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Original article

Comparison of two different rectal spacers in prostate cancer external beam radiotherapy in terms of rectal sparing and volume consistency

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ABSTRACT

Background and purpose: In external beam radiation (EBRT) of the prostate, the rectum is the dose-limiting organ at risk, and sparing of the anterior rectal wall is a prerequisite for safe delivery of doses beyond 70 Gy. Spatial sparing of the rectum can be achieved by introducing a spacer material into the retroprostatic space, thus separating the anterior rectal wall from the PTV.

Materials and methods: Two spacer technologies, Spacer OAR, a polyethylene glycol gel and ProSpace, a saline inflated balloon, were compared in terms of spacer volume, stability, and dose reduction to the anterior rectum wall in 78 patients.

Results: Both spacer systems significantly reduced the rectum surface encompassed by the 95% isodose (gel: −35%, $p < 0.01$; balloon −63.4%, $p < 0.001$) compared to a control group. The balloon spacer was superior in reducing rectum dose (−27.7%, $p = 0.034$), but exhibited an average volume loss of >50% during the full course of treatment of 37–40 fractions, while the volume of gel spacers remained fairly constant.

Conclusions: In choosing between the two spacer technologies, the advantageous dose reduction of the balloon needs to be weighed up against the better volume consistency of the gel spacer with respect to the duration of hypofractionated vs normofractionated regimens.

In the primary radiation treatment of the prostate, dose escalation is known to enhance biochemical progression free survival. However, due to the spatial proximity of the prostate to the anterior rectal wall, rectum toxicity limits the maximum dose which can be safely delivered to the PTV while maintaining a low level of toxicity. Rectal sparing technologies are therefore a prerequisite for dose-escalation to the prostate.

The rapid technological advancements in the last decade with evolving technologies such as IGRT and IMRT have allowed to increase the dose to roughly 78 Gy while maintaining an acceptable toxicity profile [1–3].

However, further dose escalation and/or hypofractionation are supposed to enhance biochemical free survival. Since a rectal dose beyond 70 Gy is a predictor for rectal toxicity [4], the rectum remains to be the primary organ at risk (OAR) [5] in EBRT, warranting research into more efficient rectum sparing strategies.

In addition to advanced treatment and image guidance techniques provided by to date's radiation treatment devices, a 'geometric' rectum sparing can be achieved simply by enlarging the space between the prostate and anterior rectal wall by injecting a spacer material into the retroprostatic space [6–8]. This has been shown to effectively reduce rectum doses in retrospective planning studies [9].

Two main strategies in spacer technology are in the market today. While the basic principle remains the same – to widen the retroprostatic space – different filling materials are promoted to accomplish separation of prostate and rectum (reviewed in [10]).

SpaceOAR™ System (Augmenix Inc., Waltham, MA) is a polyethylene glycol gel (PEG) that polymerizes in seconds creating a hydrogel space. Following hydrodissection with a saline solution and confirmation of proper needle location, the two liquid hydrogel precursors are injected where they expand the perirectal space and then polymerize. The water and PEG composition result in a

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high degree of tissue compatibility without local or systemic toxicity. It maintains space for approximately three months and is compression resistant The hydrogel should be absorbed in approximately six months, with the degradation products cleared via renal filtration.

ProSpace™ (BioProtect Inc., Kfar-Saba, Israel) Balloon is composed of biodegradable polymers. Once the balloon is in situ, it is inflated with sterile saline to reach its final configuration [11]. The balloon remains inflated during the entire treatment period and allegedly biodegrades in the body within 3–6 months.

In the present study, we have prospectively compared the two spacer systems in terms of volume consistency, degradability and their ability to reduce the dose to the rectum as determined by dose surface histograms.

Materials and methods

Patients characteristics

78 patients eligible for primary radiation of the prostate in the period from 05/2012 until 07/2013 were included in our study, of which 30 received a gel spacer and 29 received a balloon spacer, respectively. The design of this prospective observational study was approved by the local ethics committee. The patients' allocation to the respective spacer group was consecutive, also in dependency of the availability of the device. All patients gave informed consent.

During this recruitment period, 19 Patients not eligible for spacer application due to internistic contraindications such as compulsory anticoagulation therapy or severe co-morbidities preventing them to have anesthesia served as control group.

