The effect of rectal retractor on intrafraction motion of the prostate

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Abstract

Rectal retractors (RR) are used in prostate radiotherapy to retract part of the rectal wall further from the prostate in order to lower the rectal dose and toxicity. The aim of this study was to investigate the effect of RR on intrafraction motion of the prostate. Intrafraction motion of the prostate with RR and without it was recorded with electromagnetic real-time tracking system. Intrafractional motion data of 260 RR fractions and 351 non-RR fractions from 22 patients was analyzed. 3D and unidirectional motion patterns between RR and non-RR fraction datasets were compared in terms of percentage time at displacement \( \geq 1, 2, 3, 4, 5 \) and 6 mm over 6 and 10 min of tracking time. Temporal patterns of the prostate motion were evaluated by re-binning the motion data in 1 min time intervals. The percentage time at displacement was larger in RR data compared to non-RR data in every direction (except anterior) and for every motion magnitude considered. For non-RR fractions the percentage of time of \( \geq 1, 2, 3, 4, 5 \) and 6 mm 3D displacements within 10 min of tracking time were 44.8\%, 16.0\%, 6.4\%, 2.9\%, 1.4\% and 0.5\%, respectively. For RR fractions the corresponding percentages were 69.6\%, 32.8\%, 15.3\%, 7.4\%, 3.7\% and 2.2\%, respectively. The difference in 3D motion between the datasets was statistically significant \((p < 0.03)\). Largest increase in the motion was seen in inferior and posterior directions when the RR was used. Motion increased linearly as a function of elapsed tracking time in both RR and non-RR datasets but the increase was more rapid in RR fractions. The use of RR increases the intrafraction motion of the prostate which can lead to inaccurate treatment localization and delivery thus questioning the justification of its use.

1. Introduction

In recent years there has been growing interest in hypofractionated radiotherapy (RT) for prostate cancer. This is due to the fact that prostate cancer is considered to have a low alpha–beta ratio relative to surrounding normal tissues tissues (Dasu and Toma-Dasu 2012, Vogelius and Bentzen 2013). In radiobiological point of view hypofractionation could lead to a better tumor control with fewer or same level of normal tissue complications compared to standard fractionation (Brenner and Hall 1999). Compared to standard fractionation, lower number of fractions and increased fraction doses may lead to a more significant underdosage of the target and overdosage of the normal tissues if the target is not hit accurately. As a consequence more emphasis should be laid on preserving the normal tissue doses at acceptable level and on accurate treatment localization.

In order to minimize rectal toxicity, several methods to reduce the dose to the rectum have been proposed. Among these are spacer gels and biodegradable balloons that are implanted to the interspace of prostate and rectum to increase the prostate-rectum separation. These methods can create a separation even up to 20 mm which results in significantly diminished rectal volumes exposed to high doses (Mok et al 2014). Disadvantages of these methods are related to the positioning of the spacer that usually cannot be corrected and to the invasive implantation procedures that can cause complications (Mok et al 2014). Another method for rectum sparing is the use of inflatable endorectal balloon (ERB) (Wachtler et al 2002, Smeenk et al 2010). This method increases the distance of posterior rectal wall from the prostate but pushes the anterior rectal wall against the prostate. Reductions in high- and intermediate-dose regions of rectum wall have been reported (Smeenk et al 2010).
Disadvantage of the ERBs is the variation in daily reproducibility of the ERB position and shape that can cause deformations in the prostate (Jones et al 2013).

An alternative to spacer gels and rectal balloons in rectum dose sparing is a rectal retractor (RR). In this method a rectal rod is inserted into the rectum and the distance between rectum wall and the prostate is increased by retracting the rectum posteriorly (Isacsson et al 2010, Nilsson et al 2014, Nicolae et al 2015). One comparative treatment planning study shows that the RR significantly decreases rectal wall doses in the high dose region (Nilsson et al 2014) whereas in another study with similar device statistical differences were not found (Nicolae et al 2015).

It has been assessed from transrectal ultrasound (US) imaging during RT and from comparison of pre- and post-RT cone beam computed tomography (CBCT) images that RR may minimize intrafraction movement of the prostate during RT (Holupka et al 1996, Nicolae et al 2015). However, this has not been measured for the same patient group using real-time motion data recorded during actual RT.

In the present study the effect of RR (Rectafix™, Scanflex Medical AB, Taby, Sweden) on prostate intrafraction motion is investigated. This is accomplished by comparing real-time intrafraction motion data of patients treated partly with the RR and without it. Three dimensional (3D) and unidirectional displacements in anterior–posterior (AP), superior–inferior (SI) and left–right (LR) directions are determined in terms of percentage time at a displacement and compared between the RR and non-RR fractions. It is commonly assumed that the RR has stabilizing effect on prostate motion and the goal was to evaluate the magnitude of this effect. If the prostate motion was halted by the RR, the need for a real-time motion tracking could be questioned. The intrafraction motion data was acquired using real-time electromagnetic tracking system, RayPilot® (Micropos Medical AB, Gothenburg, Sweden). The study is part of a clinical trial (ClinicalTrials.gov ID: NCT02319239) which aims at developing extremely hypofractionated protocol for prostate cancer with minimized rectal toxicity.

