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ASSESSMENT OF SET UP ERRORS AND DETERMINATION OF PLANNING TARGET VOLUME MARGINS IN IMAGE GUIDED RADIOTHERAPY FOR CERVICAL CANCER PATIENTS TREATED IN SUPINE POSITION

Oncology

Dr. Apurba Kumar Kalita MD, DMRT, DMRD, Professor and Head of the Department of Radiation Oncology, BBCI

Dr. Ghritashee Bora* Post Graduate Student, MD, Radiation Oncology, BBCI. *Corresponding Author

Dr. Mouchumee Bhattacharyya MD, Additional Professor, Department of Radiation Oncology, BBCI

Moirangthem Nara Singh DRP, Medical Physicist cum RSO, Dept. of Radiation Oncology, BBCI

Dr. Partha Pratim Medhi MD, Assistant Professor, Dept. of Radiation Oncology, BBCI

Dr. Shashank Bansal Post Graduate Student, MD, Radiation Oncology, BBCI

ABSTRACT

BACKGROUND: Proper positioning of a patient during radiotherapy treatment delivery is crucial for successful implementation of a treatment plan ensuring maximum dose to the target while minimising the dose to the normal tissues. The purpose of this study is to assess the set up errors and to determine the optimal Clinical Target Volume (CTV) to Planning Target Volume (PTV) margins for Cervical Carcinoma patients treated in supine position by Image guided Radiotherapy.

METHODS AND MATERIALS: 219 kVCBCT images were acquired for 10 cervical cancer patients treated with Conformal External Beam Radiotherapy using Image Guidance. Daily set-up errors along the three translational directions were analysed, evaluated for systematic and random errors and optimal CTV-PTV margin determined.

RESULTS: Corresponding CTV-PTV margins in the X, Y and Z directions were 0.7cm, 1.7cm and 0.4cm respectively.

CONCLUSION: IGRT is imperative for ensuring adequate target volume coverage and eliminating geographic miss in IMRT treatment.

KEYWORDS

Cervical cancer, IMRT/IGRT, kV-CBCT.

INTRODUCTION:

Cervical cancer is the 2nd most common malignancy among women in India as per the GLOBOCAN 2018 report [1]. The current standard of care is External beam Radiotherapy with concurrent Platinum based Chemotherapy followed by Brachytherapy.

Several studies have recently reported that three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated Radiotherapy (IMRT) are superior to conventional whole pelvis irradiation in the treatment of gynaecological malignancies [2-4].These techniques employ beams that tightly conform the high dose to the shape of the target volume while presenting steep dose gradients at the margin. Thus, a slight geometrical deviation could result in an under dose to the target volume and/or an overdose to the nearby critical normal tissues [5].For this reason, accurate margin determination is crucial to successfully achieve the treatment goal of conformal treatment.

To overcome this problem, the International Commission of Radiation Measurements and Units (ICRU) 50 and 62 recommends creating a PTV with a margin to the CTV to ensure that it adequately receives the tumoricidal radiation dose [6,7].

The PTV margins depend on various factors like: uncertainties in target delineation, poorly representative simulation, intra-fraction organ motion, inter-fractional patient set-up errors etc., which if not taken into account may lead to a decrease in the Therapeutic Ratio of Radiation [8].Inter-fraction set-up errors is an important determinant in this context and hence, Image-Guided Radiation Therapy (IGRT) provides an excellent solution to quantify for these errors in modern day practice. It aims at acquiring 2D or 3D volumetric cone beam CT (CBCT) images of the patient with respect to the treatment beam prior to the radiation delivery [9].

This study is an attempt to assess for the set-up errors during conformal Pelvic radiotherapy for patients treated in supine position and thus determine the optimal PTV margin.

MATERIALS AND METHODS:

Patient selection:

A retrospective review on set-up error measurements was conducted for 10 locally advanced cervical carcinoma patients treated with Conformal External Beam Radiotherapy in the supine position. A total of 219 kV-CBCT data sets were taken for analysis.

Immobilisation and Simulation:

Patients were first immobilized in the supine-position using four clamp customized thermoplastic mould or Vac-loc. For Radiotherapy planning purpose a Contrast-Enhanced CT scan was performed after asking the patients to void urine 1 h before the scan and then drink 500 ml of water. This procedure was repeated in each treatment session for day to day reproducibility. CT Simulation was done by taking 3 mm contiguous sections on PHILIPS Brilliance Big Bore CT Simulator machine. The data was then transferred to the CMS Xio treatment planning system (TPS)(4.80.002 version, ELEKTA).The target volumes were contoured as per the standard contouring guidelines with appropriate margin to the CTV and an isotropic margin of 10mm around it to create the PTV. The organs at risk were also delineated. The prescribed dose was 50Gy in 25#.

3DCRT and IMRT plans were generated for the patients where the prescribed dose should cover 95% of the PTV. The treatment was delivered in a 6 Mv Linear Accelerator (Elekta Synergy).

