



## Prostate cancer image guided radiotherapy: Why the commotion over rectal volume and motion?

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### ABSTRACT

**Introduction:** Distended rectums on pre-radiotherapy scans are historically associated with poorer outcomes in patients treated with two-dimensional IGRT. Subsequently, strict rectal tolerances and preparation regimes were implemented. Contemporary IGRT, daily online registration to the prostate, corrects interfraction motion but intrafraction motion remains. We re-examine the need for rectal management strategies when using contemporary IGRT by quantifying rectal volume and its effect on intrafraction motion.

**Materials and methods:** Pre and during radiotherapy rectal volumes and intrafraction motion were retrospectively calculated for 20 patients treated in 5-fractions and 20 treated in 20-fractions. Small (rectal volume at planning-CT  $\leq$  median), and large (volume  $>$  median) subgroups were formed, and rectal volume between timepoints and subgroups compared. Rectal volume and intrafraction motion correlation was examined using Spearman's rho. Intrafraction motion difference between small and large subgroups and between fractions with rectal volume  $<$  or  $\geq 90$  cm<sup>3</sup> were assessed.

**Results:** Median rectal volume was 74 cm<sup>3</sup>, 64 cm<sup>3</sup> and 65 cm<sup>3</sup> on diagnostic-MRI, planning-CT and treatment imaging respectively (ns). No significant correlation was found between patient's rectal volume at planning-CT and median intrafraction motion, nor treatment rectal volume and intrafraction motion for individual fractions. No significant difference in intrafraction motion between small and large subgroups presented and for fractions where rectal volume breached 90 cm<sup>3</sup>, motion during that fraction was not significantly greater.

**Conclusion:** Larger rectal volumes before radiotherapy and during treatment did not cause greater intrafraction motion. Findings support the relaxation of strict rectal diameter tolerances and do not support the need for rectal preparation when delivering contemporary IGRT to the prostate.

### Introduction

Prostate cancer (PCa) is the most common male cancer in Europe; 473,344 new cases were diagnosed in 2020 [1]. More than 30% of PCa patients receive radical radiotherapy (RT) [2] with five-year progression free survival rates of 80.5–90.6% achieved [3–6]. However biochemical failure rates following radical RT to localised PCa have historically been reported as higher in patients with larger rectal volumes on pre-radiotherapy scans [7–9]. The literature posits that distended rectums, stipulated as having a cross-sectional area greater than ( $>$ ) 11.2 cm<sup>2</sup> [7],

greater than or equal to ( $\geq$ ) 16 cm<sup>2</sup> [8] or a volume  $>$  90 cm<sup>3</sup> [9], promoted excessive prostate motion during RT causing target underdosing [7–9].

These findings provoked the adoption of rectal preparation regimes and strict rectal diameter constraints, as essential tools to improve RT accuracy in the era of two-dimensional bone-based image-guided RT (IGRT). Advancements in IGRT have since quelled initial fears regarding PCa outcomes [10,11], however rectal volume management strategies continue to be advocated [12,13]. We ask, are these still necessary when employing contemporary IGRT protocols?

**Abbreviations:** PCa, Prostate cancer; RT, Radiotherapy; IGRT, Image Guided Radiotherapy; dMRI, diagnostic Magnetic Resonance Image; pCT, planning Computer Tomography; MRL, Magnetic Resonance Linac; CAL, C-arm Linac; PACS, Picture archiving and communication system; CBCT, Cone Beam Computer Tomography; MRI, Magnetic Resonance Imaging; LR, Left-Right; SI, Superior-Inferior; AP, Anterior-Posterior.

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Contemporary protocols advocate daily online volumetric IGRT, aligning to the prostate gland [12,13], correcting for interfraction motion. Most RT platforms do not correct for intrafraction motion, but the impact of rectal volume on this residual motion could not be found in the literature. The aim of this study was therefore to investigate rectal volume changes during extreme and moderately hypofractionated PCa radiotherapy and examine for correlation between rectal volume and intrafraction motion.

## Materials and methods

### Data inclusion

The rectal volume and intrafraction motion of 40 patients who received radical RT for localised PCa were reviewed. Twenty patients were prescribed 36.25 Gy in 5-fractions on the Unity MR-linac (MRL) (Elekta, Sweden) and 20 were prescribed 60 Gy in 20-fractions on TrueBeam c-arm linac (CAL) (Varian, USA). Patients gave permission to use their images for research as part of standard radiotherapy consent.

### Rectal volume

Patient's rectums were contoured from the rectosigmoid flexure to the anorectal junction. Rectal volume, delineated on radiotherapy planning computer tomography (pCT), was drawn by the clinical team and approved by a clinical oncologist as per standard clinical practice on RayStation (RaySearch, Sweden) for the MRL group and Eclipse (Varian, USA) for the CAL group. One therapeutic radiographer (RTT) (SA), with independent contouring competency, retrospectively delineated rectums on:

- Large field of view, axial slice thickness 3 mm, T2-weighted diagnostic magnetic resonance images (dMRI) imported from PACS to RayStation (RaySearch, Sweden).
- T2-weighted, axial slice thickness 1 mm, treatment images, acquired daily for online adaptive planning in the MRL group, on Monaco (Elekta, Sweden).
- Cone beam CT (CBCT) scans, axial slice thickness 1.5 mm, acquired before beam delivery at fractions 1, 5, 11, 15 and 20 in the CAL group on Eclipse (Varian, USA).

Bowel preparation was not given for dMRI. Micro enema rectal preparation was used by all patients, for two days prior to and on the day of pCT. Preparation was re-introduced two days before first RT treatment, the MRL group continued enema use throughout treatment while the CAL group ceased enema use after fraction ten. Enema duration during treatment differed due to RT prescription not treatment platform. All patients were asked to drink 350 ml of water 30–60 min prior to pCT and treatment.

Data was analysed using R-Studio (RStudio, USA), normality was tested using a Shapiro-Wilk test. Median rectal volume and volume range at each timepoint was calculated for the whole cohort. MRL and CAL groups were then compared separately to minimise RT prescription and enema variation bias. Wilcoxon signed-rank tests were performed to compare subgroup rectal volumes at each timepoint against rectal volume on pCT. A significance level  $< 0.01$  was set to account for multiple comparisons.

