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Adaptive radiotherapy

A comparison between two clinically applied plan library strategies in adaptive radiotherapy of bladder cancer

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ABSTRACT

Background and purpose: The predominant approach to clinically applied adaptive radiotherapy (ART) for bladder cancer is daily selection of treatment plans from a plan library. In this study we have compared two clinical strategies for creating multiple planning target volumes (PTV) for ART of bladder cancer.
Material and methods: Online ART delivering 60 Gy in 30 fractions to the whole bladder was simulated for ten patients using two methods of creating plan libraries. In the RepeatCT method four planning CT scans were acquired at 15-min intervals, generating four CTVs with different bladder volumes. In the RepeatCBCT method one planning CT and four daily cone-beam CT images were combined using Boolean operators to form three composite CTVs. Plan selection rates and PTV volumes were evaluated, with the selected volumes averaged across 30 treatment fractions (PTV_{mean}).
Results: The PTV_{mean} volume was on average 80 cm^3 smaller ($p < 0.001$) in the RepeatCT method than in the RepeatCBCT method. Compared to the non-adaptive treatment, the PTV_{mean} was reduced by 46% (range 33–53%, RepeatCT) and 36% (range 27–44%, RepeatCBCT).
Conclusions: Both methods reduced the PTV_{mean} volume compared to the non-adaptive approach, but the reduction was larger using the strategy with repeat planning CT imaging. However, the strategy with combined CT and repeat CBCT imaging produced a more adequate range of PTV volumes.

The concept of adaptive radiotherapy (ART) was formalized by Yan et al. [1] as a radiotherapy process using systematic feedback of measurements to modify the treatment plan during the course of treatment. ART has been an active field of research during the last decade, and it is now being implemented in clinics. As pelvic anatomy is prone to constant physiological changes, the pelvic tumour sites, such as the urinary bladder, are particularly suitable for ART [2].

In urinary bladder cancer the predominant ART strategy that is currently being applied clinically is treatment plan selection from a library of pre-calculated treatment plans, guided by daily cone-beam CT (CBCT) imaging [3–8]. Essentially two kinds of approaches have been introduced on how to measure the deformations of the bladder, in order to define the adaptive target volumes for bladder cancer in a treatment plan library-based method. The first approach aims at capturing the whole range of different volumes from empty to full bladder by multiple successive planning CT (pCT) scans [5–7]. In the second approach the deformation and the positional changes of the empty bladder are monitored using the CBCT images acquired during the first treatment fractions [4,8]. The logic behind the two approaches is different, as the first aims at providing a solution to the varying amount of bladder filling while also allowing some deformation, whereas the second takes into account the daily variations in the shape and position of the empty bladder, caused by filling of the rectum or bowel loops adjacent to the bladder. Hence, a different range of adaptive PTV volumes is produced using these strategies, potentially causing different effectiveness in improving conformity over treatment.

In this paper we therefore compare two different methods of generating a treatment plan library for bladder ART. These methods are currently in clinical use in our institutions [8,9] as well as elsewhere. The primary aim of this study was to investigate if one of the proposed methods was superior in producing an adequate range of target volumes while sparing normal tissues as much as possible. For this purpose, we created two hypothetical hybrid workflows combining features from the workflows of our institutions.

Materials and methods

Ten patients (8 male and 2 female) that received ART for muscle-invasive bladder cancer in the Helsinki University Central

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Hospital (HUCH) during 2010–2014 were included in the analysis. According to the ART protocol in HUCH, four pCT scans were acquired using 15-min intervals after emptying the bladder and drinking 800 ml of water. All patients included in the study received ART in at least 30 fractions using daily CBCT imaging. The patients were instructed to empty their bladder before treatment.

Creation of the two treatment plan libraries

The four pCT and 30 CBCT images of each of the ten patients were used in this retrospective study to simulate online ART delivering 60 Gy in 30 fractions to the whole bladder. The simulation was repeated with two treatment plan libraries using different methods of creating the adaptive bladder PTVs, the RepeatCT method and the RepeatCBCT method. In this simulation we used the same CTV to PTV margins and pCT to CBCT registration strategy for both approaches, to solely enable a comparison of the different PTV creation methods (Table 1).

