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Original Research Article

Retrospective analysis of random and systematic errors in radiation therapy of head and neck cancer patients and its clinical predictive implications with VMAT treatment

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ABSTRACT

Background: The accuracy of radiotherapy is based on the matching of 2D portal/CBCT image with a reference image. The aim of this study is to determine the random and systematic setup errors (in cm) in radiotherapy of head and neck cancer patients and to derive the setup margin and its clinical implications.
Methods: Author retrospectively reviewed the records of 25 head and neck cancer (HNC) patients treated with radiotherapy between Dec 2017 and July 2018. After immobilization, setup accuracy was assessed by registration of XVI image with planning reference image using Elekta XVI image guidance system and the isocenter correction was applied. For each patient 10 CBCT image sets were taken. The translational errors in X, Y and Z directions were used to estimate systematic (Σ) and random (σ) errors and to derive the final setup margin by using van Herk's formula (2.5Σ + 0.7σ).
Results: The mean translational errors ranges from -0.23 cm to 0.32 cm in Lateral (X), -0.15 to 0.16 cm in Longitudinal (Y) and -0.11 to 0.17 cm in vertical (Z) directions. The Mean and SD for systematic errors 0.21±0.13, 0.11±0.18, 0.14±0.11 and random error (in cm) are -0.03±0.33, 0.00±0.21 and 0.05±0.30 in X, Y and Z axis respectively. The final total margin for CTV to PTV including setup margin in the X, Y and Z directions (in cm) were 0.56, 0.61, and 0.47 respectively.
Conclusion: Thus, the precise immobilization techniques are very important to reduce the setup margins, and the number of CBCTs during head and neck radiotherapy treatment.

Key words: CBCT image, Head and neck cancer, Immobilization, Random and systematic errors, Radiation therapy, Setup margins

INTRODUCTION

The main aim of radiation treatment (RT) is to deliver the prescribed dose to the targets with precision as planned in the treatment planning system. Therefore, it is very important to achieve the setup with proper immobilization as on the day of simulation. Errors in setup will lead to geographical miss at the target site which may lead to treatment failure as well as inadvertent radiation to the organs at risk leading to unacceptable acute and late toxicities. Therefore, reproducibility in daily treatment setup is considered to be an important factor for accurate radiotherapy treatment delivery. The planning target volume (PTV) is defined as the clinical target volume (CTV) plus a margin to account for patient setup uncertainties, beam alignment and organ motion (i.e. setup errors and internal margin).[1] Setup errors directly effect on the coverage of the target area. Thus, these should be help to prevent inadvertent irradiation of organ at risks (OARs).[2,3] The geometric uncertainties during the treatment delivery can lead to potential inadequate dose delivery to tumor volumes and over radiation nearby critical structures.[4] The patient setup at each fraction of radiotherapy treatment is affected by various setup uncertainties such as variations in patient positioning, mechanical uncertainties of the equipment (sagging of gantry, collimators, and couch), transfer set up errors from computed tomography (CT) simulator to the treatment unit, and also human factors. These setup uncertainties constitute systematic error. The Systematic errors are reproducible errors, occurring in the same direction and magnitude but random (day-to-day) errors can vary in direction, magnitude and are unpredictable. The purpose of study is to determine the setup error (random & systemic setup errors) for HNC Radiotherapy using inbuilt kilo-voltage cone beam computed tomographic scanner (KV-CBCT) within the linear accelerator, and to derive the setup margin for clinical implications.

METHODS

Study Design

This is a retrospective study. 25 head and neck cancer patients who received radiotherapy in Nayati Multi Super Specialty Hospital, Mathura, Uttar Pradesh, India between Dec 2017 and July 2018 were enrolled. We evaluated the inter-fractional setup errors by using an X-ray volumetric imaging system (XVI Elekta) and 2D portal imaging system with digitally reconstructed radiographs (DRR). Then we calculated the CTV to PTV margin for head and neck treatment sites, with the help of XVI image guidance and determine the optimal PTV margins.

