Original Research Article

Received : 13/09/2023 Received in revised form : 11/10/2023 Accepted : 20/10/2023

Keywords:

Planning target volume, External beam radiotherapy, Intensity Modulated Radiation Therapy, Portal imaging.

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DOI: 10.47009/jamp.2023.5.5.262

2011 101 1009, julip:2020.0.01202

Source of Support: Nil, Conflict of Interest: None declared

Int J Acad Med Pharm 2023; 5 (5); 1324-1330



PROSPECTIVE EVALUATION OF INSTITUTIONAL PLANNING TARGET VOLUME MARGIN FOR HEAD AND NECK CANCERS TREATED ON LINEAR ACCELERATOR

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Abstract

Background: As radiation technology has advanced, treatment planning and delivery have become progressively more precise, optimal PTV margins required for radiotherapy delivery have become much more critical. The systematic errors are mainly introduced during the preparatory stages of radiotherapy and are considered to influence each treatment fraction in the same way and thereby causing a shift in the dose distribution. Random errors are dayto-day displacements that will cause a blur in the dose distribution. Though undesirable, they are an inherent part of the radiation treatment process. The aim is to generate appropriate PTV margins for the head and neck tumors using IMRT technique in our department from the daily shifts detected using portal imaging. Materials and Methods: This prospective study has observed the systematic and random setup errors which occurred while treating head and neck cancer patients on Linear accelerator with EBRT. A total of 61 patients of head and neck cancers who satisfied the eligibility criteria were analyzed in this study. Result: The age range of patients was 23-80years with a median age of 57 years. 78% of the population are males and 22% are females with no paediatric population. The most common primary site in the patients was noted to be tongue i.e., 28 % of the population. Of the errors noted in vertical, longitudinal and lateral directions, the deviation noted in longitudinal direction was the maximum. Change in errors in vertical, lateral and longitudinal direction in the weeks 1 to 7 were not significant. PTV Margins are Medio lateral direction – 4.1mm Anterio-posterior direction –3.9 mm, Superio inferior direction – 4.8 mm. The maximum error occurred in superoinferior direction. CTV to PTV margin in this study was within 5mm in all directions. Conclusion: Good immobilization device can reduce the systematic errors and also on maintenance of nutritional status that can have an impact on setup errors and treatment outcome.

INTRODUCTION

Cancer of the head and neck is the sixth most common cancer worldwide. 6.4 lakh Head & Neck Cancers are diagnosed worldwide per year, account for 30% of all cancers and 1.5 lakh in India per year i.e., approximately 20% of the worldwide incidence. The optimal management of head and neck cancer requires a multidisciplinary approach. Surgery and radiotherapy are the major treatment modalities. Radiotherapy is an integral part of head and neck cancer treatment either as definitive treatment for organ preservation or as an adjuvant treatment with or without concurrent use of chemotherapy to improve tumor control.^[1,2]

The aim of radiotherapy delivery is to conform the dose to the target while reducing the dose to surrounding normal structures. As regional lymph nodal stations in the neck are also treated, the treatment volume is usually large.^[1] This highlights the importance of improving existing radiotherapy techniques to reduce the dose in relevant structures

with the use of Intensity modulated radiotherapy.^[3] As the techniques have evolved in becoming more conformal and reducing the volume of normal tissue irradiated, there is a need for a thorough verification process which include identification, adherence and effectiveness of

- the management process whether there was a designated verification team and components of that team in terms of specifying the disciplines involved.
- Quality assurance programs for maintaining the safety and accuracy of verification equipment.
- Protocols for image acquisition and analysis for each tumor site.
- Action levels and correction strategies and responsibilities within these protocols.
- Protocols for incorporating the set-up accuracies measured in margin calculations for common treatment sites where verification is particularly relevant to the application of highly technical radiotherapy; for example, prostate cancer and head and neck cancer.^[3,4]
- Training and competencies programs, preferably benchmarked to standards set out elsewhere.
- Inclusion of peer review standards into any audit once these have been revised.