2. Materials and methods

2.1. Patients and treatment

Study was approved by ethical committee of Pirkanmaa Hospital District (R14009) and the written consent to participate was obtained from each included patient. Twenty-eight patients with biopsy-proven prostate adenocarcinoma were recruited in the study between April 2014 and July 2015. They were treated with volumetric modulated arc therapy (VMAT) on a Varian TrueBeam STx accelerator (Varian Medical Systems, Palo Alto, CA) using two full arcs and 6 MV flattened beams. Twelve patients were treated using moderate hypofractionation schedule 20 × 3 Gy based on CHHiP-trial (Dearnaley et al 2012). Ten patients were treated using conventional schedule with 39 × 2 Gy. If seminal vesicles (SV) were included in the treatment, the dose to SVs was 20 × 2.3 Gy in moderate hypofractionation schedule administered by simultaneous integrated boost technique and 28 × 2 Gy in conventional schedule. RR was used in first 10 out of 20 or in first 15 out of 39 fractions to increase the distance between rectum wall and prostate.

2.2. Treatment planning and localization

Three gold seed fiducial markers were implanted transrectally in US guidance into the prostate for treatment localization. Before pre-RT imaging and treatment sessions, patients were instructed to empty their rectum and to have full bladder. Enemas were used before the magnetic resonance imaging (MRI) and CT simulation but not before treatment sessions because repetitively administered enemas were thought to be too exhausting to patients in long treatment course. A few days after the implantation, an MRI scan without the RR was acquired for target delineation. After the MRI, a RayPilot transmitter was implanted into the prostate for real-time electromagnetic motion tracking. Transmitter implantation was performed transperineally, using endorectal US guidance. The aim was to place the transmitter centrally into another, preferably more prominent one, of the lateral lobes of the prostate, trying to avoid the urethra, and midway of the apex and base of the prostate. Two computed tomography (CT) scans, first without the RR and immediately after with the RR, were acquired for treatment planning. Treatment plans were generated for both CT scans as the treatment consisted of RR and non-RR fractions. Toshiba Aquilion LB with 0.5–1 mm slice thickness was used to detect transmitter central point with high precision. 2 mm slices were reconstructed for the actual dose calculation. The planning target volume (PTV) was formed adding 5 mm isotropic margin around the clinical target volume that was either prostate alone or prostate and full SVs. The choice of 5 mm PTV margins was based on clinical protocol of daily image-guided marker alignment. Dose optimization and calculation was performed using Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA). To ensure the correct position of the RR and bladder filling, CBCT-scan was acquired before each treatment with RR. CBCT was acquired also for every other non-RR fraction to check the bladder and rectum filling. The actual target localization was performed by acquiring orthogonal KV-image pair of the prostate and matching it to the reference image pair obtained from the planning CT using three implanted gold seeds as fiducial markers. Treatment couch corrections proposed by image
matching were performed to match the plan isocenter to the machine isocenter. Prostate intrafraction motion was tracked continuously starting immediately after the initial patient positioning on treatment couch (non-RR fractions) and when RR placement was accomplished (RR-fractions). Thus the tracking included CBCT- and kV-imaging and ended after the radiation delivery was complete. As the tracking was started after initial positioning procedures, the observed motion was not influenced by extraneous disturbances, such as RR placement. If the position of the RR had to be adjusted after the CBCT check, the tracking was stopped, reset and started over after the correction was done. Couch correction shifts during the tracking were canceled out from the observed motion data by subtracting the couch shift values in question from subsequent data points. Tracking the motion during the imaging in addition to irradiation provides information for planning of the timeline of the whole treatment session, e.g. potential stabilization time needed after patient setup and prostate movement during image guidance and treatment delivery.

### 2.3. Rectal retraction

The RR consists of a cylindrical rectal rod (diameter 20 mm, length 110 mm) which is locked to an adjustable vertical column. The column and leg support are attached to a baseplate (figure 1) which is fixed to the treatment couch or RayPilot detector plate. Indexed fixation holes on the leg support ensure the reproducible positioning of the leg support relative to vertical column. Electrically non-conductive fixation bars were used for fixation of the RR to avoid electromagnetic interference on RayPilot motion detection. The retraction of the rectal wall is achieved by mechanically pushing the rectal rod posteriorly. Vertical position of the rectal rod can be recorded with the help of a numeric scale on both sides of the vertical column. The extent of the retraction was limited by the discomfort of the patient and the achieved retraction (vertical position of the rectal rod) at the CT simulation was recorded for reproducible retraction at the treatment sessions. The positioning of the patient and the retraction achieved at the CT simulation were reproduced at every treatment fraction. The use of recorded retraction index and CBCT-imaging at every RR fraction to check the vertical and longitudinal position of the rod minimized the variability in RR position between fractions and different persons performing the retraction. The retraction was reproduced with millimeter precision and the depth of the RR insertion into the rectum had to cover the prostate and differ less than 1–2 cm compared to planning CT. Since the mechanical stretching may induce rectal complications if the RR would be used in large number of fractions (Nilsson et al 2014), the use of the rod was limited to 10 fractions with moderately hypofractionated patients and to 15 fractions with conventionally fractionated patients. RR was chosen to be used at the beginning fractions of the treatment course as the rectal mucosa usually becomes more irritated along the treatment course due to the irradiation. Langen et al (2008) studied the prostate intrafraction mobility during treatment course finding no difference between the observed motion at the beginning and end of the treatment course. Based on this, the choice of non-randomized scheduling of RR fractions was considered justified.

