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Prospective observational study to estimate set-up errors and optimise PTV margins in patients undergoing IMRT for head and neck cancers from a Government cancer centre of Eastern India

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Abstract

Background: The head and neck cancers as a whole are the most common cancers among males in India. Technological advancements have led to an improvement in radiation therapy (RT) techniques with subsequent reduction in normal tissue complications. To correct patient set-up errors, an off-line correction method like no action level (NAL) protocol may be used as a preferred protocol particularly for a busy department. The objectives of the study were to measure the translational set-up errors using kV cone-beam computed tomography (CBCT) in patients undergoing intensity modulated radiotherapy (IMRT) in head and neck cancers and also to optimise clinical target volume (CTV) to planning target volume (PTV) margin using NAL protocol.
Material and methods: On the first 5 days of RT, patient's position was verified by kV-CBCT and then weekly during the course of treatment. The comparison between the reference and kV-CBCT images was performed, and the shifts measured and recorded. The mean error from the initial five consecutive fractions was corrected on the sixth daily fraction. Displacements in all the directions were measured. The population systematic and random errors were determined and used to estimate PTV margins according to the van Herk formula.
Results: A total of 322 images were analysed. Before correction, 15, 12 and 9% patients had systematic error ≥3 mm on *X*, *Y* and *Z* axes, but after correction this was reduced to 9, 0 and 0%. The total percentage of patients whose set-up margin was ≥5 mm before correction was 5, 6·25, 3·75%, but after correction it reduced to 1·88, 0, and 0·63%. The margins of total population were reduced to 63, 65 and 56% after correction on *X*, *Y* and *Z* axes, respectively.
Conclusion: A simple off-line NAL protocol can correct the set-up errors without daily on-line imaging in patients undergoing IMRT and hence acting as a resource sparing alternative. Five millimetre margin to CTVs was adequate and safe to overcome the problem of set-up errors in head and neck IMRT.

Introduction

The head and neck cancers as a whole including lip and oral cavity, pharyngeal, laryngeal and other cancers are the most common cancers among males in India.[1] The head and neck region has a complex anatomy with the presence of different critical structures in close proximity to the tumour-bearing area making radiation therapy (RT) planning quite challenging for these cancers.

Technological advancements have led to an improvement in techniques of RT in head and neck cancers and with the advent of 3D conformal techniques, especially intensity modulated radiotherapy (IMRT), treatment-related normal tissue complications have been reduced to a certain extent.[2–4]

Increasing the accuracy and precision of RT delivery has always been a therapeutic goal, but set-up errors are an inherent part of the radiation treatment process. Image guidance (IG) has provided an excellent mechanism to account and correct patient set-up errors over the course of treatment.

With the availability of 3D IG facilities like kV cone-beam computed tomography (kV-CBCT), adequate 3D volumetric image acquisition and set-up verification with both bony and soft tissue visualisation prior to treatment delivery are possible.[5–7]

There are two types of set-up errors: systematic and random, which cause variations of treatment plan from the actual daily treatment delivery.

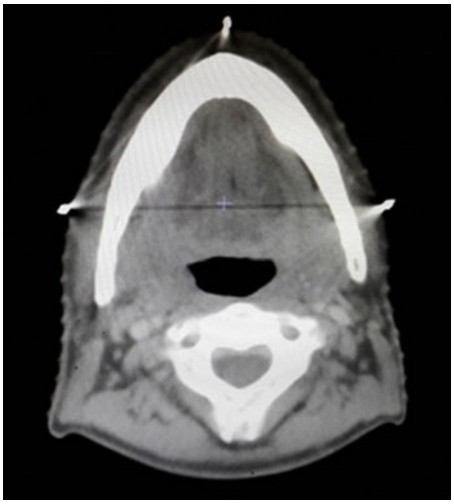

Figure 1. CT scan axial view with three fiducials in situ.

Systematic error (Σ) is the treatment preparation error (during simulation, target delineation and planning). This affects the patient set-up in the same manner during each fraction of treatment. Random error (σ) is the treatment execution error which occurs because patient's position may not be exactly reproduced, inducing a blurred effect on the planned dose distribution.

Ideal clinical target volume (CTV) to planning target volume (PTV) margin can be calculated using van Herk formula[8]

$$\text{Set up margin}(M) = 2.5\sum + 0.7\sigma$$

Daily use of IG technique produces best possible patient's position over the course of treatment, but it is time consuming particularly for a busy department with large number of patients, and also there are some concerns regarding daily additional radiation doses to the patient.[9] Both systematic and random errors are corrected by on-line correction protocol, but the imaging and image analysis is difficult for departments with huge patient loads and limited number of radiotherapy machines. On the other hand, systematic error correction and margin reduction are possible by the off-line correction protocol where tools and procedures are simpler and easily implementable.