The accuracy of the dose to the tumor and to the surrounding tissues and the precision in the spatial geometry of treatment volume are the main aspects of radiotherapy. Set-up displacement is the difference between the intended and actual treatment position. Systematic errors are introduced during the preparatory stages of radiotherapy and are considered to influence each treatment fraction in the same way and thereby causing a shift in the dose distribution.^[5-12] Random errors are day-to-day displacements that will cause a blur in the dose distribution.^[9,12] Though undesirable, they are an inherent part of the radiation treatment process.

The purpose of the PTV margin is to compensate for various uncertainties related to treatment delivery, if not corrected, it may cause differences between the intended and actual delivered dose distribution to the CTV.^[3,6] This CTV to PTV margin is much more important for intensity modulated radiation therapy (IMRT) plans as they usually have high dose gradients between tumor volume and adjacent normal tissue.^[5]

This study is planned at our Radiation Oncology Department which is equipped with kV x ray portal imaging (PI) to detect daily translational set up errors in 3 dimensions (X, Y, Z). The final aim of this study is to generate appropriate PTV margins for the head and neck tumors treated with IMRT technique in our department from the daily shifts detected using portal imaging. The findings in the study guide us to generate planning target volume more accurate which can reduce the irradiated area in patient's body and decrease treatment related toxicities. At the same time, under-dose or geographical miss of the tumor can be avoided.

MATERIALS AND METHODS

This study conducted in Department of Radiation oncology, Apollo Cancer Hospital, Hyderabad for a period of 15 months from January 2019 to April 2020 in 61 patients of head and neck cancers treating under IMRT in Novalis TX linear accelerator with thermoplastic immobilization device.

For estimating sample size for this study, we utilized the data from the study of Saha and Mallick et al 5. The required average PTV margin in head and neck cancers was found that 5.73 ± 1 from the previous published study. Considering $Z\alpha/2 = 1.96$ the critical value of the Normal distribution at $\alpha/2$ (with confidence level of 95%, α is 0.05). $Z\beta = 0.842$ is the critical value of the Normal distribution at β (power of the test is 80%, $\beta=0.20$). $\sigma 2 = 2.89$ is the estimated population variance based on the previous study. Considering d =1 is the expected difference between the means.

$$n = \frac{\left(\frac{Z_{\frac{\alpha}{2}} + Z_{\beta}}{2}\right)^2 \times 2 \times \sigma^2}{d^2}}{(1.96 + 0.842)^2 \times 2 \times 2.89} = 45.379 \cong 46$$

∴The minimum required sample per group is 46.

Based on the Apollo Hospital statistics from January 2018 to December 2018, approximately 120 head and neck cancer cases were registered in our department and had been treated with radiotherapy.

With this, we estimate at least 50 patients can be entered and the total number of fractions assessed are in range of 1500-1650. This is the expected sample size allowing for those patients who do not meet study criteria, or refusals, or dropouts.

Inclusion Criteria: All head and neck cancer patients, of age- 18-70 yrs, with Eastern Cooperative oncology group (ECOG) performance status between 0-2, treated in supine position with four clamp immobilization device. Patients with recurrent tumor are also included.

Exclusion Criteria: Tumors in which neck is not a part of treating area and immobilization device other than four clamp.

Immobilization - Patients were immobilized in supine position with hands by the side of body on AIO board with customized thermoplastic mask after placing appropriate neck rest. Head was extended depending on the location of tumor.

Simulation - By using 64 slice Philips CT simulator, 2-3 mm CT axial cuts of head, neck and thorax of the patient are acquired with immobilization device and fiducials. Radiation fields were simulated and optical field projection was marked on the thermoplastic mould for subsequent positioning and treatment. Fiducials are used to mark virtual isocentre and it was also useful to reproduce the simulated position while treating.

Treatment Planning Process - The CT images are exported to Eclipse 13.6 planning system in DICOM

format. Fusion of CT simulator images and Preop/diagnostic images were performed. The Radiation Oncologist delineates critical organs and Clinical Target Volume (CTV) on the fused images. After this, isotropic margin of 5-7 mm applied around CTV, yielding Planning target volume (PTV). Inverse planning technique featured by the treatment planning software Eclipse 13.6 (Varian Medical System, Palo Alto, US) was applied to elaborate the IMRT plan. IMRT plan is generated by medical physicist, evaluated and approved by radiation oncologist. The DRR images were acquired from the CT simulation images in both anterio-posterior and lateral directions.