Within fractions without the RR, in-house developed knee support having femur angle comparable to most commercial solutions was used (figure 2).

### 2.4. Intra-fraction motion tracking

The RayPilot system consists of a transmitter which is implanted into the prostate and a receiver plate which is positioned on the treatment couch. The transmitter consisting of the transmitting part (length 17 mm, diameter 3 mm) and a cable (length 383 mm, diameter 1.6 mm) is attached to the receiver plate during each fraction to activate the transmitter. Signal sent by the transmitter is read by the receiver antennas in the receiver system and the position of the transmitter is
located. The position is given in LR, SI and AP directions at 30 Hz frequency. The system measures also the rotation around the vertical axis (yaw) and rotation around the lateral axis (pitch). The active measurement volume is 10 cm × 10 cm × 10 cm and the vertical position of the measurement volume is adjustable. The operation limits for the transmitter angle are ±40° ±5% (pitch and yaw). Reported 3D resolution of the system, measured in laboratory environment, is 0.8 mm (±0.6) mm (Kindblom et al 2009). The RayPilot system is calibrated to the treatment room isocenter and based on the known relationship between transmitter center and treatment isocenter in the planning CT the system allows treatment localization, in addition to motion tracking. However, in this study the RayPilot was only used for the tracking of the intrafraction motion. The collected intrafraction motion data was saved in 1 s time resolution for further analysis. No treatment interruptions were made based on the detected intrafraction motion of the prostate.

2.5. Data processing

There was a small, sub-millimeter, bias in initial zero-point position tracked which is a result of a finite measurement resolution of the RayPilot system. The bias was eliminated by subtracting the initial position reading from subsequent position points in all translational directions. As the tracking time included treatment couch corrections, the shifts made to the couch were seen in raw tracking data. To analyze the pure prostate motion, the shifts were canceled out by subtracting couch shift values in question from subsequent data points. The effect of instrumental noise and radiofrequency disturbances were reduced by filtering the data using first order low-pass filter. To avoid the changes in phase response, the data was filtered bidirectionally in time and averaged. Gaussian measurement noise characteristics of the RayPilot system differ a little bit depending on measurement direction and therefore different smoothing factors (α) for different directions were used. Smoothing factors were α = 0.15, α = 0.15 and α = 0.1 for LR, SI and AP directions, respectively. In addition to the Cartesian motion data, 3D vectors were calculated for the motion analysis.

2.6. Data analysis

Intrafraction motion was assessed by calculating absolute prostate displacement in each direction relative to its initial position at the beginning of the tracking. The extent, directionality and duration of prostate displacements were investigated. For this purpose, percentages of time at 3D and unidirectional displacements ≧1, 2, 3, 4, 5 and 6 mm were determined for 6 and 10 min tracking times. The percentage is the fraction of time when the pre-processed time-displacement curve is equal to or above the given displacement value. Temporal patterns of prostate motion were also investigated. To accomplish this, the percentages of time at displacements ≧1, 2, 3, 4, 5 and 6 mm were determined for 1 min tracking time intervals ranging from 0 to 10 min. The percentage times were determined separately for all RR fractions and all non-RR fractions and separately for the whole patient population and individual patients. Due to the variability in the duration of treatment sessions, the percentage times at displacements were calculated up to 10 min of tracking time to maintain adequate amount of data at the last minutes. The effect of RR on intrafraction motion was evaluated by comparing 3D and unidirectional motion patterns between RR and non-RR fractions. Comparisons between the RR and non-RR fractions were made for individual patients and for the whole patient population.

2.7. Statistical analysis

To evaluate the time dependence of prostate displacement, Pearson correlation coefficients between percentage time at a displacement and tracking time were calculated for each direction and 3D vector. Correlation was defined for displacements ≧1, 2, 3, 4, 5 and 6 mm.

Nonparametric two-sample Kolmogorov–Smirnov test was used to estimate differences in intrafraction motion patterns between the RR and non-RR fractions. The distributions of percentage time at a displacement in 1 min intervals within 10 min tracking time were compared between both fraction datasets. The comparisons were made for displacements ≧1, 2, 3, 4, 5 and 6 mm in each direction.

