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MV CBCT based assessment of setup uncertainties and planning target volume margin in head and neck cancer

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ABSTRACT

Background: Set-up errors are an undesirable part of the radiation treatment process. The goal of online imaging is to increase treatment accuracy by reducing the set-up errors. This study aimed to determine the daily variation of patient set-up uncertainties and planning target volume (PTV) margins for head and neck cancer patients using pre-treatment verification by mega voltage cone-beam computed tomography (MV-CBCT).

Materials and methods: This retrospective study was internal record base of head and neck (H&N) cancer patients treated with definitive radiotherapy, adjuvant radiotherapy, and hypo-fractionated radiotherapy at our institution since the implementation of Halcyon™ 2.0 machine (Varian, US). Errors collected from each patient setup were recorded and evaluated for each direction [medio-lateral (ML), supero-inferior (SI), antero-posterior (AP)] discretely. For each patient, the systematic error (Σ) and random error (σ) were collected. Clinical target volume (CTV) to planning target volume (PTV) margin was calculated using International Commission on Radiation Units and Measurements (ICRU) 62 (PTV margin = $\sqrt{(\sum^2 + \sigma^2)}$), Stroom's (PTV margin = $2\Sigma + 0.7\sigma$), and Van Herk's (PTV margin = $2.5\Sigma + 0.7\sigma$) formula.

Results: A total of 7900 pre-treatment CBCT scans of 301 patients were analyzed and a total of 23,000 error measurements in the ML, SI, and AP directions were recorded. For all of our H&N cancer patients, the CTV to PTV margin, calculated from the van Herk formula for the head and neck patients was 0.49 mm in the anteroposterior axis.

Conclusions: An isometric PTV margin of 5 mm may be considered safe if daily imaging is not being done. In case daily online pretreatment imaging is being utilized, further reduction of PTV margin is possible.

Key words: radiotherapy; planning target volume; set up errors; imaging

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Introduction

Modern radiotherapy techniques are becoming highly precise to target cancer. Radiotherapy is a core treatment option for head and neck cancer in the definitive, adjuvant, and palliative setting. Techniques of radiation for the management of head and neck (H&N) cancer have improved significantly over the last few decades. With time, conventional two-dimensional fields have been extensively replaced by more sophisticated 3D conformal radiotherapy (3DCRT) techniques all over the world and, more recently, even 3DCRT is being replaced by intensity-modulated radiation therapy (IMRT), which is more conformal and, hence, spares surrounding organs better [1,

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2]. However, to achieve this high conformality and sharp dose gradients, we need enormous efforts to reduce uncertainties like tumor delineation, precise patient positioning, and control of the organ motion [3]. A margin from clinical target volume (CTV) is given to generate the planning target volume (PTV) to account for the uncertainties during patient positioning. The same is done for serial organs at risk (OARs) to generate planning organ at risk volume (PRV) [4]. This CTV to PTV and OAR to PRV margin is not fixed. The margins depend on multiple factors including systematic and random errors that occur during patient simulation, planning, and treatment delivery. The accuracy of treatment may vary from center to center and have to be determined at the institute level. The present study aimed to report our clinical experience in the treatment of H&N cancer, with the following aims:

- to define the proper CTV to PTV margins to be adopted in our target delineation protocol for head and neck cancers treated radically, immobilized using thermoplastic cast;
- to describe the overall accuracy of our set-up procedures.

Materials and methods

Patient selection

This was a record-based retrospective analysis of H&N cancer patients treated with definitive radiotherapy, adjuvant radiotherapy, and hypo-fractionated radiotherapy for the management at our institution since the implementation of Halcyon™ 2.0 machine (Varian, US). The study period was between September 2020 to December 2021. Inclusion criteria were immobilization with 5 clamp thermoplastic mask and set-up measurements were available for daily imaging before radiation delivery. This analysis dealt mainly with set-up accuracy and PTV margins in H&N radiotherapy. Set-up data of a total of 298 patients (7900 MV-CBCT) treated between study period were collected and reviewed. Institutional ethics committee approval was obtained before the commencement of study.

Immobilization and simulation

All patients were positioned supine and immobilized with a 5-point thermoplastic mask with an appropriate headrest to ensure daily reproducibility. In-room lasers were used to mark the position of the reference isocentre on the mask. The planning CT scan was acquired with a 2.5-mm slice thickness for all patients. CT data were transferred into the treatment planning system for contouring and planning.