Equipment and process

To provide adequate immobilization of the HNC patients we are using AIO (All in one) alignment board, standard thermoplastic immobilization (from macro medics solution radiation therapy), headrest No. 2, 3, 4 and additionally shoulder retractor to retract the shoulders away from the treatment fields. After completion of the mould room procedures patients were positioned on CT simulator couch as shown in Figure 1. Then planning CT was acquired and transferred to MONACO planning system, where contouring of the targets and organs at risk are done followed by plan generation and evaluation after which the 3D reference planning CT of each patient was transferred from MONACO planning system to XVI imaging system.

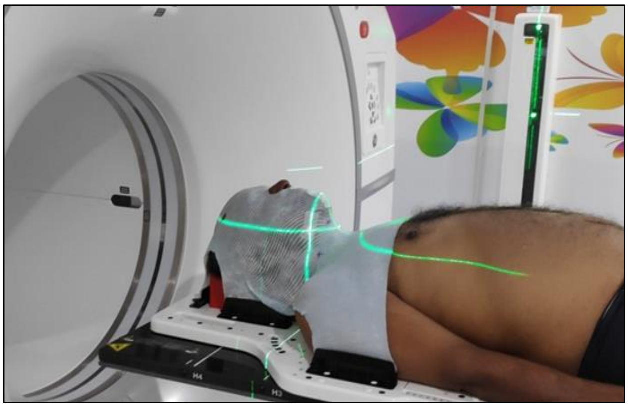

Figure 1: CT simulation procedure for HNC patients using five-clamp orfit with AIO board.

Then CT images were imported and ROI (region of interest) for matching was selected by using clip box method as shown in Figure 2.

Figure 2: Image showing fusion of CBCT and planning image using clip box registration method for head neck image verification using XVI system.

In the treatment room, the patient is positioned with immobilization mask for treatment as done in mould room procedure and in CT Simulation. The isocenter shifts in three directions (RL, AP and SI) were applied from CT reference markers to planning CT origin by using the planning system generated shift charts. Then the shifts are verified by comparing the SSD on patient with the SSD value mentioned in shift chart.The setup accuracy was assessed daily for each patient by doing CBCT or 2D Imaging. While doing CBCT registration the automatic "bone to bone" match method was used to verify the isocentre position in all three directions with rotation correction. The elekta XVI image guidance system is a highly précised and optically guided patient localization system, which affords sub-millimetre set-up accuracy in IGRT treatments. In this study, total data of 250 CBCT images taken for 25 patients. For each patient total 10 CBCT image sets were taken, which includes first three days CBCT's and weekly once 3D images. During the course of treatment and for remaining 4 days in a week DRR imaging (2D IMAGE) were taken to check the setup error in three directions. While CBCT image sets were registered with the reference planning CT image set using clip box registration method, the translational errors in all three directions were noted down (lateral 'X', longitudinal 'Y', and vertical 'Z') as shown in Figure 2. After an automatic match with the reference image the obtained translational shift was applied to couch correction in all three directions and these data are noted and compiled in an excel sheet. To obtain appropriate CTV-PTV margin Van Herk's formula $2.5^* \Sigma+0.7\sigma$ (Σ-systematic error and σ– random error) is used for HNC patients. Patients were treated after couch corrections are applied. Set-up error corrections are done for each patient in daily basis in all three translational directions (weekly once CBCT and four days DRR). The standard workflow, starting from mould room procedure to treatment setup verification for HNC Radiotherapy at our institute is shown in Figure 3.