The paired Wilcoxon signed-rank test was applied to test the difference in percentage times with and without the RR at displacements ≧1, 2, 3, 4, 5 and 6 mm within 6 and 10 min. Differences in left, right, superior, inferior, anterior, posterior and 3D directions were tested. In addition to comparisons between fraction datasets over whole population, comparisons of 3D motion patterns were made for all individual
patients. For a small subgroup of four patients having very small prostate motion the testing was limited to displacements ≥1, 1.5, 2, 2.5, 3 and 3.5 mm. All tests were conducted with significance level of 0.05.

3. Results

3.1. 3D motion analysis for RR and non-RR data

Technical problems with the cables of three of the implanted transmitters and transmitter pitch or yaw angle being out of operating limits with three patients prevented motion data collection partly or entirely thus leading to exclusion of these patients from the analysis. As a consequence, usable motion data was available for 22 patients out of 28 patients recruited, and the final number of fractions analyzed was 260 with the RR and 351 without it. Mean tracking time ± standard deviation for fractions with the RR was 540 ± 150 s and 450 ± 150 s for fractions without the RR. Difference in mean tracking times largely resulted from the different number of CBCTs between RR and non-RR fractions and the time required for RR position confirmation in RR fractions. Tracking time of 247 RR fractions (95.0%) and 276 non-RR fractions (80.7%) covered at least 6 min whereas 58 RR fractions (22.3%) and 26 non-RR fractions (7.5%) covered at least 10 min. The percentage time of 3D prostate displacements over 6 and 10 min of tracking time for both fraction datasets are shown in figure 3. The percentage time at 3D displacement was larger in RR fractions compared to non-RR fractions for every motion magnitude considered within both 6 and 10 min of tracking time. For non-RR fractions the percentage times of 1, 2, 3, 4, 5 and 6 mm 3D displacements were 37.2%, 11.0%, 3.5%, 1.4%, 0.6% and 0.3% within 6 min, and 44.8%, 16.0%, 6.4%, 2.9%, 1.4% and 0.5% within 10 min, respectively. For RR fractions the corresponding percentages were 59.0%, 21.8%, 9.7%, 4.2%, 2.0% and 1.2% within 6 min, and 69.6%, 32.8%, 15.3%, 7.4%, 3.7% and 2.2% within 10 min, respectively. The difference in 3D motion between RR and non-RR fractions was statistically significant (p < 0.03) for both 6 and 10 min of tracking time. The power of the test for the 3D differences within 10 min of tracking time was 0.90.

3.2. 3D analysis for individual patients

The percentage time of 3D displacements of the prostate in RR and non-RR fractions over 10 min of tracking time for individual patients are shown in table 1. The analysis reveals that for 13 patients out of 22 the 3D motion of the prostate was significantly larger (p < 0.05) with RR than without it. For two patients the observed motion was milder within RR fractions compared to non-RR fractions and the difference was statistically significant (p < 0.05). For
rest of the patients statistically significant difference was not seen.

3.3. Directional analysis

Percentage times at unidirectional displacements within 6 and 10 min tracking time for both fraction datasets are shown in tables 2 and 3, respectively. Least motion was seen in LR direction. LR displacements \( \geq 5 \) mm were not seen in RR data and were negligible (0.01%) in non-RR data. The motion was quite evenly distributed between left and right directions, although the movement was slightly more emphasized in left direction in both RR and non-RR data and more frequent in RR data than in non-RR data \((p = 0.08 \text{ left},\ p = 0.90; p = 0.07 \text{ right},\ p = 0.76)\).

SI motion in non-RR fractions was approximately of the same order as LR motion in non-RR fractions and no displacements \( \geq 5 \) mm were seen. In RR fractions SI motion was notable larger. Motion was more frequent in RR fractions than in non-RR fractions in superior and especially in inferior direction. Differences between the two datasets were statistically significant \((p < 0.03,\ power \geq 0.86)\) in both superior and inferior directions.

### Table 1. Percentage time of 3D prostate displacements in RR and non-RR fractions within 10 min of tracking time for individual patients.

