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Utilization of Electronic Portal Imaging Device (EPID) For Setup Verification and Determination of Setup Margin in Head and Neck Radiation Therapy

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ABSTRACT

Introduction: Radiation therapy involves a multistep procedure; therefore, the error in patient set up is an inherent part of the treatment. Main purpose of this study was to determine the clinical target volume (CTV) to planning target volume (PTV) in head and neck cancer patients.

Material and Methods: A total of 15 patients who had daily portal images during the treatment courses were randomly selected in the present study. Systematic (Σ) and random (σ) errors were evaluated in three directions. The Isogray treatment planning system and Elekta linear accelerator were used in this study. Moreover, we had used MOSIAQ software as a record and Verify system. Setup margins were calculated using three published margin recipes, including the International Commission on Radiation Units and Measurements (ICRU) report 62, as well as Stroom's and van Herk's formulae.

Results: Average magnitude of the translational errors was reported between 0.7 and 10 mm. The systematic and random errors for head and neck cancer patients were 3.55 (2.58-4.52) and 1.83 (1.56-2.10) mm, respectively. According to the ICRU report 62, as well as Stoorm's and van Herk's formulas, the required margins to cover the target were obtained within the ranges of 3.1-4.9, 6.4-10.5, and 7.7-12.7 mm, respectively.

Conclusion: According to the results of the present study, 6.5-10.5 mm extension in CTV to PTV margin can ensure that 90% of the head and neck cancer patients will receive a minimum cumulative CTV dose higher than or equal to 95% of the prescribed dose.

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Introduction

As radiation therapy treatment becomes more complex, it becomes more important to evaluate various uncertainties that affect the treatment procedure [1]. Recently, several institutions can perform conformal treatments under computer control and verify patient positioning. Patient positioning is a critical step in head and neck treatment to prevent missing the target for recurrence and avoid the extreme dose to eyes and thyroid as an organ at risk [2]. In previous studies, positioning verification was performed by cassette films [3, 4]. As mentioned in these studies, it is a time-consuming process that causes the reduction of the film quality after a long time for scanning.

Nowadays, Electronic Portal Imaging (EPI) becomes one of the devices used to verify the treatment process that has originally been developed for positioning verification prior to radiation therapy. As shown in a previous study [5], Electronic Portal Imaging Device (EPID) can be used to improve patient alignment and patient positioning prior to dose delivery with good quality, especially in head and neck cases with more bony markers [6]. The portal image systems consist of a two-dimensional array of diode dosimeters that are capable of acquiring megavoltage images in the form of Digital Imaging and Communications in Medicine [1].

The EPIs have some advantages in comparison with cassette films; however, they have also some limitations. Low-Quality image of EPIs is the most important limitation that makes the soft tissues invisible in the image. Anatomical structures, such as bony structures and body contour or radio-opaque markers (if any), could be shown on port image generated just before radiation therapy and perform the registration process with reference image for patients positioning verification.

Cartesian coordinates were used because we have setup errors in three directions. All the errors are divided into two main groups, including systematic

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(Σ) errors and random (σ) errors or interfraction uncertainties defined as the same deviation in the same direction. Such uncertainties related to mechanical uncertainties in medical devices are repeated in each fraction in the whole courses of treatment [1]. Incorrect setting of laser lights, problem in the collimator system, and changes in machine efficiency are the examples of systematic errors. However, random errors or interfraction uncertainties include day-to-day errors, such as incorrect block shields, as well as beam(s) and patient position, that can be different for each patient [1].

$\Sigma_{\text{sytematic}}$ and σ_{random} represent the standard deviations of systematic and random population errors, respectively. The clinical target volume (CTV) contains the gross tumor volume and a centimetre margin covering subclinical disease that cannot be fully imaged [7]. Planning target volume (PTV) is a geometrical concept that considers the net effect of all the possible geometrical variations in order to properly deliver dose to the CTV. It is important to get the optimum PTV margin because there is a potential for recurrence if a part of CTV is missed.

