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Evaluation of Patient Set Up Errors in Head and Neck Three-Dimensional (3D) Conformal and Intensity-Modulated Radiotherapy Using Electronic Portal Imaging Device

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ABSTRACT

Introduction: Interfractional set-up variations may cause deviation of the delivered dose from the planned dose distribution. This study aimed at calculating random and systematic set-up errors using an electronic portal imaging device (EPID) to set the optimum planning target volume (PTV) margins in patients with head and neck cancer who were under treatment with three-dimensional conformal (3DCRT) and intensity-modulated radiotherapy (IMRT).
Material and Methods: In this study, 50 patients underwent 3DCRT along with weekly electronic portal image (EPI), and daily IMRT imaging was performed on 50 others. The EPIs were compared with Digitally Reconstructed Radiographs (DRRs) to quantify the systematic, random, and 3D vector length of set-up errors in three translational directions (X, Y, Z). The PTV margins were measured utilizing International Commission on Radiation Units and Measurements report 62, Stroom's and van Herk's models.
Results: For 3DCRT and IMRT techniques, the overall mean 3D vector length of displacement was obtained at 3.9 and 2.7 mm, respectively. The maximum systematic and random errors were 1.3 and 1.9 mm for the IMRT technique and 2 and 2.9 mm for 3DCRT, respectively. PTV margins in the three acquisition directions were 2-7.2 mm.
Conclusion: It was found that a 7 mm extension of the clinical target volume (CTV) to PTV margin ensures that 90% of head and neck cancer patients have received 95% of the planned dose.

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Introduction

The patient's set-up at each fraction affects the efficacy of the radiation therapy for accurate dose delivery to the target volume with minimal toxicity of normal tissues. Beam alignment and organ motion safety margins are applied to the clinical target volume (CTV) to determine planning target volume (PTV), which accounts for such inter-fractional treatment uncertainties as patient positioning (1). Optimization of safety margins can minimize unintended irradiation to adjacent normal tissues. Each set-up uncertainty includes both random and systematic components. The systematic component of errors occurring with similar magnitude and direction for each fraction within the treatment course results in a shift of the cumulative dose distribution concerning the clinical target. Incorrect laser setting and changes in gantry stability are examples of systematic errors (2). However, the random errors are unpredictable and vary in magnitude and direction from day to day such as incorrect block shields and patient position (3). Nowadays, imaging techniques such as electronic portal imaging devices (EPIDs) provide guidance for patient set-up verification and target localization. The Electronic portal images (EPIs) can efficiently reduce set-up errors and reduce treatment margins, which leads to improvement of local control at the tumor site (4). Several studies have been reported on portal imaging (PI) guided set-up corrections and PTV margins specifically to the center in head and neck cancer (2, 5, 6). Generally, the

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determination of population random and systematic set-up errors for various treatment techniques and all anatomical regions treated in a separate department allows to define an appropriate treatment planning margins for each technique (7). These local data would aid in the derivation of site-specific protocols for margin generation. This study aimed at quantifying random and systematic inter-fractional setup errors using EPI for a total of 100 head and neck cancer patients undergoing 3DCRT and IMRT to determine the optimum CTV to PTV margins required for covering the target.

Materials and Methods

Patient Selection

This retrospective study was carried out on 100 randomly selected head and neck cancer patients who were referred to Reza radiation oncology cancer center, Mashhad, Iran, from September 2018 to April 2019. Fifty of them underwent 3DCRT, while the remaining fifty underwent IMRT of the head and neck region.

Immobilization, treatment simulation, and planning

The five-point thermoplastic fixation masks were utilized to immobilize patients in a proper anatomic position, who were then scanned in a head-first supine position with 3 mm slice thickness on a (16 slices) computed tomography (CT) scanner (Siemens Healthcare, Forcheim, Germany). The thermoplastic mask was marked using radio-opaque labels under laser beams guidance to indicate the isocenter. All CT images were transferred to the Prowess Panther treatment planning system (TPS) (Version 5.5, Prowess Inc., Concord, CA, USA) to constitute CTV and PTV for 3DCRT and IMRT treatment planning. The treatment plans were performed in consistency with the International Commission on Radiation Units and Measurements (ICRU) 50, 62, and 83 guidelines (8-10). An overall dose of 70 Gy/30 fractions (fx) was administered to patients for both 3DCRT and IMRT.