| Patient | RR | non-RR | RR | non-RR | RR | non-RR | RR | non-RR | RR | non-RR | RR | non-RR |
|---------|----|--------|----|--------|----|--------|----|--------|----|--------|----|--------|
| 1       | 75.7 | 44.3 | 35.0 | 16.0 | 17.3 | 8.8 | 1.3 | 6.6 | 0.0 | 2.6 | 0.0 | 0.5 |
| 2       | 70.8 | 68.2 | 36.3 | 36.4 | 2.5 | 13.2 | 0.0 | 5.4 | 0.0 | 2.8 | 0.0 | 0.4 |
| 3*      | 71.6 | 38.2 | 38.8 | 13.0 | 22.6 | 2.2 | 11.1 | 0.0 | 6.2 | 0.0 | 2.3 | 0.0 |
| 4*      | 77.4 | 5.6 | 53.5 | 0.0 | 25.4 | 0.0 | 13.8 | 0.0 | 11.1 | 0.0 | 10.7 | 0.0 |
| 5*      | 70.2 | 23.4 | 21.4 | 8.8 | 10.0 | 0.0 | 0.9 | 0.0 | 0.3 | 0.0 | 0.1 | 0.0 |
| 6*      | 90.1 | 70.3 | 67.7 | 34.8 | 49.3 | 9.8 | 28.3 | 3.9 | 16.6 | 0.2 | 4.6 | 0.0 |
| 7*      | 66.9 | 49.9 | 44.4 | 8.7 | 25.6 | 2.4 | 14.9 | 1.0 | 6.9 | 0.3 | 3.3 | 0.0 |
| 8       | 69.5 | 58.2 | 22.8 | 24.8 | 2.1 | 8.1 | 0.0 | 2.9 | 0.0 | 0.2 | 0.0 | 0.0 |
| 9*      | 65.0 | 12.0 | 29.6 | 0.2 | 2.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 10**    | 66.9 | 70.4 | 13.4 | 27.9 | 0.0 | 11.3 | 0.0 | 9.7 | 0.0 | 4.8 | 0.0 | 0.0 |
| 11*     | 57.4 | 29.1 | 13.5 | 1.4 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 12*     | 57.1 | 26.1 | 6.4 | 1.3 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 13*     | 88.2 | 74.8 | 65.2 | 43.0 | 50.5 | 17.9 | 28.4 | 5.7 | 11.3 | 3.2 | 7.6 | 0.9 |
| 14*     | 85.1 | 34.2 | 65.9 | 7.7 | 39.5 | 1.2 | 21.8 | 0.2 | 9.4 | 0.0 | 7.1 | 0.0 |
| 15*     | 59.1 | 24.5 | 5.1 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 16      | 49.2 | 40.3 | 5.0 | 6.5 | 0.0 | 1.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| 17      | 62.2 | 31.5 | 7.2 | 9.5 | 0.0 | 3.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 18*     | 80.4 | 35.9 | 39.1 | 5.7 | 21.4 | 4.8 | 15.7 | 1.1 | 8.2 | 0.0 | 7.5 | 0.0 |
| 19      | 73.2 | 65.9 | 40.8 | 37.1 | 8.5 | 20.8 | 0.0 | 10.7 | 0.0 | 4.7 | 0.0 | 1.2 |
| 20**    | 46.5 | 75.5 | 17.4 | 41.0 | 0.5 | 20.3 | 0.0 | 3.9 | 0.0 | 1.8 | 0.0 | 0.4 |
| 21*     | 87.5 | 76.4 | 69.7 | 49.7 | 40.9 | 30.3 | 22.1 | 14.9 | 13.3 | 7.3 | 5.7 | 3.5 |
| 22      | 64.4 | 46.7 | 19.3 | 16.1 | 4.6 | 9.2 | 0.3 | 8.0 | 0.0 | 6.0 | 0.0 | 5.0 |

\(*p < 0.05,\ RR\text{-}motion\ larger\ than\ non-RR\ motion.\)

\(**p < 0.05,\ non-RR\ motion\ larger\ than\ RR\ motion.\)

### Table 2. Percentage of time of unidirectional prostate displacements for RR and non-RR fractions within 6 min of tracking time.

| Displacement | RR | non-RR | RR | non-RR | RR | non-RR | RR | non-RR | RR | non-RR |
|--------------|----|--------|----|--------|----|--------|----|--------|----|--------|
| Left         | 6.8 | 1.9 | 0.8 | 0.1 | 0.0 | 0.0 |
| Right        | 7.2 | 1.6 | 0.2 | 0.1 | 0.0 | 0.0 |
| Superior     | 4.0 | 1.3 | 0.6 | 0.2 | 0.0 | 0.0 |
| Inferior     | 26.4 | 6.4 | 2.6 | 1.2 | 0.6 | 0.6 |
| Anterior     | 6.1 | 2.0 | 0.9 | 0.4 | 0.1 | 0.1 |
| Posterior    | 24.2 | 6.9 | 2.6 | 1.5 | 0.8 | 0.7 |

Biomed. Phys. Eng. Express 2 (2016) 035021 A Vanhanen and M Kapanen
Most of the motion in non-RR group was seen in AP direction. Anterior motion was comparable between the groups whereas posterior motion was more frequent in RR group than in non-RR group. The difference in posterior motion distribution between the groups was statistically significant ($p < 0.03$, power = 0.90).

### 3.4. Time dependence

Temporal patterns of the prostate motion were evaluated by re-binning the percentage of time at displacements against 1 min tracking time intervals. Temporal pattern of 3D motion is plotted for displacements $\geq 2$, 3, 4, 5 and 6 mm (figure 4) and unidirectional temporal patterns are plotted for displacements $\geq 2$, 3 and 5 mm (figure 5). 3D motion of the prostate increased as a function of elapsed tracking time whether the RR was used or not and the correlation of the percentage time of 3D displacement with tracking time was significant for all the displacements considered. For 3D deviations $\geq 2$, 3, 4 and 5 mm the increment of percentage time at displacement was linear with tracking time in RR and non-RR fractions, though the linearity was more pronounced in RR fractions. The 3D motion beyond 6 mm increased linearly with elapsed tracking time in RR fractions whereas displacements of at least 6 mm were rare in non-RR group and the linearity of the tracking time dependence was not evident. Common for all the displacements considered was that the percentage time at displacement grew faster in RR fractions than in non-RR fractions.

