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# Verification of Setup Errors in Head and Neck Cancer Patients Treated by 3D-CRT and IMRT using Electronic Portal Image Device (EPID) .

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## ABSTRACT

**Purpose:** To study the geometric uncertainties in the treatment and evaluate the adequacy of the margins employed for PTV generation in the treatment of patients undergoing head and neck cancer radiotherapy.
**Material & Methods:** Weekly portal images of setup fields in anterior-posterior and lateral directions were obtained for each patient. These images were matched with the reference image from Varian Acuity simulator. Six anatomical landmarks were selected for comparison. The displacement of portal image from the reference image was recorded in X (Left-Right, L-R) and Z (Anterior-Posterior, A-P) direction for anterior field and Z (Anterior-Posterior, A-P) & (Superior-Inferior, S-I) Y direction for lateral field. The systematic and random errors for individual and population were calculated.
**Results:** The estimated population systematic errors were 2.9 mm for (L-R), 2.7 mm for (A-P) for anterior field & 2.1 mm for (S-I) for the lateral field. The estimated population random errors were 1.9 mm for (L-R), 2.4mm for (A-P) for anterior field & 1.8 mm for superior-inferior (S-I) for the lateral field. Using the ICRU recommendation, the CTV-PTV margin in the, ML, AP, and SI direction were 7.5, 6.4 & 5.6 mm, respectively.
**Conclusion:** The calculated population-based margin is more than the empirical one (5 mm), thus the margin does not provide sufficient coverage for all of the patients. Collected data confirmed the need for a strict check of patient position reproducibility

## INTRODUCTION

The goal of radiotherapeutic treatment for cancer is to provide optimal target coverage while minimizing the dose to normal organs. The introduction of new technology such as intensity modulated radiation therapy (IMRT) and 3-D conformal radiation therapy (3D-CRT) poses new challenges for delivering the intended dose while minimizing toxicity to critical normal structures. This is accomplished by conforming the treatment fields to the target volume using appropriate margins to account for treatment uncertainties. [1, 2]

To determine these margins between the clinical target volume (CTV) and field borders, the concept of the planning target volume (PTV) has been introduced by the International Commission on Radiation Units and Measurement (ICRU) [3].

The PTV is the CTV plus a margin to allow for geometrical uncertainty in the shape and variations in its location relative to the radiation beam due to organ mobility, organ deformation and patient setup variations. At present, a CTV-to-PTV margin 5 mm is prescribed to patients undergoing IMRT of head and neck cancer at our department guided by radiation therapy oncology group (RTOG) recommendation .However, a too small CTV-to-PTV margin will result in a geometrical miss at some or even all treatment fractions. Therefore, it became increasingly important to define adequate CTV to PTV margin. Extreme caution is recommended by ICRU reports on this task, suggesting the transition from expert-guess margin assignment to departments own measurements of uncertainties for margin estimations[3].The RTOG protocol H-0022, suggests using a uniform CTV-to-PTV margin of at least 5 mm until the institution-specific uncertainty has been evaluated. [4]

Pretreatment patient positioning constitutes one important element in determining treatment accuracy. Significant improvements in both accuracy and efficiency of detecting and correcting setup errors can, in principle, be achieved by using electronic portal imaging devices where the setup is verified prior to each treatment and, in some situations, also during the treatment [5]

Currently, weekly electronic portal films is a standard method for assessing patient positioning accuracy. The electronic portal imaging device (EPID) provides a possible means by which patient setup could be more accuracy monitored . [6, 7]

## MATERIAL & METHODS

This retrospective study included 50 patients with pathologically proven head and neck cancer whom presented to Kasr El Ainy center of Clinical Oncology and Nuclear Medicine (NEMROCK) between 2014 &2015 and were treated by IMRT & 3D CRT techniques with a suitable bony landmarks in their EPID.

### *Immobilization and Computed Tomography (CT) simulation*

Thermoplastic mask with five point stabilization of the head were used to immobilize all patients in suitable anatomic positions. S shaped Head-Neck-Shoulders Mask, S Frame thermoplastic mask was used for IMRT patients ( made in china ). Proper neck supports were chosen by considering the primary tumor localization for the patient lying in supine position. Slice thickness was 3 mm and the mask of the patient was marked with radio opaque labels with the help of laser beams.