Gildersleve J et al. [8] investigated 290 portal images related to 12 head and neck patients who had thermoplastic immobilization. In the aforementioned study, systematic and random setup errors were reported within the ranges of (1.7-1.4) cm, (2.2-1.4) cm, and (1.8-1.4)cm for anterior-posterior (AP), cranial-caudal (CC), and medial-lateral (ML) directions, respectively. In another study carried out by El-Gayed AA et al. [9], systematic and random errors were reported within the ranges of (2.6-2.8)cm, (2.5-1.7)cm, and (2.4-1.8)cm for AP, CC, and ML directions, respectively. In addition, immobilization was not used for 10 rectal tumor patients.

Purpose of the present study was to determine the range of setup errors and propose the optimum CTV to PTV margin in head and neck cancer patients treated with conformal radiation therapy (CRT) at Imam Reza hospital of Mashhad, Iran. In this regard, the systematic and random errors were evaluated in head and neck cancer using EPID. The present study was performed for the first time in our institution (Imam Reza hospital, radiation oncology department). Moreover, setup errors and CTV-PTV margins were determined for head and neck cancer patients. It is necessary for all physicians to know the range of systematic and random errors in their radiation department to consider the best margin for a specific organ.

Materials and Methods

Patient Selection

This retrospective study was conducted on 15 patients randomly selected with head and neck cancer treated with three-dimensional (3D) -CRT technique at Imam Reza Radiation Oncology Center of Mashhad, Iran. All the patients were firstly scanned in the head supine position using radio-opaque labels under laser beams guidance in computed-tomography (CT) scanner (16 slices, Neusoft Medical System Co., Shenyang, China). Then, these markers were tattooed on the thermoplastic frame (because the face skin is more sensitive, and all the patients had their own thermoplastic) just to remain until the last session.

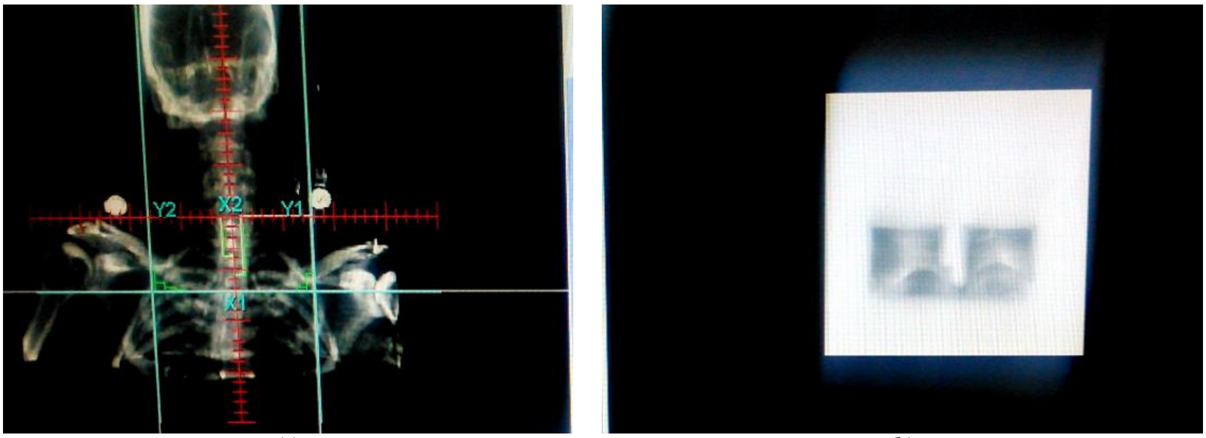
For daily setup, the treatment isocenter was aligned with the sagittal and transverse treatment room lasers with three-point tattoos on the thermoplastic. If the isocenter point was placed on a hole of thermoplastic, a sticky paper was used on the thermoplastic and marked the laser cross lines on it. An immobilization device was applied for all the patients. In addition, a thickness of 3 mm was implied for all the subjects.

