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Original article

Spacer stability and prostate position variability during radiotherapy for prostate cancer applying a hydrogel to protect the rectal wall

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ABSTRACT

Background and purpose: The aim was to evaluate the spacer dimensions and prostate position variability during the course of radiotherapy for prostate cancer.

Materials and methods: CT scans were performed in a group of 15 patients (G1) after the 10 ml injection of a hydrogel spacer (SpaceOAR™) and 30 patients without a spacer (G2) before the beginning of treatment (CT1) and in the last treatment week, 10–12 weeks following spacer implantation (CT2). Spacer dimensions and displacements were determined and prostate displacements compared.

Results: Mean volume of the hydrogel increased slightly (17%; $p < 0.01$), in 4 of 15 patients >2 cm^3. The average displacement of the hydrogel center of mass was 0.6 mm (87% ⩽ 2.2 mm), −0.6 mm (100% ⩽ 2.2 mm) and 1.4 mm (87% ⩽ 4.3 mm) in the *x*-, *y*- and *z*-axes (not significant). The average distance between prostate and anterior rectal wall before/at the end of radiotherapy was 1.6 cm/1.5 cm, 1.2 cm/1.3 cm and 1.0 cm/1.1 cm at the level of the base, middle and apex (G1). Prostate position variations were similar comparing G1 and G2, but significant systematic posterior displacements were only found in G2.

Conclusions: A stable distance between the prostate and anterior rectal wall results during the radiotherapy course after injection of the spacer before treatment planning. Larger posterior prostate displacements could be reduced.

External beam radiation (EBRT) is a well established curative treatment for prostate cancer [1–4]. Increasing doses are known to improve biochemical control [5], but rectal toxicity is dose-limiting [6]. Rectal bleeding rates have been frequently evaluated in the literature [7–9]. Additionally, symptoms like pain, incontinence, frequency and urgency can potentially reduce quality of life [10,11]. Major technical advances, as intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT), are increasingly adopted to allow accurate targeting with the best possible protection of normal tissues [12–17].

The application of a spacer to increase the distance between the prostate and the anterior rectal wall is an innovative technique helping to protect effectively the rectal wall [18–21]. Studies applying a hydrogel spacer have shown that the rectal wall volume inside the 70 Gy isodose can be decreased by >50% [20,21]. As rectal toxicity is known to be associated with both total dose to a specific volume and the volume inside a specific isodose [5–9,22], a considerable reduction of toxicity can be expected.

A consistent protection of the rectal wall throughout a fractionated treatment is essential for a successful outcome. An ideal spacer is required to remain at the injected position and maintain the distance between the prostate and the rectum that has been calculated in the initial treatment planning computed tomography (CT) scan.

The aim of this study was to analyze changes throughout the treatment by comparing planning CT scans with CT scans performed in the last week of treatment. Spacer dimensions, spacer displacements, prostate displacements and changes of the distance between the prostate and anterior rectal wall were determined. Additionally, a group of conventionally treated patients was used as a reference for the displacements and distances without a spacer (CT scans performed at the same intervals).

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 < 3 + 4) in our department after local ethics committee approval. These patients have been in-

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cluded in a multi-institutional phase II clinical trial (study sponsor: Augmenix Inc.). All patients have signed informed consent before being included in this study.

The SpaceOAR™ System is a polyethylene glycol gel (PEG) that polymerizes in seconds, creating a hydrogel space. In use, a 18 gauge needle is advanced via the transperineal approach to the space between the prostate and the rectum under transrectal ultrasound guidance. Following confirmation of proper needle location, the liquid hydrogel precursors are injected where they expand the perirectal space and then polymerize, or solidify without measurable temperature rise. The hydrogel amount was limited to 10 ml (15 ml for first patient). The hydrogel must maintain space for approximately three months during the complete duration of EBRT. It is absorbed in about six months with the degradation products cleared via renal filtration.

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) using a five-field intensity-modulated radiotherapy (IMRT) technique and daily ultrasound-based image-guided radiotherapy (IGRT).

Imaging

CT scans were performed before treatment (CT1) and in the last treatment week (CT2) in the group of patients after spacer gel injection (G1) to determine organ volumes and spacer volumes/dimensions, distances between the prostate and anterior rectal wall, as well as prostate (clinical target volume) displacements. CT scans were performed with a slice thickness of 5 mm from the anal canal up to the sacral promontory with a full bladder and a supine patient position. No bowel or intravenous contrast enhancement was used. The data were transferred to a commercially available planning system (Brainlab®, Heimstetten, Germany) for this analysis. In every CT scan the bladder, rectum, spacer gel, prostate and seminal vesicles were contoured by identifying the external contours. Rectum volume included the rectal wall and filling between the rectosigmoid flexure and the anal canal (flexure not included). All contours have been defined by the same observer (M.P.) to exclude inter-observer variations.