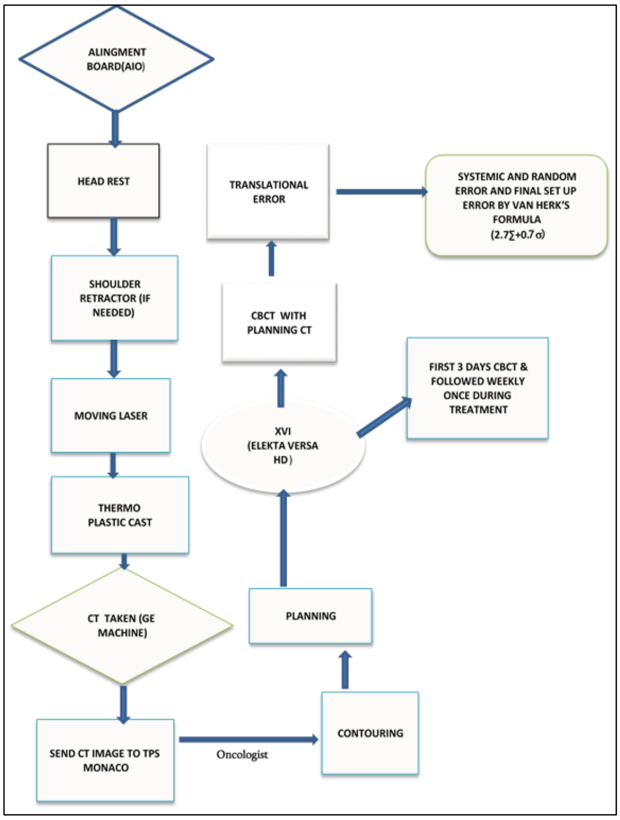

Figure 3: The standard workflow for head and neck cancer patient's radiotherapy.

Statistical analysis

Individual patient data were entered in MS excel and the X (lateral), Y (longitudinal), Z (Vertical) data were categorized into Systematic and Random errors based on their occurrence i.e. 'Systematic errors' as those data which had data variation in the same direction and the data having variation in bi-direction were taken as 'Random errors'. All the systematic and random error data were segregated separately for all patients to further evaluate the Mean and Standard Deviation.

RESULTS

For total 25 patients, the data were analyzed for calculating the mean displacement in X (Lateral), Y (Longitudinal) and Z (Vertical) directions, from where the mean systematic and random errors were derived. These shifts (displacements) were used for calculation of the final PTV margins by using Van Herk's formula. The calculated mean (±SD) systematic errors in the X (Lateral), Y (Longitudinal) and Z (Vertical) directions were 0.21cm±0.13 cm, 0.11cm±0.18 cm, 0.14cm±0.11 cm and the mean(±SD) random errors were-0.03cm±0.33 cm, 0.00cm±0.21 cm and 0.05cm±0.30 cm respectively as shown in Table 1.

Table 1: Mean and Standard Deviation (SD) value for systematic and random error in all three directions (lateral X, longitudinal Y, and vertical Z)

Directions	Systematic error (cm)		Random error (cm)	
	Mean	SD	Mean	SD
Lateral (X)	0.21	0.13	-0.03	0.33
Longitudinal (Y)	0.11	0.18	0.00	0.21
Vertical (Z)	0.14	0.11	0.05	0.30

The final setup margin was calculated by using the Van Herk's formula. Here we found the setup margins in Lateral (X), Longitudinal (Y) and Vertical (Z) directions were 0.56 cm, 0.61 cm and 0.47 cm respectively were shown in Table 2.

Table 2: Setup Margin in X, Y, Z direction, using Van Herk's formula.

Direction	Setup Margin (in cm) calculated using Van Herk's formula
Lateral (X)	0.56
Longitudinal (Y)	0.61
Vertical (Z)	0.47

The mean translation shifts in X, Y, Z direction were calculated for each patient. Figure 4 shows the mean displacement in X (Lateral) direction for individual patients. The maximum mean displacement in lateral direction ranges from -0.23 cm in right and 0.32 cm in left direction.