### *Target Volume Delineation and Treatment Planning*

The findings on clinical examination , CT and/or MRI before RT were used to constitute the GTV (Gross Tumor Volume), the CTV (Clinical Target Volume) and the PTV (Planning Target Volume). GTV tumor delineation was done to include the primary tumor and GTV lymph nodes. CTV (tumor and node) volumes were constructed by adding margins to GTV volumes as per clinical protocols and experiences for probable microscopic extension of disease. PTV volumes were planned empirical by adding 0.5 cm to the CTV, for possible set-up errors. The 3D-CRT &IMRT treatment plans were performed in consistency with the ICRU (50 , 62, 83) guidelines.[8, 9]

### *EPI Evaluation Protocol*

Orthogonal pair set-up fields (anterior and lateral) were obtained with an amorphous silicon detector electronic portal imaging device integrated in the linac (Varian aS500, Varis Vision™, Varian Medical systems®). Digitally reconstructed radiographs (DRRs) of those fields were generated by the Treatment Planning System (Varian Eclipse™ Varian Medical Systems®) and transferred into Vision 6.5 as the reference images for verification purposes.

### *Frequency of the EPI*

Four hundred-and-twenty-four EPIs (212 anterior, 212 lateral) were obtained for all patients, For each patient 3–6 (average 4) portal images per field were acquired during the course of fractionated RT.

### *Reference bony landmarks for the comparison of the EPI*

Lateral (L) image: base of the skull, body and spine of C2 vertebra and the other visible bony structures. (Figure 1)

Antero posterior (AP) image: nasal septum, maxillary sinus, base of posterior skull, vertebras. (Figure 2)

### *Evaluation of the EPI*

Evaluation protocol was an offline procedure. Reference Digitally Reconstructed Radiography (DRR) images were compared to the EPIs and the differences between the EPI and the DRR using bony landmarks were measured in cranio-caudal (CC), anterior-posterior (AP) and medio-lateral (ML) directions.

### *EPI and Statistical analysis*

All statistical calculations, data management and analysis were performed using computer programs Microsoft Excel version 2007. This program calculates the mean, median values and standard deviations. Then the random (σ) and the systematic (Σ) components of the errors were calculated. CTV-PTV margins were calculated using (ICRU) Report 62, Stroom's and van Herk's formula.

The systematic error (m individual) is the mean set-up error for an individual patient. It is calculated by summing the measured set -up error for each imaged fraction (Δ1+ Δ2+ Δ3…) then dividing by the number of imaged fractions (n).

The overall mean set-up error (M pop) is the overall mean for the analyzed patient group. The systematic error for the population (∑set-up) is defined as the standard deviation SD (spread) of the individual mean set-up errors about the overall population mean (M pop). For each individual patient, the random displacement( σ individual) for a particular direction was assessed by the substraction of the systematic displacement (m individual) from

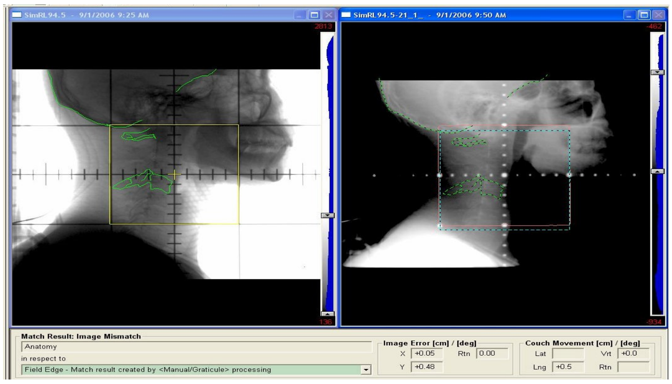

**Figure 1: (Left)** Simulator image of a right lateral setup field with contours outlined skull bones, C1 and C4. **(Right)** Corresponding treatment portal image matched to skull bones. An additional match was performed on this image to C1 and C4.

