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Bladder motion

Inter- and intra-fractional bladder motion during radiotherapy for bladder cancer: A comparison of full and empty bladders

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ABSTRACT

Purpose: To compare inter- and intra-fraction bladder volume variations and bladder wall motion during radiotherapy (RT) for bladder cancer with full and empty bladder protocols.

Materials and methods: Bladder volumes, filling rates and bladder wall movement were retrospectively analyzed for 24 patients with at least 4 sets of delineable pre and post treatment cone beam CT (CBCT)-scans. Eight patients were treated with an 'empty bladder' (EB) protocol and sixteen patients with a 'full bladder' (FB) protocol.

Results: 24 planning CT-scans and 356 CBCT-scans (178 sets) were analyzed. The average time between pre and post irradiation CBCT was 8 min (range 6–18 min). Median filling rate was 1.94 ml/min and did not differ between EB and FB. Random variation in bladder volume and inter-fraction wall movement was slightly but not significantly larger for FB, whereas intra-fraction bladder wall movement was slightly but not significantly smaller for FB. The largest inter- and intra-fraction bladder wall movement was found in the cranial anterior direction.

Conclusion: Empty and full bladder protocols show similar inter- and intra-fraction wall motion, and therefore treatment choices could be purely based on organ at risk criteria.

For patients with muscle invasive bladder cancer, the current standard treatment is cystectomy. Inoperable patients and those who prefer a non-invasive treatment, or would like to retain their bladder, are referred for radiotherapy (RT) with or without chemotherapy.

There are basically two methods to treat bladder cancer with external beam RT (EBRT). The most common method is to irradiate the whole bladder. For this method, patients are generally instructed to empty their bladder before the planning CT-scan and each treatment, to minimize the target size. The second method of treating bladder cancer with EBRT is to irradiate the tumor alone, i.e., partial bladder RT. Partial bladder RT is only used for patients with a solitary bladder tumor. Only a few institutes perform partial bladder RT [1,2]. Some institutes use a combination: they electively irradiate the whole bladder and add a boost to the primary tumor area [3,4]. For boost or focal treatments in bladder RT there is a debate whether treatments should be done with a full bladder (FB) or an empty bladder (EB).

Full bladders are expected to move healthy tissue, such as small bowel and healthy part of the bladder, away from the treatment fields. Studies on FB during EBRT for cervical cancer, prostate cancer and rectal cancer showed for example a reduced small bowel volume irradiated, reducing toxicity. [5–8]. A disadvantage of FB is that they are expected to be less reproducible causing larger inter-fraction motion at the superior and anterior borders [9]. Inter-fraction motion however could be compensated when daily tumor alignment is available. Cone beam CT (CBCT) is increasingly used to align patients before each treatment fraction. In our clinic we currently use a protocol to align the tumor before each treatment fraction, based on the alignment of lipiodol markers surrounding the tumor [10]. If the tumor is aligned daily, intra-fraction motion remains as main source of error.

Although inter-fraction and intra-fraction bladder motion is already studied extensively by many authors [9,11–14], intra-fraction motion was never studied for bladder cancer patients with FB. A study on healthy volunteers with a FB showed greater filling rates and concomitant wall displacements when comparing with a study on bladder cancer patients and other pelvic patients with an EB [15,16]. Therefore, EB are believed to have less intra-fraction motion and hence smaller margins needed than FB. However, the behavior of FB and EB was never compared in bladder cancer patients.

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The aim of this study is therefore to compare and quantify inter- and intra-fraction bladder volume and position variation during RT of bladder cancer, using both empty and full bladder protocols.

Materials and methods

Patients and treatments

Twenty-four patients, twenty-one male and three female, with T1–T4 bladder cancer were retrospectively included in this study. Inclusion criteria were (1) no catheter and (2) at least four sets of pre- and post treatment CBCT-scans with a delineable bladder. All patients had maximal trans urethral resection of their bladder tumor prior to RT. Patient and treatment characteristics are given in Table A (Appendix). Eight patients were scanned and treated with an empty bladder (EB): they were instructed to void their bladder just before the planning CT-scan and each treatment fraction. The other sixteen patients were instructed to empty their bladder and drink 250 ml water one hour before the planning CT-scan and each treatment fraction, which is called the full bladder (FB) protocol.

According to our clinical shrinking action level protocol for setup verification, all patients had at least two CBCT-scans in the first week of treatment, and at least one CBCT-scan in all subsequent weeks [19]. Whenever a pre-treatment CBCT-scan was made, another CBCT-scan was made after the treatment for treatment evaluation and for bladder filling and wall movement analysis. Pre- and post treatment CBCT-scans acquired during one fraction will be called a "set" from now on.

