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RETRACTED - Determination of geometrical margins in external beam radiotherapy for prostate cancer

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Original Article

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Abstract

Introduction: The focus of this study is to find the optimal clinical tumour volume (CTV) to planning tumour volume (PTV) margins for precise radiotherapy treatment of prostate cancer. The geometrical shape of the target volume posses challenges in accurately identifying the CTV to PTV margins, especially when the organ affected by cancer demonstrates anatomical variations and the surrounding organs have high radio-sensitivity, in comparison to the organ of origin of the cancer. *Materials and methods:* The geometrical margins of CTV to PTV are investigated using portal imaging, in three directions. This study is carried out on 20 patients treated by the external photon beam radiotherapy of prostate cancer using standard accelerator without stereotaxic and without prostate markers. *Results and discussion:* Based on previous studies and the findings of our work, we propose CTV to PTV margin of 5·84 mm in the lateral direction, of 5·1 mm in the cranio-spinal direction and of 7·3 mm in the antero-posterior direction for external photon beam radiotherapy of prostate cancer. *Conclusion:* The proposed CTV to PTV margins ensure high radiotherapy treatment precision of prostate cancer.

Introduction

In many locations in the body, radiotherapy is currently accepted as one of the most reliable treatment modality for localised cancer. The International Commission on Radiation Units and Measurements (ICRU) recommends, in reports 50 and 62, protecting healthy tissue and the organs at risk (OAR) for high-dose treatment.[1,2] These recommendations aim to reduce the dose to the OAR and to increase treatment efficiency of the cancer by definition of target volumes, such as gross tumour volume, clinical tumour volume (CTV) and planning tumour volume (PTV).[3] In this work, we are interested in the radiotherapy treatment of prostate cancer.

In the United States, prostate cancer is the most common cancer, but it is also curable if found in the early stages. In 2017, the American Cancer Society predicted that there will be around 161,360 new diagnoses of prostate cancer, and that around 26,730 fatalities will occur because of it.[4,5] The prostate is a gland found only in men and is located inferiorly to the bladder and anterior to the rectum, and both these organs are subjected to organ motion depending on organ filling.

In radiotherapy treatment, the prescribed dose will be delivered to the PTV and the determination of the CTV to PTV margins is important to reduce the probability of the late effects of radiation in normal tissues and ensuring greater radiotherapy efficiency.[6–8] The determination procedures are an integral part of quality assurance in practice for radiotherapy treatment, which is taken seriously by the International Atomic Energy Agency (IAEA) and American Association of Physicists in Medicine (AAPM).[9–12]

The accurate CTV to PTV margins are determined by considering all anatomic variations in the pelvis. The main cause of prostatic displacement is involuntary movements of neighbouring organs such as rectal filling variation and bladder filling. These movements are constant and are associated with the movement and displacement of the prostate gland. The amplitude of the prostate motions can be managed with rectal and bladder filling protocols, these parameters have been previously studied and described.[13,14]

In this study, we evaluate the ideal CTV to PTV margins for high radiotherapy precision of prostate cancer and for the protection of the OAR. The CTV to PTV margins are estimated in three anatomical directions, the lateral direction, cranio-spinal direction and antero-posterior direction, using two Van Herk methods as used in previous studies.[15]

Materials and methods

For the purpose of this study, 20 prostate cancer patients were selected at random and over four consecutive days, the CVT and PTV margins were statistically determined.

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Patients were simulated, supine and in treatment position using a Siemens CT scanner (Siemens, Erlangen, Germany). Reference points were defined to guide daily treatment position. Data were transferred to the treatment planning system and an optimal treatment plan produced.

The treatment was carried out by three-dimensional conformal radiotherapy using an Elekta Synergy Platform (Elekta, Sweden, Stockholm) linear accelerator (without stereotaxic and prostate markers) at Hospital University Centre Hassan II Fez Morocco. The daily portal imaging was undertaken using an Iview of an Elekta imager (Elekta).

Treatment prescription

The patient is placed in the same position on the treatment table according to the reference points defined in the pre-treatment computed tomography (CT) localisation scan. During treatment, to ensure CTV and PTV reproducibility, this requires reduced inter-fraction organ movement. This is achieved by daily portal imaging and this image is then compared with the pre-treatment localisation CT scan. Figure 1 presents two medical mages used to ensure accuracy of treatment for prostate cancer, in the left image the reference image serves to determine the displacements due to anatomic variations. The difference between the reference image and the portal image allows us to evaluate the daily displacement in three directions of space.

The treatment operator ensures the patient is in the correct treatment position and uses reference points and the portal image to verify that the positioning is correct.