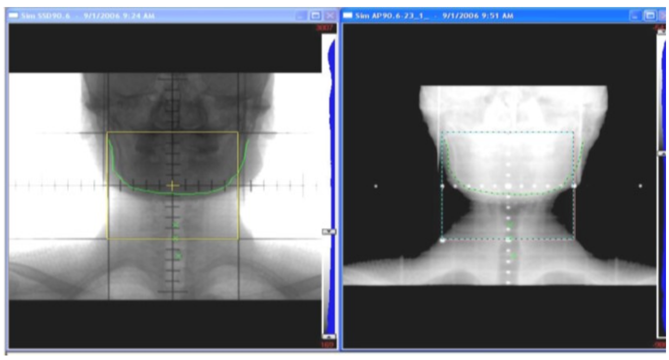

**Figure 2: (Left)** Simulator image of an anterior setup field with contour outlined mandible and spinous process. **(Right)** Corresponding treatment portal image matched to mandible. An additional match was performed on this image to spinous process.

the daily displacement. *Population random error* (σ set-up) is the mean of all the individual random error (σ1, σ2, σ3….)

## RESULTS

Data of 50 patients with pathologically proved head neck cancer presented to Kasr El Ainy center of Clinical Oncology and Nuclear Medicine (NEMROCK) between 2014 &2015 whom were treated with IMRT & 3D CRT and had regular verification of their treatment plan regarding set up errors by using EPI's were collected and statistically analyzed .

### *Results of EPI evaluation*

424 EPIs (212 anterior, 212 lateral) were obtained for all patients with an average of 4 portal images for every patient over each course.848 transitional displacements were measured in three directions. The distribution of all set-up displacements measured both in anterior and lateral EPIs are shown in Figures 3 & 4.

After phantom data analysis, displacements, for all patients, were analyzed considering the average of values obtained from anterior and lateral EPID.92% of the set-up deviations were within 5 mm in all three directions. The percentage of EPID images in which the errors exceed 3 mm along longitudinal, lateral and vertical directions were equal to 28%, 26 %, and 16 %, respectively.

### *Systematic and random errors*

Systematic (Σ) and random (σ) errors were calculated as per conventionally defined norms [5, 6].The systematic component of the displacement represents displacement that was present during the entire course of treatment.

For an individual patient, the systematic displacement was assessed by mean values of all the displacements .For the whole population, the systematic error was represented by the standard deviation (SD) from the values of mean displacement for all individual patients. The random errors represent day-to-day variation in the set-up of the patient. For each patient, dispersion around the systematic displacement was calculated to assess the random displacement.

For the whole population, the distribution of random displacements was expressed by the root mean square of SD of all patients. The estimated population systematic errors (Σ) were 2.9 mm for (L-R), 2.7 mm for (A-P) for anterior field & 2.4 mm for (A-P) & 2.1 mm for (S-I) for the lateral field. The estimated population random errors (σ) were 1.9 mm for (L-R), 2 .4mm for (A-P) for anterior field & 2 mm for (A-P) & 1.8 mm for superior-inferior (S-I) for the lateral field.

### *Margin calculation*

CTV - PTV margins were calculated using the ICRU Report 62, Stroom's [10], and van Herk's [11-13] formulae as shown in table (1)

Using the ICRU recommendation, the CTV-PTV margin in the ML, AP and SI directions were 7.5, 6.4 & 5.6 mm respectively. The corresponding values were 7.6, 6.7 and 5.6 mm with Stroom's formula and 9, 8 & 6.7 mm with van Herk's formula .