The Isogray (Dosisoft, Cachan, France) treatment planning system was used in our institution. Therefore, all CT images were imported into Isogray, and digitally reconstructed radiographs (DRRs) were computed as the reference images. The target and soft tissues were contoured by an oncologist. The prescription dose was 70 Gy with 2 Gy per fraction delivered to PTV with 6, 10, and 18 MV photon beams on the linear accelerator (Elekta Precise model, Stockholm, Sweden) equipped with amorphous silicon EPID and multileaf collimators with 40 leaves on each side. Consequently, all the patients were treated with 3D-CRT technique in the present study.

Treatment Process

No particular change was considered in the routine treatment steps, except for the port image taken on certain days. The subjects were set up by the treatment room laser and tattoo markers on the immobilization device. Before the initiation of the treatment, orthogonal portal images were obtained at gantry angles 0˚ (i.e., AP direction) and 90˚ (i.e., lateral [LAT] direction) using 6 MV photon beams and typical exposure time 3 monitor units (MU) per field at a dose rate of 400 MU/min with the same field size and shape of a treatment field.

Pretreatment portal images were obtained for the first three fractions for each patient. Then, the comparison was performed between the portal image and DRR. If the deviations were acceptable (i.e., standard displacements were set at <3 mm [10]) the next image would be taken every week. Some bony landmarks were used in the head and neck for the estimation of the deviations between DRRs and electronic portal images in each anterior and LAT projections (Figure 1). Some reference landmarks were utilized in the electronic portal images, such as cervical vertebrae in neck diseases, as well as maxillary sinus and mandible in the head diseases of LAT image and rib bone and skull base of AP projection.



(a) (b)

Figure 1. Offline review by MOSAIQ software; obvious and poor determination of bony landmarks in digitally reconstructed radiograph (a) and port image (b), respectively

Total port images taken from 15 head and neck cancer patients were 92 images. For analysis, plus and minus signs represented right and left shifts for the *X* axis, respectively. Plus and minus signs for the *Y* axis denoted superior and inferior shifts, respectively. The LAT port image was used to assess the *Z* shift with a plus sign for upward (i.e., anterior) and minus sign for downward (i.e., posterior) patient movement.

Statistical Analysis

Random and systematic errors combined in µ symbol were defined as patient setup deviation. Errors were separately documented for all 15 patients for the three directions. Therefore, random errors were represented by σ defined as standard deviation of the day-to-day setup position, and systematic errors were represented by Σ defined as average setup deviation per patient. Estimation of these standard deviations depends on the total number of patients P and total images used in this study N. $m_p$is the mean deviation of $n_p$images defined as a systematic set up deviation for a patient P.

m as *the* overall mean deviation is the average value over all fractions and all patients in a given direction as follows [1] :

$$m_p = \frac{1}{n_p} \sum_{i=1}^{n_p} \mu_{(PI-DRR)_i} \quad (1)$$

Random set up deviation for a patient (*P*) in a given direction is shown as follows [1]:

$$\sigma_{rand,p} = \sqrt{\frac{1}{n_p} \sum_{i=1}^{n_p} (\mu_{(PI-DRR)_i} - m_p)^2} \quad (2)$$

Overall mean systematic errors in a given direction for all the patients is [1]:

$$m_{overall} = \frac{1}{N} \sum_{p=1}^{P} n_p \, m_p \quad (3)$$

Random setup errors of the $\sigma_{rand,p}$ distribution for all the patients in a given direction were obtained from [1]:

$$\sigma_{setup} = \frac{1}{P} \sum_{p=1}^{P} \sigma_{rand,p} \quad (4)$$

And the final equation is considered systematic setup errors for all the patients in a given direction as follows [1]:

$$\Sigma_{setup} = \frac{1}{P} \sum_{p=1}^{P} m_p \quad (5)$$

Statistical analysis was performed using Microsoft Office Excel (2010).