The discrimination of the spacer was possible in both CT scans for 15 patients who were finally included in this analysis. The reference group consisted of 30 patients (G2) who were treated conventionally (1.8 Gy fractions, 15 MeV four-field technique up to a dose of 70.2 Gy, without IGRT) without a spacer gel. CT scans have also been performed before the beginning of EBRT and in the last treatment week. Patients selected for the G2 subgroup have been consecutive patients with localized prostate cancer.

Evaluation of changes during treatment

Apart from bladder, rectum and spacer volumes, spacer dimensions were determined along the *x*-, *y*- and *z*-axes. Anterior–posterior (*x*-axis) and lateral spacer gel dimensions (*y*-axis) were measured at three different levels: base (third most superior slice), middle and apex (third most inferior prostate slice). Superior–inferior (*z*-axis) dimensions were determined in the mid-sagittal plane (sagittal reconstruction). Displacement of the center of mass (anterior, right and superior displacements are represented by positive numbers) and distances between prostate and anterior rectal wall (base, middle, apex) were determined after fusion of the prostate volumes.

Prostate center of mass and posterior prostate/seminal vesicle displacements were determined after fusion of the pelvic bones. Posterior displacements have been analyzed at three different representative levels in the mid-sagittal plane: the superior prostate/seminal vesicle (point P1), the level of the bladder neck (point P2), and the inferior prostate (point P3). The spatial difference of a specific point at different points in time in the same coordinate system after image fusion corresponded to a prostate/seminal vesicle displacement.

The explained definitions of the base, middle and apex, as well as points P1, P2 and P3 are demonstrated in Fig. 1.

Statistical analysis

Statistical analysis was performed using the SPSS 19.0 (SPSS, Chicago, IL), software. To determine differences between volumes at different points in time Wilcoxon's matched pairs test was used. Concerning volume changes of different patient groups, the Mann–Whitney *U*-test was applied. A homogeneity of variance test (Levene's test) and the chi-square test (for the frequency of a displacement within certain distances) served to compare displacements for the subgroups with or without the spacer gel. All *p*-values reported are two-sided, $p < 0.05$ is considered significant.

Results

Prostate, rectum and bladder volumes in both subgroups at the specific intervals are presented in Table 1. Mean bladder and rectum volumes decreased in both groups (G1: 49 cm^3 and 9 cm^3; G2: 69 cm^3 and 13 cm^3, statistically significant only in G2). Comparing the subgroups G1 and G2, the only significant difference resulted for the bladder volume in the last treatment week. It was significantly smaller in the G2 subgroup ($p < 0.01$). No significant differences were found comparing the percentages of patients with a neoadjuvant hormonal therapy, Gleason score < 6, T stage < 2a or PSA $\leqslant$ 10 ng/ml. In contrast to the G1 subgroup, three patients in the G2 group had a biopsy Gleason score > 3 + 4 and two patients a PSA > 20 ng/ml.

Hydrogel was identified in all levels (base, middle, apex) before treatment and in the last treatment week for patients with prostate volumes up to 69 cm^3. No spacer was seen at the level of the base only for the patients with larger prostates of at least 70 cm^3 ($p < 0.01$ in chi-square test).

The average displacement of the spacer center of mass was 0.6 mm (87% $\leqslant$ 2.2 mm), −0.6 mm (100% $\leqslant$ 2.2 mm) and 1.4 mm

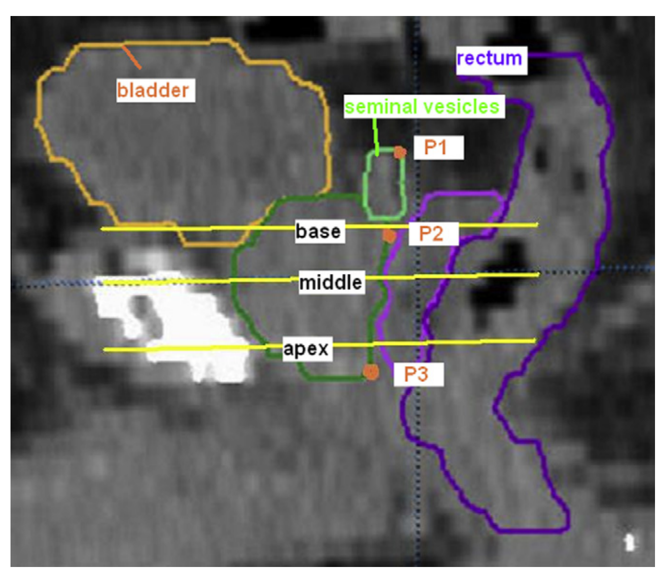

Fig. 1. Sagittal CT reconstruction demonstrating the definition of the levels of the base, middle and apex, as well as the points P1 (superior prostate/seminal vesicle), P2 (level of the bladder neck) and P3 (inferior prostate).

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