Radiotherapy and Oncology 100 (2011) 436–441

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Dosimetry

Application of a spacer gel to optimize three-dimensional conformal and intensity modulated radiotherapy for prostate cancer

Michael Pinkawa [a,*], Nuria Escobar Corral [a], Mariana Caffaro [a], Marc D. Piroth [a], Richard Holy [a], Victoria Djukic [a], Gundula Otto [a], Felix Schoth [b], Michael J. Eble [a]

[a] Department of Radiation Oncology; and [b] Department of Diagnostic and Interventional Radiology, RWTH Aachen University, Germany

ARTICLE INFO

Article history:
Received 6 April 2011
Received in revised form 6 September 2011
Accepted 10 September 2011
Available online 29 September 2011

Keywords:
Prostate neoplasm
Conformal radiotherapy
Intensity-modulated radiotherapy
Treatment planning
Toxicity
Spacer gel

ABSTRACT

Background and purpose: The aim was to evaluate the impact of a spacer gel on the dose distribution, applying three-dimensional conformal (3D CRT) and intensity modulated radiotherapy (IMRT) planning techniques.

Material and methods: The injection of a spacer gel (10 ml SpaceOAR™) was performed between the prostate and rectum under transrectal ultrasound guidance in 18 patients with prostate cancer. 3D CRT and IMRT treatment plans were compared based on CT before and after injection (78 Gy prescription dose).

Results: In contrast to the PTV and bladder, significant advantages ($p < 0.01$) resulted in respect of all analysed rectal dose values comparing pre spacer with post spacer plans for both techniques. Rectal NTCP (normal tissue complication probability) reached the lowest percentage after spacer injection irrespective of the technique, with a mean reduction of >50% for both IMRT and 3D CRT. Significantly ($p < 0.01$) higher D_{mean}, and V_{78} for the PTV were reached with IMRT vs. 3D CRT plans, with a smaller rectum V_{76} but larger rectum V_{50}.

Conclusions: The injection of a spacer gel between the prostate and anterior rectal wall is associated with considerably lower doses to the rectum and consequentially lower NTCP values irrespective of the radiotherapy technique.

As demonstrated in randomized trials, higher doses have consistently shown improved biochemical control rates for prostate cancer in studies applying three-dimensional conformal radiotherapy (3D CRT) techniques [1–4]. This benefit was associated with increased rectal toxicity [1,5], known to be the dose-limiting toxicity [6]. Rectal toxicity is associated with both the rectum volume within a particular dose level and the dose to a particular rectal volume [5–11].

Major technical advances that are increasingly adopted for external beam radiotherapy for localized prostate cancer are intensity-modulated radiotherapy (IMRT) [12,13] and image-guided radiotherapy (IGRT) [14]. In comparison to 3D CRT, dose conformality can be improved using the IMRT technique [15–17]. The volume of organs at risk can be especially reduced within the high dose region. The application of IGRT before each fraction for prostate localization is the crucial prerequisite for the reduction of safety margins to account for prostate motion. Posterior margins of 0.75–1.00 cm have been shown to be inadequate particularly for patients with initially larger rectum volumes – with decreased biochemical recurrence free survival rates [18]. As recently reported, 1.5 cm posterior margins are needed without IGRT, whereas 0.4 cm are sufficient with daily IGRT [14].

As the prostate is directly adjacent to the rectal wall, the anterior rectal wall cannot be spared completely from the high dose region irrespective of the treatment technique. The placement of a spacer gel between the prostate and anterior rectal wall is a new and very promising approach for radiotherapy of prostate cancer patients that might improve treatment tolerance and prevent serious long-term rectal toxicity [19–21].

The aim of this study was to compare dose distributions in 3D CRT and IMRT treatment plans before and after the injection of a spacer gel. Dose-volume histograms and equivalent uniform doses (EUD) were evaluated and normal tissue complication probability (NTCP) for the bladder and rectum compared.

Materials and methods

Hydrogel implant

The injection of a spacer gel (SpaceOAR™ System, Augmenix Inc., Waltham, MA) was performed in 18 patients with prostate cancer (PSA < 20 ng/ml, Gleason score $\leqslant 3+4$, mean patient age 71 years) after signing informed consent. The SpaceOAR™ System is a polyethylene glycol gel (PEG) that polymerizes in seconds,

* Corresponding author. Address: Department of Radiation Oncology, RWTH Aachen University, Pauwelsstrasse 30, 52057 Aachen, Germany.
E-mail address: MPinkawa@ukaachen.de (M. Pinkawa).

0167-8140/$ - see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.radonc.2011.09.005

creating a hydrogel space. A 18 gauge needle is advanced via the transperineal approach to the space between the prostate and the rectum under transrectal ultrasound (TRUS) guidance. Following hydrodissection with a saline solution and confirmation of proper needle location, the liquid hydrogel precursors are injected where they expand the perirectal space and then polymerize. The hydrogel amount was limited to 10 ml (15 ml for first patient, volume reduced to minimize potential toxicity). The water and PEG composition result in a high degree of tissue compatibility without local or systemic toxicity. It maintains space for approximately three months and is compression resistant (information from Augmenix Inc.). The hydrogel is absorbed in approximately six months with the degradation products cleared via renal filtration.

The distance between the prostate and anterior rectal wall was determined in TRUS before and after spacer gel injection in the sagittal view in a comparable plane at the base, apex and a medial plane.