MRL and CAL groups were further subdivided; patients with a rectal volume on pCT less than or equal to median volume were categorised as small rectum, while those with a rectal volume on pCT greater than the median as large rectum. Mann-Whitney U tests were run to compare volume between subgroups (significant  $p < 0.01$ ).

### Intrafraction prostate motion

The difference in prostate position between the pre- and post-

treatment T2-weighted MRI was taken as MRL intrafraction motion. Motion was measured independently by two experienced observers (SA and RW) on Monaco (Elekta, Sweden). Disagreements greater than two millimetres triggered re-review for transcription or registration errors. The average left–right (LR), superior–inferior (SI) and anterior–posterior (AP) displacements from the two observers was recorded.

MRL intrafraction motion represents total on couch motion not just motion during radiation beam on. This method was used as it is most akin to the CAL dataset. Any motion corrections made online, using the adapt to position (ATP) workflow, were not subtracted from total motion. Fractions where the patient got off the couch before treatment were excluded.

CAL intrafraction motion was the deviation in prostate position on post-treatment CBCT from planned, after pre-treatment motion correction. Post treatment CBCT acquisition was undertaken as part of institutional protocol to appraise PTV margins [12]. Image registration was undertaken in offline review (Varian, USA) by one of four competent RTTs (SA, NK, RH, RL) and checked by a second RTT.

Median (range) intrafraction motion in the LR, SI and AP direction were calculated. Intrafraction deviation in three directions was also converted to a single vector ( $\sqrt{\Delta X^2 + \Delta Y^2 + \Delta Z^2}$ ) [14] for magnitude comparison.

Data was analysed using R-Studio (RStudio, USA), normality was established using a Shapiro-Wilk test.

### Rectal volume and intrafraction prostate motion

Correlation between rectal volume at pCT and during treatment, and intrafraction prostate motion was examined using Spearman's rho (significant  $p < 0.01$ ). The difference in intrafraction motion between 'small' and 'large' rectum groups was compared using a Mann-Whitney U test (significant  $p < 0.01$ ). Effect on intrafraction motion was also examined for patients with pCT rectal volumes in the fourth quartile versus those in volume quartiles one to three, and treatment fractions where rectal volume was  $<$  or  $\geq 90 \text{ cm}^3$ . Mann-Whitney U tests were used to examine for significance (significant  $p < 0.01$ ).

## Results

Rectal volume and intrafraction prostate motion data was not normally distributed. Rectal volume data was available for 40 pCT, 39 dMRI and 200 fractions. All data from the CAL patient without dMRI data was removed from the rectal volume analysis to avoid data skew. This patient's data is however included in motion and correlation analysis as dMRI volume is not used. Individual's raw rectal volume and intrafraction motion data is available in [supplementary material one](#).

### Rectal volume analysis

Median (range) rectal volume was  $74 (31\text{--}246) \text{ cm}^3$  on dMRI,  $64 (33\text{--}162) \text{ cm}^3$  on pCT, and  $65 (31\text{--}212) \text{ cm}^3$  on treatment imaging, inclusive of all patients. For both the MRL and CAL group, rectal volume on dMRI differed more than on-treatment volumes from pCT, however a significant volume difference was not reached at any timepoint ([Table 1](#)).

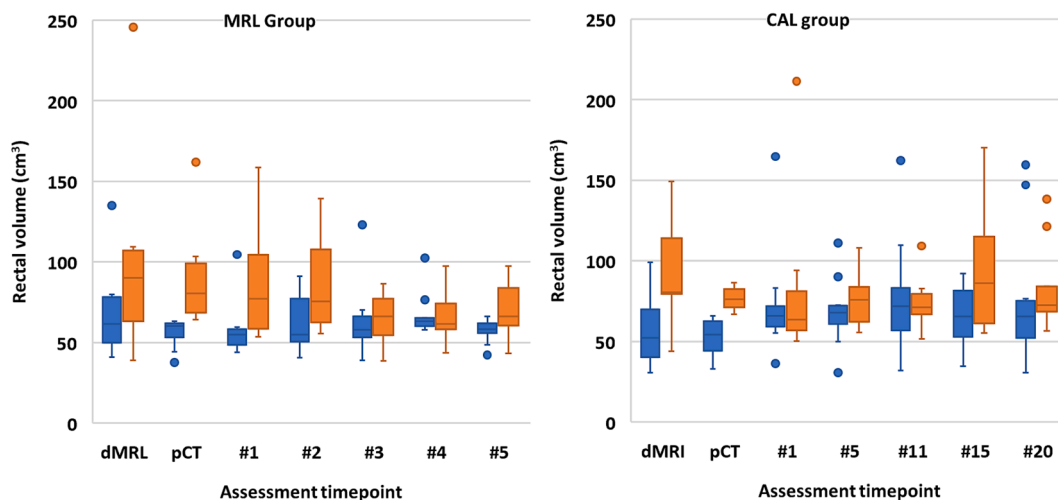
### Rectal volume subgroup analysis

Patients classified into the large rectum subgroup on pCT, maintained larger rectal volumes throughout treatment ([Fig. 1](#)). However, the difference in volume between small and large rectum subgroups was only significant at the pCT timepoint ( $p < 0.01$ ), not at dMRI or treatment timepoints ([Table 2](#)).

