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CTV to PTV Margins Based On CBCT Method for Prostate Cancer of Patients Treated With VMAT Technique

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ARTICLEINFO	A B S T R A C T	
Article type: Original Paper	 Introduction: Patient repositioning in treatment radiotherapy is one of the main factors that increase error of target irradiation. However additional margin is necessary to consider the uncertainties created along and around X, Y and Z-axis. Material and Methods: Set-up and random errors were calculated in translational and rotational axis for a sample of 20 prostatic patients; using daily IGRT-CBCT method. The aim of this study was to determine the additional margin that should be added from clinical target volume (CTV) to prevent toxicity and increase the irradiation precision in radiotherapy. The van Hark formula (PTV margin =2.5Σ +0.7σ) was used for all patients to perform PTV margin for prostatic localization. Results: The research performed for a sample of 20 consecutive patients. With respect to systematic error along the lateral axis, longitudinal and anterior-posterior was 2.32, 2.42 and 3.54 respectively. The Random error was 1.82, 2.19 and 1.76° along lateral axis, longitudinal and anterior-posterior axis respectively. The Random error was 1.78, 1.75 and 1.63° around lateral, longitudinal and anterior-posterior axis respectively. The calculated safety margin to cover clinical target volume (CTV) taking the prostate variability into account measured 7.55, 8.08 and 10.79 mm for lateral, longitudinal and anterior posterior respectively and 7mm would be enough in the posterior side. Rotational set-up errors for almost 95% of patients were between -2° and 2°. Conclusion: The calculated safety margin in all direction was smaller than 1 cm except in anterior side that was 1 cm or more. 	
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Introduction

Advanced techniques in radiation thearapy such as intensity modulated radiation therapy (IMRT and Volumetric modulated arc Therapy (VMAT) accurately shape the radiation dose to the tumor and enhance protection of healthy tissues. These techniques affect Higher gradients of dose distribution which necessitate accurate determination of the target position; otherwise, one can miss the target "entirely" 2].Furthermore, several studies have been [1, previously confirmed that VMAT generate better planning quality than IMRT for prostate cancer [4-7]. For example, Enzhuo M. Quan, et al.[4] have performed a study showing that the VMAT plan quality and the delivery efficiency may be considered in better modality compared to that of IMRT, for Prostate cancer. Moreover, the quality of the patient's treatment plan and the sparing of the adjacent normal organs achieved better results by using VMAT technique compared to conventional irradiation, and reduced the required monitor units compared to that of IMRT [8]. The authors of Ref. [9] have performed for prostate cancer, an evaluation of planning target volume (PTV margins using electronic portal imaging (EPID and IMRT techniques. The obtained result was 10 mm in all directions, which is comparable to the previous works [10, 11].

The mean factor that increases the variation of the target volume position in the treatment of the prostate is its motion characteristics proportional to the surrounding bony anatomy. According to the online imaging protocol (once a week or more frequently), the treatment margins can be decreased when the online setup correction based on the implanted radio-opaque markers and megavoltage radiography.

However, many authors have been previously shown the capability of gold nanoparticles to enhance the effect of physical dose radiation on tumor cells [12, 23]. H. Khosravi et al. demonstrated that administration of gold nanoparticles (GNPs based on keV photon energies were in good agreements with previous studies, and for MeV photon energies the dose factor was enhanced to its maximum value for 2 and 6 MeV photon beams at the depths of é.6 and 5.6 cm, respectively [24]. In addition,

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Khosravi et al. evaluated the implementation of the GNPs to identify its impact on dose distribution for the treatment of the prostate under the internal Ir-192 and external 18MV radiotherapy. However, the presence of GNPs increased the mean dose by 15% and 8% compared to the relevant results without GNPs under the internal and external radiation therapies, respectively.

These results are reduced by 1% using MC simulation under the same conditions [25].All treatment delivery needs high precision of volumes delineations for increasing treatments quality.

More and more attention is conducted to determine errors of patients positioning as well as the determination of the PTV margin and the impact of its dosimetric errors. Based on the CT scanner, GTV and/or CTV delineations are defined for each patient.

Determination of target volumes for photon radiotherapy have been previously published by International Commission on Radiation Units and Measurements (ICRU) in 1993 [26].

During the patient positioning, uncertainties in the target volume involved related to the treatment beams, however, an additional margin should be added to CTV to ensure an adequate tumor irradiation. This expansion of CTV is the Planning target volume (PTV) that is a compromising between the risks under-dosage to target volume and the risk of toxicity to the irradiation healthy tissue. Hence, Patient positioning related to the treatment beams and tumor localization within the patient are the main sources of the uncertainties in the target volume, consequently internal and set-up margin probabilistically added to consider both systematic and random errors. Thus, Image-guided radiation therapy (IGRT) is the preferred method for curative treatment of tumor localization, because it considers derivation in 3-Dimentions, translation and rotation as it allows smaller treatment margins and escalate dose to the target volume [27].