Imaging and Verification - All patients were treated by Linear accelerator machine with source to axis distance (SAD) 100 cm using 6MV energy. Patients were positioned in accordance with the treatment beam using treatment room lasers and marks on the immobilization device.

For set up verification, On-Board imaging system and EPID were used. Before each treatment fraction 2 orthogonal images were generated, one anterio posterior image by EPID and the lateral image by on board kV imaging device. Portal images were acquired using EPID system consisting of amorphous silicon flat panel detector. The model used was EPID receptor model aS1000. It is mounted iso-centrically on the Linear Accelerator with a detector size of $40 \times$ 30 cm. A single exposure portal image of the anterioposterior field was obtained. On board image system (OBI) is placed on the gantry at 90 degrees offset to primary beam and detection system is similar as EPID. The small dose delivered by portal imaging and kV imaging were not considered in calculating the final total dose.

Reference images from CT simulator were used for comparison with the images taken throughout the treatment. As our imager is not equipped with automatic anatomy matching and fusion ability, the evaluation of translational set-up errors was done by manual matching of two reproducible and easily identifiable bony landmarks in upper and lower part of the treatment field each in anterior and lateral images. Patient setup was adjusted for errors exceeding 2-5 mm. Subsequent off-line analysis was utilized to give insight into the magnitude of clinical setup error in the visually accepted images.

After demonstration of the technique by a radiation therapy technologist, radiation oncologist checked the resulting deviations based on bony anatomy and deviations were recorded to avoid interobserver variation.

For the purpose of documentation and analysis anterior, superior, and right sided shifts were coded as positive shifts and posterior, inferior, and leftsided shifts as negative shifts.

Some of the potential sources of errors such as laser alignment, display accuracy, iso-centric accuracy and jaw reproducibility were not taken into consideration for the final match result. It was assumed that the routine periodic quality assurance employed for the Linear Accelerator would ensure minimal impact of the aforesaid on daily set-up.

Statical Analysis

In this study, 61 patients are enrolled and analyzed. Mean, Standard deviation is calculated for X, Y, Z axis. Systematic and Random error are derived and Planning Target Volume margin is generated by using Van Herk's formulae.^[13]

All the qualitative variables like gender, diagnosis, histology of head and neck tumor are represented as frequencies and percentages. Quantitative parameters like age, PTV margin in X, Y, Z axis is represented with descriptive statistics like mean, standard deviation. All the data entered and maintained in MS. Excel and analyzed by using SPSS23.0v. For calculation of weekly errors and their comparison, p value is calculated by using Post Hoc tests with ANOVA at 95 % confidence interval. p value is considered significant when p is less than or equal to 0.05.

RESULTS

The study has been conducted in the Department of Radiation Oncology, Apollo Cancer Institute, Hyderabad. A total of 61 patients, who satisfied the eligibility criteria, were studied. Zero patients defaulted/died during treatment. 78 % of population are males and 22 % of population are females. 54% of the population consumed smokeless tobacco in many forms like Paan, ghutka, jarda and betel quid with tobacco and had smoking history. \Box 57 % of the history population gave of alcohol consumption. 36% of the population received concurrent chemotherapy with an average of 5 cycles of weekly Cisplatin at a dose of 40 mg/m2 or at a dose of 100mg/m2 for every 3 weeks. [Table 1]

| Table 1: Demographic data distribution in present study | | | | |
|---|-----------|------------|--|--|
| Gender | Frequency | Percentage | | |
| Male | 48 | 78 | | |
| Female | 13 | 22 | | |
| Total | 61 | 100 | | |
| Smoking History | Frequency | Percentage | | |
| Yes | 33 | 54 | | |
| No | 28 | 46 | | |
| Alcohol History | Frequency | Percentage | | |
| Yes | 35 | 57 | | |
| No | 26 | 43 | | |
| Concurrent Chemotherapy | Frequency | Percentage | | |

| Yes | 22 | 36 |
|-------|----|-----|
| No | 39 | 64 |
| Total | 61 | 100 |

| Table 2: Descriptive statistics of the Histopathological types | | | | |
|--|-----------|------------|--|--|
| HPE | Frequency | Percentage | | |
| Well differentiated SCC | 23 | 40 | | |
| Moderately differentiated SCC | 24 | .41 | | |
| Poorly differentiated SCC | 3 | .5 | | |
| Spindle cell variant, SCC | 1 | 2 | | |
| Not graded | 7 | -12 | | |
| Adenoid cystic carcinoma | 3 | 5 | | |