Target volume delineation and treatment planning

In all cases of definitive radiotherapy or chemoradiotherapy gross tumor volumes (GTVT, N) were contoured. The high-risk, intermediate-risk, and low-risk clinical target volumes (CTV HR, IR, LR) were contoured according to institute protocol. In the adjuvant setting, there were only two CTV volumes (CTV IR, CTV LR) unless high-risk features like margin positivity or extracapsular extension were present. As per the institute policy, we gave an isotropic margin of 5 mm in all directions to compensate for the geometrical uncertainties, in all cases, to each CTV to create the corresponding PTV. A margin of 3 mm was added around the OARs eg. the spinal cord and the brainstem to generate a planning organ at risk volume (PRV). All the patients were planned with volumetric modulated arc therapy (VMAT) with a single or dual arc in the treatment planning system (Eclipse 16.1, Varian treatment planning system, US).

Portal imaging

Halcyon™ 2.0 is provided with a S1200 Electronic Portal Imaging Device (EPID). The imaging panel measures 43 × 43 cm and has 1280 × 1280 pixel matrix. A spatial resolution of 2.98 mm^{-1} is afforded by the above specification. With a frame refresh rate of 24 frames/sec, it does not saturate when used for a 6MV flattening filter free (FFF) beam. the source to imager distance (SID) is 154 cm.

Image guidance protocol

Patients were repositioned on the treatment couch with the help of the reference isocentre, aligning it with the treatment room lasers. Couch shifts were made as per prescription to align the machine isocentre with the treatment isocentre. A portal imager was used to generate mega voltage cone beam CT (MV CBCT) on all treatment days. Image registration was performed by the automatic bone window-based algorithm using a region of interest that includes the planning target volumes. Following automatic registration, the matches were checked man-

ually to ensure that there are no significant volume changes, the treatment volumes are not missed and no significant changes in the location of organs at risk have occurred. Rotational corrections that arose during automatic matching were ignored and compensatory translational movements were accepted as determined by the algorithm. These matches were done online by radiotherapy technologists and in selected cases, registration was optimized manually by the physician. When the shifts after matching were 10 mm or more, patients were repositioned and rescanned. A senior physicist or radiation oncologist was involved in repositioning these patients. Translational displacements (errors) observed before treatment in the 3 axes [supero-inferior (SI), antero-posterior (AP), medio-lateral (ML)] were recorded and always applied before treatment.

Error analysis and margin calculation

Errors collected from each patient's set-up were entered into the database and analyzed separately for each direction (ML, SI, AP). For each patient, the individual mean and standard deviation (SD) of all recorded errors were calculated. Systematic error is calculated as the standard deviation of the individual mean errors in each of the three directions. Random error is calculated as the mean of the individual standard deviations of errors (Fig. 1).

