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ORIGINAL ARTICLE

Defining the Planning Tumor Volume by analyzing Setup of Head & Neck (H&N) Carcinoma in Radiotherapy

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ABSTRACT

Aim: To find out the setup error of Head and Neck patients treated with Intensity modulated radiation therapy (IMRT) on CLINAC-IX at Center for Nuclear medicine and Radiotherapy (CENAR) Quetta by using inbuilt electronic portal imaging device (EPID) to obtain the setup margin for clinical investigation.
Methods: A total of 35 patients of head & neck carcinoma were treated with Intensity modulated radiation therapy (IMRT) total dose of 69.96Gy in 33 fractions at CENAR from 1st January 2021 to 31st December 2022 were consider this retrospective study. PTV margin for different directions (Vertical, lateral &Longitudinal) were analyzed by Van Herk's formula
Results: Data analyzed for calculating the mean displacement in X (Lateral), Y (Longitudinal) and Z (Vertical) directions, from where the mean systematic and random errors derived. These shifts (displacements) used for calculation of the final PTV margins by using Van Herk's formula. The calculated mean (±SD) systematic errors in the Z (Vertical), X (Lateral) and Y (Longitudinal) and directions were 0.10cm, 0.06cm, and 0.07cm and the mean(±SD) random errors were 0.01cm, 0.004cm and 0.01cm respectively.
Conclusion: In our study, less than3 mm is an optimal margin for GTV- PTV for head and neck cancer patients. The reduction in setup margin helps in prognosis of treatment results, reduce radiation related complication in normal tissue and reduce the local recurrence. Imaging guidance techniques is effective tool for setup margin.
Keywords: Electronic Portal Imaging Device, Van Herk Equation, Systematic Error, Random Error, Head & Neck Carcinoma,

INTRODUCTION

One of the world's largest health issues is cancer[1]. The most important objective of radiotherapy treatment is to deliver the recommended dose to the targets with accuracy as planned in the treatment planning system. Therefore, it is very significant to attain the setup with appropriate immobilization as on the day of simulation. Errors in setup will lead to miss the tumor, which may directly effects the organs at risk (OAR's) leading to intolerable acute and late toxicities. Hence, reliability in daily treatment setup is considered as a significant factor for precise radiotherapy treatment delivery. The planning target volume (PTV) is characterize as the clinical target volume (CTV) plus a margin to consider patient setup variation, beam alignment and breathing motion [2]but setup errors directly effect on the coverage of the target area. Thus, these setup errors should be minimizing to prevent OAR's from radiation[3]**.** Due to setup error, the geometric miss throughout the treatment delivery can lead to incomplete dose delivery to tumor and over radiate the nearby organs. [4].During treatment, patient setup affected by different variations like patient positioning, setup error from computed tomography (CT) simulator to the treatment equipment, and human error. These setup uncertainties show systematic error. The Systematic errors are linearity errors, occurring in the same direction.

Although, in high dose radiotherapy planning precision is needed in preparing patient and to control the dose of organs at risk and precise positioning of the patient during radiotherapy session. For precise radiotherapy treatment, imaging by Imaging Device is useful which uses three–dimensional images that give accurate information on patient setup[5]**.** The purpose of the imaging system involve daily or as per protocol verification of patient setup on the treatment machine using 2D MV orthogonal X-ray images permits to minimize the geometrical mistake as a result of intra- and inter fraction motion. Minimization of inter fraction systematic and unsystematic errors permits to lessen the margins between the clinical tumor volume (CTV) and the planning target volume (PTV)[6]**.**

The rule for secure radiotherapy, both in conformal and dynamic techniques, is high accuracy of linearity of the treatment plan geometry. Therefore, depiction of the clinical tumor volume (CTV), Organs at risk (OAR's) and margins for the PTV are critical. Categorization of the target volume considerably effects successful treatment. Generally, the CTV and the OAR could be specifically identify on diagnostic images, while the PTV depends on a geometric perception, which depends on the variation in the contour of target volumes basis on motion of the organs at risk and both random and systematic errors[7].