CTV to PTV margin determination

The CTV and PTV displacements were collected over 4 consecutive days for each patient. Displacements determination was performed on a total of 300 portal images. PTV was defined as 99% of CTV and received at least 95% of the dose in 90% of treated patients; these were the conditions set for displacement determination. For CTV to PTV margins determination, two parameters were used: the systematic error Σ and the random error σ that are described by Van Herk and improved by Wang et al.[16,17]

Two formulas used to estimate the CTV to PTV margins. The first Van Herk formula is as follows:

$$\text{Margin} = 2 \cdot 5\Sigma + 0 \cdot 7\sigma - 3\,\text{mm} \quad (1)$$

where Σ is the systematic error; is defined as standard deviation of averaged motions of all patients. σ is the random error; is defined as square route of averaged sum of all standard deviation square for each patient.

The second Van Herk formula is as follows:

$$\text{Margin} = \sqrt{2 \cdot 7^2\Sigma^2 + 1 \cdot 6^2\sigma^2} - 2 \cdot 8\,\text{mm} \quad (2)$$

For a comparison, the obtained CTV to PTV margins were compared to the results of previous studies.[18–20] The overall uncertainties of the displacements determination are less than 2% and they are in respect to limits recommended by IAEA.[11]

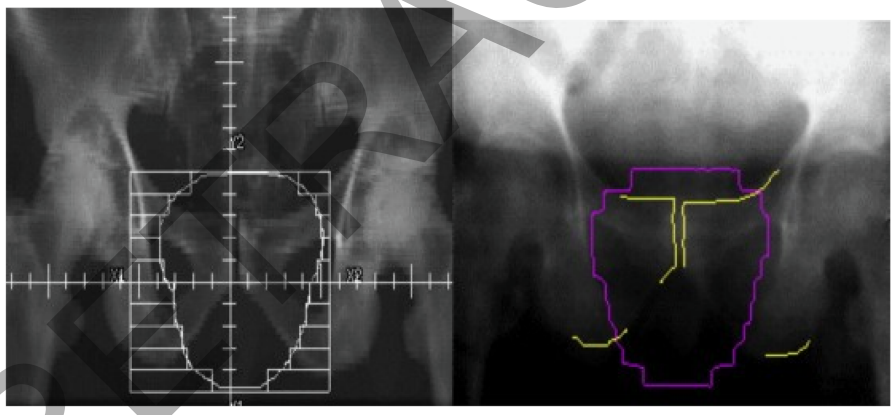

Figure 1. At left the reference image and at right the portal image to verify positioning.

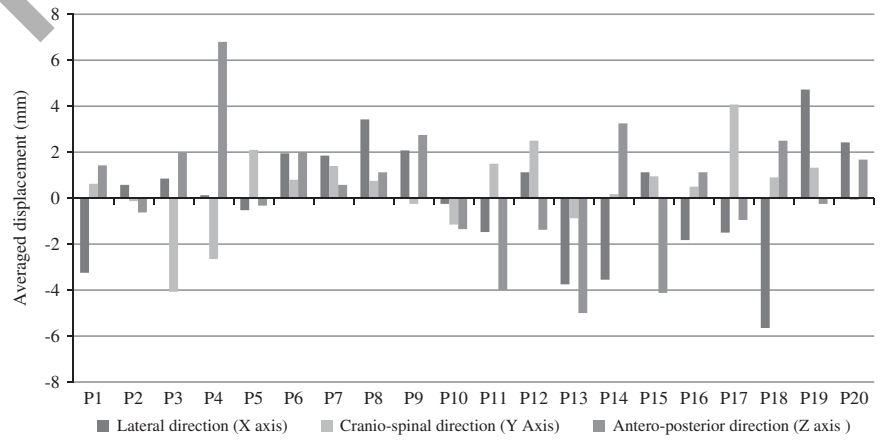

Figure 2. Averaged displacement for each treated patient in three directions of space.

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Results and discussion

The difference between the actual position displayed on the portal image and the planned theoretical position displayed on the pre-treatment CT scan image served to determine the displacement of the CTV and PTV in three directions of space: lateral direction (*X* axis), cranio-spinal direction (*Y* axis) and antero-posterior direction (*Z* axis) seen in Figure 2.

Figure 2 presents averaged displacements related to each direction over 4 days for each patient.

From the results displayed in Figure 2, we noted that prostate motions occur randomly and varied from one patient to another. The CTV to PTV margins were statistically evaluated to measure for treatment precision. The random error and the systematic error were evaluated and introduced into both Van Herk formulas 1 and 2.

