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Measuring Radiotherapy Setup Errors in IMRT Treated Head and Neck Cancer Patients Requiring Bilateral Neck Irradiation, NCI-Egypt Experience

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Abstract

Objective: We aim to quantify the magnitude of setup errors in intensity-modulated radiotherapy (IMRT) treated Head and Neck cancer patients and recommend appropriate PTV margin. **Methods:** 60 patients with head and neck cancer required bilateral neck irradiation were planned and treated by simultaneous integrated boost IMRT technique either treated radically or postoperative. Patients undergoing image-guided radiotherapy (IGRT) each with once weekly scheduled cone beam computed tomography (CBCT). The 3D displacements, systematic and random errors were calculated. The appropriate PTV expansion was determined using Van Herk's formula. **Results:** Mean 3D displacement was 0.16 cm in the vertical direction, 0.14 cm in the horizontal direction and 0.16 cm in the longitudinal direction. **Conclusion:** Use of weekly CBCT allows the planning target volume (PTV) expansion to be reduced according to our setup. The appropriate clinical target volume (CTV)-PTV margin for our institute is 0.30 cm, 0.38 cm, and 0.33 cm in the horizontal, vertical, and longitudinal directions, respectively.

Keywords

IMRT, CBCT, Setup Errors, Head and Neck

1. Introduction

In the last decade, there is a progress in the treatment of head and neck cancer (HNC). More aggressive treatment regimens, either delivery of radiotherapy with concomitant chemotherapy or altered fractionation schedules, improve tumour control and survival [1], but at the expense of increased acute and late effects, which may have a more profound effect on function and quality of life (QOL). HNC arises in structurally complex and functionally important areas. Impairment of these areas from both disease and therapy can interfere with basic functions [2].

This highlights the importance of improving existing radiotherapy techniques to reduce the dose in relevant structures as much as possible with the use of new computer assisted optimization methods, such as intensity-modulated radiotherapy (IMRT) treatment plans with highly conformal dose distributions can be obtained [3].

IMRT is a highly conformal technique that allows the dose to be shaped around normal structures but full therapeutic doses to be delivered to the tumor and regions at high risk for disease [4].

So it is important to take into consideration setup errors during patient positioning which can be defined as a discrepancy between the anatomy of the patient at the planning CT and during treatment. These errors can be divided into systematic errors (which are reproducible consistent errors, occurring in the same direction and magnitude) and random errors (which vary in direction and magnitude). The systematic errors cause a shift of the cumulative dose distribution [5].

The rationale for the PTV margin is to minimize the effects of geometric (systematic errors) and residual (random errors) uncertainties [6].

2. Patients and Methods

2.1. Selection

Sixty patients with Head and Neck squamous cell carcinoma who presented to the National Cancer Institute (NCI), Cairo University, from September 2015 till October 2016 with 3D imaging verification via CBCT were enrolled. Patients and tumour characteristics are shown in **Table 1**.

2.2. CT Simulation

All patients were immobilized using a thermoplastic mask with 5-point fixation and had contrasted CT scan from the vertex to mediastinum with 2.5 mm slice thickness with the patient placed on a neck rest that provided full neck extension.

2.3. Treatment Planning

Patients received 70 Gy/33 fx to the PTV1, 60 Gy/33 fx to PTV2 (high risk CTV), 54 Gy/33 fx to PTV3 (low risk CTV) in case of radical treatment. In the postoperative setting, two volumes were identified: CTV1 including the tumor bed and high-risk nodal areas and CTV2 including elective lymphatic areas. These volumes were irradiated to a total dose of 60 Gy/30 fx and 54 Gy/30 Fx,

Table 1. Patients' characteristics.

Characteristics	Number of patients (%)
Gender	
Male	39 (65)
Female	21 (35)
Age (years)	
Mean ± SD	50.3 ± 14.9
Median (range)	54 (21 - 81)
Primary site	
Oral cavity	11 (18.3)
Oropharynx	3 (5)
Hypopharynx	10 (16.7)
Larynx	18 (30)
Nasopharynx	16 (26.7)
Sinonasal	2 (3.3)
T classification	
T1	5 (8.3)
T2	24 (40)
T3	25 (41.7)
T4	6 (10)
N classification	
N0	30 (50)
N1	4 (6.7)
N2	23 (38.3)
N3	3 (5)
Stage	
I	3 (5)
II	7 (11.7)
III	28 (46.7)
IV	22 (36.7)
Treatment	
Adjuvant	14 (23.3)
Definitive	46 (76.7)
Radiotherapy completion	
Yes	54 (90)
No	6 (10)

respectively using the simultaneous integrated boost (SIB) technique. All patients were optimized using a step and shoot technique (Monaco Eleckta software planning system, Stockholm, Sweden), using Monte Carlo algorithm.

2.4. Daily Setup and Image Guidance

IGRT using either kilo-voltage cone beam CT (KV-CBCT) and/or electronic portal imaging device (EPID). Images were done weekly for all patients as shown in Figure 1.