Patients with hip transplants were excluded from our study. In patients who received pelvic lymph node irradiation, dose contribution of the pelvic fields was not accounted for in our analysis.

For volume dynamics assessment of the balloonspacer, a separate set of 18 consecutive patients who had received a balloonspacer were analyzed as described below.

Injection procedure

The application of both spacers was performed by urologists in a short general anesthesia according to the manufacturer's protocol. The type of spacer was selected in a random fashion at physician's discretion. Balloons were filled with either NaCl 0.9% or a mixture of NaCl and contrast agent (Visipaque 270 mg J/ml, GE Healthcare) at a ratio of 1:4. In the same session, four gold marker fiducials were inserted into the prostate under rectal ultrasound guidance.

Planning

Planning CT and MR were performed the same day and fused based on the implanted goldfiducials. For the planning MR, a turbo field echo sequence was used, optimized to visualize metal artefacts, anatomical (prostate) and liquid (spacer) structures. Prior to image acquisition patients were instructed to have a full bladder and empty their bowels. Routine use of mild laxatives was recommended.

Contouring of the prostate CTV was performed on the MR in transversal plane, aided by saggital and coronary plane contours when needed. In addition, the rectum, bladder, femoral heads and the spacer have been contoured in the transversal plane of the co-registered planning MR.

The PTV was CTV+ 6 mm in sup/inf and 5 mm in all other directions according to a standardized institutional protocol which was reported previously [12]. Total dose to the PTV was 75.85 Gy in daily fractional doses of 1.85 Gy prescribed to the 95% isodose using multisegmental 7-field step-and shoot IMRT. Dose–volume constraints for rectum and bladder were V70 < 20% and V70 < 35%, respectively, as recommended by QUANTEC. Interfractional IGRT to the marker fiducials was performed daily, followed by aperture based portal corrections in case of translatory and rotatory deviations [13].

Spacer volume assessment

In order to assess spacer volume, spacer consistency and degradation of both spacers MR imaging was performed at the start of RT, 3 weeks into RT (sagittal views) and 6 months after completion of radiotherapy in each group.

To visualize the balloon spacer in kilovolt X-ray images, contrast media was added to the saline used for filling the balloon (ratio 1:4). This allowed using the daily orthogonal kV images at 140° and 230° which are routinely assessed for gold fiducial registration and correction [13] to estimate spacer volumes by measuring the diameters of the balloon. Volumes were calculated using the volume formula for an ellipsoid cylinder:

$$V = r1 * r2 * h * \pi$$

kV images were obtained using the cone beam CT panel. kV-images as well as cone-beam datasets were exported into our in-house developed software *open radART* where image acquisition and analysis were carried out [14].

Rectal dose estimation

To transfer the dose distribution onto the surface of the rectum a three dimensional dose matrix was generated with *Oncentra Masterplan 4.1* (Nucletron, Columbia, USA). The dose values for each point of the rectum structure were calculated in *open radART* by trilinear interpolation of the corresponding values in the dose matrix. Based on these values, surface doses were generated by averaging point doses of three vertices of a triangle to obtain a color coded three dimensional dose-surface mesh of the structure (see Fig. 3) and dose surface histograms (DSH).

Toxicity assessment

Acute toxicity was scored using common toxicity criteria of adverse events (CTCAE vers.4) at the end of RT and 3 months after its completion. In addition, all patients were subjected to rectoscopy and scored using the Vienna rectoscopy score [15] at the same intervals.

Statistical analysis

Statistical differences of volume reduction between groups were tested using a single-sided paired Student's t-test choosing a significance level of $p = 0.01$. Statistical differences of toxicities were carried out using Chi-squared test (Brandt-Snedecor) for CTC scoring and Kruskal–Wallis test for VRS scoring at a significance level of $p = 0.05$. Data analysis was carried out using MS Office Excel 2007, SP3.

Results

Spacer volume and stability

Demarcation and visibility of spacers were excellent in T2 weighted MR images yielding a strong hyperintense signal. In the planning CT, however, both spacers imposed hypodense but were difficult to detect. In comparison, the balloon spacer demarked

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