-room megavoltage CT or CBCT images acquired before daily treatment. The aim of this study is to evaluate planning target volume (PTV) changes in patients undergoing IMRT using daily kV-CT scans acquired before each treatment fraction on a LINAC machine.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted with 60 head and neck patients who completed their IMRT treatment between July 2019 to February 2022 at the Elekta™ Synergy linear accelerator unit, Apeksha Hospital, Maharagama, Sri Lanka. Patients treated with IMRT under kV-CT image guidance, with a minimum prescribed dose of 60 Gy in 30 fractions, and immobilized using a 5-point fixation thermoplastic shell were included in this study. Patients who did not complete their radiotherapy treatment were excluded. The details of the selected patients are shown in Table 1.

Table 1: The details of the selected patients and treatment protocols.

Age (years)	Between 20 to 80	
Gender	Male	49 (81.7%)
	Female	11 (18.3%)
Diagnosis	Oropharynx	36
	Larynx	5

	Oral cavity	6
	Nasopharynx	4
	Hypopharynx	3
	Salivary gland	6
Dose fractionation	70 Gy in 35 fractions	54
	60 Gy in 30 fractions	6
Neck irradiation	Unilateral	14
	Bilateral	46

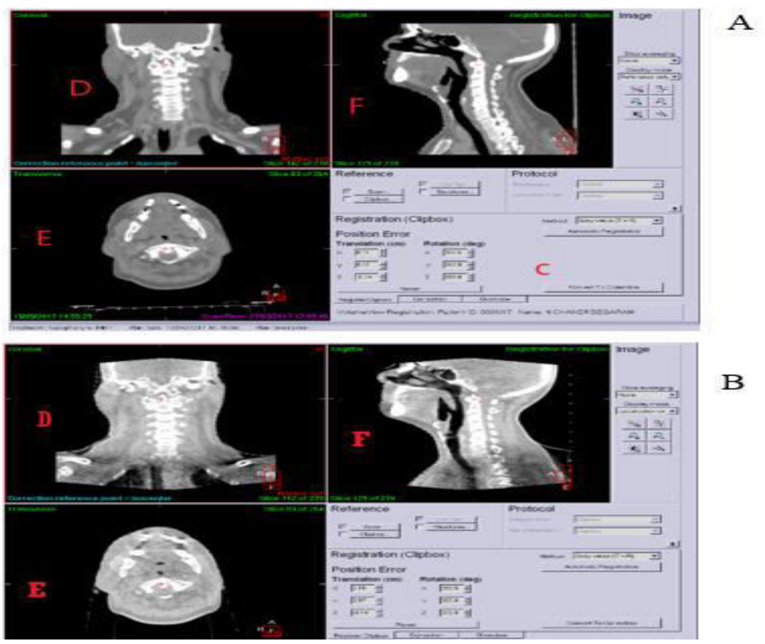


Figure 1: A-Planning CT image generated by treatment planning system. B-CBCT image obtained just prior to the delivery of treatment. C-Automatic registration. D-Coronal plane window. E-Axial plane window. F-Sagittal plane window.

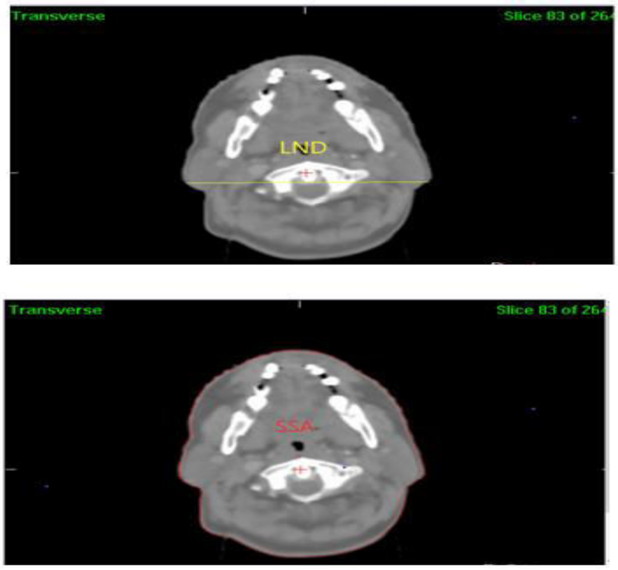
CBCT is an important tool for verifying patient setup in relation to the position of the radiation beam. An isocentrically mounted Elekta iViewGT™ CBCT imaging system was used to acquire volumetric cross-sectional CBCT images. Typically, an X-ray radiation beam with an energy of 120 kVp is used for the acquisition of CBCT images. Visual comparisons between CBCT images and the planning CT images were performed by matching clearly visible soft tissue and bony landmarks in the area of interest. CBCT images acquired during the first fraction, mid fraction, and, last fraction of treatment were selected for this study to compare with planning CT images. All images captured by the Elekta iViewGT™ system are automatically stored for review purposes. These images can be reviewed offline using the MOSAIQ® oncology information system as shown in Figure 1.