In the MRL small rectum subgroup, rectal volume at each timepoint was not significantly different to rectal volume on pCT. For the MRL large rectum subgroup, rectal volume at #4 was significantly smaller ( $p$

**Table 1**  
Median (range) rectal volume and difference in rectal volume at each timepoint compared to pCT volume.

Assessment timepoint (MRL/CAL)	Whole cohort Median (range) volume in cm <sup>3</sup>	MRL group Median (range) volume in cm <sup>3</sup>	Difference in median volume (cm <sup>3</sup> ) from pCT (p)	CAL group Median (range) volume in cm <sup>3</sup>	Difference in median volume (cm <sup>3</sup> ) from pCT (p)
dMRI	74 (31–246)	75 (39–246)	11 (0.29)	74 (31–149)	9 (0.33)
pCT	64 (33–162)	64 (38–162)	NA	66 (33–86)	NA
<b>During treatment (all)</b>	65 (31–212)	61 (39–159)	-3 (0.62)	70 (31–212)	4 (0.33)
#1 / #1		58 (44–159)	-6 (0.62)	65 (36–212)	-1 (0.33)
#2 / #5		66 (40–139)	2 (0.90)	72 (31–111)	6 (0.08)
#3 / #11		62 (39–123)	-2 (0.22)	71 (32–162)	5 (0.20)
#4 / #15		62 (44–102)	-2 (0.37)	69 (35–170)	3 (0.04)
#5 / #20		61 (42–98)	-3 (0.18)	70 (31–160)	4 (0.35)



**Fig. 1.** Rectal volume comparison between small (blue) and large (orange) volume subgroups. Median, interquartile range, range and outliers displayed.

**Table 2**  
Rectal volume differences between small and large rectal volume subgroups and difference in subgroup rectal volume at each timepoint compared to subgroup pCT volume.

MRL Group					
Timepoint	Small rectum group median (range) volume cm <sup>3</sup>	Large rectum group median (range) volume cm <sup>3</sup>	Difference in median volume cm <sup>3</sup> between groups (p)	Difference in small median volume cm <sup>3</sup> from small median pCT (p)	Difference in large median volume cm <sup>3</sup> from large median pCT (p)
dMRI	62 (41–135)	90 (39–246)	29 (0.19)	2 (0.19)	9 (0.70)
pCT	60 (38–63)	81 (64–162)	21 (<0.001)**	NA	NA
#1	55 (44–105)	77 (54–159)	22 (0.01)	-5 (0.85)	-4 (0.63)
#2	55 (40–91)	75 (56–139)	20 (0.03)	-5 (0.70)	-6 (1.00)
#3	58 (39–123)	66 (39–87)	8 (0.53)	-2 (0.70)	-15 (0.05)
#4	63 (58–102)	61 (44–98)	-2 (0.80)	3 (0.11)	-20 (<0.01)*
#5	58 (42–66)	66 (43–98)	8 (0.09)	-2 (0.92)	-15 (0.10)
CAL Group					
dMRI	52 (31–99)	81 (44–149)	28 (0.02)	-2 (0.85)	5 (0.36)
pCT	54 (33–66)	76 (67–86)	22 (<0.001)**	NA	NA
#1	66 (36–165)	63 (50–212)	-2 (1.00)	12 (<0.01)*	-13 (0.25)
#5	68 (31–111)	76 (56–108)	8 (0.32)	14 (<0.01)*	0 (0.91)
#11	72 (32–162)	71 (52–109)	-1 (0.90)	18 (0.02)	-5 (0.43)
#15	66 (35–92)	86 (55–170)	21 (0.13)	12 (0.01)	10 (0.50)
#20	66 (31–160)	73 (57–138)	7 (0.40)	12 (0.04)	-3 (0.57)

Note \* = p < 0.01, \*\* = < 0.001.

< 0.01) than at pCT, the other timepoints were not significantly different.

In the CAL small rectum subgroup, rectal volume at fraction-1 and fraction-5 was significantly larger (p < 0.01) than at pCT, the other timepoints were not significantly different. For the CAL large rectum subgroup, rectal volume at each timepoint was not significantly

different to rectal volume on pCT.

*Prostate intrafraction motion analysis*

Coupled prostate intrafraction motion and rectal volume data was available for 169 treatment fractions: 75 in the MRL and 94 in the CAL

group. Intrafraction motion was greatest in the AP direction, followed by SI, then RL (Table 3). Motion range was higher in the MRL group. Intrafraction motion (from completion of pre-treatment MRI to completion of post-treatment T2-weighted MRI) was measured over a median time of 46.13 min (34.23–66.65 min) in the MRL group. Compared to 8.33 min (6.40–16.06 min) in the CAL group (from completion of pre-treatment corrections to completion of post treatment CBCT).

#### Rectal volume and prostate intrafraction motion analysis

There was no significant correlation between patient's pCT rectal volume and median intrafraction motion over their RT course; LR  $r_s$  (38) = -0.23,  $p$  0.15; SI  $r_s$  (38) = -0.14,  $p$  0.40; AP  $r_s$  (38) = -0.09,  $p$  0.57; 3D vector  $r_s$  (38) = 0.05,  $p$  0.74 (Fig. 2).

There was no significant correlation between patients on treatment rectal volume and intrafraction motion for that fraction:

- MRL group correlation; LR  $r_s$  (73) = -0.03,  $p$  0.80; SI  $r_s$  (73) = 0.09,  $p$  0.46; AP  $r_s$  (73) = 0.20,  $p$  0.08; 3D vector  $r_s$  (73) = -0.01,  $p$  0.94.
- CAL group correlation; LR  $r_s$  (92) = -0.17,  $p$  0.11; SI  $r_s$  (92) = -0.10,  $p$  0.32; AP  $r_s$  (92) = 0.02,  $p$  0.82; 3D vector  $r_s$  (92) = 0.07,  $p$  0.51.

#### Rectal volume subgroup and prostate intrafraction motion analysis

For each volume subgroup, prostate intrafraction motion for all available fractions was compared. There was no significant difference in intrafraction motion between the small and large rectal volume subgroups (Fig. 3A). There was no significant difference in intrafraction motion in patients with rectal volume at pCT in the fourth quartile; > 79 and 75 cm<sup>3</sup> for the MRL and CAL groups respectively, versus those in volume quartiles one to three (supplementary material 2). For fractions where patient's rectal volume breached 90 cm<sup>3</sup> on daily MRI or CBCT imaging, intrafraction motion during that fraction was not significantly greater (Fig. 3B).

## Discussion

Rectal volume did not significantly change during extreme or moderately hypofractionated PCa RT and no correlation between rectal volume and prostate intrafraction motion was found.

