Radiotherapy and Oncology 106 (2013) 210–214

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Rectal spacing in prostate RT

Interstitial biodegradable balloon for reduced rectal dose during prostate radiotherapy: Results of a virtual planning investigation based on the pre- and post-implant imaging data of an international multicenter study ☆

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ARTICLE INFO

Article history:
Received 6 December 2011
Received in revised form 27 December 2012
Accepted 27 January 2013
Available online 26 February 2013

Keywords:
Prostate
Rectal dose
Tissue separation
OAR dose reduction

ABSTRACT

Purpose: To evaluate dose reduction caused by the implantation of an interstitial inflatable and biodegradable balloon device aiming to achieve lower rectal doses with virtual 3D conformal external beam radiation treatment.

Materials and methods: An inflatable balloon device was placed, interstitially and under transrectal ultrasound guidance, into the rectal–prostate interspace prior treatment initiation of 26 patients with localized prostate cancer, who elected to be treated with radiotherapy (3D CRT or IMRT). The pre- and post-implant CT imaging data of twenty two patients were collected (44 images) for the purpose of the 3D conformal virtual planning presented herein.

Results: The dorsal prostate–ventral rectal wall separation resulted in an average reduction of the rectal V70% by 55.3% (±16.8%), V80% by 64.0% (±17.7%), V90% by 72.0% (±17.1%), and V100% by 82.3% (±24.1%). In parallel, rectal D2 ml and D0.1 ml were reduced by 15.8% (±11.4%) and 3.9% (±6.4%), respectively.

Conclusions: Insertion of the biodegradable balloon into the prostate–rectum interspace is similar to other published invasive procedures. In this virtual dose distribution analysis, the balloon insertion resulted in a remarkable reduction of rectal volume exposed to high radiation doses. This effect has the potential to keep the rectal dose lower especially when higher than usual prostate dose escalation protocols or hypo-fractionated regimes are used. Further prospective clinical investigations on larger cohorts and more conformal radiation techniques will be necessary to define the clinical advantage of the biodegradable interstitial tissue separation device.

Although radiation therapy has the potential to cure locally confined prostatic tumors in selected patients, it can also result in significant morbidity, potentially leading to lifestyle restrictions and psychological distress. Patient quality of life (QoL) following primary treatment of localized prostate cancer is, to a large extent, influenced by adverse changes in bowel, urinary, and sexual function. While local dose escalation has been shown to significantly improve outcomes of radiotherapy of local and locally advanced prostate cancer [1,2], rectal toxicity [3] limits the extent of acceptable escalation [4]. A number of technical developments aim to reduce rectal radiation dose [5–8], some of which rely on tissue separation between the dorsal prostate and ventral rectal wall [9–13].

A biodegradable and inflatable balloon device (ProSpace®, BioProtect Ltd./Israel) has been designed to be transperineally implanted within the prostate–rectum interspace, before treatment initiation, to increase the gap between the prostate–rectum. The device remains inflated during the entire treatment period and biodegrades in the body some weeks after termination of treatment. In the BPI-01 international, multicenter study (NCT00918229), the device proved to increase the prostate–rectum distance 10-fold (mean 0.22 ± 0.2 cm to 2.47 ± 0.47 cm), and to remain stable during radiotherapy. In parallel, a significant mean reduction in calculated rectal radiation exposure was achieved. The implant procedure was well tolerated and the adverse events included mild pain at the perineal skin and in the anus. Three patients experienced acute urinary retention, which may have been triggered by the use of general anesthesia, and resolved within a few hours of conservative treat-

☆ The paper was partly presented at ESTRO 30 in London as a poster presentation. All authors read and accepted the manuscript before submission.

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http://dx.doi.org/10.1016/j.radonc.2013.01.007

ment. No infections or thromboembolic events occurred during the implant procedure or during radiotherapy [12–14].

As each treatment center in the BPI-01 study used its standard institutional radiation protocols (3DCRT, IMRT), which included different radiation techniques and dosages, the present work provides a centralized, radiation technique-independent analysis of the changes in rectal radiation exposure. A virtual radiation dose model, based on pre- and post-implant CT image series is presented.

Material and methods

In the framework of an international multicenter study (BioProtect, BPI-01), conducted after approval by the local Institutional Review Boards, FDA and the respective Ethics Committees and Ministries of Health, ProSpace (BioProtect Ltd., Israel) was transperineally implanted, under transrectal ultrasound guidance and local/general anesthesia, within 2 weeks of the start of radiotherapy, within the prostate–rectal interspace of 26 patients with histologically confirmed, localized prostate cancer [12–14]. Weekly CT/US scans were performed during EBRT and at 3, 6 and 12 months after balloon implantation, to evaluate stability and subsequent degradation of the balloon. Radiation treatment planning and delivery were executed as per the standard protocols of the participating center. The pre- and post-implant CT images of 22 study patients were collected to virtually determine the dose at the treated region before and after implantation. CT series of 4/22 patients were not eligible for this analysis, due to varying slice thicknesses. The implantation procedure as well the feasibility study results were described elsewhere [12–14]. Radiation treatment planning and delivery were executed as per the standard protocols of the participating center.

