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Treatment planning

Testing the new ICRU 62 'Planning Organ at Risk Volume' concept for the rectum

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Abstract

***Background and purpose*: To study the impact of the new ICRU 62 'Planning organ at Risk Volume' (PRV) concept on the relationship between rectum dose-volume histogram (DVH) data and toxicity.**

***Patients and methods*: The acute gastro-intestinal (GI) RTOG toxicity in 127 prostate cancer patients prescribed a total dose of 70 Gy with conformal irradiation to either the prostate, the prostate and seminal vesicles or the whole pelvis (initial 50 Gy only) were analysed. DVHs were derived for the rectum only and for rectum extended with six PRV margin sets (narrow/intermediate/wide; anterior/anterior and posterior). The data was analysed using permutation tests, logistic regression and effective uniform dose (EUD) calculations.**

***Results*: Acute Grade 2 GI toxicity was seen in 22 of 127 cases (17%). Permutation tests showed that the difference between DVHs for patients with and without Grade 2 effects was significant, both for rectum only and rectum PRVs (*P*-value range: 0.02–0.04), with generally lower *P*-values for the PRVs. In the logistic regression, the fractional DVH variables (i.e. volumes) were significantly related to toxicity, with approximately 2–3 times as many significant dose levels for the PRVs as for rectum only. E.g. with wide anterior and posterior margins (16 and 11 mm, respectively) the relation was significant at 26 different dose levels (6–7, 13–14, 35–43, 60–71 and 73 Gy), compared to nine levels (38–40, 43–44 and 71–74 Gy) for rectum only. EUDs were significantly different for patients with and without Grade 2 effects both for rectum only and the PRVs (95% confidence interval for EUD increase with Grade 2 effects: 0.1–3.1 Gy).**

***Conclusions*: All statistical methods applied indicated a small, but definite difference in DVH parameters between patients with versus those without Grade 2 effects. The difference was most pronounced when margins of 16 mm anterior and 11 mm posterior were applied.**

Keywords: Pelvic radiotherapy; Acute toxicity; Geometrical uncertainties; Rectum; Planning organ at risk volume; Margins

Optimization of radiotherapy (RT) for pelvic malignancies, and in particular prostate cancer, has gained huge clinical and scientific interest throughout recent years [5,11,14,21,26]. The prostate has been the test site for introduction of both conformal RT (CRT) and more recently, intensity-modulated RT (IMRT), techniques that require a high degree of geometrical accuracy. Normal tissue dose-volume histogram (DVH) parameters derived from the planning scan have been used to predict the risk for complications in the major organs at risk (ORs) in prostate irradiation—the rectum and bladder—for a given beam configuration. However, a considerable geometrical uncertainty has been documented in pelvic radiotherapy [20,22,24], reducing the confidence one should place on DVH parameters derived from the planning scan only. Recently the ICRU report no. 62 introduced the Planning Organ at Risk Volume (PRV), a volume containing a specific OR and a safety margin around it to account for its anatomical and geometrical variability, in analogy with the target volume definitions of the same report [9]. It was suggested that DVH data of the PRV would be useful in RT reporting.

The rationale for use of margins around ORs is that the resulting DVH for the OR with margins, i.e. the PRV, includes the dose in the region in space where the OR is likely to be located [16,19]. For ORs such as the rectum where the organ motion is large compared to the extent of the organ, it seems particularly important to capture the dose distribution in the volume in which the OR can move. However, this is probably also linked to the organization of the radiosensitive structures in the organ. In particular if the organ is of serial nature, i.e. the risk for complications

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Table 1
Combinations of rectum margins (mm) used in the series of prostate cancer patients

Margin combination no.		Anterior	Posterior
PRV 1	Narrow anterior margin	6	1
PRV 2	Intermediate anterior margin	11	1
PRV 3	Wide anterior margin	16	1
PRV 4	Narrow anterior and posterior margins	6	5
PRV 5	Intermediate anterior and posterior margins	11	8
PRV 6	Wide anterior and posterior margins	16	11

is determined by the maximum dose or other peak dose parameters, it should be worthwhile to investigate if DVH parameters for the PRV correlates better to the risk for complications than DVH parameters for the OR alone. For ORs of more parallel nature, adding margins appears only to increase the total volume, possibly diluting the often quite subtle relation between DVH data and toxicity. Moderate to severe rectum toxicity (mostly bleeding) has in several independent series been related to the maximum or peak doses [4,11,12,23].