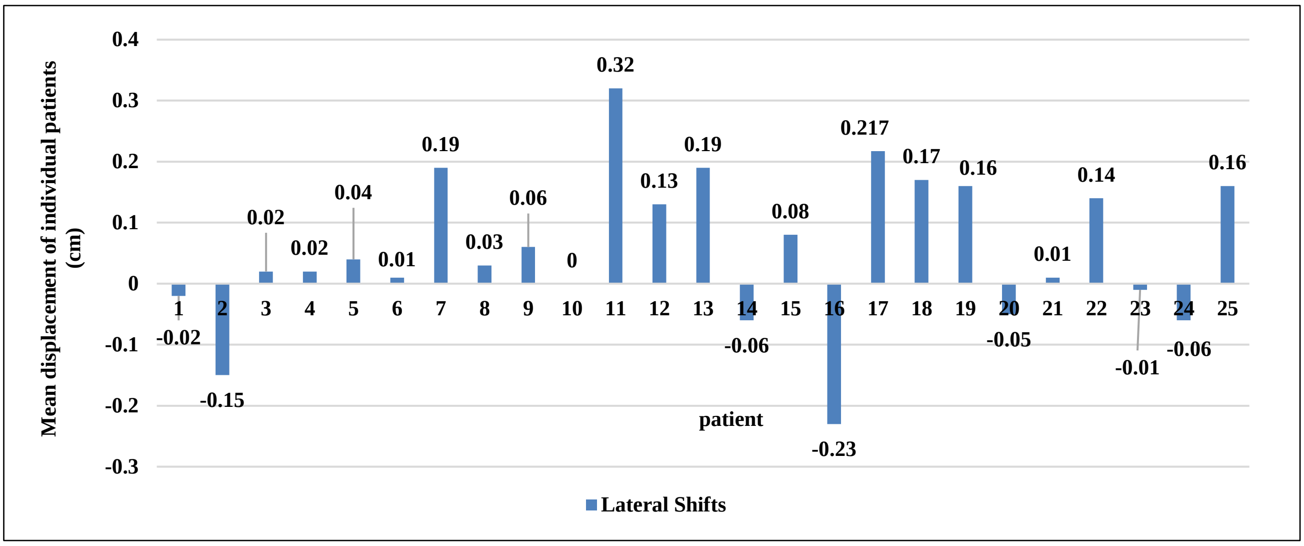

Figure 4: Mean setup variation in X (Lateral) direction for 25 patients.

