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Dependence of the safe rectum dose on the CTV–PTV margin size and treatment technique

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ABSTRACT

Background: Late rectal injury is a common side effect of external beam radiotherapy for prostate cancer.
Aim: The aim of this study was to evaluate what total dose may be safely delivered for prostate patients for 3DCRT and IMRT techniques and the CTV–PTV margin.
Materials and methods: 3DCRT and IMRT plans were prepared for 12 patients. For each patient PTV was defined with CTV–PTV margins of 0.4, 0.6, ..., 1.0 cm, and total doses of 70, 72, ..., 80 Gy, with 2 Gy dose fraction. NTCP values for the rectum were calculated using the Lyman model. Both techniques were compared in terms of population mean DVH.
Results: Significantly smaller NTCPs for IMRT were obtained. For both techniques diminishing the margin CTV–PTV of 2 mm leads to decreasing the NTCP of about 0.03. For total dose of 80 Gy the NTCP was smaller than 10% for the 4 mm margin only. The QUANTEC dose volume constraints were more frequently fulfilled for the IMRT technique than for the 3DCRT technique.
Conclusions: The IMRT technique is safer for prostate patients than the 3DCRT. If very high total doses are applied the CTV–PTV margin of 0.4 cm and the IMRT technique should be used. If the CTV–PTV margin of 0.6 cm is applied, the NTCP is smaller than 10% for the 3DCRT and IMRT techniques for the total doses smaller than 74 Gy and 78 Gy, respectively.

1. Background

Late rectal injury is a common side effect of external beam radiotherapy for prostate cancer, especially if very high dose is prescribed. This observation was confirmed by many retrospective and prospective studies.[1–3] The total doses of values larger than 80 Gy delivered with 2 Gy per fraction are recommended for prostate cancer treatment.[4] It is quite common to treat patients with larger doses per fraction.[5] A shorter course with increased dose per fraction becomes the standard, however this increased the risk of rectum injury. To keep the risk of rectum injury at acceptable level, image guided radiotherapy is used with the Intensity Modulated Radiotherapy (IMRT).[6]

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The larger the equivalent prescribed dose is delivered, the larger is the risk of rectum injury and, therefore, significant efforts are being undertaken to diminish the CTV–PTV margin. To diminish the dose to the rectum, in some clinics the endorectal balloons or hydrogel spacers are used.[7,8]

Recently, the Quantitative Analysis of Normal Tissue Effects in the Clinic Group (QUANTEC) reviewed the published data on the dose-volume determinants of late rectal injury after external beam therapy. The meta-analysis of QUANTEC revealed that the Lyman–Kutcher–Burman model gave the best estimates of Grade ≥2 late rectal toxicity or rectal bleeding.[9] Using this model it is possible to evaluate quantitatively the safety of irradiation of patients with prostate cancer.

2. Aim

The purpose of this study was to evaluate what total dose may be safely delivered for prostate patients depending on the irradiation technique and the CTV–PTV margin.