Defining the margin of PTV is very important in treating the tumor effectively and simultaneously minimizing irradiation of the OAR and reducing the risk of radiation complications[8].

In radiotherapy, margin for the PTV not well defined in case of head and neck cancer (H&N).Researchers had determined margin from 0.2cm to 0.5cm around the clinical tumor volume that based on clinical knowledge but not proved practically[9]**.**

Earlier available data on the PTV margins for head and neck cancer (H&N) specify that these margins are not symmetrical and vary for the lateral plane (X axis), longitudinal plane (Y axis) and vertical plane (Z axis)[10].

The objective of study is to find out the setup error for Head and Neck Carcinoma (H&N) Radiotherapy using inbuilt electronic portal imaging device (EPID) and to obtain the setup margin for clinical investigation.

This is an experimental learning, which try to describe the intra-fraction motion in Head and Neck (H&N) cancer patients throughout treatment sessions depends on the EPID Electronic Imagining Device (EPID) and defining the margins around the clinical tumor volume required to define the PTV.

The objective of this field's research has been to reduce local recurrence brought on by inadequate coverage and radiotherapy-related toxicities by focusing on proper setup and error corrections that aid in the prediction of treatment outcomes, especially when using highly conformal radiation techniques like IMRT and VMAT.

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MATERIAL AND METHOD

Thirty five Head & Neck cancer patients were treated with Intensity modulated radiation therapy (IMRT) therapy on CLINAC-IX with the total dose of 69.96Gy in 33 fractions at Center for Nuclear medicine and Radiotherapy (CENAR) Quetta from 1st January 2021 to 31st December 2022. Head & Neck patients were immobilized by using standard thermoplastic mask & headrest to reduce movement of patient. After preparation of the thermoplastic mask, patients were position on Toshiba Aquilion Compute Tomography (CT) couch. Lead markers were place on thermoplastic mask to mark isocenter. Pre and post contrast CT scan conducted. Omnipaque used as CT contrast. Images obtained from CT simulator and transferred to ECLIPSE planning system, where contouring of the targets and organs at risk are done by clinical oncologist and the planned by medical physicist, after planning clinical oncologist again verified all doses of target volumes and OAR'S. After verification and preparation, treatment plan transferred from ECLIPSE planning system through ARIA communication system to start treatment.

Patients positioned by application of the electronic portal-imaging device (EPID) before each radiotherapy session. The location and position of the patient was determined based on the bony structures on radiological images by the anterior posterior and lateral projections by electronic portal imaging device (EPID).

Reference landmarks in electronic portal images

Treatment Site	Reference bony landmarks in lateral image	Reference bony landmarks in AP image
Head and Neck	External mandible profile and the spinous process of one of lower cervical vertebrae	Internal & External mandible profiles, Skull base and cervical vertebra bodies(C2-C4)

Figure: 1 Standard workflow, starting from mould room procedure to treatment setup verification

Patient positioned in treatment room same as done in CT simulation. On the 1st day of treatment, the iso-center analyzed in three directions (Lng, Lat and Vrt) applied from CT reference markers. The setup accuracy evaluated after every two fraction by doing 2D imaging via EPID.In this study, total data of 448 images taken for 35 patients through MV imager. When treatment start than first two days images taken followed by every two fraction, total 12 image sets taken for each patient by following this protocol. Before start of next treatment, medical physicist verifiedthe image of patient. The translational errors in all three directions noted down (lateral 'X', longitudinal 'Y', and vertical 'Z').
To obtain appropriate GTV-PTV margin Van Herk's formula: 2.5* Σ+0.7σ (Σ-systematic error and σ– random error) is used for HNC patients. Patients treated after shift applied. Set-up error corrections are done for each patient as per protocol in all three translational directions. The standard workflow, starting from mask preparation to treatment setup verification for HNC Radiotherapy at our institute.