The RepeatCT method was based on repeat planning CTs, i.e. four successive scans acquired at 15-min intervals while the bladder was filling. The bladder was contoured in each CT, generating four CTVs with different bladder volumes. In the RepeatCBCT method one planning CT with an empty bladder and four CBCT images acquired during the first week of treatment were contoured, and the bladder contours were combined using Boolean operators to form two adaptive composite CTVs and one non-adaptive CTV. A 3-mm margin was added around the two adaptive CTVs to form plan selection volumes (PSV), followed by 5-mm intrafractional margin expansion to create PTV_{small} and PTV_{medium}. PTV_{large} was based on the empty bladder contoured in the pCT and expanded with population-based margins of 20 mm superior/anterior, 15 mm posterior and 10 mm in the other directions, followed by set-up margins of 8 mm superior/inferior and 5 mm in the other directions [8]. On the first week of treatment with the simulated RepeatCBCT method PTV_{large} was used on every fraction. In order to compare the two strategies of constructing the plan libraries, the same adaptive margins of 3 mm (PSV margin) and 5 mm (intrafractional margin) were also applied in the RepeatCT workflow to generate the four PSV and PTV contours (PTV A–D), respectively.

The treatment simulation and statistics

The bladder was contoured in the four pCT and 30 CBCT images per patient by a single observer. The PSV and PTV volumes for the RepeatCT and RepeatCBCT plan libraries were formed based on these contours. The simulated treatment plan selections were made by using manual bladder matching between the pCT and the CBCT images (MiM Software Inc., version 6.1, Cleveland, OH, USA). In this method the registration was manually adjusted to fit the daily bladder contour in the CBCT image completely inside the smallest possible PSV contour. Only translational shifts were applied, rotations were not corrected. The plan selection process started by fitting the bladder contoured in the CBCT image inside the smallest PSV contour. If the bladder expanded outside the PSV, the next larger PSV was evaluated. If the second largest PSV couldn't accommodate the bladder, the largest PTV was chosen, and it was recorded if the bladder was completely encompassed by the largest PTV. The plan selection rates were recorded and the volumes of the selected PTVs were evaluated. The mean selected PTV volume was calculated as an average of all 30 fractions. The daily bladder volumes (CTV_{daily}) were also subtracted from the selected PTV volumes to represent a surrogate measure for normal tissue irradiation. In addition, a comparison of both methods to a non-adaptive method was performed by using PTV_{large} of RepeatCBCT method as the non-adaptive PTV in all 30 fractions. In the comparison of the mean selected PTV volumes paired *t*-test (two-tailed) was used to test the statistical significance.

Results

The mean PTV volumes A–D generated by the RepeatCT method had a range of 333–496 cm^3 between the smallest and the largest PTV, whereas the RepeatCBCT method gave a wider range of 365–767 cm^3 between the mean values of PTV_{small} and PTV_{large} (Fig. 1). Due to the large anisotropic CTV to PTV margin, the volume of PTV_{large} in the RepeatCBCT library was consistently larger than the largest PTV (D) in the RepeatCT library.

In the RepeatCBCT method the different adaptive treatment plans were more evenly used than the plans in the RepeatCT method (Fig. 2). In the RepeatCBCT method the small, medium and large PTVs were selected in 51%, 26% and 23% of the simulated fractions on average, respectively. The selection frequencies for PTVs A, B, C and D in the RepeatCT method were on average 28%, 11%, 17% and 44%, respectively. For two patients only the two largest PTVs (C and D) were selected from the RepeatCT library, and there were two single instances of the largest PTV not fully encompassing the bladder (i.e. 0.7% of all treatment fractions).

The mean volume of the selected PTVs, averaged across all 30 treatment fractions, was 80 cm^3 smaller (range 39–155 cm^3, $p < 0.001$) in the RepeatCT method (414 ± 80 cm^3, mean ± 1SD)

Table 1
The differences between the plan creation strategies for the RepeatCT method and the RepeatCBCT method. For the comparison, CTV to plan selection volume (PSV) margin, intrafractional margin and the planning CT (pCT) to cone-beam CT registration method were set equal in the two workflows.

Method	PTV selection	Images used for defining adaptive PTVs	Bladder contour combinations	PSV + intrafractional margins
Repeat CT	PTV A-D	4 pCTs, every 15 min	None	3 mm + 5 mm
Repeat CBCT	PTVsmall	1 pCT + 4 CBCTs	Union of at least 2	3 mm + 5 mm
	PTVmed	1 pCT + 4 CBCTs	Union of all 5	3 mm + 5 mm
	PTVlarge	1 pCT	None	15–28 mm anisotropic CTV to PTV margin