There are several off-line correction methods available but the no action level (NAL) protocol[10] has been the most extensively used and studied[11] and recommended as a standard off-line protocol.[12] According to this protocol, set-up images are taken daily for initial 3–5 consecutive fractions; and from the daily set-up errors, the mean error is calculated that is used to shift the isocentre on the next treatment day. From then to the end of treatment course, weekly set-up image is taken. This protocol requires less imaging and therefore less work load and less time taking for busy departments and can be evaluated for sites such as head and neck radiotherapy.

The objectives of the study were to measure the translational set-up errors using kV-CBCT in patients undergoing IMRT in head and neck cancers and also to optimise CTV to PTV margin using NAL protocol.

Material and Methods

This study was conducted at Chittaranjan National Cancer Institute, Kolkata, India which is a Government Regional Cancer Centre in the state of West Bengal, India. Patients with histologically proven head and neck cancers, who were advised to receive RT by the weekly multidisciplinary head and neck tumour board and scheduled for IMRT, were part of this study. The patients included in this study were both definitive and post-operative adjuvant RT candidates. The time period of the study was from 1st June 2017 to 30th April 2018.

The study was commenced after the due approval of the Ethical Committee of the Institution. All the eligible patients were informed about the fullest extent of their disease, nature of the treatment, pros and cons of the treatment, and regarding their set-up and treatment data collection in the language and terms they were able to understand. Patients who were willing to take part in the study were included after taking proper informed consent. Other inclusion criteria were patient age—up to 70 years, tumour stage—I to IV B (T1–T4, N0–N3,M0) according to the American Joint Committee on Cancer 7th Edition, 2010[13] and Eastern Cooperative Oncology Group[14] performance status 0–2.

This was an institutional prospective observational study. Data were collected from 32 head and neck cancer patients, who were treated with either definitive or adjuvant intent with IMRT technique with or without concurrent chemotherapy.

Radiation therapy technique

The radiotherapy machine, which was used in this study, was a dual-energy (6 MV and 15 MV) Linear Accelerator (Elekta Synergy®) (Elekta, Stockholm, Sweden) owned by the Institute.

CT simulation was done on a wide bore 16 slice CT Simulator (GE Healthcare, USA) owned by the Institute equipped with a flat table-top identical to the treatment table-top (Elekta Synergy Linear Accelerator). The contrast-enhanced CT scans were taken from vertex to sternal angle with slice thickness of 2·5 mm.

Prior to CT simulation, patients were immobilised in supine position and the lasers were aligned over the mask with three points marked at the crossing of longitudinal and transverse lasers at the midline and two at the lateral ends.

Markings were done near the bony landmarks (like angle of mandible, mentum) and denoted by radiopaque ball bearing sticker (fiducials), Figure 1.

These acted as the CT reference points and with respect to these marks, patients were aligned to the planning isocentre during set-up.

Data acquired by the CT simulation were first transferred to the contouring workstation through DICOM network for delineation of different target volumes [gross tumour volumes, CTV and PTV] as well as organs at risk on each axial slice of the CT dataset as per ICRU-62,[15] and the PTVs were generated by adding 5 mm margin in all directions to the respective CTV.

Treatment planning was done on Monaco 3D Treatment Planning System (Elekta, Stockholm, Sweden).

Patient set-up

Patients were repositioned on the Linear Accelerator according to the CT reference points (fiducials), and the couch was shifted in the x, y, z direction according to the planning isocentre, Figure 2.

Image acquisition

On the first 5 days of RT, patient's position was verified by kV-CBCT [X-ray volumetric imaging (XVI Release 5.0.2 b72)] and then weekly during the course of treatment to check the reproducibility of patient set-up, Figure 3.

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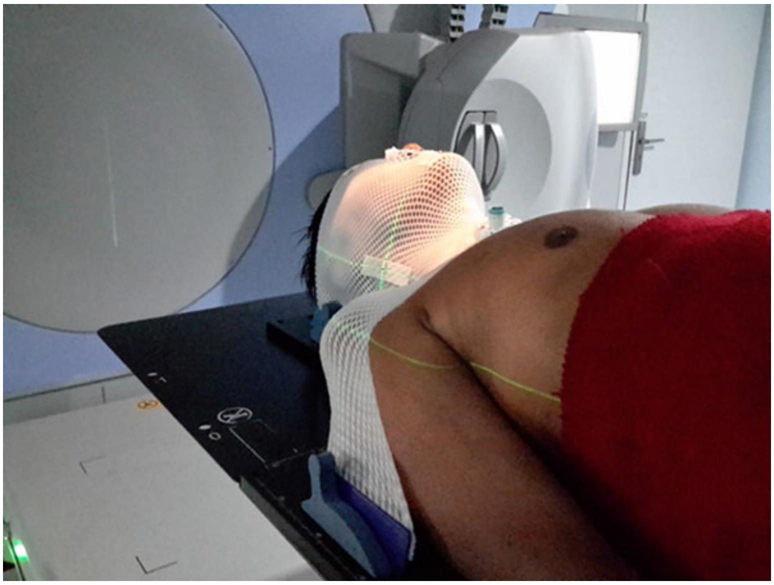

Figure 2. Patient set-up and laser matching.

