Assessment of Three-Dimensional Set-up Errors in Head and Neck Cancer Patients Treated by Intensity Modulated Radiotherapy using Electronic Portal Imaging Device.


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**Background**

Set-up errors are an inherent part of radiation treatment process. Coverage of target volume is a direct function of set-up margins, which should be optimized to prevent inadvertent irradiation of adjacent normal tissues. The aim of this study is to evaluate set-up errors and propose optimum margins for target volume coverage in head and neck radiotherapy.

**Methods**

Twenty six head and neck cancer patients received intensity modulated radiation therapy (IMRT) included in the study. The weekly portal images taken after correction of the systematic error -if any- were evaluated. The systematic error tested and corrected by taking portal images in the 1st 3 days of treatment by using the VARIS offline review system. Three hundred sixty four portal images matched anatomically with anterior and lateral digitally reconstructed radiographs (DRRs). Five hundred forty six points used to evaluate isocenter displacement in antero-posterior direction (AP), supero-inferior direction (SI) and right-left direction (RL).

**Results**

The mean isocenter displacement in AP, RL, and SI directions were 1.5 ± 1.6 mm, 1.3 ± 1.4 mm and 2.13 ± 1.6 mm. Ninety six percent of the isocenter deviations were within 4 mm in all three directions. The displacement more than 4 mm (negative or positive) was 4% in the vertical direction, 7% in the longitudinal direction and 1.6% in the lateral direction. There is insignificant increase of the isocenter shift in the last weeks of radiotherapy especially in the vertical and longitudinal directions.

**Conclusion**

The current setup for irradiating head and neck cancer patients using IMRT in our department is accurate. The 4 mm CTV-PTV margin is enough.

**Key words**

Portal images, set up errors, CTV-PTV margin.
variability \(^{(2)}\). Another approach to the overcome problem of isocenter targeting that is often used in conjunction with the margin expansion method is the employment of a verification process to ensure and correct for accurate delivery of radiation treatment to the target volume by electronic portal images (EPIs) \(^{(3)}\).

Set-up errors, though undesirable are unavoidable. It is defined as the difference between the actual and intended isocenter position.

Treatment planning in accordance with the recommendations of the ICRU 62 report requires the definition of a clinical target volume (CTV), which must encompass the gross tumor and subclinical disease and possibly involved lymph nodes. The CTV must be expanded to a planning target volume (PTV) by some geometrical margin. This margin must guarantee adequate coverage of the CTV during treatment and should therefore be based on knowledge of internal organ motion and possible daily set up errors. However, the ICRU 62 report did not give a clear recommendation for the CTV-PTV margin. In head and neck cancers the possibility of internal organ motion is negligible, so the coverage of target volume is a direct function of set-up margins, which should be optimized to prevent under-dosage. The evaluation of these errors is necessary to enable optimal definition of PTV margins. So, each radiation therapy center should have its own studies to set the optimal margin around CTV \(^{(4, 5)}\).

The use of portal imaging to measure set-up errors is accepted standard practice \(^{(6, 7)}\). The experience, training, commitment and time available with radiation therapy staff can have a major impact on daily positioning accuracy.

The set up errors include systematic and random errors. Many formulae were developed to calculate for CTV-PTV margin with high weight to systematic error as documented by Stroom \(^{(8)}\) and Herk \(^{(9)}\).

In many institutions (including our own in the past) it is customary to mark the final beam setup at the simulator, after the planning has been performed. The definition of the final isocenter is based on visual inspection, and therefore may deviate from the intended CT plan isocenter. This simulator setup error results in a set-up systematic error \(^{(10)}\).

The setup errors at the treatment unit relative to the reference setup have a systematic and a random component. The systematic component may be reduced with portal imaging and setup corrections based on an off-line decision protocol by taking 3 consecutive portal images during the 1st 3 days of treatment and then correction of systematic error if present \(^{(11, 12, 13)}\), So finally the random error will control the PTV margin in each institution.

**Aim of the study**

This study performed to evaluate set up accuracy and PTV margins used in our radiotherapy treatment protocols for head and neck cancer IMRT using EPIs.

**Patients and Methods**

Head and neck cancer patients planned to receive radiation by IMRT technique were included in the study.

**Immobilization and simulation**

The patients were immobilized in supine position on a four clamp base plate with customized thermoplastic mask from Med-Tec with thickness of 2.3 mm on an appropriate neck rest. CT scanning was performed with setting of reference point (lasers intersection point) as per site of the primary tumor. IMRT planning was done on ECLIPSE treatment planning system with creation of anterior and lateral set up reference images.