The reproducibility of the patient position in his immobilization system is a fundamental requirement to ensure an optimal treatment of cancers. The daily use of imaging before each radiotherapy session permits the detection and almost total correction of the set-up error. This is realized by moving the processing table along the three axes X, Y and Z(lateral, longitudinal and anterior-posterior) equal to the measured error. Rotational errors correction was also considered.

For this, the aim of our work was conducted to 20patients with Prostate Cancer to investigate PTV margin determination in the IGRT using cone-beam computed tomography (CBCT) or kilo voltage (kV/kV) radio-opaque fiducial markers (FM) imaging.

Materials and Methods

We conducted our study on a sample of 20 consecutive patients who had been irradiated for Prostate cancer in our department. All patients were immobilized with arms folded over the chest, pillow under the head and a wedge under the knees. And thermoplastic mask attached at five fixation points to a carbon fiber plate support.

CT simulation was performed in 3-mm slices with a resolution of 0.97 mm along the X and Y axes using Siemens Somatom Sensation Open CT (Siemens, Erlangen, Germany).Target volumes and OARs were delineated using ELEKTA SOMAVISION Focal workstations v.10.0.28 (ELEKTA, Palo Alto, CA, USA).

Three points had been tattooed on the patient's skin to allow their positioning under the treatment device. Before each Computed Tomography (CT) acquisition, radio-opaque beads were placed on these three points to make them appear in the image.

All planning techniques were customized for each patient to obtain high dose conformity distribution. A uniform margin of 10 mm wide from CT to PTV in all directions, except in the dorsal side 5mm was used, including the prostate, seminal vesicles, and in the patients at high risk, also regional lymph nodes. The dose prescription was 76 Gy in 38 fractions.

VMAT technique using two full arcs for each patient was delivered with 6MV by a linear accelerator (Elekta Oncology Systems, Crawley, UK).The dose prescribed to cover 98% of the PTV. CBCT was derived for each patient prior to treatment fraction for a sample of 20 patients suffers from Prostate and Cancer.125 kVp and 1.6mAsper projection were the selected parameter.



Figure ure 1. Schematic illustration of systematic and random errors [29]

Each treatment session for all patients was delivered with half full bladder and empty rectum. Automatic rigid volumetric image registration of the CBCT to the planning CT was performed on XVI (Elekta Oncology Systems, Crawley, UK)to correct patient's set-up errors in the treatment. However, registration of correction setup errors was per performed in three translations T(x, y, z) and three rotations R (θx , θy , θz). Here X, Y, and Z were lateral, longitudinal and anterior-posterior directions respectively, in treatment machine coordinate. The calculation of set-up error was performed by calculating the distance between the field margin and selected bony structures for pelvis of the digitally reconstructed radiographs (DRRs). The images were displayed, compared and measured by the multi-access computer program, Version 8,00J0, Impact medical system.

In most treatment machines, the set-up error correction in translational directions is acquired manually; these corrections may produce rotational errors that can only be eliminated by robot treatment couch. However, the robot six-degree couches certainly not available in all radiotherapy departments.

In this study, the rotational correction was done manually on treatment couch, to consider any misalignment for the purpose of PTV calculation.

Van Herk et al. [28] assumed minimum dose to CTV to be 95% for 90% of patients. The equation for PTV margin calculation is given by: $M_{PTV} = 2.5\Sigma + 0.7\sigma$

Random errors are mainly composed of the positioning error of the patient and anatomical variations occurring between two irradiation sessions or during a session.

The impact of random errors can be simulated by blurring the dose distribution (by convolution of the dose distribution with distribution laws of the position of the organ).

Results

This study was performed on a sample of 20 patients with prostatic cancer treated with VMAT technique. Daly

Table 1. Translational errors in X, Y and Z-axis for Prostate

CBCT imaging was mad for each individual patient, to measure the intra fraction set-up errors deviation in translational T (X, Y, Z) and rotational R (X, Y, Y) axis. However, bladder and rectum filling were prepared prior each treatment session to control as much as possible the variability of the prostate.

According to our measurements, the deviation along the lateral axis ranged from -15 to +15mm, along the anterior-posterior axis from -13 to +15 mm, and along the superior-inferior axis from-11 to +11 mm Figure 2.

The rotational deviation around lateral axis ranged from-5 to 5° , around the longitudinal axis from 2 to 5° , and around the anterior-posterior axis from -2 to 4° Figure 3.

The total results for systematic error calculation along the lateral axis, longitudinal and anterior posterior were 2.32, 2.42 and 3.54 respectively. Moreover, Random error was 1.82, 2.19 and 1.76 along lateral axis, anteriorposterior and superior inferior respectively Table 1. In addition, the rotational systematic error was calculated for all the studied patients, and the results were as follow: 1.49, 2.04 and 2.14 around lateral, longitudinal and anterionposterior axis respectively. Random error 1.78, 1.75 and 1.63° anround lateral, longitudinal and anterior-posterior axis, respectively (Table2).