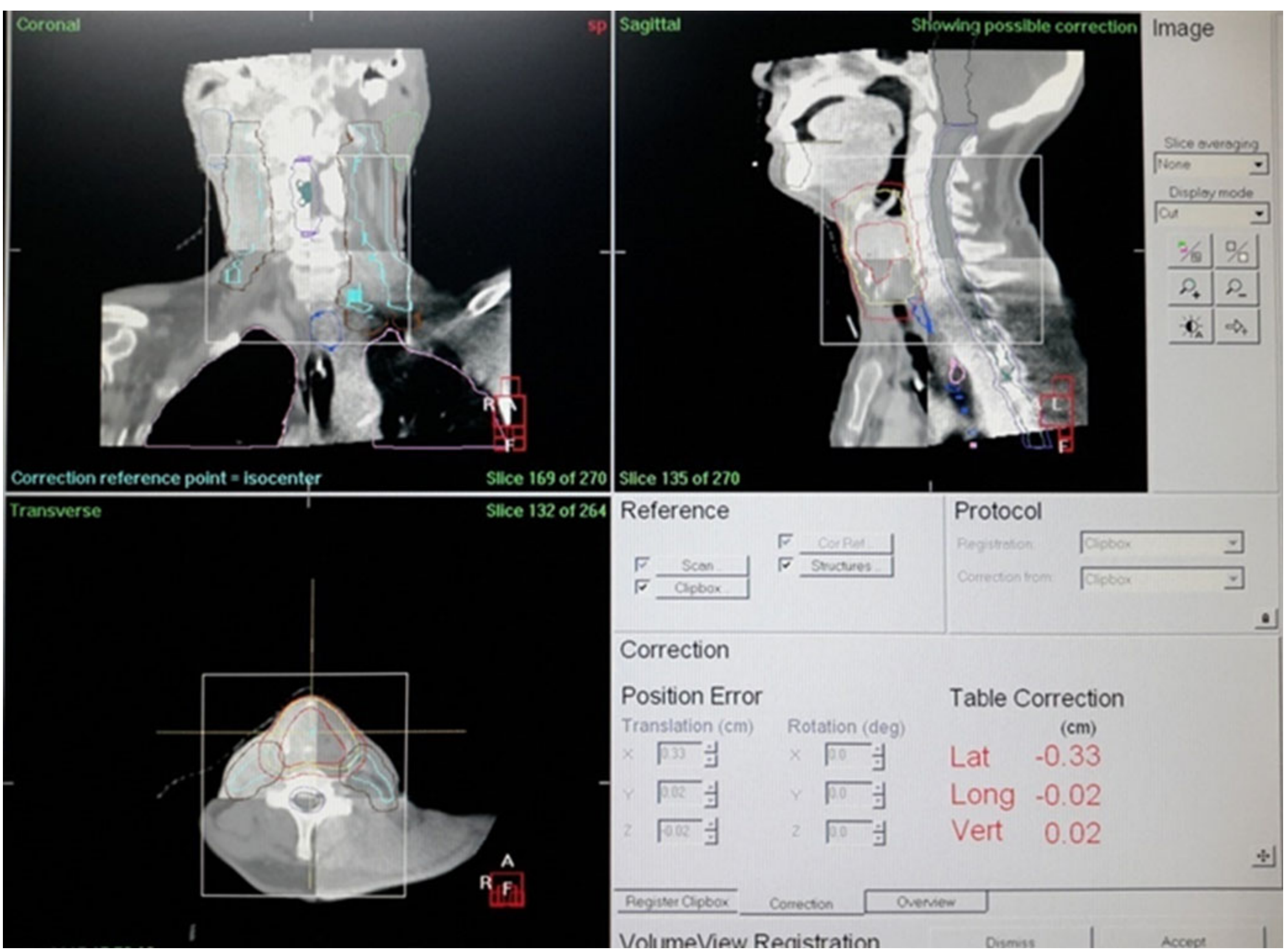

Figure 3. Patient's position verification by XVI.