#### Rectal volume

Rectal volume for the group was 74 (31–246) cm<sup>3</sup> on dMRI, 64 (33–162) cm<sup>3</sup> on pCT, and 65 (31–212) cm<sup>3</sup> on during RT imaging. No other literature was found to present rectal volume on diagnostic MRI. Average rectal volume on pCT for this group sits at the smaller end of

**Table 3**

Median prostate intrafraction motion and motion range.

Group	Direction	Median motion (mm)	Motion range (mm)
Combined cohort	LR	0.1	-9.0 to 10.0
	SI	0.2	-15.5 to 9.2
	AP	-1.0	-30.2 to 12.6
	3D vector	2.9	0.3–34.1
MRL	LR	0.2	-9.0 to 10.0
	SI	0.0	-15.5 to 9.2
	AP	-0.4	-30.2 to 12.6
	3D vector	3.8	0.6–34.1
CAL	LR	-0.1	-7.7 to 10.0
	SI	0.5	-7.7 to 7.5
	AP	-1.3	-7.9 to 7.0
	3D vector	2.2	0.3–10.4

reported pCT rectal volumes; 56.1 (±19.6) [15], 63.27 (19.64–183.51) [16], 73.3 (47.5–104.7) [17], 83.3 (41.5–154.5) [18] and 114.6 (43.9–259.1) [19] cm<sup>3</sup>. On treatment volume sits in the middle of previous reported data; 49.6–54.4 [15], 50.86 (+/- 9.34) [20], 54.65 (19.2–174.82) [16], 67.4 (36.2–150.1) [17], 86.1 (49.5–147.6) [18] and 94.3 (41.9–278.8) [19] cm<sup>3</sup>. Note the large volume range in our group (all using enemas) is synonymous with prior literature, volume variability occurs irrespective of the intensity of bowel preparation advice given; diet and enema management [15], simple emptying advice [16,17] or no instruction [19,20], indicating that rectal volume variability is dependent on the individual, governed by anatomical boundaries [21] and intrinsic patient and environmental factors [22].

Stable median rectal volumes during treatment, compared to pCT, are observed. Contradictory to previous studies [15,16,19,23] rectal volume did not significantly reduce with increasing fraction number. Rectal volume was quantified for every fraction of the MRL group and at regular intervals in the CAL group making results more comprehensive than some previous studies, reliant on volume assessments at limited timepoints [23,16]. The direction of rectal volume change is not unified in the literature, it is also reported as increasing during treatment [18,24,25] and not significant [26]. Varying analysis timepoints, bowel preparation, RT prescriptions and patient populations likely contribute to inconsistent findings.

CAL small rectum subgroup analysis detected significantly larger rectal volumes at fraction one and five of treatment compared to pCT, with rectal volume remaining larger throughout RT than at pCT. This finding in isolation would suggest that smaller rectal volumes at pCT have the propensity to change more during radiotherapy as there is room for organ expansion. Miralbell et al (2003) identified a trend for patients with smaller rectal volumes at pCT to have increased volumes during RT however their small-rectum threshold was <75 cm<sup>3</sup>, considerable higher than our CAL small group threshold (<66 cm<sup>3</sup>). This trend was not seen in the MRL group. Despite inconclusive evidence of this association, it does raise some doubt on the appropriateness of imposing rectal tolerances at pCT [12,13] which may not be achievable during RT.

Enema use is a confounding factor biasing our rectal volume results. As all patients used enemas the extent to which they altered rectal volume cannot be quantified. One could construe this data to endorse the use of enemas to maintain a stable rectal volume from pCT through RT. However, the lack of a significant difference in rectal volume between pCT and dMRI, fraction-11, 15 and 20, where no enemas were used, suggests enemas had little effect. A comprehensive review of rectal emptying strategies found no robust evidence to support the use of one preparation strategy over another and questioned the need for intensive regimes when using IGRT [27]. To address this issue, further work is needed to evaluate rectal volume changes in patients using and not using bowel preparation.

#### Intrafraction motion

Median intrafraction motion in our patient group was small and similar to previously reported studies [28–30]. The values reported account for all on couch motion, intrafraction bony anatomy shifts were not subtracted as per some previous studies [29]. This decision was taken as motion can cause target coverage compromise, irrespective of source, we recognise however that our motion results are therefore not solely attributable to internal anatomy changes.

Using pre-post treatment images to measure intrafraction motion risked overestimating errors, as each measurement contains matching uncertainty and possible motion after treatment cessation [31]. A truer assessment of intrafraction motion could have been gained through during treatment monitoring, using transperineal ultrasound [32], electromagnetic tracking [30] or cine MRI [21]. However, these solutions are not commonplace, so pre-post imaging continues to be a valid methodology. Further work is planned to retest our MRL dataset using cine MRI acquired during treatment [33].