**Portal imaging and evaluation**

Portal images were acquired using Varian portal imager (Varian a-Si 1000 flat panel detector with IAS 3 on Exact arm). EPIs were acquired at a reduced dose rate of 100 Monitor Units (MU) per minute and 1-2 MUs were delivered per field for portal acquisition. A double exposure portal images for both the anterior and lateral fields were obtained. Portal images were taken in the 1st 3 days of treatment and then weekly during the radiation course. The 1st 3 portal images were evaluated to correct systematic error if present (Figure 1). The 3rd day corrected isocenter position will be included in the final analysis as the 1st week isocenter position. The weekly obtained portal image after that will be included in the study. Reference images from ECLIPSE treatment planning system were used for comparison with the portal images. Automatic
overlaying and fusion ability in the VARIS offline review system used for anatomical match between DRRs and portal images after defining representative bony landmarks in the DRRs. The results of D isocenter shift were documented as shown in (figure 1). The anterior, superior, and right sided shifts coded as positive shifts and posterior, inferior, and left-sided shifts as negative shifts. One radiation oncologist carried out all the measurements to avoid inter-observer variation.

**Statistics**

Statistical Package for Social Sciences (SPSS version 10.0) was used for statistical analysis.

**Results**

A total of 26 head and neck cancer patients treated by radiotherapy using IMRT technique were included in the study. Seventeen patients were nasopharyngeal carcinoma, 3 patients laryngeal carcinoma, 4 patients oral cavity tumour, 1 patient salivary gland tumour and 1 patient maxillary carcinoma. Five hundred forty six isocenter shifts were evaluated for vertical, longitudinal and lateral shifts representing weekly portal images for each patient during the course of radiation. The 1st week portal image represented by the 3rd day corrected portal image for systematic error if any.

**Isocenter displacement**

Three dimensional isocenter displacements were measured in 364 (182 anterior and 182 lateral) portal images and assessed in vertical or AP, lateral or RL and longitudinal or SI directions. The isocenter shift for all patients in AP, RL and SI directions were illustrated in (Figures 2, 3 and 4), respectively. The absolute mean isocenter shift for all patients was 1.5±1.6 mm in the vertical axis, 1.3±1.4 mm in the lateral axis, and 2.13±1.6 mm in the longitudinal axis as shown in (Table 1).

Ninety six percent of the isocenter deviations in all directions were within 4 mm. The displacement more than 4 mm (negative or positive) was 4% in the vertical direction, 7% in the longitudinal direction and 1.6% in the lateral direction. The isocenter displacements in each week for AP, RL and SI directions were shown in (figure 5, 6, 7) respectively and Table 1.

<table>
<thead>
<tr>
<th>Week of radiation (W)</th>
<th>Mean (mm) ± SD</th>
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<tbody>
<tr>
<td></td>
<td>SI</td>
</tr>
<tr>
<td>W1</td>
<td>1.8±1.1</td>
</tr>
<tr>
<td>W2</td>
<td>2.2±2.3</td>
</tr>
<tr>
<td>W3</td>
<td>1.8±1.3</td>
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<tr>
<td>W4</td>
<td>2.2±1.4</td>
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<td>W5</td>
<td>2.1±1.3</td>
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<tr>
<td>W6</td>
<td>2.9±2.2</td>
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<tr>
<td>W7</td>
<td>1.9±1.7</td>
</tr>
<tr>
<td>ALL WEEKS</td>
<td>2.13±1.6</td>
</tr>
</tbody>
</table>

Table 1: The isocenter displacement in SI (longitudinal), RL (lateral) and AP (vertical) directions for all patients and according to the week of radiation.
The figures and table showed marginal increase of the isocenter shift in the last weeks of radiotherapy (week 6 and week 7) in the vertical and longitudinal directions. The mean vertical displacement in week 1 was 0.96 ± 1 mm and in week 6 (the largest difference) was 2.1 ± 2.6 mm with non significant p value 0.16. The longitudinal shift in week 1 was 1.8 ± 1.1 mm and in week 6 (the largest difference) was 2.9 ± 2.2 mm with p value 0.5.
Discussion

Numerous publications have presented data on setup uncertainties for head-and-neck cancers (10-17), and some setup correction schemes have been proposed (8, 9). In all of these reports, portal images were used exclusively to measure setup accuracy.

