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Original article

Optimal image guided radiation therapy strategy for organs at risk sparing in radiotherapy of the prostate including pelvic lymph nodes

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ABSTRACT

Background and purpose: Purpose of this study was to quantify the OAR dose for different position correction strategies, and to determine which strategy is most optimal for treating patients on the prostate and pelvic lymph nodes.

Materials and methods: For 30 patients, four different treatment plans were made reflecting different correction strategies: online correction on bony anatomy; offline correction on bony anatomy; online correction on the prostate fiducials; using 1 cm margins around both CTVs. The dose to the PTVs and OARs was quantified and a pairwise statistical analysis was performed.

Results: No statistically significant differences were observed in the dose to the PTVs, ensuring that any OAR sparing is not caused by differences in PTV coverage. Dose to the rectum and anal canal was lowest when applying an online correction on prostate fiducials, although the total PTV volume was higher. Dose to the small bowel bag and femoral heads was slightly higher compared to online correction on bony structures, but well within clinically acceptable limits.

Conclusion: Although the total PTV volume is higher when applying an online correction on the prostate, this strategy leads to the most optimal sparing of relevant OARs, at the cost of a slightly higher dose to the femoral heads and small bowel bag.

The treatment for lymph node positive prostate cancer, often consists of radiotherapy combined with Androgen Deprivation Therapy (ADT). The target volume includes the pelvic lymph nodes (PLN), prostate and seminal vesicles (SV).

Ensuring that the target volume receives the planned dose can be a challenge due to the fact that the PLN and prostate can move with respect to each other due to changes in rectal filling [1–3]. Different correction strategies can be chosen to ensure either correct positioning of the prostate or the pelvic nodes, resulting in different CTV-PTV margins for both target volumes. Larger margins and treatment volumes results in higher OAR dose and higher toxicity [4,5]. In a previous study, the required setup margins for different correction strategies were calculated based on pre-treatment CBCT images of 20 patients [6]. Calculation was based on the Van Herk formula [7,8]. This study showed that when a patient setup correction is performed on a match of the bony anatomy, larger margins are required for the prostate to account for baseline shifts with respect to the PLN. These baseline shifts can be accounted for by applying an online setup correction on the prostate, but this will lead to larger PTV margins around the PLN. In a similar study, Kershaw et al. recently quantified the prostate motion in relation to the PLN and SV to define the setup margins [9]. They concluded that neither a prostate or bone registration is optimal, and that further research is required to determine which strategy results in the lowest OAR doses. A number of studies have investigated the coverage of the target volumes for a given PTV margin, but did not report on OAR dose [1,10,11]. Hsu et al., Rossi et al. and Eminowicz et al. investigated different correction strategies, but also focused on target coverage. A dosimetric analysis of these different correction strategies quantifying the OAR dose has not been published yet. The purpose of this study was to determine which setup correction strategy leads to the lowest OAR dose, and consequently, the lowest toxicity.

Materials and methods

Patients

30 consecutive patients with lymph node positive prostate cancer were included retrospectively. All patients received a lymph node dissection and were eligible for radiotherapy when a maximum of 3 micro-metastases or 2 macro-metastases in the PLN were found.

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Imaging and delineation

All patients received a planning CT scan (Philips Healthcare, Best, The Netherlands) in supine position, with a slice thickness of 3 mm. Patients were immobilised using a knee and ankle support. To reduce chance of systematic errors due to prostate shifts on the planning CT, patients were instructed to empty their bladder and defecate one hour before scanning and each treatment fraction and after that to drink 500 mL of water. If a large rectal filling was observed, the planning CT was repeated after the defecation. The CT scan was imported in the RayStation TPS (version 5.0.2.35, Raysearch Laboratories, Stockholm, Sweden). The CTV of the prostate (CTV_p) consists of the entire prostate gland and the SV were included in this CTV. Delineation of the CTV of the PLN (CTV_{PLN}) was based on consensus recommendations from the RTOG [12]. Bladder, small bowel bag (SBB), femoral heads, rectum and anal canal were delineated. The SBB was defined as the peritoneal space in which the small bowel can move. The rectum was contoured from the ischial tuberosities to the rectosigmoid junction and the anal canal was defined from anus to the musculus puborectalis. Femoral heads were defined up to and including the trochanter minor.