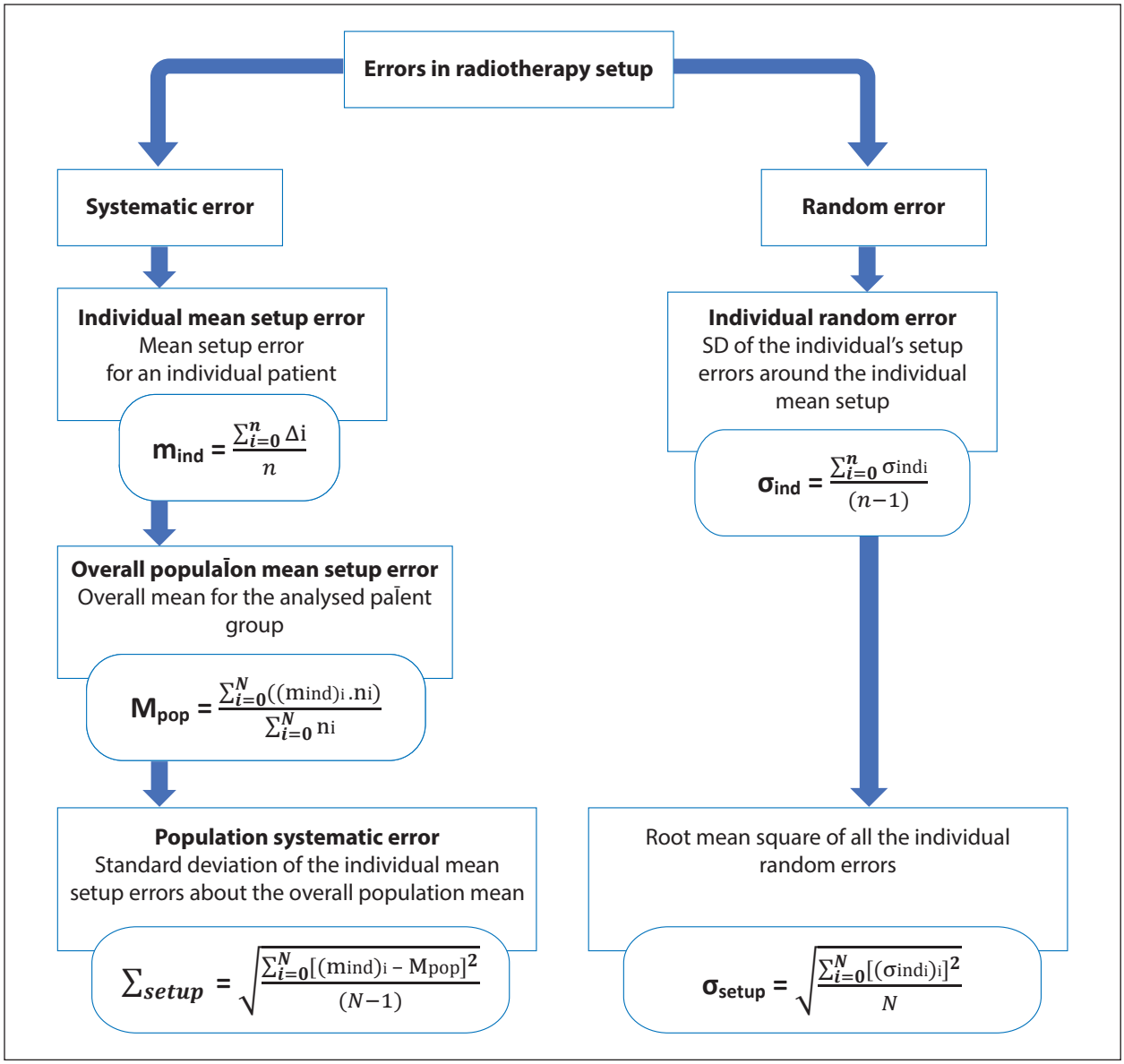

Figure 1. Figure showing various set up errors in radiotherapy

PTV margin calculation

Several methods have been proposed in the literature to calculate CTV to PTV margin. We calculated CTV to PTV margin using ICRU 62 [5] (PTV margin =), Stroom's [6] (PTV margin = 2Σ + 0.7σ), and Van Herk's [7] (PTV margin = 2.5Σ + 0.7σ) formula in this study. Here Σ and σ are the population systematic error and population random error, respectively. To adopt a PTV margin for head and neck cancer patients in our institute, we pursued Van Herk's equation, which ensures that 90% of the patients are given a CTV dose of at least 95% of the prescribed dose (Tab. 1).

PRV margin calculation

The Mc Kenzie formula (PRV margin = 1.3Σ + 0.5σ) [15] was used to calculate the margin around the spinal cord and Brain stem (Tab. 1).

Calculation of 3D vector

The 3D vector of displacement, a value combining errors recorded in all three axes, was calculated. The 3D vector of maximum displacement, r, is calculated as the square root of the sum of the squares of the PTV margins calculated in each of the axes.

Results

A total of 7900 pre-treatment CBCT scans of 301 patients were analyzed and a total of 23,000 error measurements in the ML, SI, and AP directions were recorded. For all of our H&N cancer patients, the distribution was narrow, and the maximum translational shift was less than ± 10 mm.