Contouring of prostate and rectal wall in both pre- and post-implant images was performed by one physician (GB, experienced in delineation work) and dose calculations were performed by one medical physicist (CM), with identical radiation parameters for all cases. The Planning Target Volume (PTV) was defined in 1.0 cm extensions in all directions margin to the prostate. In post-implant images the balloon was also contoured. After creating these 44 virtual plans, changes in rectal dose–volume-histograms (DVH) were measured and compared to rectal tissue dose values with and without the implanted balloon.

The potential dose reduction on the rectum due to the enlarged distance between prostate and ventral rectal wall, was calculated by determining the differences in V50%, V60%, V80%, V90% and V100% (Vxx% = the volume in % of the rectum wall receiving xx% of the prescribed dose) at the prescribed dose level of 74 Gy. Rectal wall volume data were compared by using D2 ml and D0.1 ml (Dxx ml is defined as the minimum dose in Gy in the most irradiated rectal wall volume of xx ml [15]). Similarly, when calculating affected rectal volume, presentation in percentage form allows for the most effective comparison between all 22 patients. Statistical significance of volume (Vxx%) and dose (Dxx ml) reductions were tested by a single-sided, paired Student's *t*-test. A significance level of 0.01 was chosen.

A four-field box technique was used (18 MeV photons, field at 0°, 90°, 180°, and 270°) in the treatment planning system (TPS) ECLIPSE© (Varian, Paolo Alto, USA). The planning was performed on CT data sets with a slice thickness of 2 mm. The "half-beam technique" was applied and the isocenter was placed close to the rectum in order to achieve lower rectal doses due to the lower weight of the 180° field. The field size multileaf collimators (MLC) were optimally fitted, in each case. The reference dose of 74 Gy (conventional fractionation) was prescribed on the 100% isodose. ICRU recommendations were followed. Preparation of pre- and post-implant radiation plans was performed on the basis of identical procedures: isocenters for both plans were on the same place, D_{max} values were comparable and field lengths were equal since the CTV was not changed.

GEC-ESTRO dose recording and reporting recommendations for prostate brachytherapy were adapted to rectal tissue dose reporting [16].

Results

Typical pre- and post-implant organ geometries are shown in Fig. 1. The mean measured post-implant prostate–rectum distance, on the anterior–posterior axis was 19.15 mm (range 14.6–23.4 mm). The mean latero-lateral extension of the balloon was 30.45 mm (range 21.1–36.6 mm), cranio-caudal 45 mm. The attained median dose reduction in % as well the corresponding standard deviation values (SD) is summarized in Table 1.

In an effort to normalize the different dose regimens applied at the participating centers, changes in dose are presented as the percentage of the total dose. Vxx% represents the rectal wall volume in %, which receives a dose of xx% in Gy of the prescribed dose. Dxx ml is defined as the minimum dose in Gy in the most irradiated rectal wall volume of xx ml [15].

The size of the rectum wall volume included into the radiation field is individually different. Separate CT-data result in a different size (ml) of the affected volume of the rectum wall even for the same patient. A comparison of the volume in absolute value with the unit ml is ineffective. Percent offers the option to become a comparable value to all results of the 22 patients.

The volumes receiving 37 Gy (V50%) showed very small changes on average, and ranged from volume increase of 31% in one patient to a volume decrease of 35% in another patient.

The minimum volume reduction was about 30% and the maximum nearly 100% for all volumes receiving more than 52 Gy (V70%, V80%, V90%, and V100%). The high dose values of a 2 ml volume (D2 ml) decreased by a mean 16% (SD = 11.4%; range: 3–42%). The influence of the balloon implantations was smaller for the very small volumes, and yielded a mean 4% (±6.4%; range: −1–27%) for D0.1 ml. With the exception of V50%, all volume reductions were significant. The same significance holds for the dose reduction of D2 ml and D0.1 ml.

The observed SD of ±20% seems to be relatively high – the explanation for that is apparently that the pre-implant and postimplant CT data showed differences in rectal shape and volumes in the same patient.

The reduction in rectal dose upon use of the ProSpace© balloon is highlighted when comparing the pre-implant and post-implant rectal DVHs. Corresponding anterior-posterior dose profiles are shown in the lower part of Fig. 1. The marked region indicates transposition of rectal wall volume from an area of steep dose gradients (Fig. 1, down left) into an area of lower dose plateau regions (Fig. 1 down right). Relevant influences on DVHs are presented in Fig. 2, where both pre-implant and post-implant rectal DVHs are co-plotted. A strong rectal dose fall-off expresses itself in 39–42 Gy range of the DVH, namely, at 50–60% of the prescribed dose. The DVHs also demonstrate that a much smaller rectal volume will be exposed to >42 Gy in the post-implant versus the pre-implant setup. Furthermore, DVHs show that the post-implant rectal wall volume receiving <39 Gy increases. A very small fraction of rectal volumes (2.0 and 0.1 ml) is exposed to the highest dose values.

Discussion

The use of an interstitial spacer is intended to reduce rectal dose and toxicity, where the benefit of enlarged prostate–rectum spaces