LR motion increased as a function of elapsed tracking time and the increase of the motion was linear for RR fractions in left direction. The probability of larger displacement along the elapsed tracking time increased also in right direction but the linearity was not clear. LR motion was more time independent when RR was not used.

The probability of inferior displacements $\geq 2$ and 3 mm grew as a function of tracking time ($p < 0.05$) and the increase was more linear and steep in RR fractions than in non-RR fractions. The increase of the percentage time at superior displacements $\geq 1$, 2 and 3 mm was mild and comparable between the two data-sets. Displacements of at least 5 mm in inferior direction were seen only in RR fractions and the probability of at least 5 mm displacement increased as a function of elapsed tracking time. Large displacements in superior direction were negligible and time independent.

The percentage time at displacement $\geq 1$, 2 and 3 mm increased as a function of tracking time in anterior and posterior directions in both groups ($p < 0.05$). Posterior motion beyond 5 mm was negligible in non-RR group but increased as a function of tracking time in RR group. Large ($\geq 5$ mm) anterior motion was time independent in both groups.

Statistically significant differences in temporal patterns of the motion between RR and non-RR fractions were found in inferior motion beyond 3 mm ($p \leq 0.015$) and in posterior motion for displacements $\geq 5$ mm ($p < 0.05$). Differences in inferior motion were near the significance level for displacements $\geq 1$ and 2 mm ($p = 0.055$).

### 4. Discussion

In the current study the effect of the RR on prostate intrafraction motion was examined using real-time motion tracking over every treatment fraction and the whole treatment course. Results of the study suggest that the RR increases the prostate motion instead of stabilizing it. Compared to non-RR fractions the percentage time at displacement in RR fractions was effectively larger in every direction (with the exception of anterior) and for any displacement considered. The difference in 3D motion patterns between RR and non-RR fractions was statistically significant ($p < 0.03$). Differences in 3D motion were evaluated also at individual level. For 13 out of 22 patients the RR

![Table 3. Percentage of time of unidirectional prostate displacements for RR and non-RR fractions within 10 min of tracking time.](image)
caused significant increase in intrafraction motion of the prostate. For only two patients the intrafraction motion was significantly reduced with the RR. These results are conflicting with the results of Nicolae et al (2015) who observed prostate immobilization with endorectal immobilization device (EIS) comparable to immobilization with ERB. However, it has to be pointed out that the clinical implementation of the EIS system differs from RR as the knee support used and therefore the femur angle is different between the two systems. Nicolae et al (2015) also used pre- and post-treatment CBCT-imaging as a motion tracking method which misses the motion information (e.g. transient excursions of the prostate) during the actual treatment and which has been proven to be insensitive in determining intrafraction prostate motion (Noel et al 2009). Results of the current study are based on continuous motion tracking thus representing more accurate and comprehensive view of prostate intrafraction motion between two different clinical practical implementations.

Directional analysis of the motion was performed to clarify more rigorously the effect of RR on prostate motion. Overall the LR motion was mildest and most of the motion was seen in SI and AP directions in both RR and non-RR fractions. This finding was expected as the prostate is surrounded laterally by muscular structures which restricts the LR motion of the prostate and directs the motion mainly in AP and SI directions (Lin et al 2013). The use of RR increased the intrafraction motion in all but anterior direction but the biggest differences between RR and non-RR fractions were seen in superior, inferior and posterior directions. Especially the increase in inferior and posterior motion was notable. In addition to increased frequency in inferior and posterior motion the magnitude of the motions increased in RR fractions compared to non-RR fractions. Over 3 mm displacements in inferior direction and over 4 mm displacements in posterior direction were seen only in RR fractions. Without the RR there can be seen slight emphasis on inferiorly directed motion and more clearly posteriorly directed motion which is consistent with many earlier findings (Langen et al 2008, Bittner et al 2010, Li et al 2013, Tong et al 2015).

Several reasons can explain the increased motion with RR. The RR and the retraction cause discomfort which may increase the muscular tension. Changes in tension may be larger than in normal patient setup and might lead to increased motion of the whole pelvis and the prostate. Greatly increased posterior and inferior motion could be a consequence of the posteriorly...
directed retraction which creates empty space posteriorly to the prostate eliminating the supporting act of the posterior tissues. Phenomenon seems to be opposite when compared to the use of ERBs which create supporting structure posteriorly to the prostate and which have been reported to reduce the motion especially in AP direction (Smeenk et al, 2012, Wang et al, 2012). The greatest separation between rectum and prostate with the RR is achieved at the inferior part of the prostate-rectum interface. This might direct the motion more in posterior and inferior directions as the muscular tension relaxes. Filling of the bladder during the tracking time might also push the prostate towards inferior and posterior directions.