Table 1. Summary of operations used for margin calculation

Mean of setup errors in individual patients	M
SD of setup errors in individual patients	D
Systematic error, Σ	SD of the mean setup errors (M)
Random error, σ	Mean of the SD of setup errors of individual patients (M)
PTV margin for each axis (by Van Herk's equation)	PTV margin = 2.5 Σ + 0.7 σ
PRV margin for each axis (by Mc Kenzie's formula)	PRV margin = 1.3 Σ + 0.5 σ
3D vector of displacement, r	$r = \sqrt{x^2 + y^2 + z^2}$

SD — standard deviation; PTV — planning target volume; PRV — planning organ at risk volume

Overall distribution of systematic and random error

The displacements in all 3 axes were normally distributed as depicted in Figure 2; also tested by the Kolmogorov-Smirnov test. The displacements were within 3 mm for 87.0% immobilizations in the ML direction; 87.6% in the SI direction; 81.8% in the AP direction. The displacements were within 5 mm for 97.2% in the ML direction; 96.9% in the SI direction; and 94.6% in the AP direction. Around 0.7% of the displacements in ML, 0.7% in

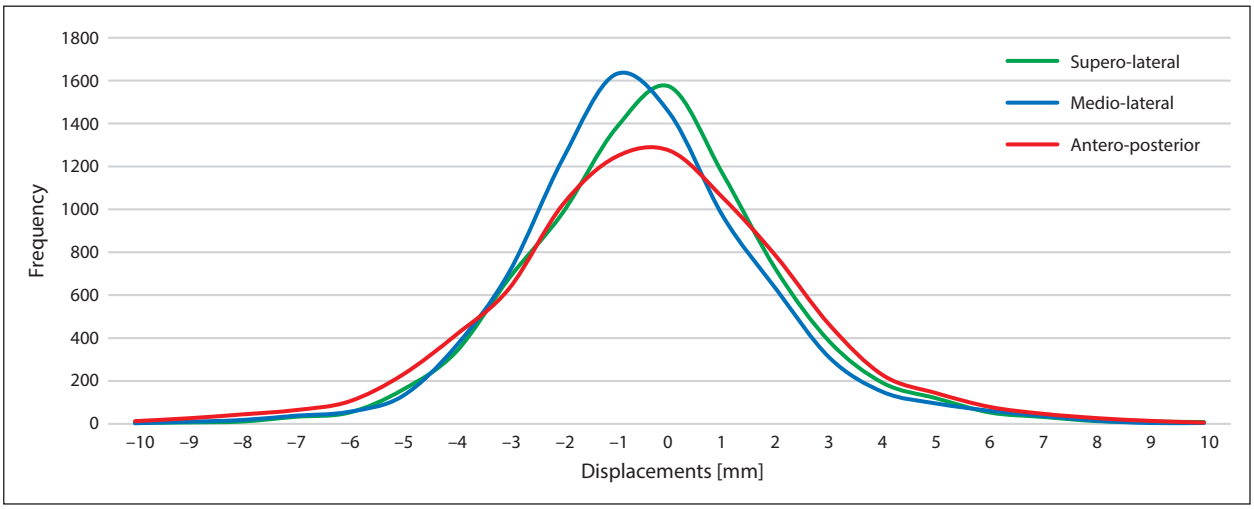

Figure 2. Frequency distribution histogram showing the distribution of measured displacements in supero-inferior, antero-posterior, medio-lateral axes

Table 2. Planning target volume (PTV) and planning organ at risk volume (PRV) margins according to International Commission on Radiation Units and Measurements (ICRU) 62, van Herk's equation, Stroom's formula and Mc Kenzie formula

	Mediolateral, X [mm]	Superoinferior, Y [mm]	Anteroposterior, Z [mm]
Systematic error, Σ	1.3	1.3	1.3
Random error, σ	2.0	2.0	2.4
PTV margin (ICRU 62)	2.4	2.4	2.7
PTV margin (van Herk's equation)	4.6	4.7	4.9
PTV margin (Stroom's formula)	4.0	4.0	4.3
PRV margin (Mc Kenzie formula)	2.7	2.7	2.9
Maximum translational displacement (r)	8.2 mm		

the SI, and 1.6% in the AP directions were more than 7 mm from the reference isocentre.

PTV and PRV margin calculation

Table 2 shows the systematic and random error components and the use of these calculated values to generate PTV margin for the treatment of H&N cancer patients. The CTV to PTV margins are calculated by ICRU 62, Stroom's, and van Herk's formula. PRV margins are also calculated; using the Mc Kenzie formula [6].