Determination of Required Margin

There are several mathematic formulae to achieve CTV-PTV margins, including the International Commission on Radiation Units and Measurements (ICRU) report 62 (i.e., sqrtΣ^2+σ^2) [11], as well as Stroom (i.e., 2Σ+0.7σ) [12] and Van Herk (i.e., 2.5Σ+0.7σ) [13]. According to the ICRU report 62, systematic and random uncertainties have an equal contribution to the dose distribution in which they should be added in quadrature to produce CTV-PTV margins.

As demonstrated by Gupta et al., the random errors affect the dose distribution; however, the systematic errors have another effect, such as a shift in the cumulative dose distribution. Therefore, considering the same contribution of these two kinds of error might not be necessarily true[14]. Heijmen, Stroom, and van Herk et al. suggested formulae for incorporating these differential effects using coverage probability matrices and dose population histograms.

The margin recipe (i.e., 2**Σ**+0.7σ) suggested by Stroom's states that at least 95% of the prescribed dose is received by 99% of the CTV. The margin recipe (i.e., 2.5**Σ**+0.7σ) suggested by van Herk confirms that at least 95% of the prescribed dose will be received by the CTV in 90% of patients [13]. It was declared that motion in organs caused random errors and systematic errors familiarized by setup errors, target volume delineation, and organ motion. It could be reduced by using multimodality imaging, such as positron emission tomography or magnetic resonance images and electronic portal imaging with decision rules.

In addition, clear delineation protocols and correct procedures of CT scan could be useful for uncertainties errors. Systematic errors have more effect on the required margin about 3 to 4 times more than random errors. In addition, more geographical misses occurred through large systematic errors. Indeed, biological margin recipes are more reliable and are more frequently cited than physical margin considerations [15].

Results

The equations (1), (2), (3), (4), and (5) were used for systematic setup deviation for a patient, random setup deviation for a patient, overall mean systematic errors, random setup errors for all the patients, and systematic setup errors for all the patients, respectively. Table 1 tabulates the aforementioned data.

Number of initial days of portal measurement depends on the magnitude of the random setup error. To obtain a 95% confidence level in prediction, an empirical formula should be used as follows:

$n = \min\{9, 4 + 2(\sigma - 1)\}$

Where σ is the predicted random error, and n is the number of required daily portal image. For any $\sigma \geq 1$ mm, 4-9 days of portal imaging will be required for a confident prediction [16]. Because all the patients used thermoplastic in this study, $\sigma \leq 1$ mm was considered. All of the displacements were measured in 92 portal images, including 47 anterior and 45 LAT projections.

The systematic and random errors were calculated in the present study. The systematic errors existed during the whole courses of treatment. The random errors represented day-to-day variation in the set-up of a patient. The population systematic errors in LAT, longitudinal, and vertical axes were reported as 0.3398, 0.2858, and 0.4529 cm, respectively. Furthermore, the population random errors in the corresponding axes were reported as 0.1561, 0.1692, and 1.2790 cm, respectively (Table 2).

Figure 2 shows the total deviations in three directions, including (a) caudocranial longitudinal (b) left-right LAT direction from the AP field but (c) caudocranial longitudinal and (d) dorsoventral vertical direction from the LAT field.

The CTV to PTV margins were estimated with three popular formula recommended by the ICRU report 62, Stroom, and van Herk. The CTV to PTV margins in the LAT, longitudinal, and vertical direction were 0.3740, 0.3322, and 0.4990 cm using the ICRU recommendation, respectively. The corresponding values were reported as 0.7889, 0.6901, and 1.05525 cm using Stroom's formula, as well as 0.9588, 0.8331, and 1.2790 cm by van Herk's formula (Table 2).