From the obtained systematic and random errors, the size of safety margin from CTV was derived in deferent directions, in order to compensate the error of patient positioning along and around each of X, Y and Z axis.

By using Van Herk formula, we calculated CTV to PTV margin for translational T(X, Y, Z) axis 7.55, 8.08 and 10.79 mmrespectively as shown in Table 1.

Positioning	SYSTEMATIC ERROR (Σ)	RANDOM ERROR (σ)	PTV-CTV MARGIN
error	Standard Deviation	Mean of the Standard Deviation	PTV margin = $2.5 \times \Sigma + 0.7 \times \sigma$
TX	2.32	1.82	7.55
TY	2.42	2.19	8.08
TZ	3.54	1.76	10.79

Table 2. Rotational errors in X, Y and Z-axis for Prostate

Positioning error	SYSTEMATIC ERROR (Σ)	RANDOM ERROR (σ)
	Standard Deviation	Mean of the Standard Deviation
RX	1.49	1.78
RY	2.04	1.75
RZ	2.14	1.63

Discussion

As known on prostate cancer difficulties that make its treatment unreliable, are the intra-fractional organ movement and errors created in the subsequent repositioning of the patient. Our exacting task in this study was to determine an adequate safety margin considering translational and rotation set-up errors around and along X, Y and Z-axis. However, monitoring the prostate position variability was the main task to perform CTV-PTV safety margin. Then, the addition margin from CTV to PTV while, keeping the precision of target volume irradiation and Organ at risk protection is dependent on the precision of the patient repositions in the initial position. Several studies based on IGRT modality such a CBCT that has become of crucial importance to

According to our results performed in this work on patients repositioning, it may be considered that our data is comparable to that published by Brut Kragelj [32], on safety margin calculation for prostate cancer.



Figure 2. Distribution of translational set-up errors in X, Y, Z axes







Figure 3. Rational set-up errors around X, Y, Z axes

Van Herk and colleagues found that 7 mm margin was enough to be added from clinical target volume (CTV), without considering for intra-fraction motion of the prostate [31]. Approximately 1cm of PTV margin was reported by various authors of the studies on the prostate irradiation, except in the dorsal side which was accepted to be smaller than 1cm [33-34]. Zelefsky, reported also, if the safety margin is less than 1cm, the CTV coverage can be affected. For patient that was treated in prone position with 1cm in the anterior lateral and craniocaudal directions and of 0.6 cm at the dorsal side, the coverage of CTV at the dorsal side is 85 % before and 96% after the corrections for setup error and prostate displacement [35]. In our study, to consider for target volume coverage, we evaluate the translational and rotational set-up error. However, rotational seterrors most often contribute to affect the target coverage, though it is insignificant as reported by Zhang et al [36]. Results of translational set-up errors for all measurements of our patients are in the form of symmetric Gaussian distribution, and more than 95% of the patients in the interval of -7mm to 7mm except for the lateral left side that was between -9mm and 10mm. Anterior-posterior measurements varied from -7mm to 11mm and this means the calculated 10.79mm additional safety margin should be reduced to almost 7mm in the dorsal side Figure 2. The calculate CTV to PTV margin along translational axis, were 7.55, 8.08 and 10.79 mm for the lateral, longitudinal and anteriorposterior respectively as shown in Table 1.Our total mean Intra-fraction prostate movement measurements for all patients were 2.32; 2.42 and 3.54. However, these values can change with treatment time as resulted from the literature (Σ was 1-2mm) for around 90 seconds [37]. Prolonged Radiotherapy treatment duration can increase intra-fraction prostate movement up to 3-6 mm [38]. Consequently, the safety margin will also increase. Furthermore, rotational uncertainties can potentially cause target messing during irradiation especially for the region away from treatment center. A study published by Laursen et al, suggested increasing the margin with the distance from the isocenter in order to take rotational errors into account [39]. In this study, we evaluated also rotational errors, that was almost symmetric in the interval between -5° and $+5^{\circ}$ but most of the deviations was between -2° and $+2^{\circ}$ as show in Figure 3.

Conclusion

The main objective of this study concentrated on evaluating the set-up error; taking into account the translational and rotational variability of patients treated for prostate cancer by VMAT technique. Applying Van Herk formula in PTV calculation provides comparable results with the previous study.

The use of CBCT methodbefore each treatment, allowed us to obtain a safety margin smaller than 1 cm in all directions, except in the anterior side that should be 1cm and perhaps more; to ensure an adequate treatment of the target volume while, sparing organs at risques, and almost 2° of deviation around X, Y and Z axis.

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