3. Materials and methods

3.1. *Treatment technique*

Here is a short description of the technique of irradiation of patients with prostate cancer in our clinic. Twelve patients with localized prostate carcinoma (T2–3 N0 M0) treated in our clinic in 2010 were randomly selected. The median age of treated patients was 71 years and 6 months, PSA median 7.9 ng/ml (range 4.8–22.7 ng/ml), and Gleason score median 4.0 (range 3–7). During the CT scanning, patients were positioned supine with a knee-roll for position's stabilization. According to the protocol, images were taken with empty rectum and full bladder. To achieve this before investigation, patients were asked to empty their bladder and drink half a liter of water 1 h prior to a planning CT scan.[10] The same procedure was followed before each treatment session. If the patient was not able to empty the rectum the additional Cone Beam CT was made to correct the patient's position. CT treatment simulation was performed with a CT scanner (Somatom Open, Siemens) with a slice thickness of 3 mm. Images were sent to a contouring station (ROP, CompArt) where the prostate, seminal vesicles, rectum, posterior wall of rectum, bladder and femoral heads were delineated by a physician. The rectum was delineated in all CT slices containing CTV and was extended by 3 cm craniocaudally. The rectum was regarded as the solid organ including the rectal content. The PTV is drawn by adding the margins: cranial–caudal and anterior–posterior margin was 0.7 cm, left-right margin was 0.4 cm. The 15 MV energy photon beams were used. The prescribed dose was 65 Gy delivered in 25 fractions 5 times a week. Dose distributions fulfilled the recommendations of the ICRU Reports 50 and 62: minimum dose to PTV > 95% and maximum dose < 107%. Additionally, according to our internal protocol, minimum dose to CTV > 97%, and maximum dose to CTV < 103% of the prescribed dose were recommended. The rectum dose-limiting constraints were: 25% of the rectum volume could receive the dose of 61 Gy or larger, 2% of the posterior wall of the rectum could receive the dose of 56.2 Gy or larger. The bladder dose-volume limiting constraint was: 50% of the bladder volume could receive the dose of 52 Gy or larger. Treatment plans were prepared with the Eclipse system, version. 10 with an Anisotropic Analytical Algorithm.

For this study additional plans were prepared by the authors of this paper. For each patient four PTVs (Planning Target Volume) were drawn consisting of the prostate gland CTV (Clinical Target Volume) and seminal vesicles with uniform margins of 0.4, 0.6, 0.8, and 1.0 cm. For each patient two treatment plans were prepared: (1) 3D conformal plan with a three field arrangement (AP and two lateral opposed fields, with a wedge as required), and (2) IMRT plan (sliding window) consisted of 5 beams at angles of 0°, 45°, 115°, 245° and 315°. For each patient, each margin, and each total dose the optimized plan was prepared. The optimization was performed for total doses of 70, 72, ..., 80 Gy and 2 Gy dose per fraction. For Organs at Risk the QUANTEC dose-volume constraints were used.[10] The dose was always prescribed to the isocenter which was defined as a center of mass of the CTV.

3.2. *Normal Tissue Complication Probability and data analysis*

Differential absolute dose volume histograms with dose bins of 1 Gy for each patient, and for each plan were calculated and saved in the computer file. No fractionation correction was made. Using this numerical data in Excel, the Normal Tissue Complication Probability (NTCP) values for the rectum were calculated using the Lyman model with model parameters recommended by QUANTEC for Grade ≥2 late toxicity or rectal bleeding: $n = 0.09$, $m = 0.13$, and $TD50 = 76.9$ Gy.[10–12] Population mean Cumulative Dose Volume Histograms were calculated for each margin and both techniques separately. Average population Cumulative Dose Volume Histograms were compared with dose volume constraints proposed by Michalski, i.e. V50 < 50%, V60 < 35%, V65 < 25%, V70 < 20%, and V75 < 15% (VX is the partial volume of an organ which receives dose smaller than X Gy).[10]

It was assumed that the treatment is safe, if the NTCP of rectum is not larger than 10%.

4. Results

In Fig. 1 the average population DVHs for the 3D-CRT and IMRT techniques is shown (for some points the standard deviation is added). Similar differences in shape of DVHs were observed for all patients. Comparison of the population average dose distribution in the rectum obtained for IMRT and 3DCRT shows that: for the IMRT technique, smaller volume of the rectum was exposed to doses larger than 70% and smaller than 35% of prescribed dose. For doses in the range between 35% and 70% of prescribed dose the DVH is similar for both techniques. Figs. 2 and 3 show the dependence of the NTCP on the total dose for 3D-CRT and IMRT for all CTV–PTV margins. The increase of NTCP with dose is more pronounced for larger CTV–PTV margins, e.g., for 4 mm and 8 mm for dose of 80 Gy the difference between the NTCP for IMRT and 3DCRT are about 5% and 8%, respectively. Fig. 4 shows a comparison