Table 1. Brief results of the population systematic (Σ) and random (σ) errors considering two fields of view and four directions

Field	Anterior-Posterior		Lateral	
	Caudocranial longitudinal	Left-Right lateral	Dorsoventral vertical	Caudocranial longitudinal
Min deviation [cm]	0.7	0	0	0
Max deviation [cm]	0.7	0.9	0.61	0.8
$M_{overall}$ [cm]	0.28	0. 33	0.46	0.25
Σ_{setup} [cm]	0.28	0.33	0.45	0.25
σ_{setup} [cm]	0.17	0.15	0.21	0.18

Table 2. Population systematic and random errors, as well as clinical target volume to planning target volume margins [cm]

	Systematic (Σ)	Random (σ)	ICRU report 62 [11]	Stroom [12]	Van Herk [13]
X	0.3398	0.1561	0.3740	0.7889	0.9588
Y (Anterior-Posterior)	0.2858	0.1692	0.3322	0.6901	0.8331
Y (RLAT)	0.2586	0.1882	0.3198	0.6490	0.7783
Z	0.4529	0.2094	0.4990	1.0525	1.2790

ICRU: International Commission on Radiation Units and Measurements; RLAT: Right Lateral

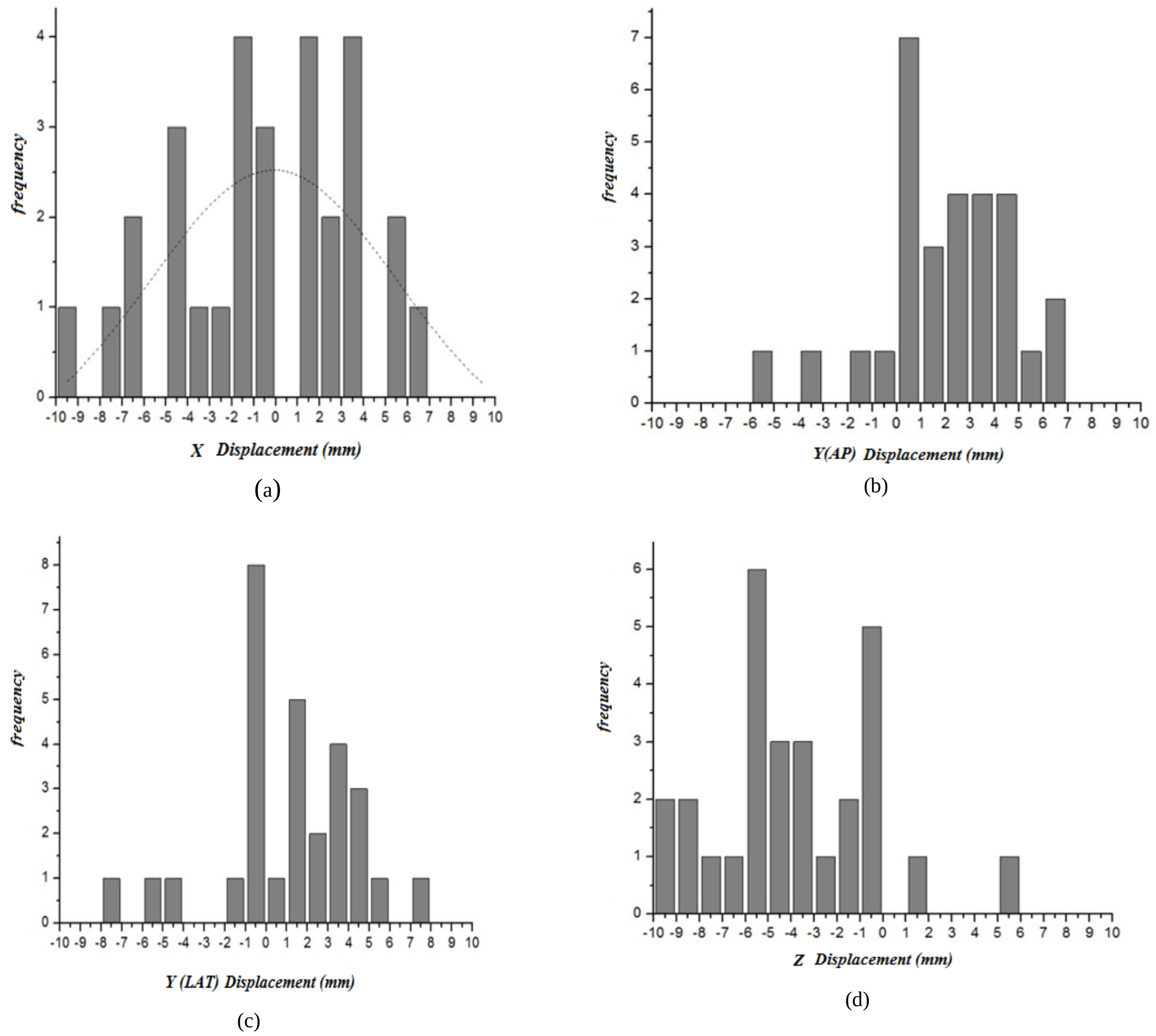


Figure 2. Distribution of total deviations at (a) left-right lateral direction, (b) caudocranial longitudinal direction from the anterior-posterior field, and (c) dorsoventral vertical direction from the lateral field

Discussion

This study reported the accuracy rate of the head and neck radiation therapy of patients treated with CRT in Imam Reza Hospital of Mashhad. Main goal of the present study was to determine the CTV to PTV margins by which the target volume will be covered through radiation.

Out of 92 treatment fields, 31 (31%) cases were modified to be corrected for setup errors included in 10 of the 15 patients. Most of these modifications were related to the images of the first treatment session. Yan et al. [16] reported that the off-line registration of portal images could reduce the setup errors, especially at the initial sessions. For each subject, the length of the 3D vector was calculated and averaged for obtaining the mean 3D vector of displacement. Mean 3D vector of displacement was reported as 4.64 mm.