The clinical target volume (CTV) locations are given in Table A. The planning target volumes (PTVs) were constructed as follows: for whole bladder irradiation, the clinical target volume (CTV) was defined as the bladder with any extravesical tumor spread, with PTV margins of 2.0 cm cranial, 1.5 cm dorsal and 1.0 cm in the other directions. For partial bladder irradiation the CTV, in most cases the gross tumor volume (GTV), was expanded with a PTV margin of 2.0 cm in all directions. For nine patients, indicated with an 'A' in Table A, the partial bladder RT was combined with an adaptive radiotherapy (ART) technique. For them the PTV was the encompassing GTV of 6 CT-scans expanded with a 1.0 cm margin. This technique is described in more detail by Pos et al. [2].

Data acquisition and delineation

All patients were scanned and treated in supine position. The planning CT-scan (24-slice Somatom-Sensation-Open, Siemens, Forchheim Germany) was performed with a resolution of $0.098 \times 0.3 \times 0.098$ cm^3. The CBCT-scans were acquired using an Elekta Synergy system using the following parameters: 130 kV, 360 degree, FoV medium, a scan time of 2 min and a scan dose range of 1–6 cGy (1280–2000 mAs). No bowtie filter was used.

The external bladder wall was delineated by one experienced radiographer on both planning CT-scan and each pre- and post treatment CBCT-scan using in-house software. For each set of CBCT-scans only the pre-scan was completely delineated, while the post-scan delineation was a manually adjusted copy of the pre-scan delineation, to reduce the influence of delineation uncertainties.

Volume, increase and position analysis

Bladder volume, volume increase, expansion rate and bladder wall movement were studied for EB and FB separately.

Bladder volumes were calculated from the manual delineations. Volume increase was calculated per CBCT-set, subtracting the pre-treatment bladder volume from the post-treatment volume. Filling rate was then calculated by dividing the volume increase by the time between pre-and post-treatment CBCT-scans as recorded by the equipment.

Bladder wall displacement and displacement rate (i.e. the bladder wall displacement per minute) were calculated using scalar maps, similar to height maps of a globe. This technique is described in detail by Lotz et al. [15]. To create those maps, a reference point inside the bladder was chosen as follows: from the center of the symphysis 2.0 cm along the longitudinal axis of the pubic bone, then 2.0 cm in dorsal direction and 2.0 cm in cranial direction. In case the entire bladder wall was not visible from that point, the reference point was shifted. The distance of the bladder wall to the reference point was determined for 2500 directions (for 50 azimuth angles and 50 polar angles of a spherical coordinate system), generating 2500 'domains' on the bladder wall. The movement of each bladder wall domain was found by subtracting the pre-treatment distance to the reference point from the post-treatment distance to the reference point. Bladder wall displacement rate was determined by dividing the bladder wall displacement by the time between pre- and post-treatment CBCT-scans.

Statistics

The statistics of bladder volumes was based on all pre-treatment CBCT bladders and the planning CT bladder. Statistics of the variations for the population of patients was calculated as follows: the group mean was calculated as the mean of the averages per patient, the systematic error ($\sum$) was calculated as the standard deviation (SD) of the averages per patient; and the random error (σ) was calculated the root mean square over all patients of the SDs over all fractions per patient [17].

We tested whether group statistics significantly differed between the EB and FB group. Mean inter-fraction wall movement was compared using an independent-samples *t*-test, its systematic error using Levene's test for equality of variance, and its random errors using the Mann–Whitney test [18]. Bladder volume, volume increase and intra-fraction bladder wall movement were not normally distributed and were therefore compared using a rank test (Mann–Whitney test). Since all tested variables are correlated, no Bonferroni correction is used.

Time-trends of bladder volumes (planning volume and pre-treatment volumes) and volume increases were studied using linear regression. The day of the planning CT-scan was considered as day 0 and the first day of radiotherapy was considered as day 1. The relation between significant time trends and the treatment variables ART, drinking protocol, tumor location, PTV and dose were tested using the Fischer's Exact test, since it is applicable for small sample sizes.

Results

The average treatment duration, including weekends, was 36 days, range 25–49 days. The average time between pre and post CBCT-scan was 8 min (range 6–18 minutes). A total of 356 CBCT-scans (178 CBCT-sets) and 24 planning CT-scans were analyzed. All patients were able to follow the voiding and drinking instructions. Eight patients had some hydronephrosis, and eleven patients had elevated levels of creatine, both did not correlate significantly with bladder volume or filling. None of the patients received concurrent chemotherapy.

Inter-fraction volume and position variation

A summary of the results can be found in Table 1. Fig. 1 shows for four patients a sagittal reconstruction of the planning CT-scan with all CBCT delineations overlaid. This figure gives an impression