95% of the population had histopathology as squamous cell carcinoma, of which 40% were having well differentiated, 41 % were moderately differentiated, 5% were poorly differentiated, 2% were spindle cell variant and 12 % were not graded. 5% had adenoid cystic carcinoma.

| Table 3: Descriptive statistics showing Intent of radiotherapy | | | | |
|--|-----------|------------|--|--|
| Intent of Radiotherapy | Frequency | Percentage | | |
| Adjuvant | 39 | 64 | | |
| Radical | 22 | 36 | | |
| Total | 61 | 100 | | |
| Location of Tumor | Frequency | Percentage | | |
| Oral Cavity | 31 | 51 | | |
| Larynx | 15 | 25 | | |
| Oropharynx | 5 | 8 | | |
| Hypopharynx | 5 | 8 | | |
| Paranasal Sinuses | 3 | 5 | | |
| Salivary gland | 2 | 3 | | |

36 % of population received radical radiotherapy and 64 % of population received adjuvant radiotherapy.

51% of the population had primary in oral cavity, 25% in population had primary in larynx followed by 8% in oropharynx, 8% in hypo pharynx and 5% had primary in para nasal sinuses and 3% of population had primary in salivary gland.

55% of tumors in oral cavity are tongue primary and 45% are buccal mucosa tumors.

Table 4: Derivation of PTV Margin using ICRU62, Strooms, Van Herk formulae

| Table 4: Derivation of FTV Margin using ICK002, Strooms, Van Herk formulae | | | | | |
|--|-------|--------|------------------------------|---------------------------------|-----------|
| DIRECTION (mm) | SE -∑ | RE - σ | ICRU 62 | STROOMS 2Σ +0.7 σ | VAN HERK |
| | | | $\sqrt{\Sigma^2 + \sigma^2}$ | | 2.5Σ+0.7σ |
| LATERAL/ X AXIS/ ML | 0.9 | 2.6 | 2.7 | 3.6 | 4.1 mm |
| LONGITUDINAL/ Y AXIS/ SI | 1.2 | 2.5 | 2.7 | 4.2 | 4.8 mm |
| VERTICAL/ Z AXIS/ AP | 1.0 | 2.1 | 2.3 | 3.5 | 3.9 mm |

In addition to generation of PTV margin, weekly errors were calculated and compared. WEEKLY ERRORS

| Table 5: Descriptive Statistics of weekly errors | | | | |
|--|------|-------|---------|--------|
| Week | Max | Min | Mean | SD |
| Lateral direction (X- Axis) | | | | |
| 1 | 0.46 | -0.14 | 0.0675 | 0.1305 |
| 2 | 0.36 | -0.30 | 0.0380 | 0.1234 |
| 3 | 0.54 | -1.36 | 0.0410 | 0.2278 |
| 4 | 0.34 | -0.42 | 0.0302 | 0.1503 |
| 5 | 0.34 | -0.18 | 0.0446 | 0.1242 |
| 6 | 0.34 | -0.66 | 0.0233 | 0.1544 |
| 7 | 0.35 | -0.60 | 0.0241 | 0.1838 |
| Longitudinal direction (Y-Axis) | | | | |
| 1 | 1.02 | -0.38 | 0.0262 | 0.2084 |
| 2 | 0.32 | -0.96 | 0.0095 | 0.1894 |
| 3 | 0.54 | -0.46 | 0.0269 | 0.1562 |
| 4 | 0.34 | -0.50 | -0.0013 | 0.1398 |
| 5 | 0.54 | -0.50 | 0.0330 | 0.1861 |
| 6 | 0.68 | -0.42 | 0.0348 | 0.1773 |
| 7 | 0.66 | -0.33 | 0.0169 | 0.2200 |
| Vertical direction (Z – Axis) | | | | |
| 1 | 0.26 | -0.22 | 0.0230 | 0.1156 |
| 2 | 0.42 | -0.50 | 0.0308 | 0.1375 |
| 3 | 0.66 | -0.18 | 0.0403 | 0.1364 |