The margins for planning tumor volume against gross tumor volume were estimated according to the Van Herk (2004), Stroom and Heijmen (2002) and ICRU Report 62 formulas which anticipated that the margins for the PTV should be defined as follows:

$M = 2.5\ \Sigma + 0.7\sigma$ (Van Herk, 2004)
$M = 2.0\Sigma + 0.7\sigma$ (Stroom and Heijmen, 2002)
$M = \text{sqrt}(\Sigma^2 + \sigma^2)$ (ICRU Report 62)

- Σ- SD of systematic errors
- σ- SD of random errors

The formulas include both systematic and random errors, which obtained from motion of internal organs, which failed to attain the position from the CT scanner during the session of radiotherapy

RESULTS

For total 35patients, the data analyzed for calculating the mean displacement in X (Lateral), Y (Longitudinal) and Z (Vertical) directions, from where the mean systematic and random errors derived. These shifts (displacements) used for calculation of the final PTV margins by using Van Herk's formula. The calculated mean (±SD) systematic errors in the Z (Vertical), X (Lateral) and Y (Longitudinal) and directions were 0.10cm, 0.06cm, and 0.07cm and the mean(±SD) random errors were 0.01cm, 0.004cm and 0.01cm respectively as shown in Table 1.

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

Directions	Mean	SD
Lateral(x)	0.03	0.10
Longitudinal(Y)	-0.01	0.07
Vertical (Z)	0.03	0.06

The final setup margins were calculated by using the Van Herk's formula. Here found the setup margins in Lateral (X), Longitudinal (Y) and Vertical (Z) directions were 0.2cm;0.2 cm and 0.3 cm respectively shown in Table 2.

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

Directions	Setup Margin in X, Y, Z direction, using Van Herk's formula.
Lateral(X)	0.2cm
Longitudinal(Y)	0.2cm
Vertical (Z)	0.3cm

The mean translation shifts in X, Y, Z direction calculated for each patient

Figure: 2 Setup margins for PTV from GTV according to the Van Herk Equation, Stroom and Heijmen Equation and ICRU Report 62 Formula:

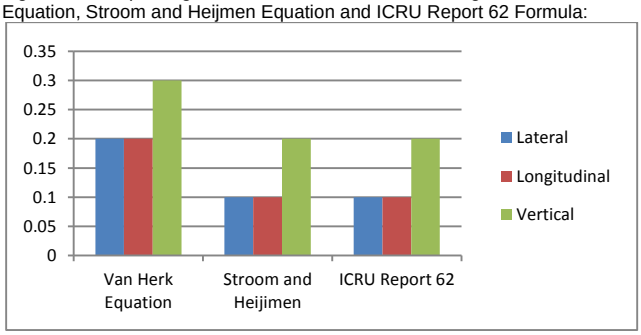


Figure: 3 Mean Setup Variation in Lateral (X) Direction.

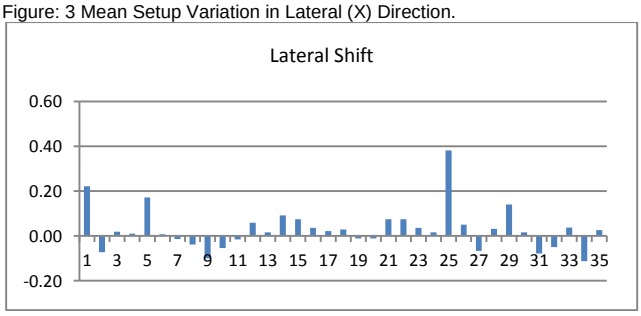
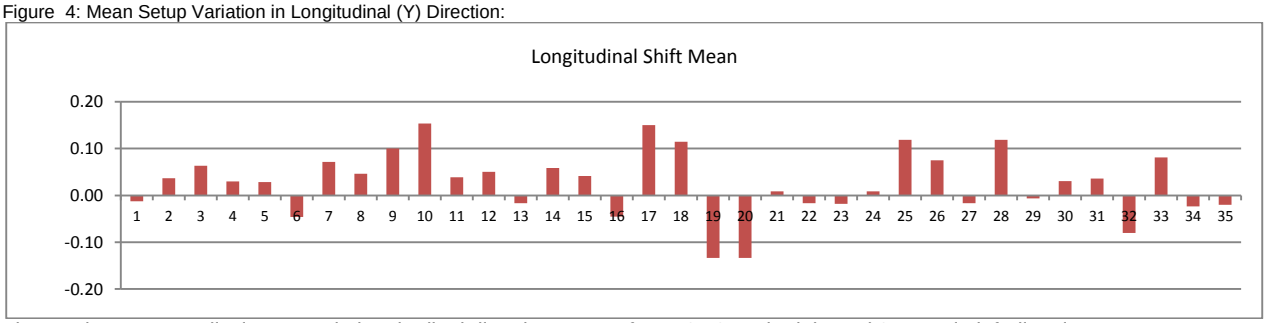