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Table 1. The number of patients, whose systematic errors were ≥3 mm

	Pre-correction	Post-correction
X	5 (15%)	3 (9%)
Y	4 (12%)	0 (0%)
Z	3 (9%)	0 (0%)

Table 2. The number of patients, whose random errors were ≥3 mm

	Pre-correction	Post-correction
X	3 (9%)	2 (6%)
Y	5 (15%)	0 (0%)
Z	2 (6%)	0 (0%)

Image matching

The image registration was done within a region of interest (clip-box). Images were analysed by matching anatomical landmarks such as bone and soft tissue of CT reference images. The comparison between the reference and XVI images was performed using the template-matching technique. The software allows improvement of the image quality using different filters and contrast changing tools (grey matching or soft tissue, bony matching). Both the field edges of reference and the XVI images were matched by automatic settings. The match template was then adjusted using translation (x, y, z) to get the best correspondence between the template and the anatomical landmarks seen on the XVI. The software then calculated these displacement/set-up errors of the XVI relative to the reference image. The set-up errors were reflected as the shift of the patient, relative to these marks. These shifts were measured and recorded.

Isocentre correction protocol

The displacements were recorded in a worksheet for mean and standard deviation (SD) calculation. Pre-treatment (on-line) correction of the isocentric position on the first five daily fractions was restricted to set-up errors >5 mm (0·5 cm). After on-line corrections, the isocentre was turned back to the original position for the next fraction; otherwise treatments were delivered in uncorrected position.

The mean error from the initial five consecutive fractions, whatever its magnitude, was corrected on the sixth daily fraction. The corrected isocentre was fixed for the next fractions until the treatment end. The corrected isocentric position was verified weekly thereafter. Residual set-up errors recorded again in the worksheet, and new residual mean and SD were calculated.

Data analysis

Displacements in all the directions [right–left (*X*), supero-inferior (*Y*) and antero-posterior (*Z*)] were measured. The overall mean error on each axis was computed as the mean value of the errors measured in every XVI image for every patient in the study. The individual patients' systematic error was the mean value of errors of initial 5 days (pre-correction) and the mean value of the weekly data. The population systematic error (Σ) on each axis was the SD of individual patient mean errors. So, it was the SD of 32 patients' mean value of total systematic error (daily + weekly). Finally, the population random error (σ) on each axis was the mean value of the SD of individual patient errors. Population systematic and random errors were used to estimate PTV margins according to the van Herk formula[8] and published margin recipes.[16,17]

Pre- and post-treatment weights were documented. This study also tried to evaluate whether the errors tended to differ based on weight loss and how the set-up accuracy changed in patients who had <5% weight loss compared with those who had 5% or more weight loss.

All collected data were recorded in the Case Record Form.

Results

A total number of 322 images (160 pre-correction and 162 post-correction) were analysed. Displacements in the three directions were measured.

Pre-correction and post-correction systematic errors per patient

Before correction, 15, 12 and 9% patients of total population had systematic error ≥3 mm on *X*, *Y*, and *Z* axes, but after correction this was reduced to 9, 0, and 0%, Table 1.

Pre-correction and post-correction random errors per patient

Individual patient random errors on *X*, *Y* and *Z* axes before correction were ≥3 mm on 9, 15 and 6%, respectively. Corresponding values after correction were 6, 0 and 0%, Table 2.

Population (32) systematic and random errors

The values of pre- and post-correction systematic and random errors of the population of head and neck cancer patients are displayed in the table. The reduction of population systematic error after correction was 21, 19 and 19% in *X*, *Y* and *Z* axes, respectively.

The estimated margins from CTV to PTV to compensate for set-up errors were calculated according to the formula suggested by van Herk et al.[8]

The total percentage of patients whose set-up margins were ≥5 mm before correction was 5, 6·25 and 3·75%, but after correction the chance reduced to 1·88, 0 and 0·63% on *X*, *Y* and *Z* axes, respectively.

From Tables 3 and 4, we are able to conclude that 5 mm margin in all direction is adequate to compensate for set-up error. Table 5 shows that total 15% of patients required set-up margin more than 5 mm before correction but after correction, it was reduced to 2·51%.

We also analysed differences in set-up uncertainties based on treatment intent—definitive or adjuvant because it was hypothesised that, during definitive treatment, more volume changes occur due to primary or tumour shrinkage. In this study, 15 patients were treated with definitive intent and 17 patients with adjuvant intent. Each group was further subdivided according to weight loss—>5% and <5%. In the definitive group, 7 patients had weight loss <5% and 8 patients had >5%. In the adjuvant group, 7 patients had weight loss <5% and 10 patients had >5%. There was no statistically significant difference between these two intents.

To assess the impact of weight loss, all the 32 patients were divided into two groups: <5% and >5%. We found that there was a marginal increase in systematic and random error in *X* and *Z* axes in patients whose weight loss were >5%, but the 5 mm PTV margin was adequate for all patients.