| 4 | 0.36 | -0.32 | 0.0475 | 0.1388 |
|---|------|-------|---------|--------|
| 5 | 0.38 | -0.26 | 0.0410 | 0.1450 |
| 6 | 0.58 | -0.26 | 0.0584 | 0.1726 |
| 7 | 0.46 | -0.87 | -0.0166 | 0.2312 |

| Cable 6: Comparison of week | ly errors | | | |
|----------------------------------|-----------|-----------------------|------------|---------|
| Time (I) | (J) Time | Mean Difference (I-J) | Std. Error | Sig. |
| Comparison of weekly errors in X | K- Axis | | | |
| Week1 | Week2 | 0.02951 | 0.02868 | 0.304 |
| | Week3 | 0.02656 | 0.02868 | 0.355 |
| | Week4 | 0.03738 | 0.02868 | 0.193 |
| | Week5 | 0.02295 | 0.02868 | 0.424 |
| | Week6 | 0.04426 | 0.02868 | 0.124 |
| | Week7 | 0.04348 | 0.03457 | 0.209 |
| Comparison of weekly errors in Y | Z- Axis | | | |
| Week1 | Week2 | 0.0167 | .0.0328 | 0.6109 |
| | Week3 | -0.0007 | 0.0328 | 0.9841 |
| | Week4 | 0.0275 | 0.0328 | 0.4021 |
| | Week5 | -0.0067 | 0.0328 | 0.8379 |
| | Week6 | -0.0085 | 0.0328 | 0.7953 |
| | Week7 | 0.0094 | 0.0396 | 0.8133 |
| Comparison of weekly errors in Z | Z - Axis | | | |
| Week1 | Week2 | -0.00787 | 0.02734 | 0.77365 |
| | Week3 | -0.01738 | 0.02734 | 0.52542 |
| | Week4 | -0.02459 | 0.02734 | 0.36899 |
| | Week5 | -0.01803 | 0.02734 | 0.50992 |
| | Week6 | -0.03541 | 0.02734 | 0.19604 |
| | Week7 | 0.03951 | 0.03296 | 0.23129 |

The change in errors in lateral, longitudinal and vertical direction in the weeks of 1 to 7 are not significant.

| Table 7: Comparison of Population Systematic and Random errors (mm) in different studies | | | |
|--|------------------|--------------|--|
| Study | Systematic error | Random Error | |
| Tejpal Gupta et al, ^[11] | 0.96 - 1.2 | 1.94 - 2.48 | |
| Suzuki et al, ^[9] | 0.7 - 1.3 | 0.7-1.6 | |
| Zhang et al, ^[14] | 1.5 - 3.2 | 1.1-2.9 | |
| Present Study | 0.9-1.2 | 2.1-2.6 | |

| Table 8: Comparison of PTV margins (mm) in Tata Memorial Hospital Study (TMH), Mumbai 13 and Present study | | | | |
|--|--|---|--|--|
| Direction | PTV Margin (Van Herk Formula) TMH. ^[13] | PTV Margin (Van Herk Formula) PRESENT STUDY | | |
| Anterio-posterior | 3.76 | 3.9 | | |
| Medio-lateral | 3.83 | 4.1 | | |
| Supero-inferior | 4.74 | 4.8 | | |

DISCUSSION

The study was conducted in Dept. of Radiotherapy, Apollo Cancer Institutes, Hyderabad. A total of 61 patients of head and neck cancers who satisfied the eligibility criteria were analyzed in this study. This report attempts to evaluate the set-up accuracy in patients receiving radiotherapy for head and neck cancers with IMRT at radiotherapy unit of Apollo Cancer Institutes by using OBI and EPID systems. As the main aim of delivering radiotherapy is to give adequate tumoricidal dose and spare nearby normal tissues, maintaining accuracy plays a crucial role. In general, attempts to reduce treatment related uncertainties begin from accurate delineation of the tumor which is the Gross Tumor Volume (GTV) and giving an appropriate margin, i.e., CTV (clinical target volume) around the GTV to cover the microscopic extent of the disease by predicting the routes of loco regional spread based on the primary tumor site.^[6,7] In order to ensure not to miss the target volume, a PTV margin (Planning target volume) is

given around the CTV to account for the setup errors. Every attempt has to be made to look into the possible causes of the errors and measures have to been taken to correct them.