Continuous drifting describes well the motion type of the prostate in majority of the fractions investigated in the present study. This supports the hypothesis that the observed motion is mainly a consequence of a muscle relaxation. With many patients the prostate was quite stable and sudden excursions, related probably to peristaltic motion (Langen et al, 2008), were seen rarely. However, as pointed out by earlier studies, there can be substantial transitions in the prostate motion that can be unpredictable (Kupelian et al, 2007, Tong et al, 2015).

Flattening of the motion curves as a function of elapsed tracking time were seen in some of the individual fractions in both RR and non-RR datasets but was not evident in motion patterns over all fractions except for small (≤1 mm) 3D motions (data not shown). Instead, temporal patterns of the motion (figures 4 and 5) reveal that the motion increased linearly as a function of elapsed tracking time in both fraction datasets for most of the displacements considered. For RR fractions the increase in motion was notably faster. Generally, our findings of increasing probability of prostate intrafraction motion with tracking time are consistent with previously reported results (Langen et al, 2008, Ballhausen et al, 2015, Tong et al, 2015). Li et al (2013) reported that the magnitude of the intrafraction motion of the prostate would not significantly change after 9 min of treatment time. Their tracking

![Figure 5. Percentage of time at unidirectional prostate displacements as a function of elapsed tracking time. Largest increase in the motion was seen in inferior and posterior directions when the RR was used.](image-url)
...data did not include the localization time which might take even 4–6 min from initial setup to the start of treatment delivery based on our own clinical experiences. Taking into account the localization time the possible saturation of the magnitude of the motion could be seen actually 13–15 min after the initial setup and might be impractical to wait in normal clinical routine. Possible stabilization that could be related to a relaxation of the patient was not seen in neither of the fraction datasets within the examined 10 min of tracking time in the present study. This suggests that within the first 10 min after the initial setup no stabilizing or relaxing time is needed between patient setup, image guidance and treatment with and without the RR. Relative differences in 3D motion are nearly the same between 6 and 10 min datasets for both fraction datasets reflecting the linear increase in the probability of the motion and indicating that the observed difference in intrafraction motion between RR and non-RR fractions is independent of tracking time. However, it has to be pointed out that the effect of RR on intrafraction motion with longer than 10 min tracking times after the initial setup is not known.

Increase in the probability of the motion with elapsed tracking time emphasizes the importance of shorter treatment times that are achievable with modern treatment techniques such as VMAT and flattened filter free (FFF) beams. It should also be realized that the prostate motion affects also to the accuracy of image guided treatment localization and thus the delay between imaging and couch corrections should be minimized. The time that is required for image guidance depends on the imaging modality and the experience of the personnel. Orthogonal kV imaging based image guidance in prostate RT takes about 2.5 min in our department and delivery of 2 Gy fraction dose with two full VMAT treatment arcs will take approximately 2 min. Using 10 MV FFF beams even the dose of 7.25 Gy, that is common in prostate SBRT, can be delivered within 2 to 3 min.

The observed 3D motion of the prostate in non-RR fractions was generally smaller than seen in literature: the percentage of time at displacements $\geq 3$ mm and $\geq 5$ mm within 10 min of tracking time was 6.4% and 1.4%, respectively. Tong et al (2015) observed 12% accumulated time of at least 3 mm displacement for all treatment fractions completed within 10 min. For at least 5 mm displacement the corresponding percentage was about 2% (Tong et al 2015, figure 2). Wang et al (2012) observed prostate displacements of $>3$ mm and $>5$ mm for 11.7% ± 7.0% and 3.1% ± 2.2% within 6 min of tracking time. Corresponding percentages for 6 min tracking time in the current study were 3.5% and 0.6%. Langen et al (2008) observed prostate displacements of $>3$ mm and $>5$ mm for 13.6% and 3.3% of total treatment time (mean tracking time 10 ± 2 min), respectively. Nearly similar percentages of time observed also Li et al (2009) (13.4% and 1.8%) for tracking times ranging from 10 to 20 min. However, these results are not fully comparable to the current results as they are proportional to different tracking times. The assessments of motion pattern were restricted to maximum of 10 min of tracking time because majority of the fractions were completed in less than 10 min and low number of longer tracking times might not represent well the motion in general population. There are many explanations for the differences in non-immobilized motion. One reason might be the differences in treatment preparation, e.g. rectum and bladder filling. In the present study the patients were concisely instructed to empty the rectum before each treatment whereas in the study of Langen et al (2008) bladder or rectum preparations were not performed before CT-simulation or daily treatment fractions. No special requirements for rectum filling before treatments in non-EBRT group have been mentioned in the study of Wang et al (2012) either and there is no mention about it in the study of Li et al (2009). However, in the study of Tong et al (2015) patients were instructed to come to all simulations and treatments with empty rectum and full bladder. Rectal movements and related rectal distension have been shown to result in significant displacements of the prostate (Padhani et al 1999) which implies that empty rectum in the current patient data might explain some of the differences between the current and literature results.