Matching is done between the online image and the planning CT image in three directions; vertical, horizontal and longitudinal. The vertical direction accounts for the anterior-posterior error, the horizontal direction accounts for the change of position along the right to left axis while the longitudinal direction accounts for the change along the superior-inferior direction.

2.5. Data Collection

Study data were collected and managed using REDCap research electronic data capture tools V6.10.12 (Radiation Oncology Record, Vanderbelt University, Nashville, TN) and statistical analysis was done using SPSS v23 (IBM inc., Chicago, IL).

3. Results

Sixty patients were included, 18 patients (30%) had a primary cancer in the larynx, 16 patients (26.7%) in the nasopharynx, 11 patients (18.3%) in the oral cavity, 10 patients (16.7%) in the hypopharynx, 3 patients (5%) in the oropharynx and 2 patients (3.3%) sinonasal. 54 patients ended radiotherapy treatment and 6 didn't continue treatment (2 patients developed Grade 3 mucositis and refused to continue, 1 patient developed diabetic coma and died, 2 patients

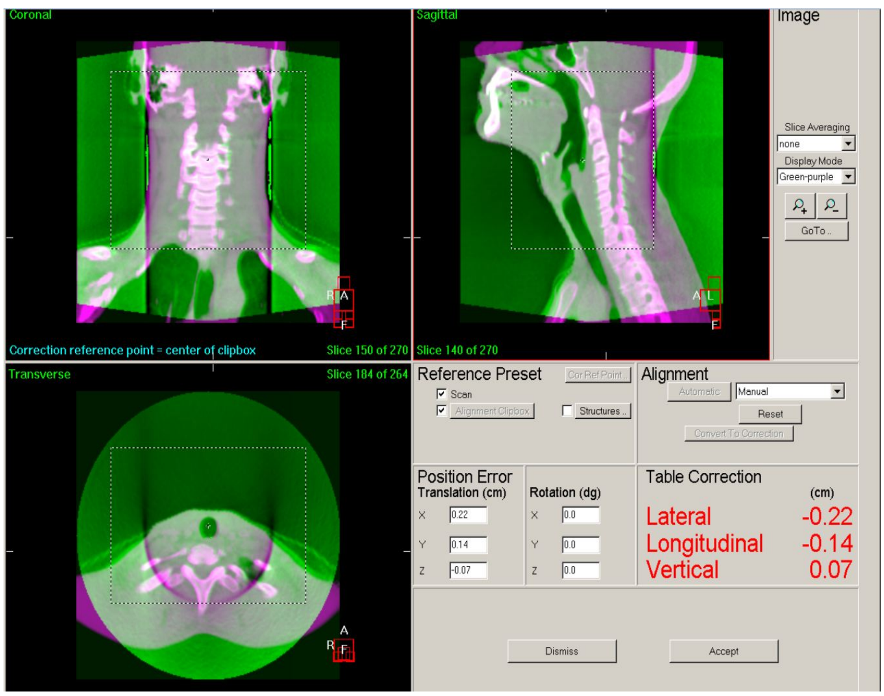

Figure 1. Matching between digitally reconstructed image (DRR) and image taken prior to treatment.

Table 2. Set up errors (in cm) using online verification.

	Horizontal	Vertical	Longitudinal
All cases (53)			
Mean ± SD	0.14 ± 0.14	0.16 ± 0.11	0.16 ± 0.11
Median (range)	0.14 (0 - 0.56)	0.14 (0 - 0.43)	0.16 (0 - 0.56)
Radical (40)			
Mean ± SD	0.15 ± 0.14	0.18 ± 0.13	0.16 ± 0.09
Median (range)	0.14 (0 - 0.56)	0.14 (0 - 0.48)	0.17 (0 - 0.4)
Postoperative (13)			
Mean ± SD	0.1 ± 0.14	0.13 ± 0.1	0.15 ± 0.15
Median (range)	0.07 (0 - 0.4)	0.14 (0 - 0.3)	0.12 (0 - 0.56)

Table 3. Difference in set up errors according to tumor location.

	Horizontal	Vertical	Longitudinal
Nasopharynx (16)			
Mean ± SD	0.09 ± 0.09	0.14 ± 0.1	0.16 ± 0.1
Median (range)	0.09 (0 - 0.28)	0.14 (0 - 0.37)	0.17 (0 - 0.35)
Oropharynx (2)			
Mean ± SD	0.17 ± 0.25	0.32 ± 0.15	0.14 ± 0.09
Median (range)	0.17 (0 - 0.35)	0.32 (0.21 - 0.43)	0.14 (0.07 - 0.21)
Hypopharynx (9)			
Mean ± SD	0.19 ± 0.14	0.17 ± 0.1	0.19 ± 0.11
Median (range)	0.25 (0 - 0.4)	0.21 (0 - 0.35)	0.18 (0 - 0.4)
Larynx (15)			
Mean ± SD	0.15 ± 0.18	0.13 ± 0.1	0.14 ± 0.07
Median (range)	0.09 (0 - 0.56)	0.12 (0 - 0.42)	0.16 (0 - 0.23)
Oral cavity (9)			
Mean ± SD	0.15 ± 0.15	0.19 ± 0.1	0.15 ± 0.18
Median (range)	0.14 (0 - 0.4)	0.18 (0 - 0.35)	0.09 (0 - 0.56)
Sinonasal (2)			
Mean ± SD	0.17 ± 0.04	0.07 ± 0	0.22 ± 0.08
Median (range)	0.17 (0.14 - 0.19)	0.07 (0.07 - 0.07)	0.22 (0.16 - 0.28)

Table 4. Systematic and random error and recommended CTV-PTV margin in the present study (53 cases).