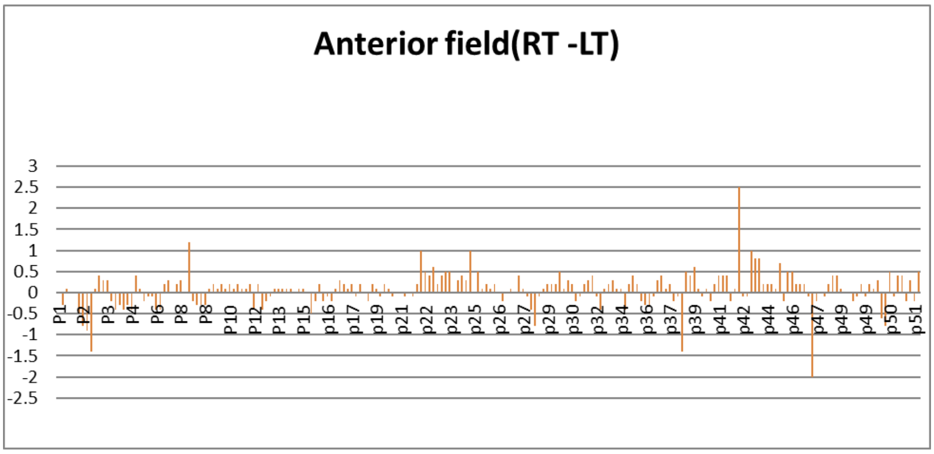


**Figure 3.** Set- up error displacements distributions obtained by orthogonal images: Anterior projection (EPI 90). RT-LT direction (mean values of the displacements measured )

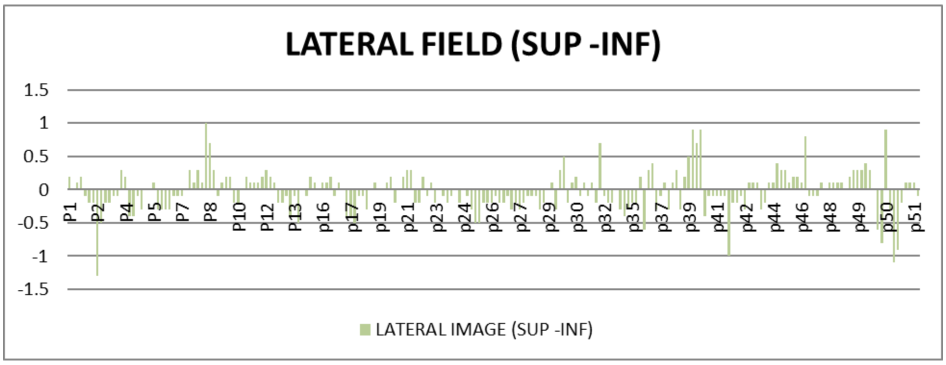


**Figure 4.** Set- up error displacements distributions obtained by orthogonal images: lateral projection (EPI 90). superior-inferior direction (mean values of the displacements measured)

**Table 1. Population systematic, random errors and CTV-PTV margin**

| Population set-up errors | | | | CTV to PTV margins (mm) | | |
|---|---|---|---|---|---|---|
| ***Direction*** | ***Overall mean*** | ***Systematic (Σ)*** | ***Random (σ)*** | ***ICRU 62 (Sqrt Σ2 + σ2)*** | ***Stroom (2Σ + 0.7σ)*** | ***van Herk (2.5Σ + 0.7σ)*** |
| ML | 0.7 | 2.9 | 2.4 | 7.5 | 7.6 | 9.0 |
| AP | 1.4 | 2.6 | 1.9 | 6.5 | 6.7 | 8.0 |
| SI | 0.2 | 2.2 | 1.8 | 5.6 | 5.6 | 6.7 |

## DISCUSSION

This study attempts to evaluate the set-up accuracy in patients receiving radiotherapy for head and neck cancers with antero-lateral portals at our radiotherapy cancer center using a camera-based portal imaging system. Image analysis was carried out by comparing the reference simulator image with portal image using fixed bony landmarks, a good surrogate for target localization in head and neck cancers.

As there exists a possibility of variation in manual measurements six anatomical landmarks were selected for comparison were used for evaluation of displacements in each direction. Emphasis was laid on the technique of manual measurements by precisely choosing the same points on reference and portal images. Matching was done by three radiation oncologists to ensure the quality of image analysis.

The set-up errors was normally distributed in the vertical axis, slightly skewed more to the outer in longitudinal axis and to the left in lateral axis. 92% of the set-up deviations were within 5 mm in all three directions. The CTV to PTV margin was more than 5 mm in all directions. This does not compare reasonably well with the published head and neck data using head cast and thermoplastic immobilization devices.