CTV-PTV margins

The CTV-PTV margins used in this study are shown in Table 1 and depend on the position correction strategy:

A. online correction on bony anatomy;
B. offline Shrinking Action Level (SAL) correction protocol on bony anatomy ($n = 3$, $\alpha = 10$) [13];
C. online correction on the prostate fiducials;
D. CTV-PTV margin of 1 cm around both CTV_p and CTV_{PLN}

The setup margins were determined in a previous study, and account for translational patient setup errors as well as baseline shifts between the prostate and PLN [6]. Depending on the correction strategy, this results in either larger margins to the prostate or the PLN to account for these baseline shifts. An additional margin was included to account for rotation and delineation uncertainties. For a bony anatomy match, both an online and offline correction was included as the positional errors in the pelvis are usually small, however an offline strategy will lead to a reduced online workload and a decreased imaging frequency. The CTVs and PTVs for all evaluated strategies are visualised in Fig. 1.

Treatment planning

For each patient, one treatment plan was made for each of the four PTV margins reflecting the different correction strategies. All plans were created for an Elekta linac with an Agility MLC (Elekta, Crawley, UK) using a single VMAT beam with a full gantry rotation and a beam energy of 10 MV. The isocentre was placed in the geometric centre of the total PTV volume ($PTV_p + PTV_{PLN}$). The prescribed dose was 50.4 Gy to PTV_{PLN} and 67.2 Gy to PTV_p in 28 fractions using a simultaneous integrated boost (SIB) technique.

A standard set of objectives was used for optimising the treatment plans. The objectives were adapted for the individual patient to achieve an optimal treatment plan. Dose criteria that should minimally be achieved for both the PTVs and OARs are summarised in Table 2 [5]. For the PTVs, 95% of the PTV volume must be covered by at least 95% of the prescription dose ($V_{95\%} \geq 95\%$). Care was taken that the PTV coverage was identical for all plans. All generated treatment plans were reviewed by the same expert medical physicist and radiation oncologist. Priority was given to reducing the rectum and anal canal dose, followed by the SBB, as this is clinically most relevant. Sparing of the femoral heads and bladder was considered to be less important.

Data collection and analysis

The dose criteria given in Table 2 were evaluated. In addition, the absolute volumes of the different PTVs (PTV_p, PTV_{PLN} and PTV_{total}), the maximum and the mean dose to the PTVs, rectum and bladder were evaluated. All parameters were automatically retrieved using the scripting functionality.

For data analysis, SPSS was used. A Shapiro–Wilk test was performed to check if the data were normally distributed. If data were normally distributed, the mean and standard deviation were calculated. Otherwise the median including minimum and maximum value was determined. A pairwise statistical analysis was performed on the data to see if a statistically significant difference in OAR dose could be observed between the different strategies, using a repeated measurements ANOVA test or a Friedman test, depending on the normality of the data. When a Friedman test was used and a significant difference was obtained, a Wilcoxon Signed Rank test was applied to point out between which correction strategies the dose was statistically significant different. A Bonferroni correction was applied to correct for multiple testing.

Results

Four treatment plans with margins reflecting different correction strategies were optimised. Patient characteristics are summarised in Table 3. The mean or median values of the evaluated parameters obtained from the treatment plans and the results of the pairwise statistical analysis are summarised in Table 4.

Differences in the average PTV volumes are statistically significant between the four strategies ($p < 0.001$). An online correction on the prostate results in the smallest PTV_p volume (average 129 cc), while an offline correction on the bony anatomy results in the largest PTV_p volume (average 192 cc). The PTV_{PLN} volume is smallest for online correction on bony anatomy and largest for online correction on prostate fiducials (average 606 cc versus 940 cc). The average volume of PTV_{total} varied between 762 cc when performing an online correction on bony anatomy and 1108 cc when using the standard margin of 1 cm. No statistically significant differences were observed in the coverage and mean dose to the PTVs, ensuring that any OAR sparing is not caused by differences in PTV dose.

Table 1
CTV-PTV margins for different correction strategies.

Strategy	Prostate margins (cm)			Lymph node margins (cm)		
	LR	SI	AP	LR	SI	AP
A	0.6	0.9	1.1	0.5	0.5	0.7
B	0.8	1.1	1.2	0.8	0.7	0.9
C	0.5, with 0.8 to apex prostate and around SV [2]			0.6	1.0	1.2
D	1.0	1.0	1.0	1.0	1.0	1.0

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