We found that the random error is related to the standard deviation and the systematic error is related to standard deviation squared. Figure 3 gives the standard deviation variation in three directions of space.

From Figure 3 we noted that the standard deviation changed from one direction to another and from one patient to another. These values are displayed in Table 1 and these were then introduced into the Van Herk formulas.

To test the reliability of this study, we compared our results to previous studies before we proposed the ideal CTV to PTV margins in each direction for treatment presision.[21,22]

In the lateral direction (*X* axis), the CTV to PTV margin is 5·83 mm given by the first Van Herk formula and 5·84 mm by the second. In previous studies, it was found to be 4·1 mm by Rudat et al. in a study on 23 patients treated by standard accelerator using an image guided technique in addition to prostate markers.[21] Although, Schallemkamp et al. had found 2·8 mm in the lateral direction in a study on 20 patients under the same conditions as Rudat et al.[21,22] In the absence of the image guidance and prostate markers, Schallemkamp et al. and Rudat et al. have proposed a margin of 5 mm. For high radiotherapy precision, we propose 5·83 mm as an optimal margin to ensure encompassing possible microscopic spread of the tumour.

In the cranio-spinal direction (*Y* axis), the CTV to PTV margin was 3·88 mm given by the first Van Herk formula and 3·91 mm by the second. These values are smaller in comparison to 5·1 mm found by Schallenkamp et al. under the same conditions of ours. For high treatment precision, we propose 5.1 mm as an optimal margin, as found by Schallenkamp et al., because it is greater than our margin and it ensures treating the microscopic spread of the tumour.

In the antero-posterior direction (*Z* axis), the CTV to PTV margin is 4·22 mm as calculated by the first Van Herk formula and 4·42 mm found by the second. These values are considerably less than 7·3 mm found by Schallenkamp et al.[22] For high radiotherapy treatment precision of prostate cancer, we propose to consider 7·3 mm as an optimal margin because it is greater than our margin and ensures treating the microscopic spread of the tumour.

Conclusion

The findings of this study are based on an experimental study of CTV to PTV margin determination for prostate cancer. For high radiotherapy treatment precision, we propose the CTV to PTV margins of 5·84 mm in the lateral direction, of 5·1 mm in the cranio-spinal direction and of 7·3 mm in the antero-posterior

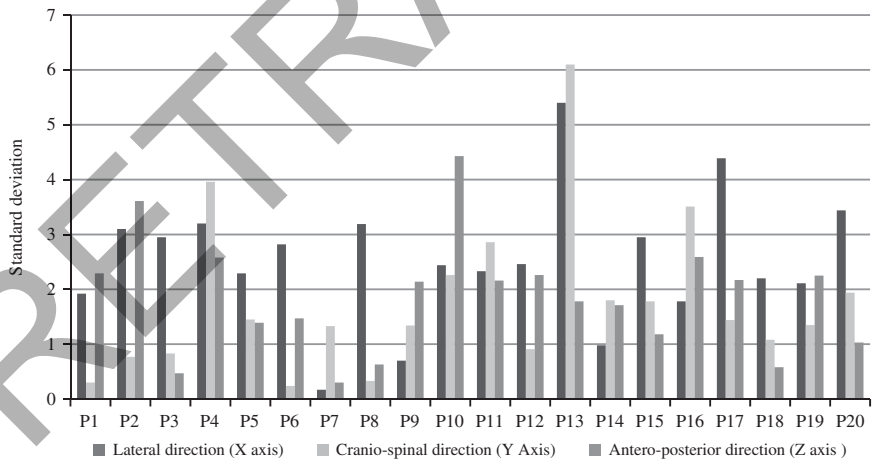

Figure 3. Standard deviation for each treated patient in three directions of space.

Table 1. the systematic error Σ, the random error σ and the clinical tumour volume (CTV) to planning tumour volume (PTV) margin on each direction

Direction of space (axis)	Lateral direction (axis *X*)	Cranio-spinal direction (axis *Y*)	Antero-posterior direction (axis *Z*)
Random error σ	2·6377382	1·76351175	2·77973636
Systematic error Σ	2·79401145	2·25687838	2·11092397
Margin (mm) (by formula 1)	5·83144538	3·87665416	4·22312537
Margin (mm) (by formula 2)	5·84413106	3·91514316	4·42946689
Difference between margins (mm)	0·01268569	0·038489	0·20634152

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direction. These margins are optimal when using a standard accelerator without stereotaxic and prostate markers.

The proposed geometrical CTV to PTV margins reduce the probability of tumour recurrence and may have an impact on disease-free survival.

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