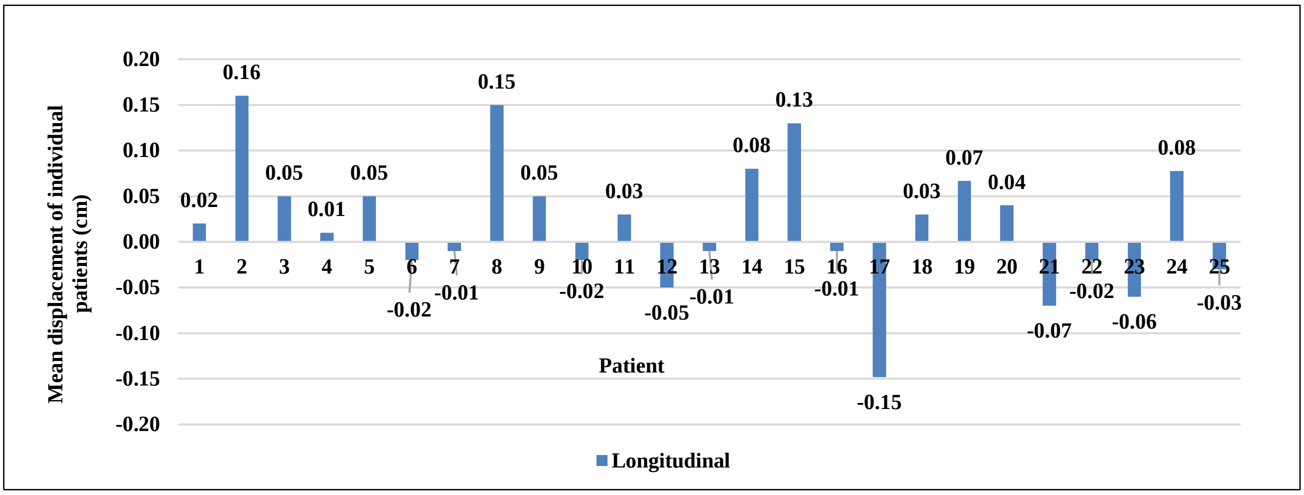

Figure 5: Mean setup variation in Y (Longitudinal) direction for 25 patients.

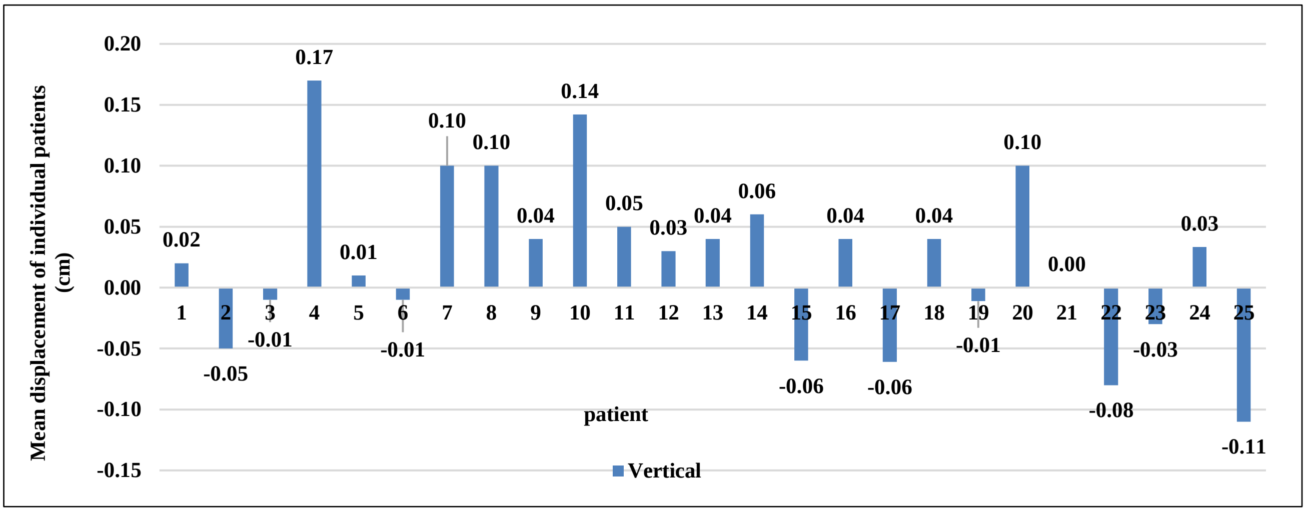

Figure 6: Mean setup variation in Z (Vertical) direction for 25 patients.

Figure 5 shows that mean displacement in Y (Longitudinal) direction for individual patients. The maximum mean displacement in longitudinal direction ranges from -0.15cm in superior and 0.16 cm in inferior direction. Figure 6 shows that mean displacement in Z (Vertical) direction for individual patients. The mean vector displacement in vertical direction ranges from-0.11 cm in posterior and 0.17 cm in anterior direction.