Discussion

As discussed by Stroom et al., and van Herk et al. [7, 8] systematic error has disproportionately larger implications on the final dose distributions of all radiation treatments. All efforts should be made to minimize systematic errors, right from simulation through quality assurance of imaging, contouring, planning, and quality assurance of treatment delivery by image guidance. In this regard, each radiation center should systematically document the displacements effected during image-guided radiotherapy, and use this data to evaluate the systematic and random error profile of their institute and develop a custom PTV margin that best suits its patient base.

The current study population, consisting of 298 head and neck cancer patients and 7900 scans, represents the largest reported series on head and neck cancer patients. The PTV margins that are generated using this database confirm that the current practice of 5 mm margins around the CTV is adequate. The systematic component of the error was around 1.3 mm in all axes, and the random component was 2.0 mm medio-laterally, 2.0 mm supero-inferiorly, and 2.4 mm antero-posteriorly. Reviewing similar studies from the literature, the systematic and random errors observed are comparable. We believe that the systematic error observed in our study may be a bit higher than some of the others found in the literature, which is attributable to the difference in IGRT protocol that is pursued between the centers. At our center, we follow the online protocol where imaging is done before each fraction of radiation, and errors are corrected following the "Zero action level" protocol. A few studies found in the literature have used orthogonal portal images for matching, in contrast to the MV-CBCT which were available for matching in this study [9]. Volumetric matching may have influenced the observed systematic errors and may explain the slightly larger systematic error determined by our study [10].

The PTV margins that are generated by our study are applicable to a conventional fractionation schedule of head and neck cancer patients. As learned from the work of Mesko et al. [11], van Herk's formula was utilized for PTV margin and they evaluated that 1.5 to 2 mm margin was sufficient in the skull base region, whereas 2–2.5 mm was required in the head and neck region. They also highlighted that van Herk or Gordon and Siebers margin do not take into account rotational errors, image registration, and treatment planning; therefore, additional margins may be required.

Ideally, the margin for PRV should be calculated based on the differences in the positions noticed of the OARs specifically under study. The CBCTs acquired in this study were fused with the CT simulation reference image reference to match

the treatment volumes; hence, the data we present here, undoubtedly, is applicable for the calculation of PTV margins. However, they were not fused again to observe the uncertainties in the position of the OARs. Hence, they do not support the idea of the generation of PRV. Nonetheless, we apply the Mc Kenzie formula over this data with the assumption that the extent of motion or set-up uncertainty in the OAR parallels the extent of the uncertainty of target volumes. Thus, it is advised to consider the PRV data generated only as a guide or to inspire further study dedicated to the same. We identified that the PRV that we generated from this study was within 3 mm, which correlates with the margins that are currently used at our institute.

Daily IGRT is not the current standard in head and neck cancer cases. Hence, we add a note on the feasibility of daily CBCT in a busy radiotherapy unit. The average additional time spent for imaging and fusion as part of the IGRT technique on Halcyon™ was approximately 2–4 minutes [12, 13]. This is better than the additional time taken for IGRT by 2D-KV verification claimed by previous studies [14, 15]. Also, even with daily IGRT, we were able to treat around 7–8 patients per hour. We had occasional patients who required repositioning as part of the institute policy to reposition if the shifts were more than 1 cm. Regardless, the number of patients treated on the machine per hour did not suffer.

Results of the present study may be used for PTV margin determination to include possible difference between bony structures and soft tissues or intra-fraction target motion if daily pre-treatment imaging is not performed. If an online imaging is done before each fraction, the PTV margins may be reduced accordingly.

Conclusions

The results of our study show that with strict adherence to the routine machine and CT simulator QA program, appropriate target delineation, and mindful patient set-up procedure; an isometric PTV margin of 5 mm and PRV margin of 3 mm may be considered safe if daily imaging is not done. In case daily online pretreatment imaging is utilized, further reduction of PTV margin is possible.

Competing interests

All authors have completed the ICMJE uniform disclosure form and declare no conflict of interest.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the Helsinki Declaration.

Ethical approval

The IEC (institution) approved the study.

Authors' contribution

All authors contributed to the conception or design of the work, the acquisition, analysis, or interpretation of the data. All authors were involved in drafting and commenting on the paper and have approved the final version.

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