Daily setup and image guidance

Patients were positioned by aligning the treatment room lasers with surface markers over the thermoplastic mask placed at the time of the simulation. Orthogonal portal images were obtained utilizing a flat-panel amorphous silicon EPID with a resolution of 1024 × 1024 pixels integrated into the linear accelerator (Siemens Medical System, Germany). Patients without set-up errors on the first digital portal image were monitored every week for 3DCRT, while daily online portal imaging was performed for the IMRT technique. The electronic portal images (EPIs) were acquired at anterior-posterior (AP) and lateral directions utilizing 6 MV photon beams and an exposure time of 1 monitor unit (MU) per field at a dose rate of 400 MU/min. The position of bony anatomical structures on the EPIs was compared with the same structures on the digitally reconstructed radiographs (DRRs) as a reference image from the TPS. Matching the EPIs and DRRs was performed on the Coherence (Siemens Medical Solutions, USA, Inc.) software system. The patient setup deviations were assessed in the left-right lateral (X) and craniocaudal longitudinal (Y) direction calculated in the AP field and dorsoventral vertical (Z) direction calculated in the lateral dimension. A threshold of 3 and 5 mm were established as the lower bound for applying corrections in IMRT and 3DCRT technique, respectively.

Statistical analysis

The patient set-up errors (μ) including both random and systematic errors were determined for each patient as well as the entire group. The individual systematic set-up errors were defined as mean set-up deviations (M_p) for a specific patient (p)(2):

$$M_p = \frac{1}{n_p}\sum_{i=1}^{n_p}(\mu_{(EPI-DRR),i}) \quad (1)$$

Where the parameter n_p is the number of portal images. The overall mean systematic set-up error (S_{overal}) for all the patients (p) in a specific direction was determined by the following formula (2);

$$M_{overal} = \frac{1}{N}\sum_{p=1}^{p} M_p \cdot n_p \quad (2)$$

Where N is the total number of images. The random set-up error (σ) of a given patient (p) was determined by the standard deviation (SD) of the day-to-day set-up errors around mean set-up deviations in

a given direction (2):

$$\sigma_{rand,p} = \sqrt{\frac{1}{n_p}\sum_{i=1}^{n_p}(\mu_{(EPI-DRR),i} - M_p)^2} \quad (3)$$

The random set-up errors for all patients (p) in a specific direction were obtained as follows (2);

$$\sigma_{set-up} = \sqrt{\frac{p}{N-p}\sum_{p=1}^{p}(\sigma_{rand,p})^2\,(n_p - 1)} \quad (4)$$

For all the patients (p) in a specific direction, the SD of the distribution of mean set-up deviations was defined as (2):

$$\Sigma_{set-up} = \sqrt{\frac{1}{N(P-1)}\sum_{p=1}^{p} n_p (M_p - M_{overal})^2} \quad (5)$$

Finally, the PTV margins were quantified based on Van Herk's formula (2.5 Σ + 0.7 σ) (11), Stroom (2Σ+0.7σ) (12), and ICRU report 62 (sqrtΣ^2+σ^2) (9). Based on this formula, 95% is the least cumulative dose to CTV, for 90% of the patients. Stroom's margin recipe ensures that 99% of the CTV will receive 95% of the determined doses. The data were analyzed in SPSS software (version 19.0). Furthermore, the 3D vector length of displacements at each treatment technique was measured by quadratically combining 1D deviations (d) in the three directions;

$$3D\ vector\ length = \sqrt{d_{AP}^2 + d_{LAT}^2 + d_{CC}^2} \quad (6)$$

Results

Totally, 3400 EPIs (1700 anterior and 1700 lateral portal images) from 100 patients were studied. Figure 1 presents the overall distributions of translational set-up errors in dorsoventral, left-right lateral (L), and craniocaudal (CC) axes for both 3DCRT and IMRT techniques.