A recent study from our institution presented margins that accounted for the geometrical uncertainties around the rectum in pelvic RT, derived from repeat CT scanning and electronic portal imaging data using both a published margin recipe and more empirical methods [19]. In addition, a series of consecutive prostate cancer patients has been followed prospectively for adverse effects at our institution [12]. In this series the treated volume varied considerably according to the defined stage and risk factors (TNM stage, PSA level and Gleason score), from volumes encompassing the prostate only, to prostate and seminal vesicles, and whole pelvic irradiation [12]. This caused a corresponding variation in rectum DVHs, which is desirable when analyzing the correlation between rectum DVH data and toxicity. In the present study we therefore analysed the rectum toxicity profiles for these patients and investigated whether the derived PRV margin proposals improve the correlation between rectum DVH parameters and the incidence of rectum adverse effects.

Methods and materials

Patient material

Throughout 2001, 132 prostate cancer patients were treated with curative CRT at Haukeland University Hospital. Treatment planning and acute effect data have been presented elsewhere [12], and only the points relevant to this study are described here.

The primary tumour was staged clinically according to the 1997 TNM classification for prostate cancer [7] while histopathologic specimens were graded according to the Gleason pattern score [17]. As many as 113 of the patients (86%) received endocrine treatment, commencing 3–4 months before CRT, to reduce the prostate volume and thereby reduce the dose of radiation delivered to the rectum and bladder. The endocrine therapy continued during and 2 months after start of RT [1].

CT scanning and organ outlining for treatment planning

All patients were planned and treated supine. The planning CT scans were acquired with patients on a flat couch, including slices from the L3/L4 vertebrae level down to the level of the perineum. Slices 5 mm thick with 5 mm interval (5/5 slices) were acquired through the region that contained the target volumes, while 10/10 slices were acquired in the abutting regions above and below. The responsible oncologist contoured the target volumes and the ORs, i.e. the rectum and the bladder. The rectum was defined as the volume within the outer wall contour, including the contents, with superior limit at the first slice below the recto-sigmoid flexure, and inferior limit at the first slice above the anal verge.

Six rectum PRVs were defined by adding six different sets of margins (Table 1) around the rectum. The margins were based on a study of geometrical uncertainties in bladder irradiation, where the narrow and large margins encompassed approximately 50 and 75% of the observed rectum variation, respectively [19]. Only anterior and posterior margins were applied, as dose gradients predominantly were found along this direction. A 1 mm margin was the smallest that could be used in our planning system, and was therefore used in the posterior direction for PRVs 1–3.

Target volume definitions, dose prescription and treatment technique

All patients were prescribed a total dose of 70 Gy (average PTV dose), and were treated with one 2 Gy fraction daily, 5 days a week over 7 weeks. Depending on the defined stage and other risk factors (TNM, PSA and Gleason score), the target volume varied from prostate only for low-stage and low-risk patients, to prostate and seminal vesicles for patients in intermediate stage and risk groups to modified pelvic irradiation (initial 50 Gy) for patients with advanced disease. A dose of 50 Gy was administered to the defined volume with wide margins (15–20 mm between PTV and prostate/prostate and seminal vesicles), while another 20 Gy was given to a smaller volume grown with narrower margins (10–15 mm between PTV and prostate/prostate and seminal vesicles). The last 20 Gy to those given the initial 50 Gy with modified pelvic fields were given to the prostate and seminal vesicles with 10–15 mm margins. Photon beams of 10–15 MV beam quality were used. All patients except one were treated with a four-field conformal box technique (anterior, posterior and two lateral beams); this patient was treated with a six-field technique (anterior, posterior and four lateral oblique fields). Multi-leaf collimators (MLCs)