XVI CBCT image acquisition:

CBCT was derived prior to each treatment fraction except for a few where it could not be done because of mechanical errors. The selected scan parameter was 120 kVp and 1056 mAs per projection. The set-up error was calculated by registration of planning CT images with the current CBCT images using the bony anatomy. After registration, only the translational errors were recorded which was determined from the automatic bone match. All translational shifts were applied and recorded in centimeters.

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

The mean and standard deviations (SDs) were calculated for all patients in all three axes - X, Y, Z for individually recorded errors.

Statistics:
The set-up error along the 3 translational directions was used to calculate the systematic (Σ) and random errors (σ) for each individual patient and the patient group.

Systematic set up error:
The systematic error of the population(Σ_{setup}) is defined as the Standard Deviation (SD) of the individual mean set up error about the overall population mean(M_{pop}).This is calculated by summing up of the squares of the differences of the overall population mean(M_{pop}) and each individual patient mean(M_n).

$$\Sigma^2 = \frac{(M1-Mpop)^2+(M2-Mpop)^2 \ldots\ldots+(Mn-Mpop)^2}{n-1}$$

Random set up error:
The Random set up error ($\sigma_{individual}$) is the SD of the set up errors around the corresponding mean individual value. ($\sigma^2_{individual}$) is calculated by summing up of the squares of the differences between the mean and the set up error from each image divided by the number of images minus one.

$$\sigma^2_{Individual} = \frac{(\Delta 1-M)^2\ +(\Delta 2-M)^2 \ldots\ldots+(\Delta x-M)^2}{x-1};$$

x = No. Of acquired data sets for individual patient
M= Mean of individual patient set up errors

$$\sigma_{\text{set-up}} = \frac{\sigma 1+\sigma 2 \ldots\ldots+\sigma n}{n};$$

n= No. Of patients

These set-up error measurements were then used to calculate the 3 dimensional CTV-to-PTV margins using van Herck's formula, where the PTV margin is given by the formula: 2.5Σ+0.7σ [10-12].

RESULTS:
The translational displacements in all the three axes: X (Medio-lateral), Y (Supero-inferior) and Z(Anterior-posterior) were recorded for the 215 kV-CBCT images in 10 patients. The Systematic (Σ) and Random (σ) errors as well as the corresponding CTV-PTV margins for the 3 directions were calculated as shown in **Table 1**.

Table 1: Systematic (Σ) errors, Random (σ) errors and CTV-PTV margins calculated using Van Herck's Formula

Directions	Systematic Error(Σ)(cm)	Random Error(σ)(cm)	Van Herck's Formula (2.5*Σ + 0.7*σ) (Cm)
X(Medio-lateral)	0.20	0.31	0.7
Y(Supero-inferior)	0.39	1.02	1.7
Z(Anterior-posterior)	0.10	0.23	0.4

DISCUSSION:
Various uncertainties can arise during the treatment planning in gynaecological malignancies; which can be due to internal organ motion or the filling status of the OARs (Bladder, Rectum) and also due to set-up variations. Uncertainties arising due to set-up variation can be caused by both inter-fraction and intra-fraction motion, the former being the greater of the two components [13].

The modern forms of Radiotherapy are equipped with Image guidance system which allows for verification of the treatment planning process. But for the correct implementation of this technique optimal margin around the target is an important step. Many factors including different patient immobilization positions (prone vs supine), varying measurement methods (electronic portal imaging device, kV-CBCT, Mv-CBCT) or measurement frequencies (daily or weekly) and different treatment techniques (3DCRT, IMRT, and VMAT) can all influence the determination of this optimal PTV margin.

The CTV-PTV margins derived in our study were 0.7, 1.7 and 0.4 cm respectively in the AP, SI and ML directions. In Yao *et al* study[14] the PTV margins obtained from inter-fraction errors were 5.6, 8.3 and 7.6 mm along AP, SI, and ML direction. Similarly, Laursen *et al*. calculated margins of 11.6, 8.2, and 9.6 mm in the AP, SI and ML directions respectively[15].Another study recommends a 7 mm CTV-PTV margins in all directions when using daily imaging for setup corrections [16]. Stroom *et al*. [17]also proposed a 5 mm CTV-PTV margin based on a study on 14 patients with user defined landmarks. In a similar study by Rash et al., mean shift valuesof 7 mm (0 -28 mm) in AP, 2.9 mm (0 -12 mm) in SI, and 3 mm (0 -7 mm) in medio-lateral directions were found in 145 cone beam CT images of 5 patients who had postoperative adjuvant RT with fiducials that had been placed in vaginal apex before treatment [18].

In this study while evaluating the translational errors it was seen that the maximum displacement was seen in the Y (longitudinal/supero-inferior) direction. The shifts in this axis were found to be in between 1 and 2 cm. Asymmetrical margins were found in all the 3 axes in our study. Thus through this study an optimal margin can be given for determining the PTV from the CTV.

CONCLUSION:
Daily CBCT thus serves as an important measure in the appropriate treatment delivery for malignancies treated with new conformal techniques. Appropriate margins to account for the set-up errors can result in maximum target coverage with minimal sparing of normal tissues. But the drawback of this study was that it did not account for the rotational errors.

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