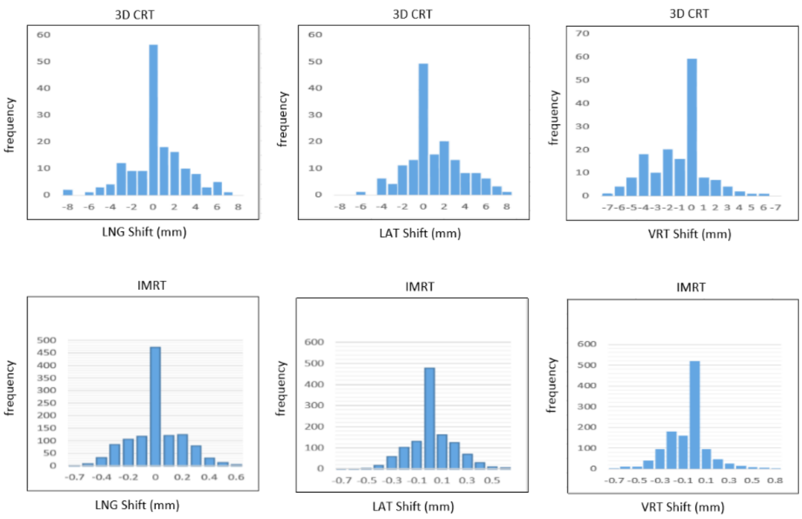

Figure 1. Distribution of total deviations at craniocaudal longitudinal, left-right lateral and dorsoventral direction

Table 1. The cumulative frequencies (%) of 3D vector lengths

	Treatment technique	
3D vector length (mm)	3DCRT	IMRT
< 3	31.5	50
3-5	44.6	45.2
5-8	23.9	4.8
> 8	0	0

Table 2. Population systematic (Σ) and random errors (σ) and CTV to PTV margins for both 3DCRT and IMRT techniques in three directions

Treatment technique	Direction	Mean error ± SD in mm	Systematic error in mm (Σ)	Random error in mm (σ)	ICRU 62 (mm)	Stroom's (mm)	Van Herk's (mm)
3DCRT	Craniocaudal Longitudinal (Y)	2.8 ± 2.17	2	2.9	3.6	6.1	7.2
IMRT		2.21 ± 1.4	1.3	1.9	2.3	3.9	4.5
3DCRT	Left-right lateral (X)	2.7 ± 2.23	1.8	2.9	3.5	5.8	6.8
IMRT		2.02 ± 1.32	0.9	1.8	2	3.2	3.5
3DCRT	Dorsoventral vertical (Z)	2.6 ± 2.15	1.6	2.7	3.1	3	5.8
IMRT		2.16 ± 1.45	1.1	1.8	2.1	3.5	4

The distribution of set-up errors was narrow, and the maximum translational shift was 8 and 7 mm in 3DCRT and IMRT, respectively. In the 3DCRT technique, the total frequency distributions of set-up displacements were within ±5 mm (correction action level in 3DCRT) in 94.4% of cases in the craniocaudal direction, 96.3% cases in the dorsoventral direction, and 93.1% of cases in the lateral direction. In the IMRT technique, the overall frequencies of set-up errors were within ±3 mm (correction action level in IMRT) in 78.2%, 82.3%, and 83.2% of cases in craniocaudal, dorsoventral, and lateral directions, respectively. Table 1 represents cumulative frequencies of 3D vector lengths of translational displacements at each treatment technique.

The highest percentages of 3D displacements were in the range of 3-5 mm and less than 3 mm in 3DCRT and IMRT techniques, respectively. In both treatment techniques, three-dimensional vector distances ≥8mm were insignificant. The mean± SD set-up errors, the systematic and random deviations for all patients, as well as the CTV to PTV margin, quantified from the ICRU report 62, Van Herk and Stroom formula for achieving adequate target coverage with a confidence level of 95% are listed in Table 2.

In both treatment delivery techniques, the mean±SD of set-up errors in the three directions was less than 3 mm (Table 2). In the 3DCRT technique, the random and systematic set-up errors were higher, compared to IMRT technique. The maximum systematic errors were 2 and 1.3 mm in the longitudinal direction for 3DCRT and IMRT techniques, respectively. The maximum value of random errors was also 2.9 and 1.9 mm in the longitudinal direction for 3DCRT and IMRT techniques, respectively. The maximal CTV to PTV margin quantified using van Herk's, Stroom, and ICRU 62 formula was estimated to be 7.2 mm, 6.1 mm, and 3.6 mm in the longitudinal direction in 3DCRT and 4.5, 3.9, and 2.3 mm in IMRT technique, respectively.

