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Adaptive radiotherapy

Evaluation of delivered dose for a clinical daily adaptive plan selection strategy for bladder cancer radiotherapy

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ABSTRACT

Purpose: To account for variable bladder size during bladder cancer radiotherapy, a daily plan selection strategy was implemented. The aim of this study was to calculate the actually delivered dose using an adaptive strategy, compared to a non-adaptive approach.
Material and methods: Ten patients were treated to the bladder and lymph nodes with an adaptive full bladder strategy. Interpolated delineations of bladder and tumor on a full and empty bladder CT scan resulted in five PTVs for which VMAT plans were created. Daily cone beam CT (CBCT) scans were used for plan selection. Bowel, rectum and target volumes were delineated on these CBCTs, and delivered dose for these was calculated using both the adaptive plan, and a non-adaptive plan.
Results: Target coverage for lymph nodes improved using an adaptive strategy. The full bladder strategy spared the healthy part of the bladder from a high dose. Average bowel cavity V30Gy and V40Gy significantly reduced with 60 and 69 ml, respectively ($p < 0.01$). Other parameters for bowel and rectum remained unchanged.
Conclusions: Daily plan selection compared to a non-adaptive strategy yielded similar bladder coverage and improved coverage for lymph nodes, with a significant reduction in bowel cavity V30Gy and V40Gy only, while other sparing was limited.
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As a bladder-conserving alternative to cystectomy, external beam radiotherapy provides an effective treatment option for muscle-invasive bladder cancer [1]. For focal tumors, combining whole bladder irradiation with a tumor boost and chemotherapy, local control rates of 67% were achieved [2]. In our department, when such a tumor boost is given, patients are treated with a full bladder which is expected to spare more of the healthy bladder from the boost dose [3]. To compensate for variations between fractions in bladder filling, size and position, large target volume margins are required to ensure target coverage, even with the use of a strict drinking protocol [4,5]. These margins result in a high dose to the organs at risk (OARs).

The introduction of pre-treatment cone beam CT (CBCT) for daily patient set-up, has enabled soft-tissue visualization during the treatment course. This allows adapting the radiation delivery according to anatomical changes during the treatment course, which is known as adaptive radiotherapy (ART). Multiple ART strategies for bladder cancer have been described, based on daily plan selection, which comprises the creation of multiple treatment plans for different bladder volumes, and daily selection of the plan best fitting the bladder volume as seen on the CBCT [6–12]. To obtain target volumes for the multiple plans, variable target margins, multiple CT-scans or the CBCT-scans acquired during the first week can be used [6,8–12]. Interpolating a registration between a full and an empty bladder delineation to generate intermediate bladder volumes, for the creation of multiple treatment plans, was also described previously [7]. This method was implemented in 2013 at our institute.

The dosimetric analyses for these adaptive strategies imply that target coverage is maintained or improved, while reducing dose to the organs at risk [6–12]. These dosimetric analyses are usually performed by summating the weighted dose calculations of the used plans during treatment. In this case, the changed anatomy of the organs of interest, i.e. bladder, rectum and bowel, are not taken into account. To understand the value of an adaptive strategy and investigate the areas of improvement, dose delivery to the target and separate OARs should be evaluated. Even though this has been investigated earlier, either for specific organs [10,11], or for the normal tissue as a whole [13], it is currently unknown whether OAR sparing is also seen in patients treated with a full bladder including pelvic lymph nodes in the target, and whether target

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coverage of bladder and lymph nodes is not compromised using an adaptive strategy, taking daily anatomical changes into account.

The aim of this study was therefore to calculate the actually delivered dose to the target and OARs when patients are irradiated with a full bladder, using a daily plan selection strategy for bladder cancer radiotherapy, and to compare this to the dose that would have been delivered with a non-adaptive approach.

Material/methods

Patients and imaging

Between March 2013 and September 2014, 11 of the 16 consecutive patients with muscle-invasive bladder cancer were treated with an adaptive strategy, of which 10 were included in this study. Patients with multiple tumors or carcinoma in situ were excluded, as well as patients with two metal hip prostheses. Patient characteristics are presented in Table 1. Patients were treated in 20 fractions to the bladder and pelvic lymph nodes, combined with a simultaneously integrated boost to the tumor

Prior to treatment, two planning CT scans with a full and empty bladder were acquired in supine position. Patients were eligible for our plan selection approach if the full bladder volume on the planning CT scan was at least twice the empty bladder volume. On both scans, the radiation oncologist contoured the bladder and GTV, which was aided by cystoscopically placed fiducial markers. On the full bladder scan, the draining pelvic lymph nodes, rectum, bowel cavity and both femur heads were delineated.