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Table 3. Population pre-correction versus post-correction systematic errors, random errors, PTV margin

	X	Y	Z		X	Y	Z
Pre-CSE (cm)	0·18	0·16	0·15	Post-CSE (cm)	0·11	0·10	0·09
Pre-CRE (cm)	0·16	0·18	0·15	Post-CRE (cm)	0·12	0·10	0·11
Pre-CM (cm)	0·56	0·53	0·48	Post-CM (cm)	0·36	0·32	0·30

CSE, correction systematic error; CRE, correction random error; CM, correction margin

Table 4. Population systematic errors, random errors and PTV margins

	X	Y	Z
SE	0·09	0·08	0·09
RE	0·18	0·17	0·16
M (cm)	0·35	0·32	0·34

Table 5. The number of patients, whose set-up margins were ≥5 mm

Axes	Pre-correction	Post-correction
X	8 (5%)	3 (1·88%)
Y	10 (6·25%)	0 (0%)
Z	6 (3·75%)	1 (0·63%)

Discussion

Studies have shown that IMRT may be an ideal technique for the treatment of head and neck cancers as it improves quality of life by improving locoregional control and reducing side effects (especially xerostomia).[18–24] The improved dose conformality that is achieved with IMRT requires greater accuracy in treatment planning and registration during the course of radiation, because reduced target delineation causes set-up errors.

Several studies had investigated set-up errors in head and neck cancers and analysed the required number (N) of first fractions to be imaged to detect systematic errors.[25–39] They also reported that weekly imaging after the first set of verifications was effective in further reducing the value of N while achieving the same accuracy.[29] The study of Houghton et al.[30] demonstrated that in head and neck cancers the systematic displacement registered after three fractions correlated well with the mean error of the other fractions delivered, and no additional benefit was noted when the mean error from the first five fractions was considered.

In our centre, we applied a protocol that included five kV-CBCT scans in the first five fractions, followed by weekly scans. Based on the results of our study, a 5 mm margin and weekly imaging after the first five daily images could reduce significant set-up error during treatment.

The availability of portal imaging devices in modern linear accelerators has become routine for detection of geometrical uncertainties.[40] ICRU reports recommend estimating the magnitude of those uncertainties in every radiotherapy unit in order to apply appropriate margins to CTV. Diverse margin recipes have been published assuming different statistical goals. For instance, van Herk et al.[41] defined a margin M such that $M = 2{\cdot}5\Sigma + 0{\cdot}7\sigma$ assures a minimum dose to the CTV of 95% for 90% of patients. Previously, Stroom et al.[42] concluded in a slightly different formulation ($M = 2\Sigma + 0{\cdot}7\sigma$) derived on the basis that >99% of the CTV should get at least 95% of the dose.

Systematic errors have a much more important dosimetric impact than random errors. Geometrical uncertainty in fractionated radiotherapy has a systematic and random component but suitable imaging protocols can easily separate them and making it possible to customise margins in every department for every patient population, for margin optimisation. Based on the available literatures and our experience, margins up to 5 mm for head and neck irradiation would be needed to compensate for set-up inaccuracies with modern conventional immobilisation techniques.

On-line correction protocols pursue total error correction, systematic protocols include specific tools, devolving in the so-called image-guided radiotherapy (IGRT), but most treatment units do not have the equipment and/or the workforce needed for daily IGRT. Off-line correction protocols pursue systematic error correction and margin reduction.[11,43,44] The tools and procedures involved in off-line correction protocols are implemented easily in every treatment unit equipped with imaging. The NAL protocol is more efficient than others, requiring less imaging and therefore less workload. The NAL protocol has been applied previously in head and neck.[43] de Boer et al.[11] quantified set-up errors in head and neck irradiation and investigated theoretically the impact of an off-line correction protocol. A retrospective analysis and Monte Carlo simulation showed that accuracy in the order of 1 mm could be obtained with the application of a NAL protocol. These authors concluded that off-line verification protocols could be particularly effective in head and neck patients due to the small size of the random set-up errors. The present study corroborates that off-line NAL protocol is effective in reducing systematic errors for head and neck irradiation, making it possible to reduce population PTV margins to 5 mm. Small systematic errors and, therefore, reduced margins are very important in highly conformal treatments for head and neck patients.

In our study, based on the van Herk formula[8] ($2{\cdot}5\Sigma + 0{\cdot}7\,\sigma$), the margin of 5 mm added from CTVs to PTVs was sufficient to overcome the set-up errors in head and neck cancers after set-up error correction.