Error	Horizontal (mm)	Vertical (mm)	Longitudinal (mm)
Systematic (S)	0.123	0.149	0.134
Random (σ)	0.3	1.4	1.2
CTV-PTV margin	3	3.8	3.3

didn't continue treatment due to social reasons, 1 patient had hypopharyngeal carcinoma rapidly deteriorating and didn't continue treatment).

Most of the cases had stage III disease (28 patients, 46.7%) and stage IV disease (22 patients, 36.7%) while only 3 patients (5%) had stage I and 7 cases (11.7%) had stage II disease. Patient's characteristics and treatment demographics are shown in **Table 1**.

All patients had online imaging using kilo-voltage cone beam CT (KV-CBCT) and/or electronic portal imaging device (EPID). Out of the 60 patients, only 53 patients had 3 consecutive weekly online verifications and the rest had EPID imaging due to machine break down. EPID was used only when the CBCT was out of function.

The mean of the detected error was 0.16 cm in the vertical direction, 0.14 in the horizontal direction and 0.16 in the longitudinal direction.

The overall mean error (M), systematic error (S) and random error (σ) were determined according to van Herk's formalism and the PTV margins were calculated using the van Herk formula [5]. Our work showed PTV margin 3.0, 3.8, and 3.3 mm for x, y, and z respectively.

4. Discussion

This paper reports our clinical experience with IGRT in the treatment of H&N cancer, with the aim to define the overall accuracy of our setup procedures and to define the proper CTV-PTV margins to be adopted in our target delineation.
Assessments of set-up variations are essential on an institute-by-institute basis as the efficacy of radiotherapy treatment depends on patient's setup, as they are dependent on factors such as immobilization devices and the clinical experience of the staff [7].

Furthermore, the inadequate definition of PTV can lead to local failure due to geographical tumour misses, or to increase the dose to the normal tissues near the CTV.

The assessment of set up errors in the present study was done using CBCT and confirmed its effectiveness in reducing setup margins. The mean of setup errors was bigger in radical cases than in postoperative cases that may be due to shrinkage of target during treatment (**Table 2**). Previous studies by Li *et al.* [8] addressed setup uncertainties for H & N treatment sites and described a number of common factors that can contribute to setup errors for these sites. The factors consist of loosening of the fixation mask due to a reduced body contour following weight loss, or tumor shrinkage and tightening of the mask by the swelling of some part of the lesion.

In consideration of these factors, the fixation mask was remade in our institution if considerable discrepancies occurred, and rescanning and replanning were performed to reduce setup errors for these sites.

We found that the mean setup error in the horizontal direction was high in hypopharyngeal cases, and in the vertical direction for oropharyngeal cases and in the longitudinal direction for the sinonasal cases (**Table 3**).

According to some authors, in HN tumors organ motion may be neglected. In fact, Hamlet *et al.* reported that in larynx tumors breathing and swallowing have no significant impacts on dose distribution [9].

Also, Van Asselen *et al.* reported that there was no need to adjust the margins around the CTV to take into account the larynx displacements occurred due to swallowing [10].

Our work showed PTV margin of 3.0, 3.8, and 3.3 mm for X, Y, and Z, respectively (**Table 4**), while these margins were 4.9, 6.4, and 5.8 mm in Mesías *et al.* [11], 5.7, 5.3, and 6.2 mm in Saha *et al.* [12], 2.3, 1.9, and 2.0 mm in Liu *et al.* [13], and 3.0, 1.3, and 2.6 mm in Su *et al.* [14].

The minimum reported PTV margin is 1.9 mm. The PTV margin that is suggested in our present work falls within the reported margins. Nevertheless, each margin is institution specific and small differences are to be expected even though the methodology is the same. However, in the case of close proximity of OAR and high-dose regions, or when re-irradiation has to be performed, daily image guidance a reduced PTV margin should be strongly considered.

These consequences are reflected in some dosimetric studies which reported that PTV margin need to be larger to account for setup errors in case that daily IGRT is not used [15] [16] and that the improved setup accuracy achieved using IGRT can protect healthy tissues to a great extent [17].

5. Conclusion

Set-up variations should be obtained in each department to calculate institute-specific margins, as the planning margins reported in the literature are only indicative and range from 3 - 5 mm. Verification protocol of bony and soft tissue anatomical references information provided by CBCT improves the set-up accuracy and allows full radiation dose delivery to the target with decreasing the radiation dose to normal critical structures. According to our results, the appropriate CTV-PTV margin for our institute is 0.30 cm, 0.38 cm, and 0.33 cm in the horizontal, vertical, and longitudinal directions, respectively.

Conflicts of Interest

None of the authors has any conflict of interest to declare.

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