The cause of such errors is directly related to the immobilization tool, way of fixation, the irradiated area, the human error of daily adjustment, body weight changes during radiation, the thickness of the marks on the mask and tolerance of laser, gantry and table of the linear and simulator machines. CTV-PTV margin correct for these setup errors. The addition of these margins increases the likelihood of normal tissue complications, thus the ultimate aim is to reduce the PTV margin as much as you can. As per the causes, the isocenter shift differ from radiotherapy center to another and hence each center should revise his setup and determine the exact PTV margin required.

Different studies determine 3-5 mm as acceptable margin around the target in IMRT for head and neck cancer (4, 12, 15, 16).

At the start of IMRT at our department we choose 4 mm CTV-PTV margin based on Stoorm et al (8) and Van Herk et al (9) data.

It has been consistently shown that systematic errors (Σ) are of higher dosimetric consequences than random errors (δ). Using coverage probability matrices and dose-volume histograms, Stroom and Van Herk (16) have suggested formulae incorporating this differential effect. Stroom’s margin recipe \(2\Sigma + 0.7\delta\) ensures that on an average, 99% of the CTV receives more than or equal to 95% of the prescribed dose. The formula by van Herk \(2.5\Sigma + 0.7\delta\) ensures that 90% of CTV receive a minimum dose of at least 95% of the prescribed dose. The CTV to PTV margins using van Herk’s formula were 3.76, 3.84, and 4.74 mm in AP, RL, and SI directions respectively.

However some of the published literatures including ICRU 62 margin-generating recipes do not differentiate between random and systematic errors.

As mentioned before, the internal policy and procedure in our department for head and neck cancer radiotherapy treatment is to perform portal imaging in the 1st three days of treatment to eliminate any systematic error, so the choice of 4 mm as CTV-PTV seems to be theoretically enough based on Van Herk and Stoorn data (8, 9).

This study performed to evaluate CTV-PTV margin chosen and the set-up accuracy in head and neck patients receiving radiotherapy with IMRT at the newly commissioned radiotherapy department of Prince Sultan Haematology Oncology Center using VARIAN portal imaging system. The mean isocenter displacements for all patients were 1.5±1.6 mm in the vertical direction, 1.3±1.4 mm in the lateral direction and 2.13±1.6 mm in longitudinal direction. Ninety six percent of the isocenter deviations were within 4 mm in all three directions.

These data are comparable to Suzuki et al (14) data who analyzed portal images for 22 patients of head and neck and brain tumors treated with IMRT. The mean isocenter displacement in different directions ranged from 0.7 to 1.6 mm and appropriate PTV-margins ranged from 2 to 3.6 mm. They adopted PTV margin of 3 mm for head and neck IMRT.

Humphreys et al (12) evaluated 354 anterior and lateral electronic portal images for 20 head and neck patients. 94% of all translational displacements were within 3 mm, and 99% within 5 mm. The mean ± SE shift was 0.9 ± 0.4 mm in the Right–Left, 0.7 ± 0.6 mm in the Superior–Inferior and 0.02 ± 0.7 mm in the Anterior–Posterior directions (12). The estimated margins required for CTV–PTV were calculated according to the Van Herk formula and was 2.9mm for AP, 2.6mm for RL and 3.3mm for SI. The study concluded that the 3 mm CTV–PTV margin adopted in their department is enough.

However, caution should be exercised while comparing data from different series as each group has used different model parameters to derive cumulative set-up errors which is reflection of the experience, training, commitment, immobilization technique, machine tolerance and time available with radiation therapy staff on radiotherapy unit.

The 3D isocenter displacements in our study though comparable with previously published literature, had a displacement more than 4 mm for nearly 4% of set-up checks. Attempts are being made
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to reduce such errors by incorporating Image-guided radiation therapy (IGRT) which is an innovative and exciting approach for set-up verification that can be potentially useful for high-precision techniques with inherently conformal dose distributions and sharp dose gradients. Contemporary IGRT systems allow accurate internal target positioning and even real-time tumor tracking with a potentiality to reduce margins.

Conclusion

The current setup for head and neck patients using the Med-Tec thermoplastic mask for immobilization and EPIs with the VARIS offline review system for verification is acceptable for IMRT. The four mm CTV-PTV margin implemented in head and neck cancer patients treated by IMRT is reasonable.

References