EPID is a primary tool for quality assurance in radiation delivery. Current commercially available EPIDs use flat panel display technology, providing faster acquisition and superior image quality. In combination with a modern digital accelerator fitted with multileaf collimator, field set-up and image acquisition can be done remotely and displayed in seconds, obviating the need to re-enter the treatment room each time.

This allows more frequent treatment verification or to acquire a series of images during a single treatment for patient movement estimation. Another powerful feature is that the images are in digital form, which allows application of software tools for processing to extract information relevant to treatment verification and their managing by picture archiving and communication systems (PACS) specially designed for radiotherapy. To calculate PTV margin from the observed values of errors, few formulae have been proposed after many statistical calculations on how much margin can cover the entire target volume during treatment without missing it. Austin-Seymour et al,[11] Stroom et al,^[12] and van Herk et al,^[13] have put forth different margin recipes using the observed systematic and random error values. These formulae have taken the target CTV coverage as the ultimate goal and have tried to attain it in a range of 75 to 95 % with different adjustments in the formulae, i.e., what can be the minimum PTV margin to be given in order to achieve a reasonable CTV coverage uncertainty. By determining the inaccuracies in the treatment setup and obtaining an average error magnitude from those observed errors in three directions, one can derive a PTV margin. PTV margin should be institutionally derived and not practiced based on those given in the literature. They have to be studied in each major treatment site in the institution and implemented accordingly, once the errors are observed in the institution

This study attempted to observe the systematic and random errors while treating head and neck cancers with EBRT on Linear accelerator so as to derive an institutional PTV margin which is appropriate for this treatment setup. Patients who satisfied the inclusion criteria were immobilized with thermoplastic cast after positioning them in supine position. CT simulation was done and 2-3 mm slices were obtained from vertex to mid chest with fiducials markers placed on the thermoplastic cast.

TPS based IMRT plan was generated in the Eclipse system and the plan was exported to the treatment setup. DRR images were taken from the CT simulation and used as the first reference image. Patients were positioned and EPID image, OB kV image were taken once at the beginning of treatment and every day thereafter till the end of the treatment. To assess the deviation in all three directions, i.e., supero-inferior. anterio-posterior and lateral directions single exposure image was obtained both in anterio-posterior and lateral directions. These images were analyzed by comparing with the initial DRR image and the shift was noted after matching.

Image analysis was carried out by manual matching, comparing the reference simulator image with treatment image using fixed bony landmarks. As there exists a possibility of variation in manual measurements two different points were used for evaluation of displacements in each direction.

The age range of patients was 23-80 years with a median age of 57 years. This is in accordance with data from cancer registries in developing countries which suggest that about 80 to 90 percent of head and neck cancer cases occur in age 50 years or older. A total of 58 patients (95%) had histopathology of squamous cell carcinoma, of which 40 % were well differentiated, 41% had moderately differentiated and 5% had poorly differentiated. One patient had spindle cell variant of squamous cell carcinoma. Squamous cell carcinoma of 7 patients (12%) has not

been graded. 5% has adenoid cystic carcinoma. 78% of the population are males and 22% are females with no paediatric population. The most common primary site in the patients was noted to be tongue i.e., 28% of the population. 25% cancers were noted in larynx followed by 23% in buccal mucosa. 8% had primary in oropharynx, 8% of population had primary in hypo pharynx, 5% had primary in para nasal sinuses and 3% of population had salivary gland tumor. 36% of population received concurrent chemotherapy.

Of the errors noted in vertical, longitudinal and lateral directions, the deviation noted in longitudinal direction was the maximum. In addition to derivation of PTV margin, weekly errors were calculated and compared. Change in errors in vertical, lateral and longitudinal direction in the weeks 1 to 7 were not significant. The population systematic error (Σ) in Vertical direction was 1.0mm, lateral direction was 0.9mm and in longitudinal direction was 1.2mm. The population random error (σ) in vertical direction is 2.1mm, lateral direction is 2.6 mm and longitudinal direction is 2.7 mm. The population is 2.5 mm. This study attempted to derive PTV margin from the obtained values of systematic and random errors by using Van Herk formula.