Interestingly the observed 3D motion in RR fractions was comparable to or more frequent than findings of non-immobilized prostate motion in literature (Langen et al 2008, Li et al 2009, Wang et al 2012, Tong et al 2015). In these studies the intrafraction motion was tracked using electromagnetic Calypso® system (Balter et al 2005, Willoughby et al 2006) in which three localization transponders are implanted into the prostate. With the RayPilot used in the present study a wired transmitter is implanted into the prostate leaving the cable running out from the perineum. The cable may induce fibrosis to the perineal tissues surrounding the cable which might reduce the tissue mobility and have minor stabilizing effect on prostate as the transmitter part is connected to the cable. However, this should be verified with comparative measurements with different tracking methods and consistent patient groups.

It can be argued if the use of RR would affect the prostate motion of subsequent non-RR fractions. If this was the case, it may be assumed that the effect would have been largest at the beginning of the non-RR fractions. However, the observed prostate motion of the first five non-RR fractions did not differ from the motion of last five non-RR fractions of the treatment course. Based on these findings, it is unlikely that the use of RR would have affected to the prostate motion at subsequent non-RR fractions. To test this rigorously, would require larger cohorts of patients treated separately with or without the RR, which was out of scope of this study.
One of the limitations of the present study is the small amount of patient data that might explain some of the differences in observed non-immobilized prostate motion results between our study and literature. It is noteworthy that patient inclusion criteria excluded for example hip transplant patients and our results might not be fully representative to that particular group of patients. To compensate small number of patients, all the patients were treated partly with and without the RR thus making the comparison of the motion data between RR and non-RR fractions comparable. This also enabled the comparison of motion patterns at individual level which deepened the knowledge of RR’s effect with different anatomies. The placement of the transmitter is important as prostate deformations might have an influence on detected intrafraction motion. Comparison of RR and non-RR motion data for individual patients reduced also the possible effect of non-ideal transmitter placement on observed difference in intrafraction motion patterns as the measurement point was the same for all fractions for the same patient. It is noteworthy that RayPi-lot tracking is based on tracking of single point inside the prostate which does not necessarily reflect the motion of SVs or deformations of the prostate. Thus the analysis of intrafraction motion of the SVs and the effects of prostate deformations are not included in the present study. If SVs are included in treatment their possible motion should be compensated with reasonable margins and deformations of the prostate should always be verified with imaging, e.g. CBCT.

In the present study the analysis of motion was limited to translational movements. The analysis of intrafraction prostate rotations (pitch and yaw) and their connection to translational movements would require more extensive investigation which was out of scope of this study. The impact of increased motion with RR on treatment margins was not investigated in this study either but will be explored in future studies. However, it is obvious that increased motion should be taken into account by increasing margins or by exploiting real-time motion monitoring.

Femur angle against couch surface was steeper in RR fractions (population mean 44.2° ± 4.2°) than in non-RR fractions (population mean 16.6° ± 2.4°) due to differences in knee supports between RR and non-RR fractions. Knee support affects to the position of rectum and prostate (Steenbakkers et al 2004) but whether it has an effect on prostate motion is not known or has not bee reported in the literature. In-house developed knee support was used in all fractions with two patients in the current study. For one of these two patients the motion distributions between RR and non-RR fractions were similar and for the other the motion was significantly larger in RR fractions than in non-RR fractions. These findings suggest that the leg support is not the cause of the observed difference in motion patterns but its effect cannot be fully excluded and should be confirmed with further investigation.

The primary benefit of the RR is thought to be the rectum dose sparing in prostate RT. However, this has been questioned by the results of Nicolae et al (2015) who did not see a difference in rectum dose distribution between treatment plans calculated with and without the EIS similar to the RR. Results of the present study suggest that the use of RR increases the intrafraction motion of the prostate although the observed motion even with the RR was generally small. However, increased motion can lead to inaccurate treatment localization and delivery increasing the uncertainty of dose sparing of the RR. Based on these results, we do not recommend the use of it. Controversy in dose sparing of the RR require further investigation and the final effect of RR on rectal side effects should be verified by clinical data.

5. Conclusions

In the present study the effect of the RR on intrafraction motion of the prostate was assessed for the first time using real-time motion tracking. The results imply that the use of the RR increases intrafraction motion when compared to motion data recorded in normal patient setup without the RR. The difference in percentage time at 3D displacement was 1%–25% depending on the magnitude of the displacement and the difference between the motion patterns between RR and non-RR fractions was statistically significant. This finding is important because it is opposite to the general assumptions based on transrectal US findings. The increased movement, if not corrected properly, may lead to a degradation of the delivered dose to the target and expose organs at risk to higher doses. Further clinical and planning studies might be needed to evaluate the dose sparing effect of the RR in detail.

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