DISCUSSION

In this present study, author found out daily setup error in head and neck cancer patients using masks immobilization and three laser alignment technique. Setup errors were assessed by using CBCT and confirmed its effectiveness in reducing setup margins. In the current study setup-errors showed systematic errors systematic errors (in cm) were 0.21±0.13, 0.11±0.18, 0.14±0.11 and random error (in cm) were 0.03±0.33, 0.00±0.21 and 0.05±0.30 in X, Y and Z axis respectively. These results are found to be acceptable and comparable with previous literatures.[5,6] Hong TS et al.[7] concluded that the heavy immobilization device such as head, neck and shoulder immobilization shell may be required for highly conformal radiation therapy for head and neck cancers. However, it should be kept in mind that reproducibility of patient positioning is an important factor and it depends on the proper mould room procedure, CT simulation, treatment implementation as well as the experience and efforts of all treatment staffs. The current study found that the immobilization masks were equally important in head and neck cancer treatment for setup accuracy and shortened setup time. As per International Commission on Radiation Units and Measurements (ICRU) Report 62, margin to the PTV from CTV is required in radiation therapy for the setup uncertainty.[1] PTV margin should be calculated based on the data of the patients systematic and random errors, according to Stroom et al.[6, 8] and Van Herk et al.[9,10] Using Van Herk formula we found that 5 mm of isotropic margin for PTV is required to achieve the proper dose coverage to the target volume, which matches our head and neck practice guideline. Hurkmans et al.[11] in their review article stated that SDs of the systematic and random setup errors varies, respectively, between 1.6–4.6 mm and 1.1–2.5 mm in Head and Neck cancers. Kataria et al. [12] in their review article stated that mean errors in head-neck radiotherapy plans were between 0.12±0.05 cm laterally, 0.12±0.04 cm longitudinally, and 0.12± 0.05 cm vertically.12 In our study we also found the Mean and SDs of the setup error [systematic error (Σ) and random error (σ)] in X, Y and Z were for systematic error are 0.21±0.13, 0.11±0.18, 0.14±0.11 and random error are -0.03±0.33, 0.00±0.21 and 0.05±0.30 which is shown in table 1 which is less than the previously discussed literature. Gupta et al.[13] assessed the setup errors in 25 patients with H & N lesions using camera-based images that immobilized with thermoplastic mask. The systematic errors were 0.96 mm, 1.2 mm and 0.98 mm and random errors were 1.94 mm, 2.48 mm and 1.97 mm in the vertical, longitudinal and lateral directions, respectively. They obtained a PTV margin 3.76 mm, 4.74 mm and 3.83 mm for the vertical, longitudinal and lateral directions.[13] In our study, we found that systematic error (∑) for X, Y and Z directions were 0.21cm, 0.11 cm and 0.14 cm and random error (σ) were -0.03cm, 0.00 cm, and 0.05 cm.

The final total margin for CTV to PTV including setup margin in the X, Y and Z directions using Van Herk's formula ($2.5 * \Sigma + 0.7\sigma$) were 0.56 cm, 0.61 cm, and 0.47 cm respectively. There are several publications addressing the issue of set up uncertainties in head and neck cancers. Xu et al.[14] observed that translational setup errors in X, Y and Z directions were 1.2±0.9 mm, 1.2±1.1 mm, and 1.0±0.8 mm, respectively.[14] In this study, translational error in each direction ranged from -0.23 cm to 0.32 cm in Lateral (X), -0.15 to 0.16 cm in Longitudinal (Y) and -0.11 to 0.17 cm in vertical (Z) directions. Setup errors directly affect the coverage of clinical targets, inappropriate coverage may result in treatment failure and on other hand it may be responsible for acute and late radiation related toxicities like skin reactions, oral and oropharyngeal mucositis, xerostomia, radiation induced myelopathy and others.

CONCLUSION

In this study we found that 5 mm is an optimal setup margin for CTV- PTV to include the setup errors in radiation treatment of head and neck cancer patients. The appropriate setup error corrections help in prediction of treatment outcomes especially treating with highly conformal radiotherapy technique that are IMRT, VMAT to minimize the local recurrence due to inappropriate coverage and radiotherapy related toxicities. The online correction procedure from the XVI system has enabled an additional reduction of set-up margins. To reduce imaging dose to the patient the number of XVI volumetric images are reduced by combining the 2D portal image verification method for setup correction. The rotational setup errors, patient's weight loss and tumor shrinkage were not considered.

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