Creation of library of structures

The bladder and GTV structures as delineated on the full bladder CT were registered to the bladder and GTV structures from the empty bladder CT, using a structure-based deformable registration algorithm as implemented in Erasmus RTStudio (part of Erasmus MatterhornRT, software platform for radiotherapy research and advanced treatment). This algorithm was described previously [16]. In short, the algorithm found corresponding points between two structures. By connecting these pairs of corresponding points, deformation vectors were obtained. Linear scaling of these deformation vectors resulted in a library of structures. To represent different filling states, the following scale factors were used: 0%, 33%, 67%, 100% and 133%, with 0% and 100% structures corresponding to the empty and full bladder, respectively.

Treatment planning and delivery

The full bladder CT scan and bladder and GTV structures were imported in Oncentra treatment planning system (version 4.3, Elekta, Stockholm, Sweden). For each filling state two planning target volume (PTV) structures were created: $PTV_{elective}$, consisting of the lymph nodes and one of the five bladder volumes, with a uniform margin of 7 mm, and $PTV_{boost,}$ consisting of one of the five GTV volumes and a 9 mm uniform margin (Fig. 1). The margins are applied to account for residual errors, such as shape changes, delineation errors and intrafraction motion. The PTV_{boost} margin is larger than the $PTV_{elective}$ margin, due to larger delineation uncertainties for the tumor. Five dual arc VMAT plans were created on the full bladder CT, with a separate optimization for each combination of PTVs. Standard planning objectives were used to aim for a homogeneous fractional dose of 2 Gy in $PTV_{elective}$ (i.e. 40 Gy in 20 fractions), and 2.75 or 3 Gy in PTV_{boost} (i.e. 55–60 Gy in 20 fractions), while keeping dose to the OARs as low as possible. A prescription of 3 Gy to PTV_{boost} is preferable, but for ventrally and caudally located tumors 2.75 Gy is chosen, to spare the bowel cavity from a 3 Gy fraction dose.

Before each fraction, patients were asked to drink 0.5 liter of water 1.5 h prior to treatment, and refrain from voiding. A CBCT scan was acquired daily, and registered to the pelvic bony anatomy (XVI, Elekta). Subsequently, the five bladder contours were projected on the CBCT scan, and the smallest bladder contour encompassing the entire bladder on CBCT was selected. The plan corresponding to the chosen bladder contour was selected for treatment. The corresponding $PTV_{elective}$ and PTV_{boost} contours were projected on the CBCT. If needed, these contours were shifted manually, until maximum tumor coverage was obtained, based on the location of the tumor markers relative to PTV_{boost}, ensuring that the bladder was still located inside $PTV_{elective}$ (summarized data regarding these shifts in Supplementary Table 1). The resulting setup correction was applied before starting treatment. Irradiation time per fraction was 140–160 s.

Simulation of non-adaptive procedure

To compare the dose delivered with the daily plan selection protocol to a non-adaptive approach, a non-adaptive $PTV_{elective}$ was created. This consisted of the full bladder and lymph node delineations, with 13 mm margin ventrally and cranially to the bladder, and 7 mm margin in all other directions. To obtain a

Table 1
Patient characteristics.

Patient	Age	Sex	Tumor stage	Pre-RT treatment	Chemotherapy	GTV location	Markers	ART
1	91	M	cT2N0M0	TURT	None	Dorsal wall	Lipiodol	No
2	84	M	cT3N0M0	Partial bladder resection	None	Ventral wall and dome	Surgical clips	Yes
3	71	M	T4bN0M0	TURT	Cisplatin	Right wall	Lipiodol	Yes
4	66	M	T2N0M0	TURT	Cisplatin	Left wall and dome	Lipiodol	Yes
5	84	M	T2N0–1M0	Unknown	Cisplatin	Right wall	Lipiodol	No
6	79	M	T2–3N0M0	TURT	Cisplatin	Right wall	Lipiodol	Yes
7	66	M	T2–3N0M0	TURT	Cisplatin	Dorsal wall, dome	None	No
8	71	M	T2N0M0	TURT	None	Dome	None	Yes
9	79	F	T2N0M0	TURT	Cisplatin	Lower wall	Lipiodol	Yes
10	76	M	T2N0M0	TURT	None	Prostatic urethra	Gold markers	Yes
11	84	M	T4aN0M0	TURT	Cisplatin	Prostatic urethra	Hydrogel	Yes
12	86	M	cT3N0M0	TURT	None	Right and dorsal wall	Hydrogel	Yes
13	84	M	T2N0M0	TURT	Carboplatin	Prostatic urethra	Gold markers	No
14	81	M	T2N0M0	TURT	Cisplatin	Right wall	Hydrogel	No
15	81	M	T2N0M0	TURT	Carboplatin	Right and dorsal wall	Hydrogel	Yes
16	84	M	T2N0M0	TURT	None	Left wall	Hydrogel	Yes

TURT = transurethral resection of the tumor. Chemotherapy regimen: weekly administration of cisplatin or carboplatin. Lipiodol and hydrogel: fluid contrast agents, injected during cystoscopy procedure prior to planning CT-scans, to indicate border of the tumor [14,15]. Patient 12 was excluded from analysis, since quality of CBCT scans was not sufficient.