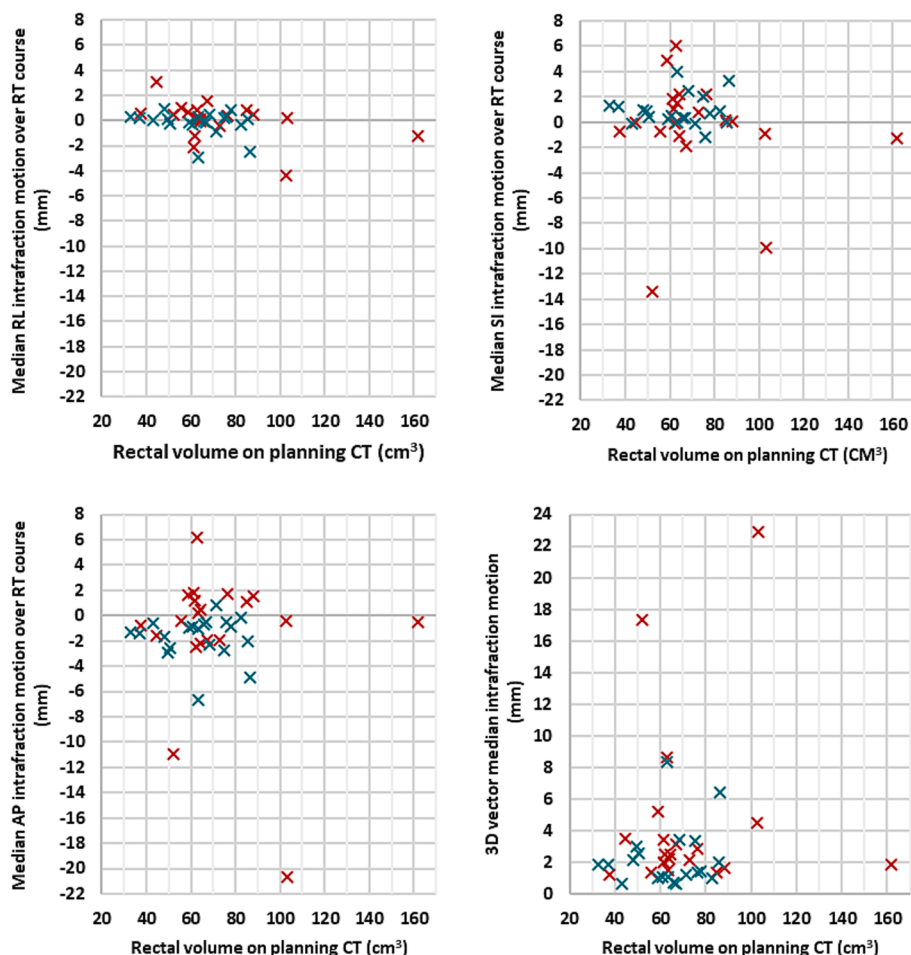


Fig. 2. Rectal volume on planning CT vs patient's median intrafraction motion over RT course (red = MRL group, green = CAL group).

Motion range was greater in the MRL group likely due to the substantially longer on-couch time, this supports prostate intrafraction motion as a random walk model, where variance continues to grow over time [21,34,35]. Twenty-one percent (16/75) of the MRL fractions triggered an ATP workflow [36] as the prostate breached the PTV margin on verification MRI, acquired just before treatment delivery. For these fractions the motion presented is larger than intrafraction motion during beam on. Shortening fraction duration is one method to limit the effect of random walk motion, but where substantial reductions are not possible, such as on the MRL, online tracking and position correction on-the-fly is the optimal mitigation strategy [34,37].

#### Rectal volume and intrafraction motion

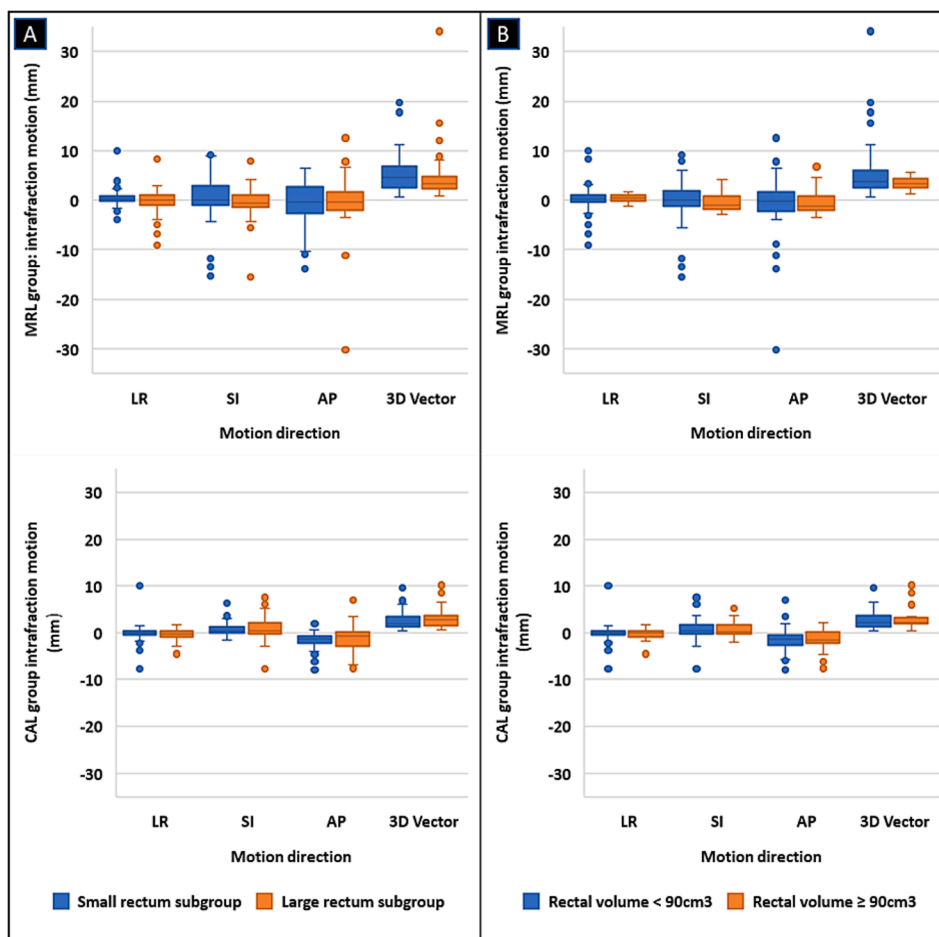
No significant correlation between patients' rectal volume on pCT and median intrafraction motion over RT course was found, refuting associations between a distended rectum on pre-radiotherapy scans, greater motion uncertainty and poorer outcomes [7–9]. Indeed, these articles are predominantly concerned with interfraction motion and recognise that the use of daily image guidance, to the prostate, offers a solution to reduce motion uncertainty and improve local control [7–9]. Further supported by Kupelian et al., (2008) and Silverman et al., (2016) who conclude that modern IGRT techniques alleviate the negative risk that rectal distension has on long-term tumour control.