The calculated PTV margin using Van Herk formula is 3.99 mm in vertical direction, 4.13 mm in lateral direction and 4.83 mm in longitudinal direction. Using ICRU 62 formula PTV margin is 2.7, 2.7 and 2.3 mm in lateral, longitudinal and vertical directions respectively. Using Stroom's formula PTV margin in vertical, lateral and longitudinal directions are 3.5, 3.6 and 4.2 mm respectively.

Population systematic (Σ) and random errors (σ) also correlated well with the published literature.

CTV to PTV margin in this study was within 5mm in all directions which is accordance with the values obtained in a study, by Tejpal Gupta et al 13done at Tata memorial hospital, Mumbai.

The value was higher in longitudinal direction in this study which is 4.83 mm. The possible explanation is loss of subcutaneous fat in the submandibular region which can lead to improper neck fixation, contributing to errors in superoinferior direction. Acute effects of radiation like mucositis, dysphagia, and dermatitis are noticed after 2 weeks of start of treatment. These acute reactions affect the patient's compliance and their general built which can have an impact on the setup variability.

Mongioj et al,^[15] investigated alignment data from a cohort of 20 patients with nasopharyngeal cancer. They found setup displacements showed no significant changes as therapy progressed, but greater errors were observed when the patient had severe weight loss or tumor node shrinkage. This emphasizes the importance of good immobilization methods and also maintenance of nutritional status without much loss of body weight.

Limitations of the Study

• Apart from the errors in vertical, lateral and longitudinal directions (translational errors), rotational errors i.e., pitch, roll and yaw rotation can occur. Errors in these directions can have a

significant impact on radiation delivery especially in highly conformal, extremely hypo fractionated treatments like SRS, SBRT. This study used Van Herk formula for calculation of PTV which is mainly used for calculating translational errors. So rotational errors were not measured. However, as set up errors constitute both translational and rotational errors, this can be a minor drawback of this study.

- Automatic anatomy matching and image fusion facility was not used in this study. Usage of both automatic and manual matching enhances accuracy of translational errors measurement.
- Subset Analysis of primary sites like oral cavity, larynx, salivary glands, para-nasal sinuses were not possible because of small sample size.

Limitations of present study can be surmounted by

- Increasing sample size.
- Considering patients of head and neck immobilized with mould other than four clamp immobilization devices e.g. 5 clamp head and neck immobilization device.
- Using both automatic and manual matching to improve accuracy of translational error measurements.
- Analysing set up errors based on primary sites and intent of treatment.

Future Recommendations

Setup errors are influenced by many factors like immobilization methods, treatment positioning inaccuracies and most importantly the patient related factors. Nutritional status of patient had a major impact on their compliance and tolerance to treatment related toxicities. As was observed in the study, maximum errors which occurred in superoinferior direction were possibly due to loss of subcutaneous fat in the head and neck region, especially the submandibular region.

Hence, maintaining nutrition should be given utmost importance. Counselling regarding the importance of maintaining nutrition should be considered prior to beginning radiation and guidance be given on the possible ways to achieve and maintain it during treatment.

When the thermoplastic mould becomes loose or is noticed to be ill-fitting due to decline in nutritional status of the patient, there is a need for consideration of re-doing mould so as to reduce the errors.

This study was done only in head and neck cancer patients where the setup errors are lesser compared to pelvic tumors. Hence, another study for assessment of setup errors in other treatment sites and comparison of errors among each other is required for critical analysis. There is need for consideration of a differential PTV margin according to their observed institutional setup errors.

CONCLUSION

This study emphasizes on the importance of good immobilization and on maintenance of nutritional status that can have an impact on setup errors and treatment outcome. It also highlights the need for institutional study in deriving a PTV margin for their own treatment setup while treating different primary sites. This should be accompanied by complete analysis of all the possible reasons that contribute to the error magnitude and the steps that need to be taken to reduce them in their treatment setup.

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