Figure 3 shows the mean displacement in X (Lateral) direction for individual patients. The maximum mean displacement in lateral direction ranges from -0.11 cm in right and 0.38cm in left direction

Table 3: The Mean Values and Standard Deviations for the Lateral, Vertical & Longitudinal Directions and the Margins for PTV Calculated According to the Van Herk (2004), Stroom and Heijmen (2002) and ICRU Report 62 Formulas

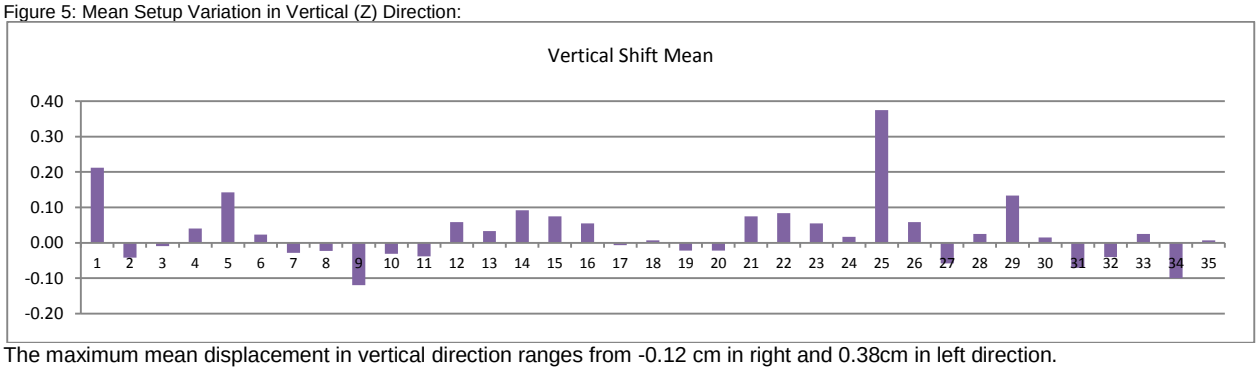
Direction	Mean (cm)	Standard Deviation (cm)	Random Error (cm)	Van Herk (cm)	Stroom and Heijimen (cm)	ICRU Report 62 (cm)
Lateral	-0.01	0.06	0.004	0.2	0.1	0.1
Longitudinal	0.03	0.07	0.01	0.2	0.1	0.1
Vertical	0.03	0.10	0.01	0.3	0.2	0.2

Figure 4: Mean Setup Variation in Longitudinal (Y) Direction:



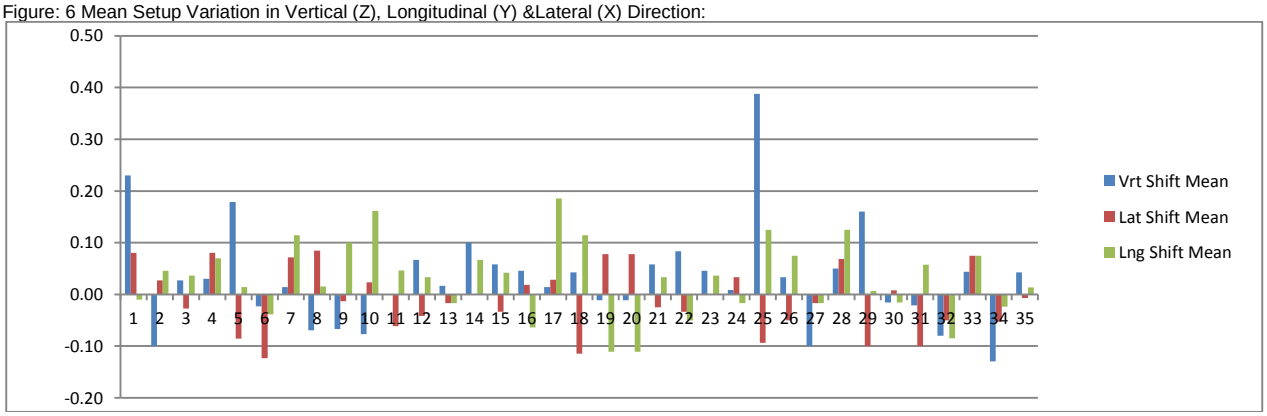
The maximum mean displacement in longitudinal direction ranges from -0.13 cm in right and 0.15cm in left direction.

Figure 5: Mean Setup Variation in Vertical (Z) Direction:



The maximum mean displacement in vertical direction ranges from -0.12 cm in right and 0.38cm in left direction.

Figure: 6 Mean Setup Variation in Vertical (Z), Longitudinal (Y) &Lateral (X) Direction:



DISCUSSION

Head & Neck cancer is a heterogeneous condition marked by aggressive and unchecked cell development in several regions including larynx, pharynx, oropharynx, hypopharynx and oral cavity. Incidences of head & neck cancer are increasing and rank among the top ten malignancies globally. The sixth most common cancer to be diagnosed is head & neck and males are far more likely than females to develop it[11].

The Nasopharynx is a large cavity that extends 10 cm or so from either side of the skull in three dimensions and is located in the middle of skull. It is asymptomatic until a lesion, such as cancer completely clogs the Nasopharynx and the nose or compresses and effects a nerve through mass effect or direct invasions[12].

It should consider that reliability of patient positioning is significant factor and it depends on the proper use of immobilization devices, CT simulation, treatment implementation as well as the experience and hard work of all treatment staffs. By Using Van Herk equation it found that 2mm to 3mm of margin for PTV is necessary to obtain the appropriate dose coverage to the target volume.

In this present, setup errors were assessed by using EPID and offline review and confirmed its efficiency in reducing setup margins. In the current research, setup-errors showed systematic

errors (in cm) were 0.06, 0.07 & 0.10 and random error (in cm) were 0.004, 0.01 & 0.01 in X, Y and Z axis respectively. In a review article, Hurksmans.et al reported that systematic and random error is less than 2mm in head and neck patients[11]. The finding of our study is comparable with Hurksman et al study[13].

In another study, setup error in 25patients assessed with H&N cancer using EPID imager. The systematic errors were 0.096, 0.12, and 0.098 (cm) in the vertical, longitudinal and lateral direction. The random errors were 0.194, 0.248 and 0.197(cm) in the vertical, longitudinal and lateral direction[14]. The finding of this study is comparable to our study.

According to Van Herk Equation (2.5* Σ+0.7σ PTV margin from GTV obtained was 0.3cm, 0.2cm and 0.2cm for the vertical, longitudinal and lateral directions respectively. Setup errors 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 our study, less than 3mm is an optimal margin for GTV- PTV for head and neck cancer patients. The reduction in setup margin helps in prognosis of treatment results, reduce radiation related complication in normal tissue and reduce the local recurrence. Imaging guidance techniques is effective tool for setup margin. The rotational setup errors, patient's weight loss and tumor shrinkage were not considered.

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1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.
4. All authors agree to be responsible for all aspects of their research work

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