Finding no association between rectal volume on pCT and intrafraction motion, means rectal measurements cannot be used as a patient specific motion prediction tool. If rectal volume at pCT is not indicative of intrafraction motion, we should reconsider the need for rectal diameter constraints at pCT, which when breached necessitate a repeat pCT

and inherent delay to the patient's pathway. We note that anecdotally patients bear the greatest burden in terms of emotional distress and time costs when rescans are performed due to failed rectal constraints [38].

No correlation between rectal volume on daily treatment images and motion during that fraction was found. Plus, no significant difference in motion was found when comparing fractions where rectal volume was  $<$  or  $\geq$  median volume or  $90 \text{ cm}^3$ . Anecdotal evidence tells us that adhering to a bowel preparation regime heightens patient's anxiety before and during PCa RT, but little data specifically addresses this issue [39]. Higher levels of anxiety are reported in PCa patients [40], preparing for radiotherapy can be a particularly stressful time [41] and distress due to information overload occurs [42]. Considering this, our findings, the inconclusive evidence supporting bowel preparation [27,38,43,44] and adherence to stringent daily volumetric IGRT protocols, we feel confident to withdraw the use of a blanket bowel preparation regime. This has potential to alleviate patient anxiety and distress, plus reduce the cost and plastic waste associated with enema use. The change will be carefully evaluated with respect to; rescan rates, inter and intrafraction motion and the psychological impact on patients.

A limitation of our pCT rectal volume motion analysis is that comparison with other studies is complicated by varying definitions of a large rectum, different volumes [9,10], cross sectional areas [7,8] or diameters [11] are described and different preparation schedules followed. Our large rectum definition 'rectal volume on pCT greater than the median' was smaller than previously used volume cut-offs [9,10], using the median value could also be criticised for including mid to large rectal volumes. Use of a large cut-off, such as  $90 \text{ cm}^3$  [9], was not appropriate as only three patients had pCT volumes higher than this. Instead, analysis was rerun dividing patients by rectal volume in the



**Fig. 3.** A: Intrafraction motion comparison between small (blue) and large (orange) volume subgroups. Median, interquartile range, range and outliers displayed. **Fig. 3B:** Intrafraction motion comparison between fractions where rectal volume on treatment imaging was  $< 90 \text{ cm}^3$  (blue) and  $\geq 90 \text{ cm}^3$  (orange). Median, interquartile range, range and outliers displayed.

fourth quartile versus those in volume quartiles one to three, still no significant difference in motion was found.

Other limitations include the measurement of rectal volume on different image datasets; MRI, CT and CBCT, the varying soft-tissue image quality achieved, and imaging parameters used may have influenced contour precision and resulting delineated volume. Contrary to this including patients with different RT prescriptions, treatment platforms and verification imaging strengthens the generalisability of findings. Rectal content was not analysed, previous research defining content as “gas, combination of gas and faeces, and faeces” found that only rectal gas significantly affected prostate intrafraction motion [14]. Having not appraised content we could not do this sub-analysis. Finally, we did not quantify the dosimetric effect of rectal volume changes. Previous research has reported both no significant [15,19,26,44,45], and significant [18] dosimetric impact due to rectal volume variation, with gas [26] and distention location [46] impacting this. Online correction of interfraction motion promotes accurate dose delivery to target irrespective of rectal volume changes [20], however appropriate caution must remain, especially for patients with locally advanced PCa, as translational isocentre shifts do not rectify seminal vesicle distortions [44]. Our next step will investigate the impact of rectal volume changes on dose.

## Conclusion

For this cohort of 40 PCa patients, treated with extreme or moderately hypofractionated radiotherapy, patient’s rectal volume remained

stable from dMRI, to pCT and through RT. Patient’s with larger rectal volumes at pCT continued to have larger rectal volumes during RT, although not significantly so. Rectal volume varied between individuals and fractions but no significant difference in volume was seen on images acquired with or without prior enema use. Larger rectal volumes on pre-treatment and treatment volumetric imaging did not predict greater intrafraction prostate motion.

Our findings support the relaxation of strict rectal diameter tolerances at pCT and do not support the need for rectal preparation when delivering contemporary IGRT to the prostate. Further work will repeat this analysis in a cohort of patients not using enemas and in addition quantify the effect on patient anxiety, RT satisfaction, workflow efficiency and RT dose.

## CRediT authorship contribution statement

**S.E. Alexander:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization. **U. Oelfke:** Conceptualization, Writing – review & editing, Supervision. **R. Westley:** Methodology, Investigation, Writing – review & editing. **H.A. McNair:** Conceptualization, Methodology, Writing – review & editing, Supervision. **A.C. Tree:** Conceptualization, Methodology, Writing – review & editing, Supervision.

## Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ctro.2023.100685>.