The set-up margins of the population of this study, before correction, were 0·56, 0·53 and 0·48 cm, but after correction it reduced to 0·36, 0·32 and 0·30 cm on x, y and z axes, respectively.

Similar findings were reported by Dionisi et al.[45] The authors concluded that a margin of 5 mm added to CTVs to obtain the respective PTVs was safe in order to overcome the problem of set-up errors.

Moreover, Xu et al.[46] concluded that adding a margin of 3 mm in all directions from the CTVs to obtain the respective PTVs was adequate to overcome the problem of set-up errors.

Finally, Velec et al.[47] compared the intra-fraction and inter-fraction set-up errors in two different thermoplastic masks in patients affected by head and neck cancers treated with IMRT and concluded that the set-up errors before and after corrections were <3 mm in any direction. There was no statistical significance between the two different thermoplastic masks, with respect to inter-fraction and intra-fraction set-up errors.

We also analysed differences in set-up uncertainties based on treatment intent—definitive or adjuvant because it was hypothesised that, during definitive treatment, more volume changes occur due to primary or tumour shrinkage. In this study, 15 patients were treated with definitive intent and 17 patients with adjuvant intent. Each group was further subdivided according to weight loss—>5% and <5%. In the definitive group, 7 patients had weight loss <5%

and 8 patients had >5%. In the adjuvant group, 7 patients had weight loss <5% and 10 patients had >5%. There was no statistical difference between these two intents ($p > 0{\cdot}05$).

The patients of adjuvant sub-group had more weight loss compared to definitive sub-group. In the adjuvant sub-group, anatomical distortions after surgery might have impacted on the percentage of systematic error.

But there was no statistical difference between the errors and margins of both these sub-groups. This needs further study with more number of patients to reach a final conclusion, whether there is any impact of treatment intension on set-up errors.

Weight loss during head and neck radiotherapy can theoretically increase set-up uncertainty by allowing more movement inside the thermoplastic mask or by the loss of posterior neck adipose tissue, resulting in a systematic antero-posterior shift as a time trend. Two prior studies retrospectively looking at the effect of weight loss did not find a significant correlation between weight loss and set-up errors.[48,49] Another study, however, found a higher set-up shift with larger PTV requirements for patients with weight loss and laryngeal cancer.[7] In another study, the systematic errors were slightly higher in the lateral and antero-posterior direction in patients whose weight loss was >5%, but the required PTV margins for set-up error were within 5 mm.[50]

Conclusion

The results of our study confirmed that image-guided kV-CBCT is very effective in evaluating set-up errors in head and neck cancer patients and a simple off-line NAL protocol can correct the set-up errors without daily on-line imaging in patients undergoing IMRT and hence acting as a resource sparing alternative. In our centre, by adding 5 mm margin in all directions to the CTVs to obtain the respective PTVs, we obtained a safe margin to overcome the problem of set-up errors including the issue of weight loss. So, with the help of serial kV-CBCT and NAL off-line protocol, systematic set-up errors of head and neck cancer patients can be reduced resulting in decreased workload and time per patient in a busy department.