In the present study, there were a few limitations. Firstly, rotational errors could not be considered because there were portal images in the AP and LAT projections; therefore, rotational shifts were not captured. Secondly, portal images did not provide information about organ motion. Although organ motion can be negligible in head and neck cancer, there were some cases with unpredictable movement. Therefore, these kinds of errors were not considered in the calculation of PTV margins. Suzuki et al. [17] reported the effects of organ motion in random and systematic setup errors ranged from 0.3-0.6 and 0.2-0.8 mm, respectively.

In our institution, the action level of translational direction was 5 mm in head and neck cases. Findings of the present study showed that 86%, 90%, and 50% of setup deviation in the LAT, longitudinal, and vertical axes were lower than 5 mm, respectively. Table 3 tabulates the comparison between the results obtained from the present study and similar studies [1, 14, 17-23].

As observed in Table 3, the findings of the present study are in line with the results of similar studies. The difference between the systematic and the random errors in our center (Imam Reza hospital, radiation oncology center) with errors in other studies was due to the accuracy of the Linac (i.e., systematic errors) and precision of the treatment procedure by the technician (i.e., random errors). However, all the differences were in range for the treatment.

As a recommendation, using appropriate immobilization methods, improving laser alignment and dimension (a laser with 2 mm dimension was used in the present study), as well as table and gantry stability, are necessary to reduce errors and achieve more reliable results. Hurkmans et al. mentioned that the immobilization device and institution affect the setup accuracy [24]. Moreover, the margin size and range of systematic and random errors depend on the treatment site. In the aforementioned review, they reported a range of systematic errors. Pelvis errors ranged from 1.1 to 4.7 mm, 1.6 to 4.6 mm for head and neck cancer, and 1.0 to 4.7 mm for breast cases.