A total of 800 planning and CBCT cross-sectional images were processed using Digimizer™ 5.4 software (MedCalc Software Ltd) as shown in Figure 2. Relevant planning CT images (used as reference CT images) were compared with CBCT images from the first fraction of treatment, the mid fraction of treatment, and the last fraction of the treatment. To evaluate anatomical deviations during fractionated radiotherapy, axial plane cross-sectional planning

CT and CBCT slices at specific anatomical vertebral levels namely, the first cervical vertebra (C1) and the fifth cervical vertebra (C5) were selected for comparison of the surface slice area (SSA) and lateral neck diameter (LND) (Table 2). The following formula was used to calculate the percentage deviation of LND and SSA at the levels of C1 and C5.

$$percentage\ deviation(\%) = \frac{planning\ CT(SSA\ or\ LND) - CBCT(SSA\ or\ LND}{planning\ CT\ (SSA\ or\ LND)} \times 100\%$$

All data were analyzed using the software of Statistical Package for the social Sciences (SPSS) version 26.

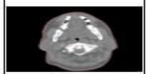
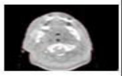
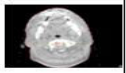
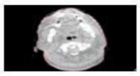
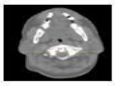
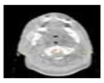
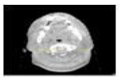
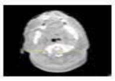
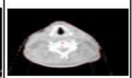
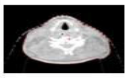
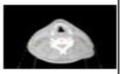
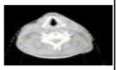
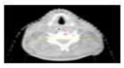


A

B

Figure 2: Analyzed images from DigimizerTM 5.4 software. A- LND measurement (distance measurement). B-SSA measurement (auto contour tool).

Table 2: Anatomical deviations explains SSA and LND at C1 and C5 levels.

	Planning CT	1st fraction of treatment	Mid fraction of Treatment	Last fraction of Treatment
C1 (SSA)				
C1 (LND)				
C5 (SSA)				
C5 (LND)				

RESULTS

Figure 3 shows the mean SSA percentage deviation at the C1 and C5 levels, while Figure 4 presents the mean LND percentage deviation at the same level. At the C1 level, the maximum and minimum anatomical deviation percentages of SSA between the planning CT and the first day of CBCT are 12.4% and 0.1%, respectively. For the mid-day of CBCT, the maximum and minimum deviations are 14.1% and 0.4%, respectively, and for the last day of CBCT, they are 17.5% and 0.1% respectively. Similarly, for LND at the C1 level, the maximum and minimum deviations between the planning CT and the first day of CBCT are 13.0% and 0%, respectively; for the mid-day of CBCT, they are 23.3% and 1%, respectively; and for the last day of CBCT, they are 23% and 0.1%, respectively.

At the C5 level, the maximum and minimum anatomical deviation percentages of SSA between the planning CT and the first day of CBCT are 21.2% and 0.1%, respectively. For the mid-day of CBCT, the maximum and minimum deviations are 28.4% and 0.1%, respectively, and for the last day of CBCT, they are 30.1% and 0.7%, respectively. For LND at the C5 level, the maximum and minimum deviations between the planning CT and the first day of CBCT are 15.7% and 0.2%, respectively; for the mid-day of CBCT, they are 20.2% and 0%, respectively; and for the last day of CBCT, they are 21.3% and 0%, respectively.

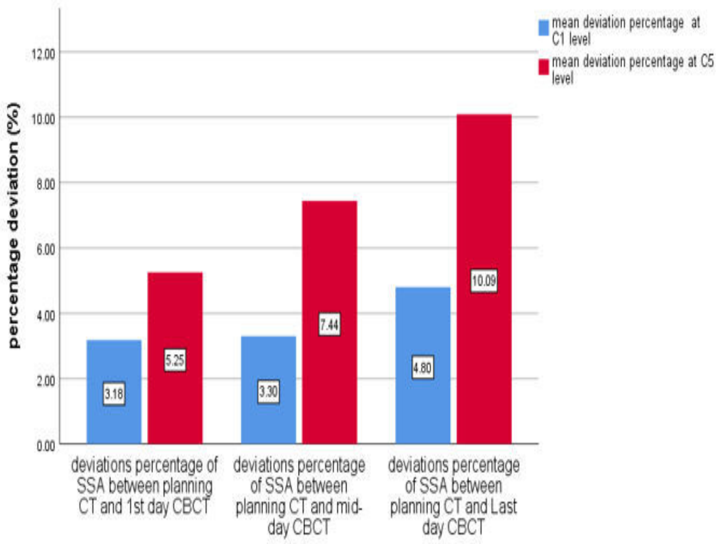


Figure 3: The mean SSA percentage anatomical deviations at C1 and C5 levels.