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References

1. Bray F, Ferlay J, Soerjomataram I, Siegel R L, Torre L A, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394–424.
2. Bucci M K, Bevan A, Roach M 3rd. Advances in radiation therapy: conventional to 3D, to IMRT, to 4D, and beyond. CA Cancer J Clin 2005; 55: 117–134.
3. Lee N, Xia P, Fischbein N J, Akazawa P, Akazawa C, Quivey J M. Intensity-modulated radiation therapy for head-and-neck cancer: the UCSF experience focusing on target volume delineation. Int J Radiat Oncol Biol Phys 2003; 57: 49–60.
4. Nutting C M, Morden J P, Harrington K J et al. Parotid- sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol 2011; 12: 127–136.
5. Jaffray D A, Siewerdsen J H, Wong J W, Martinez A A. Flat-panel cone-beam computed tomography for image-guided radiation therapy. Int J Radiat Oncol Biol Phys 2002; 53: 1337–1349.
6. Nielsen M, Bertelsen A, Westberg J, Jensen H R, Brink C. Cone beam CT evaluation of patient set-up accuracy as a QA tool. Acta Oncol 2009; 48: 271–276.
7. Den R B, Doemer A, Kubicek G et al. Daily image guidance with cone-beam computed tomography for head-and-neck cancer intensity-modulated radiotherapy: a prospective study. Int J Radiat Oncol Biol Phys 2010; 76: 1353–1359.
8. van Herk M. Errors and margins in radiotherapy. Semin Radiat Oncol 2004; 14: 52–64.
9. Sterzing F, Kalz J, Sroka-Perez G et al. Megavoltage CT in helical tomotherapy-clinical advantages and limitations of special physical characteristics. Technol Cancer Res Treat 2009; 8: 343–352.
10. Lozano E, P'erez L, Torres J et al. Correction of systematic error in breast and head and neck irradiation through a no- action level (NAL) protocol. Clin Transl Oncol 2011; 13: 34–42.
11. de Boer H C, Heijmen B J. A protocol for the reduction of systematic patient setup errors with minimal portal imaging workload. Int J Radiat Oncol Biol Phys 2001; 50: 1350–1365.
12. The Royal College of Radiologists SaCoR, Institute of Physics and Engineering in Medicine. On Target: Ensuring Geometric Accuracy in Radiotherapy. London: Royal College of Radiologists, 2008.
13. Ebookpdf.com. 2019. AJCC 7th Edition 2010.pdf – Free Download. [online]. https://ebookpdf.com/ajcc-7th-edition-2010.
14. ECOG-ACRIN. 2019. Spring 2017 Group Meeting – ECOG-ACRIN. [online]. https://ecog-acrin.org/resources/group-meetings/spring-2017-group-meeting.
15. Stroom J C, Heijmen B J. Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report. Radiat Oncol 2002; 64: 75–83.
16. Park E T, Park S K. Set-up uncertainities for inter-fractional head and neck cancer in radiotherapy. Oncotarget 2016; 7 (29): 4662–4667.
17. Kaur I, Gupta G, Rawat S, Ahlawat P, Kakria A, Saxena U. Dosimetric impact of set-up errors in head and neck cancer patients treated by image guided radiotherapy. Int J Med Phys 2016; 41 (2): 144–148.
18. Ursino S, Faggioni L, Guidoccio F. Role of perfusion CT in the evaluation of functional primary tumour response after radiochemotherapy in head and neck cancer: preliminary findings. Br J Radiol 2016; 89: 20151070.
19. Chao K S, Ozyigit G, Tran B N, Cengiz M, Dempsey J F, Low D A. Patterns of failure in patients receiving definitive and postoperative IMRT for head-and-neck cancer. Int J Radiat Oncol Biol Phys 2003; 55: 312–321.
20. Ursino S, D'Angelo E, Mazzola R et al. A comparison of swallowing dysfunction after three-dimensional conformal and intensity-modulated radiotherapy: a systematic review by the Italian Head and Neck Radiotherapy Study Group. Strahlenther Onkol 2017; 193: 877–889.
21. Eisbruch A, Kim H M, Terrell J E, Marsh L H, Dawson L A, Ship J A. Xerostomia and its predictors following parotid-sparing irradiation of head-and-neck cancer. Int J Radiat Oncol Biol Phys 2001; 50: 695–704.
22. Chao K S, Deasy J O, Markman J et al. A prospective study of salivary function sparing in patients with head-and-neck cancers receiving intensity-modulated or three-dimensional radiation therapy: initial results. Int J Radiat Oncol Biol Phys 2001; 49: 907–916.
23. Delishaj D, Ursino S, Lombardo E et al. Impact of treatment volumes in loco-regional failure of oral cancer in patients treated with IMRT. Radiat Oncol 2016; 119: 985.
24. Parliament M B, Scrimger R A, Anderson S G et al. Preservation of oral health-related quality of life and salivary flow rates after inverse- planned intensity- modulated radiotherapy (IMRT) for head-and-neck cancer. Int J Radiat Oncol Biol Phys 2004; 58: 663–673.
25. Amer A M, Mackay R I, Roberts S A, Hendry J H, Williams P C. The required number of treatment imaging days for an effective off-line correction of systematic errors in conformal radiotherapy of prostate cancer: a radiobiological analysis. Radiother Oncol 2001; 61: 143–150.