Treatment planning

3D CRT (four-field technique with 0°, 90°, 180°, 270° gantry angles) [22] and IMRT (180°, 105°, 45°, 315°, 255° gantry angles) treatment plans were compared based on computed tomography (CT) in supine position with a slice thickness of 5 mm before (CT1) and within 3–5 days after (CT2) spacer injection to allow the evaluation of the actual advantage of the spacer for the dose to the rectum (Philips Pinnacle^3 Version 8.0 m treatment planning system). Additionally, T2 weighted magnetic resonance imaging scans were performed only after injection for image fusion with CT2 for an optimal visualization of soft tissues (specifically prostate and adjacent rectal wall) and clear delineation of the spacer gel (Fig. 1).

Patients were asked to have a full bladder for the planning CT scans. They were asked to empty their bowels, if possible. Enemas have not been used and CT scans have not been repeated in case of larger rectum volumes. Patient preparation was the same before and after spacer injection. In all scans prostate volume, planning target volume (PTV), bladder and rectum were delineated by identifying the external contours. As demonstrated in a prior study, histograms for the organ contours and the organ walls hardly differ [23]. The rectum enclosed the region from the anal canal to the rectosigmoid flexure. Clinical target volume (CTV) was defined as prostate with (ten patients) or without (eight patients with PSA < 10 ng/ml and Gleason score 6) the base of seminal vesicles (corresponding to the proximal 2–4 seminal vesicle slices). The same individual (M.P.) performed all contouring to exclude inter-observer variations. For the PTV, 8 mm lateral and anterior, 5 mm superior and inferior and 4 mm posterior margins were added.

To ensure comparable target coverage in all 3D CRT and IMRT plans, a total dose of 78 Gy was prescribed to the PTV in 2 Gy fractions with 15 MeV photons for an Elekta SLi linear accelerator (multileaf collimator with leaves projecting to 1 cm at isocenter), with a minimum of 74.1 Gy (95% of prescription dose) in 99% and a maximum of 83.4 Gy (107% of prescription dose) in 100% of the PTV.

The same objectives and constraints were used for inverse IMRT treatment planning before and after spacer gel injection, respectively, based on recently published RTOG (Radiation Therapy Oncology Group) recommendations [24,25]: maximum rectum V_{50} = 50%, maximum rectum V_{70} = 20% (constraint: 76 Gy maximum rectal dose); maximum bladder V_{55} = 50%, maximum bladder V_{70} = 30%. The direct machine parameter optimization (DMPO) algorithm was applied for inverse planning with a 2 cm^2 minimum segment area, five minimum segment monitor units and a maximum number of 70 segments. The dose grid size included the PTV, organs at risk and additionally 4–5 cm of tissue in the cranial and caudal directions.

Plan evaluation

Mean doses (D_{mean}) for the PTV, rectum and bladder, as well as the respective dose-volume histograms were evaluated and compared. Additionally, the EUD and NTCP were determined. The EUD is defined as the biologically equivalent dose that, if given uniformly, will lead to the same effect in the tumour volume or the normal tissues as the actual nonuniform dose distribution. The form

$$\mathrm{EUD} = \left(\frac{1}{N}\sum_i D_i^a\right)^{\frac{1}{a}}$$

was suggested for both tumours and normal tissues [26]. In this expression, "N" is the number of voxels in the anatomic structure of interest, "D_i" is the dose in the ith voxel, and "a" is the tumour or normal tissue-specific parameter that describes the dose-volume effect. In this analysis, $a = -10$ was taken for prostate cancer [26,27], $a = 2$ for the bladder and $a = 9$ for the rectum [28,29]. NTCP for rectum (severe proctitis, necrosis, fistula) and bladder (symptomatic bladder contracture and volume loss) [28,29] toxicity was computed applying the Lyman–Kutcher–Burman model with Emami parameters (rectum: $n = 0.12$, $m = 0.15$, median toxicity dose = 80 Gy; bladder:

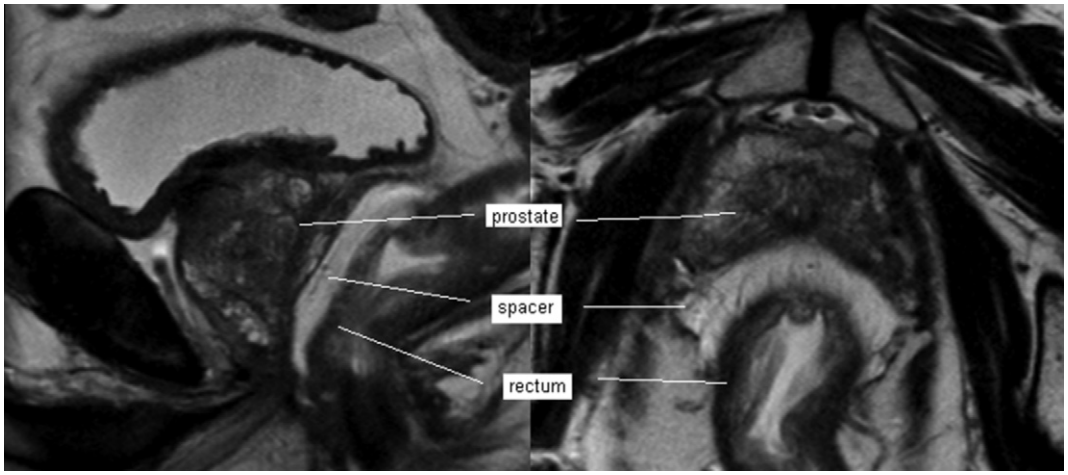

Fig. 1. Sagittal and axial T2 weighted magnetic resonance imaging scans with spacer between prostate and anterior rectal wall.