## References

- [1] The Global Cancer Observatory. Europe factsheet. <https://GcolarcFr/Today/Data/Factsheets/Populations/908-Europe-Fact-SheetsPdf> n.d. [Accessed 28.07.2023].
- [2] The Royal College of Surgeons of England. National prostate cancer audit: Annual Report 2022 NPCA Annual Report 2022 - National Prostate Cancer Audit [Accessed 28.07.2023].
- [3] Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol* 2016;17(8):1047–60.
- [4] Incrocci L, Wortel RC, Alemayehu WG, Aluwni S, Schimmel E, Krol S, et al. Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncol* 2016;17(8):1061–9.
- [5] Catton CN, Lukka H, Gu C-S, Martin JM, Supiot S, Chung PWM, et al. Randomized trial of a hypofractionated radiation regimen for the treatment of localized prostate cancer. *J Clin Oncol* 2017;35(17):1884–90.
- [6] Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. *Lancet* 2019;394(10196):385–95.
- [7] de Crevoisier R, Tucker SL, Dong L, Mohan R, Cheung R, Cox JD, et al. Increased risk of biochemical and local failure in patients with distended rectum on the planning CT for prostate cancer radiotherapy. *Int J Radiat Oncol Biol Phys* 2005;62(4):965–73.
- [8] Engels B, Soete G, Verellen D, Storme G. Conformal arc radiotherapy for prostate cancer: increased biochemical failure in patients with distended rectum on the planning computed tomogram despite image guidance by implanted markers. *Int J Radiat Oncol Biol Phys* 2009;74:388–91. <https://doi.org/10.1016/j.ijrobp.2008.08.007>.
- [9] Heemsbergen WD, Hoogeman MS, Witte MG, Peeters STH, Incrocci L, Lebesque JV. Increased risk of biochemical and clinical failure for prostate patients with a large rectum at radiotherapy planning: results from the dutch trial of 68 Gy versus 78 Gy. *Int J Radiat Oncol Biol Phys* 2007;67:1418–24. <https://doi.org/10.1016/j.ijrobp.2006.11.014>.
- [10] Kupelian PA, Langen KM, Willoughby TR, Zeidan OA, Meeks SL. Image-guided radiotherapy for localized prostate cancer: treating a moving target. *Semin Radiat Oncol* 2008;18:58–66. <https://doi.org/10.1016/j.semradonc.2007.09.008>.
- [11] Silverman R, Johnson K, Perry C, Sundar S. Degree of rectal distension seen on prostate radiotherapy planning CT scan is not a negative prognostic factor in the modern era of image-guided radiotherapy. *Oncology* 2015;90:51–6. <https://doi.org/10.1159/000441225>.
- [12] Board R. On target 2: updated guidance for image-guided radiotherapy. *Radiotherapy Board* 2021:182.
- [13] Ghadjar P, Fiorino C, Munck af Rosenschöld P, Pinkawa M, Zilli T, van der Heide UA. ESTRO ACROP consensus guideline on the use of image guided radiation therapy for localized prostate cancer. *Radiation Oncol* 2019;14:15–13.
- [14] Ogino I, Uemura H, Inoue T, Kubota Y, Nomura K, Okamoto N. Reduction of prostate motion by removal of gas in rectum during radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;72. <https://doi.org/10.1016/j.ijrobp.2008.01.004>.
- [15] Byun DJ, Gorovets DJ, Jacobs LM, Happersett L, Zhang P, Pei X, et al. Strict bladder filling and rectal emptying during prostate SBRT: Does it make a dosimetric or clinical difference? *Radiat Oncol* 2020;15(1). <https://doi.org/10.1186/s13014-020-01681-6>.
- [16] Anderson NS, Yu JB, Peschel RE, Decker RH. A significant decrease in rectal volume and diameter during prostate IMRT. *Radiation Oncol* 2011;98:187–91. <https://doi.org/10.1016/j.radonc.2010.12.005>.
- [17] Maund IF, Benson RJ, Fairfoul J, Cook J, Huddart R, Poynter A. Image-guided radiotherapy of the prostate using daily CBCT: The feasibility and likely benefit of implementing a margin reduction. *Br J Radiol* 2014;87(1044):20140459. <https://doi.org/10.1259/bjr.20140459>.
- [18] Pearson D, Gill SK, Campbell N, Reddy K. Dosimetric and volumetric changes in the rectum and bladder in patients receiving CBCT-guided prostate IMRT: Analysis based on daily CBCT dose calculation. *J Appl Clin Med Phys* 2016;17:107–17. <https://doi.org/10.1120/jacmp.v17i6.6207>.
- [19] Tøndel H, Solberg A, Lydersen S, Jensen CA, Kaasa S, Lund JÅ. Rectal volume variations and estimated rectal dose during 8 weeks of image-guided radical 3D conformal external beam radiotherapy for prostate cancer. *Clin Transl Radiat Oncol* 2019;15:113–7. <https://doi.org/10.1016/j.ctro.2019.02.003>.
- [20] Arya R, Goyal H, Naik A, Gurjar OP. A prospective observational study to analyse the influence of bladder and rectal volume changes on prostate radiotherapy using IMRT. *Rep Pract Oncol Radiother* 2020;25:312–7. <https://doi.org/10.1016/j.rpor.2020.03.004>.
- [21] de Muinck Keizer DM, Kerkmeijer LGW, Willigenburg T, van Lier ALHMW, Hartogh MDD, van der Voort van Zyp JRN, et al. Prostate intrafraction motion during the preparation and delivery of MR-guided radiotherapy sessions on a 1.5T MR-Linac. *Radiation Oncol* 2020;15:188–94.
- [22] Alexander SE, Oelfke U, McNair HA, Tree AC. GI factors, potential to predict prostate motion during radiotherapy; a scoping review. *Clin Transl Radiat Oncol* 2023:40. <https://doi.org/10.1016/j.ctro.2023.100604>.
- [23] Pinkawa M, Siluschek J, Gabel B, Demirel C, Asadpour B, Holy R, et al. Influence of the initial rectal distension on posterior margins in primary and postoperative radiotherapy for prostate cancer. *Radiation Oncol* 2006;81(3):284–90.
- [24] Miralbell R, Taussky D, Rinaldi O, Lomax A, Canales S, Escude L, et al. Influence of rectal volume changes during radiotherapy for prostate cancer: A predictive model for mild-to-moderate late rectal toxicity. *Int J Radiat Oncol Biol Phys* 2003;57(5):1280–4.
- [25] Muelas-Soria R, García-Mollá R, Morillo-Macias V, Bonaque-Alandí F, Sorribes-Carreras P, García-Piñón F, et al. The usefulness of adaptive radiotherapy in prostate cancer: how, when, and who? *Biomedicine* 2022;10(6):1401. <https://doi.org/10.3390/biomedicine10061401>.
- [26] Chen Z, Yang Z, Wang J, Hu W. Dosimetric impact of different bladder and rectum filling during prostate cancer radiotherapy. *Radiat Oncol* 2016;11. <https://doi.org/10.1186/s13014-016-0681-z>.
- [27] McNair HA, Wedlake L, Lips IM, Andreyev J, Van Vulpen M, Dearnaley D. A systematic review: Effectiveness of rectal emptying preparation in prostate cancer patients. *Pract Radiat Oncol* 2014;4:437–47. <https://doi.org/10.1016/j.proro.2014.06.005>.
- [28] Badakhshi H, Wust P, Budach V, Graf R. Image-guided radiotherapy with implanted markers and kilovoltage imaging and 6-dimensional position corrections for intrafraction motion of the prostate. *Anticancer Res* 2013;33(9):4117–21.
- [29] Choi Y, Kwak D-W, Lee H-S, Hur W-J, Cho W-Y, Sung GT, et al. Effect of rectal enema on intrafraction prostate movement during image-guided radiotherapy. *J Med Imaging Radiat Oncol* 2015;59(2):236–42.
- [30] Panizza D, Faccenda V, Lucchini R, Daniotti MC, Trivellato S, Caricato P, et al. Intrafraction prostate motion management during dose-escalated Linac-based stereotactic body radiation therapy. *Front Oncol* 2022;12. <https://doi.org/10.3389/fonc.2022.883725>.
- [31] Tudor GSJ, Bernstein D, Riley S, Rimmer Y, Thomas SJ, van Herk M, et al. Geometric uncertainties in daily online IGRT: refining the CTV-PTV margin for contemporary photon radiotherapy. *British Institute of Radiology* 2020. <https://doi.org/10.1259/geo-unc-igrt>.
- [32] Grimwood A, Thomas K, Kember S, Aldis G, Lawes R, Brigden B, et al. Factors affecting accuracy and precision in ultrasound guided radiotherapy. *Phys Imaging Radiat Oncol* 2021;18:68–77.
- [33] Goodwin E, Nil S, Dunlop A, Persson E, Alexander S, Westley R, Oelfke U. Motion prediction in 3D using 2D MR-Linac cine images: A comparative study between optical flow and template matching. Manuscript submitted for publication 2023.
- [34] Ballhausen H, Li M, Hegemann NS, Ganswindt U, Belka C. Intra-fraction motion of the prostate is a random walk. *Phys Med Biol* 2015;60:549–63. <https://doi.org/10.1088/0031-9155/60/2/549>.
- [35] Richter A, Exner F, Weick S, Lawrenz I, Polat B, Flentje M, et al. Evaluation of intrafraction prostate motion tracking using the Clarity Autoscan system for safety margin validation. *Z Med Phys* 2020;30(2):135–41. <https://doi.org/10.1016/j.zemedi.2019.12.004>.
- [36] Winkel D, Bol GH, Kroon PS, van Asselen B, Hackett SS, Werensteijn-Honingh AM, et al. Adaptive radiotherapy: The Elekta Unity MR-linac concept. *Clin Transl Radiat Oncol* 2019;18:54–9. <https://doi.org/10.1016/j.ctro.2019.04.001>.
- [37] Shimizu S, Nishioka K, Suzuki R, Shinohara N, Maruyama S, Abe T, et al. Early results of urethral dose reduction and small safety margin in intensity-modulated radiation therapy (IMRT) for localized prostate cancer using a real-time tumor-tracking radiotherapy (TRT) system. *Radiat Oncol* 2014;9(1). <https://doi.org/10.1186/1748-717X-9-118>.