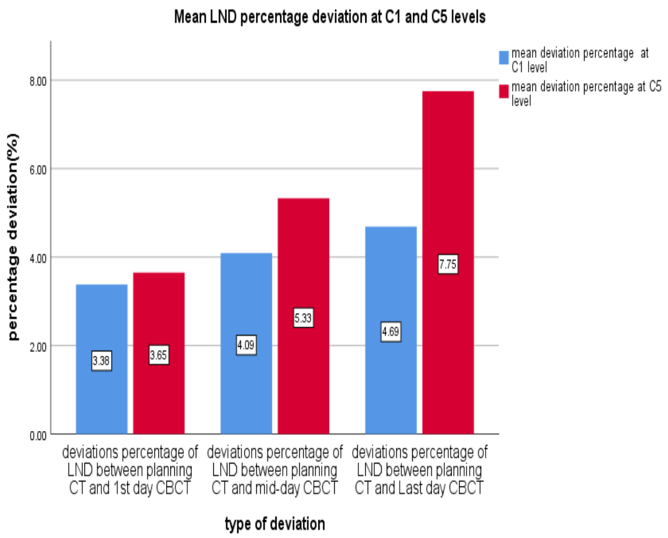


Figure 4: The mean LND percentage anatomical deviations at C1 and C5 levels.

A paired-sample t-test and related samples Wilcoxon signed rank test were performed to evaluate SSA and LND anatomical deviations between the planning CT and the first day, mid-day, and last day of CBCT. The results are presented in Table 3.

Table 3: The summary of comparison tests.

Anatomical Level		A significant difference was observed = ✓ A significant difference was not observed = ×		
		Time		
	Type of deviation	1st day	Mid- day	Last day
C1	LND	×	✓	✓
	SSA	×	×	✓
C5	LND	✓	✓	✓
	SSA	✓	✓	✓

DISCUSSION

The results of this study highlight the progressive anatomical changes that occur during IMRT for head and neck cancer, as evidenced by increasing deviations in SSA and LND at both C1 and C5 levels. These findings align with existing literature on the impact of treatment-related weight loss, tumor shrinkage, and soft tissue changes in this patient population.

The highest deviation for SSA at the C1 level was observed on the last day of CBCT, at 4.8% while the highest deviation for SSA at C5 level was 10.1% on the last day of CBCT. Similarly, the highest deviation for LND at the C1 level was 4.7% on the last day of CBCT, and the highest deviation for LND at the C5 level was 7.8% on the last day of CBCT. At the C1 level, SSA deviations ranged from a minimum of 0.1% to a maximum of 17.5%, while LND deviations reached up to 23% by the last fraction of treatment. These changes are likely attributed to soft tissue and muscle volume reductions in the upper cervical region. Similarly, the C5 level demonstrated even greater deviations, with SSA and LND reaching maxima of 30.1% and 21.3%, respectively. These more pronounced changes may reflect greater anatomical and volumetric alterations in the lower neck due to the cumulative effects of radiotherapy and concurrent weight loss.

According to this study, the findings indicate the necessity for re-planning as the results show significant deviations. However, evaluating changes in the mean value is not the sole factor contributing to the decision for re-planning. For greater accuracy in assessing significant changes, paired sample t-tests and related samples Wilcoxon signed rank tests were conducted separately for the LND and SSA datasets. At the C1 level shown in Table 3, significant differences were observed for LND on the mid-day and last day of CBCT, while significant changes in SSA were observed on the last day of CBCT.

A similar analysis was conducted for LND and SSA at the C5 level. According to the results obtained, significant changes were observed from the first day of CBCT for both LND and SSA data as shown in Table 3. Overall, deviations observed at the C5 level were greater than those at the C1 level.

The results suggest that the highest SSA and LND deviations at both C1 and C5 occurred between the mid-day and last-day treatment fractions compared to the planning CT. These deviations are attributed to shrinkage of the primary tumor and nodal volumes, edema resolution, weight loss, and other treatment-related factors. A previous study (Noble et al., 2019)[8] established re-planning criteria based on a maximum mean C1-SSA deviation percentage of 5.4%, a maximum C1-LND deviation percentage of 8.4%, and dose variations to the spinal cord. In the present study, dose variations could not be evaluated; hence, only anatomical deviations were considered.

Based on the analysis in this study, the significant differences observed between planning CT and CBCT imaging at various treatment fractions emphasize the importance of regular imaging and evaluation during IMRT. Adaptive radiotherapy (ART) has been proposed as a solution to address these anatomical variations. By updating treatment plans to reflect the patient's evolving anatomy. ART has the potential to improve dose accuracy, reduce toxicity to surrounding healthy tissues, and maintain therapeutic efficacy.

The findings reinforce the critical role of CBCT imaging in identifying and quantifying anatomical changes during treatment. Routine incorporation of mid-treatment imaging could serve as a valuable tool for early detection of significant deviations, enabling timely interventions and improved treatment outcomes.

CONCLUSION

This study demonstrates the progressive anatomical changes that occur during IMRT for head and neck cancer. Significant deviations in SSA and LND at C1 and C5 levels underscore the need for adaptive radiotherapy planning to accommodate these changes. Incorporating CBCT imaging throughout treatment allows for precise monitoring and facilitates timely modifications to treatment plans. Future studies should explore the integration of ART in clinical practice and its impact on treatment outcomes and patient quality of life.

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