26. Delishaj D, Ursino S, Lombardo E et al. OC-0274: analysis of set-up errors in head and neck cancer treated with IMRT technique assessed by CBCT. Radiother Oncol 2016; 119 (Suppl1): 127–128.
27. Bortfeld T, van Herk M, Jiang S B. When should systematic patient positioning errors in radiotherapy be corrected?. Phys Med Biol 2002; 47: 297–302.
28. Suzuki M, Nishimura Y, Nakamatsu K et al. Analysis of interfractional set-up errors and intrafractional organ motions during IMRT for head and neck tumors to define an appropriate planning target volume (PTV)- and planning organs at risk volume (PRV)-margins. Radiother Oncol 2006; 78: 283–290.
29. Su J, Chen W, Yang H et al. Different setup errors assessed by weekly cone-beam computed tomography on different registration in nasopharyngeal carcinoma treated with intensity-modulated radiation therapy. Onco Targets Ther 2015; 8: 2545–2553.
30. Houghton F, Benson R J, Tudor G S et al. An assessment of action levels in imaging strategies in head and neck cancer using TomoTherapy. Are our margins adequate in the absence of image guidance?. Clin Oncol (R Coll Radiol) 2009; 21: 720–727.
31. Bissonnette J P, Moseley D, White E, Sharpe M, Purdie T, Jaffray D A. Quality assurance for the geometric accuracy of conebeam CT guidance in radiation therapy. Int J Radiat Oncol Biol Phys 2008; 71 (suppl 1), 57–61.
32. McKenzie A, van Herk M, Mijnheer B. Margins for geometric uncertainty around organs at risk in radiotherapy. Radiother Oncol 2002; 62: 299–307.
33. Pisani L, Lockman D, Jaffray D, Yan D, Martinez A, Wong J. Setup error in radiotherapy: on- line correction using electronic kilovoltage and megavoltage radiographs. Int J Radiat Oncol Biol Phys 2000; 47: 825–839.
34. Wang J, Bai S, Chen N et al. The clinical feasibility and effect of online cone beam computer tomography-guided intensity modulated radiotherapy for nasopharyngeal cancer. Radiother Oncol 2009; 90: 221–227.
35. Barker J L Jr, Garden A S, Ang K K et al. Quantification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT/linear accelerator system. Int J Radiat Oncol Biol Phys 2004; 59: 960–970.
36. Zhang L, Garden A S, Lo J et al. Multiple regions-of-interest analysis of setup uncertainties for head-and-neck cancer radiotherapy. Int J Radiat Oncol Biol Phys 2006; 64: 1559–1569.
37. Clarizio M, Zani M, Delishaj D, Fedele D, Busutti L, Fabrini M. EP-1619: comparison between two different commercial thermoplastic mask systems in image-guided radiation therapy. Radiother Oncol 2015; 115: 887–888.
38. Osman S O, de Boer H C, Astreinidou E, Gangsaas A, Heijmen B J, Levendag P C. On-line cone beam CT image guidance for vocal cord tumor targeting. Radiother Oncol 2009; 93: 8–13.
39. van Kranen S, van Beek S, Rasch C, van Herk M, Sonke J J. Setup uncertainties of anatomical sub-regions in head-and neck cancer patients after offline CBCT guidance. Int J Radiat Oncol Biol Phys 2009; 73: 1566–1573.
40. Shalev S. Treatment verification using digital imaging. In: Smith A R (ed). Radiation Therapy Physics. Berlin: Springer, 1995: 155–173.
41. van Herk M, Remeiijer P, Rasch C. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000; 47: 1121–1135.
42. Stroom J C, de Boer H C, Huizenga H, Visser A G. Inclusion of geometrical uncertainties in radiotherapy treatment planning. Int J Radiat Oncol Biol Phys 1999; 43: 905–919.
43. de Boer H C, van Sörnser de Koste J R, Creutzberg C L, Visser A G, Heijmen B J, Levendag P C. Electronic portal image assisted reduction of systematic set-up errors in head and neck irradiation. Radiat Oncol 2001; 61: 299–308.
44. Humphreys M, Guerrero M T, Mubata C et al. Assessment of a customised immobilisation system for head and neck IMRT using electronic portal imaging. Radiat Oncol 2005; 77: 39–44.
45. Dionisi F, Palazzi M F, Bracco F et al. Set-up errors and planning target volume margins in head and neck cancer radiotherapy: a clinical study of image guidance with on-line cone-beam computed tomography. Int J Clin Oncol 2013; 18: 418–427.
46. Xu F, Wang J, Bai S, Xu Q F, Shen Y L, Zhong R M. Detection of intrafractional tumour position error in radiotherapy utilizing cone beam computed tomography. Radiat Oncol 2008; 89: 311–319.
47. Velec M, Waldron J N, O'Sullivan B et al. Cone-beam CT assessment of inter-fraction and intrafraction setup error of two head-and-neck cancer thermoplastic masks. Int J Radiat Oncol Biol Phys 2010;76: 949–955.
48. Johansen J, Bertelsen A, Hansen C R, Westberg J, Hansen O, Brink C. Set-up errors in patients undergoing image guided radiation treatment. Relationship to body mass index and weight loss. Acta Oncol 2008; 47: 1454–1458.
49. De Bari B, Ait Erraisse M, Chekrine T et al. Does weight loss predict accuracy of setup in head and neck cancer patients treated with intensity-modulated radiation therapy?. Radiol Med 2012; 117: 885–891.
50. Saha A, Mallick I, Das P, Chatterjee S, Achari R, Shrimali R K. Evaluating the need for daily image guidance in head and neck cancers treated with helical tomotherapy: a retrospective analysis of a large number of daily image based corrections. Clin Oncol 2016; 28: 178–184.