Population systematic (Σ) and random errors (σ) also miscorrelated with the published literature (Table 2) [14-20].

**Table 2- Population systematic (Σ) and random (σ) errors of selected contemporary series and correlation with probability of target volume coverage**

| Series | Σ | Σ | Displacements or errors |
|---|---|---|---|
| **Hess et al** | Not reported | Not reported | 3 mm for 50% coverage<br>9 mm for 95% coverage |
| **Bentel et al** | Not reported | Not reported | 5–10 mm (87–90% with 5 mm margin) |
| **Gibeau et al** | 1 – 2.2 | 0.7 – 2.3 | 4.5–5.5 mm for 90% probability of target coverage |
| **De Boer et al** | 1.5 – 2.0 | 1.5 – 2.0 | Probability values not specified |
| **Humphrey et al** | 0.02 – 0.9 | 0.4 – 0.7 | 3 mm for 95% of the errors. 5 mm for 99% of errors |
| **Zhang et al** | 1.5 – 3.2 | 1.1 – 2.9 | 5.5 mm for 90% probability of target coverage |
| **Suzuki et al** | 0.7 – 1.3 | 0.7 – 1.6 | 5 mm margin for PTV and 3 mm for PRV |

Coverage of target volume is a direct function of the set-up margin, which should be optimized to prevent inadvertent irradiation of adjacent normal tissues that may precipitate unwarranted radiation morbidity. However, this approach assumes that random and systematic errors have an equal effect on dose distribution, which may not necessarily be the case. Random errors blur the dose distribution whereas systematic errors cause a shift of the cumulative dose distribution relative to the target. In fact, it has been consistently shown that systematic errors are of higher dosimetric consequences than random errors.

Using coverage probability matrices and dose-population histograms, Stroom et al and Van Herk et al have suggested formulae incorporating this differential effect. Stroom's margin recipe (2Σ + 0.7σ) 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 (2.5Σ + 0.7σ) seems to be the most appropriate as it ensures that 90% of patients in the population receive a minimum cumulative CTV dose of at least 95% of the prescribed dose.

Hurkmans *et al*, 2001 published a comprehensive review on set-up verification using portal imaging for several anatomic sites. For HN-RT it was concluded that set-up errors (systematic and random) should be less than 2 mm (1 S.D.), using currently available immobilization equipment. It was stated that additional set-up correction strategies could reduce these errors even more. [21]

Caution should be exercised while comparing data from different series as each group has used different model parameters to derive cumulative set-up errors. Different margin generating recipes lead to a different probability of target volume coverage in different population setting depending on the distribution of shifts. It is therefore suggested that before adopting any published margin recipe, factors that can potentially impact upon margins should also be taken into consideration.

The 3D mean displacements was not comparable with previously published literature, had a wide range at times leading to high individual displacements (>7 mm also). This would be unacceptable for high-precision techniques. Attempts should be made to reduce such errors by incorporating offline correction strategies whenever displacements are >3 mm in any direction. Furthermore, a commercially available infrared positioning system is also being prospectively evaluated to increase the set-up accuracy particularly for high-precision conformal techniques. An alternative method of improving the repositioning accuracy would be the use of indexed patient positioning systems and fixed couch inserts.

Image-guided radiation therapy (IGRT) 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 tumour tracking with a potential to substantially reduce margins. In-room image-guidance systems are either gantry mounted or floor/ceiling mounted. The strategies for IGRT include the use of a) orthogonal radiographs either alone or in conjunction with infrared marker tracking, b) ultrasound imaging with or without implanted fiducial markers, and c) kilovoltage or megavoltage fan-beam or cone-beam computed tomography for volumetric imaging.

## CONCLUSION

The results of this study suggest that the determination of setup variation is important for the assessment of population-based margin calculation to define adequate CTV-to- PTV margin of head and neck cancer patients and improve the confidence in patient specific margin. However, in this study the population-based margin was more than 5 mm which means that our routine empirical margin 5 mm does not provide sufficient coverage for all of the patients. The collected data confirmed the need for a strict monitoring of patient set-up and raises the importance and needs for increasing the experience, training, commitment, and time available with radiation therapy staff.

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