Discussion

Improper definition of PTV may lead to deficiency in the delineation of various target volumes or an increase in the dose to the normal tissues in the CTV vicinity. In order to construct optimal CTV-PTV margins, the patients' set-up accuracy should be fully expressed in terms of systematic and random errors. This study investigated the set-up accuracy of head and neck cancer patients undergoing 3DCRT and IMRT using EPIs to define appropriate planning margins that satisfy a target dose criterion. According to our findings, 50% of the vector lengths were less than ±3 mm in the IMRT technique, while in 3DCRT, the highest percentage of displacements (44.6 %) were in the range of 3-5 mm (Table 1). For IMRT and 3DCRT techniques, the total mean 3D vector length of displacement was 2.7 and 3.9 mm, respectively. The predicted causes of these displacements could be loosening of the fixation mask owing to tumor shrinkage or weight loss and the thermoplastic mask tightening due to some distention in the treated area.

The findings are in line with some other studies showing the set-up displacements were dependent on the type of irradiation technique and were higher in the 3DCRT technique (2, 13, 14). The total magnitude of systematic and random errors were about 1.5-2 mm and 2.6-2.9 mm in the 3DCRT technique, while it was 0/9-1.2 mm and 1.8-1.9 mm in the IMRT technique, respectively. It has been found that the systematic component of set-up displacements has a greater role in physical dose distribution, compared to random set-up errors (15). This study showed that the systematic set-up errors in both treatment techniques were less than random errors that could be due to the accuracy of linac mechanical performance and precise laser alignment either of the treatment unit or the simulator. The magnitude of random (σ) and systematic errors (Σ) registered had good agreement with some previous studies utilizing EPIs for image registration in treating head and neck cancers (Table 3).

The adverse effects associated with patient set-up uncertainties were found to be greater using the IMRT technique due to sharp dose gradients between the targeted volumes and normal tissues (20). Xing et al. reported that a set-up error of 3 mm along the anterior-posterior in the IMRT technique led to a 38% reduction in the target dose and a 41% increase in the spinal cord dose as a non-target organ (21). Moreover, adding a safety margin to the clinical target volume to define a PTV is the most common approach to overcome set-up uncertainty. In order to prevent underestimation or overestimation of actual margin, the discrepancy of geometrical set-up errors must be considered in three directions. The maximum CTV to PTV margin in the 3DCRT technique, calculated from ICRU 62, stroom, and van Herk's formulas were 3.6, 6.1, and 7.2 mm in the craniocaudal direction, while they were 2.3, 3.9 and 4.5 in IMRT technique. Performing regular position corrections and improving patient positioning would lead to a small PTV margin and lower chance of normal tissue complications.

Table 3. Population random (σ) and systematic errors (Σ) in previous studies with the recommended margins for target volume coverage

Treatment technique	Study	Σ (mm)	σ (mm)	Errors / displacements
3D-CRT	Zhang (16)	1.5-3.2	1.1-2.9	5.5 mm for 90% target coverage
	Gupta (15)	0.96-1.2	1.94-2.48	CTV-PTV margin<5 mm in all directions and 93% of displacements were within 5 mm
	Gilbeau (17)	1-2.2	0.7-2.3	4.5-5.5 mm for 90% target coverage
IMRT	Suzuki (18)	0.7-1.3	0.7-1.6	5 mm margin for PTV and 3 mm for planning organs at risk volume (PRV). Probability values not specified.
	Pehlivan (19)	0.93-1.20	1.78-2.26	3-5 mm PTV margin in all directions
	Strbac (2)	1.42-1.93	1.77-1.86	6.1 mm CTV-PTV Y direction, 5.1 mm CTV-PTV X direction,4.8 mm CTV-PTV Z direction.

Conclusion

The current study demonstrates the feasibility of utilizing an EPID to identify set-up errors and improve field alignment before administration of the full RT dose. The PTV margin quantified by ICRU, Stroom, and van Herk models for both 3DCRT and IMRT techniques in three directions (Table 2) guarantees that almost the whole target volume will receive the planned dose. The EPID-based correction strategy would result in a reduction in set-up displacements and subsequently smaller PTV margins that are very important in treatment regions such as the head and neck because of their vicinity to sensitive regions like the brain stem, spinal cord, and salivary glands.

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