As shown in Table 2, the differences in positioning errors were at the highest level in the *Z* axis among the three axes. In a study carried out by Khosa et al. [25], it was reported that regardless the types of markers have a role in displacement. Osei et al. [26] demonstrated that the implanted marker was the most significant displacement in the *Z* axis, followed the *Y* axis. The most significant displacement occurred in the *Y* axis when the reference point was a bone marker. In the present study, the implanted marker (put some radio-opaque markers on their thermoplastic) was used for registration.

The EPI is a useful device for a reliable correction of various geometrical interfraction errors in radiotherapy. It is also a tool for fast checking of offline errors. It is recommended to apply EPI device in radiation therapy departments where the 3D-CRT is common. In the present study, we have found the margins in all axes were equal to 3.81±0.7, 7.95±1.57, and 9.62±1.94 mm according to the ICRU report 62, Stroom and van Herk, respectively, that should be considered for the head and neck cancer patients for the full coverage of the target. The margin sizes were obtained based on the average of the margins in the three directions.

The setup margins were <4, <8, and <10 mm at all three directions according to the ICRU report 62, Stroom, and Van Herk, respectively. It can be concluded that the 10-mm extension of CTV to PTV margin could be sufficient to ensure that 90% of all patients receive a minimum accumulative CTV dose with at least 95% of the prescribed dose, As well, by 8 mm extension in CTV to PTV margin can be ensure that on an average, 99% of the CTV receives more than or equal to 95% of the prescribed dose. An adequate correction strategy may be considered for the reduction of the margin sizes.

However, random errors remain of several uncertainty sources. It is suggested that before considering the margin size, all the factors that can potentially affect the margins should be considered to ensure receiving sufficient dose to the target. The decrease in PTV margins will cause a lower probability level of normal tissue complication [20].

Table 1. Population systematic (Σ) and random errors (σ) in some other relative studies with the recommendation of target volume coverage (14)

Series	Σ (mm)	σ (mm)	Displacements or errors
Hess (18)	Not reported	Not reported	3 mm for 50% coverage and 9 mm for 95% coverage
Bentel (19)	Not reported	Not reported	5-10 mm (87-90% with 5 mm margin)
Gibeau (20)	1-2.2	0.7-2.3	4.5-5.5 mm for 90% probability of target coverage
De Boer (21)	1.5-2.0	1.5-2.0	Probability values not specified
Humphrey (22)	0.02-0.9	0.4-0.7	3 mm for 95% of errors and 5 mm for 99% of errors
Zhang (23)	1.5-3.2	1.1-2.9	5.5 mm for 90% probability of target coverage
Suzuki (17)	0.7-1.3	0.7-1.6	5 mm margin for PTV and 3 mm for PRV Probability values not specified
Gupta (14)	0.96-1.2	1.94-2.48	CTV-PTV margin<5 mm in all directions and 93% displacements within 5 mm
Strbac (1)	1.42-1.93	1.77-1.86	<6.1 mm CTV-PTV LR direction <5.1 mm CTV-PTV CC direction <4.8 mm CTV-PTV DV direction
Present study	2.58-4.52	1.56-2.09	<7.88 mm CTV-PTV LR direction <6.9 mm CTV-PTV CC direction <10.5 mm CTV-PTV DV direction ≤1 cm for 90% probability of target coverage

† PTV: Planning target volume; *PRV:* Planning organ at risk volume; *CTV-PTV:* Clinical target volume to planning target volume; *LR:* Left-Right direction; *CC:* Caudo-Cranial; *DV:* Dorso-Ventral

Conclusion

This retrospective study showed the range of systematic and random errors that occurred in the setup interfraction of radiotherapy treatment. Results of the present study revealed that the setup accuracy of patients receiving 3D conformal head and neck radiotherapy is to some extent good in comparison with the errors reported in other studies. The present study helped to know the efficiency of the treatment in the reproducibility of patient position in our institution and feasibility of using EPID for the field setup verification. According to the obtained results of the present study, it is proposed to obtain pretreatment portal images every week to overcome random and systematic errors.

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