- [38] McGuffin M, Devji N, Kehoe L, Carty A, Russell S, Di Prospero L, et al. To prep or not to prep - that is the question: A randomized trial on the use of antiflatulent medication as part of bowel preparation for patients having image guided external beam radiation therapy to the prostate. *Pract Radiat Oncol* 2018;8(2):116–22. <https://doi.org/10.1016/j.prro.2017.10.012>.
- [39] Bristow BJ, McGuffin M, Szumacher E, Fitch M, Di Prospero L, D'Alimonte L. Assessing the psychological impact of daily bowel preparation on prostate patients who receive radiation therapy. *J Med Imaging Radiat Sci* 2018;49:70–5. <https://doi.org/10.1016/j.jmir.2017.07.004>.
- [40] Brunckhorst O, Hashemi S, Martin A, George G, Van Hemelrijck M, Dasgupta P, et al. Depression, anxiety, and suicidality in patients with prostate cancer: a systematic review and meta-analysis of observational studies. *Prostate Cancer Prostatic Dis* 2021;24(2):281–9. <https://doi.org/10.1038/s41391-020-00286-0>.
- [41] Canil T, Cashell A, Papadakos J, Abdelmutti N, Friedman AJ. Evaluation of the effects of pre-treatment education on self-efficacy and anxiety in patients receiving radiation therapy: A pilot study. *J Med Imaging Radiat Sci* 2012;43:221–7. <https://doi.org/10.1016/j.jmir.2012.05.002>.
- [42] Reinhart R, D'Alimonte L, Osmar K, Court A, Szumacher E, Bristow B, et al. Educating Our patients collaboratively: A novel interprofessional approach. *J Cancer Educ* 2014;29(2):382–8. <https://doi.org/10.1007/s13187-014-0623-0>.
- [43] Yahya S, Zarkar A, Southgate E, Nightingale P, Webster G. Which bowel preparation is best? Comparison of a high-fibre diet leaflet, daily microenema and no preparation in prostate cancer patients treated with radical radiotherapy to assess the effect on planned target volume shifts due to rectal distension. *Br J Radiol* 2013;86(1031):20130457. <https://doi.org/10.1259/bjr.20130457>.
- [44] Yaver M, Foo A, Larsen T, Fineberg H, Zeng G, McGowan T, et al. Consistency of organ geometries during prostate radiotherapy with two different bladder and bowel regimens. *J Med Imaging Radiat Sci* 2015;46:380–7. <https://doi.org/10.1016/j.jmir.2015.09.001>.
- [45] Bostel T, Sachpazidis I, Splinter M, Bougattf N, Fechter T, Zamboglou C, et al. Dosimetric impact of interfractional variations in prostate cancer radiotherapy—implications for imaging frequency and treatment adaptation. *Front Oncol* 2019;9. <https://doi.org/10.3389/fonc.2019.00940>.
- [46] Fuchs F, Habl G, Devečka M, Kampfer S, Combs SE, Kessel KA. Interfraction variation and dosimetric changes during image-guided radiation therapy in prostate cancer patients. *Radiat Oncol J* 2019;37:127–33. <https://doi.org/10.3857/roj.2018.00514>.