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# Dealing with rectum motion during radiotherapy: How can we anticipate it?

Julien Pierrard [a,b,*], Sofie Heylen [b], Ad Vandermeulen [b], Geneviève Van Ooteghem [a,b]

[a] UCLouvain, Institut de Recherche Experimentale et Clinique (IREC), Center of Molecular Imaging, Radiotherapy and Oncology (MIRO), Brussels, Belgium
[b] Department of Radiation Oncology, Cliniques Universitaires Saint-Luc, Brussels, Belgium

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ABSTRACT

*Introduction:* Intra- and inter-fraction rectum motion is important for pelvic radiotherapy (RT). This study assesses how RT session duration, the presence or the absence of an intra-rectal tumour, and the distance from the anorectal junction (ARJd) impact rectal motion.

*Materials and methods:* Analyses used cone-beam computed tomographies (CBCTs) from RT patients treated for rectal and prostate cancer. Three structures were evaluated: (1) the entire rectum in patients without a rectal tumour ($Rectum_{Prostate}$); (2) the non-invaded portion ($Rectum_{Rectum}$) and (3) the tumour-invaded portion ($Rectum_{Tumour}$) in rectal cancer patients.

Intrafraction motion was assessed using the Hausdorff distance 95% and the Mean distance-to-agreement between structures delineated on the first CBCT and the 2 subsequent CBCTs within a same RT session. Interfraction motion was quantified by comparing structures delineated on the planning-CT and the first CBCT of each session. Linear mixed model evaluated rectum motion in relation to time, tumour presence, and ARJd, respectively.

*Results:* We included 10 patients with and 10 without rectal cancer, collecting 385 CBCTs. A significant correlation ($p < 0.05$) between rectum motion and RT session duration was found. Intrafraction motion was significantly higher in prostate cancer patients ($Rectum_{Prostate}$ motion > $Rectum_{Rectum}$ and $Rectum_{Tumour}$, $p < 0.01$). For interfraction motion, only the mean distance to agreement was significantly higher for $Rectum_{Prostate}$ ($p < 0.05$). Motion increased significantly with ARJd for all three structures ($p < 0.001$).

*Conclusions:* Session duration, absence of a tumour, and ARJd are associated with larger intra- and interfraction rectal motion. This highlights the need for tailored RT treatment, including online-adaptive RT, to manage intra- and interfraction variations. Rectal motion should be handled differently for patients with prostate cancer and those with rectal cancer.

## Introduction

Managing rectum motion is crucial for pelvic radiotherapy (RT) planning, as the rectum could be either part of the target volume in locally advanced rectal cancer (LARC) or an organ-at-risk, such as in prostate or cervix cancer [1–6].

For LARC, a neoadjuvant radiotherapy (RT) and chemotherapy combination is increasingly recommended before surgery [1–3]. Recent trials with total neoadjuvant strategies have improved the progression-free survival in first line and, also, increased complete pathological response rates, questioning the need for surgery [7–9]. Interest in conservative treatments, such as "Watch and wait" approach has certainly risen since then. Given the demonstrated relationship between the RT dose to the primary tumour and the complete response rate, RT dose escalation is increasingly investigated for organ preservation [10–12]. However, delivering an external beam RT boost can be limited by the unavoidable dose to organs-at-risk such as the bladder and the small bowel [13]. Moreover, multiple uncertainties restrain this RT dose escalation, including the rectum tumour motion.

On the other hand, in pelvic RT for other malignancies, the rectum is an important organ-at-risk that must be preserved to avoid toxicities that can negatively impact the quality of life of the patient [4–6]. In these

* Corresponding author at: UCLouvain, Institut de Recherche Experimentale et Clinique (IREC), Center of Molecular Imaging, Radiotherapy and Oncology (MIRO), Avenue Hippocrate 54, boîte B1.54.07, Brussels, Belgium.
*E-mail addresses:* julien.pierrard@uclouvain.be (J. Pierrard), sofie.heylen@saintluc.uclouvain.be (S. Heylen), ad.vandermeulen@saintluc.uclouvain.be (A. Vandermeulen), genevieve.vanooteghem@saintluc.uclouvain.be (G. Van Ooteghem).

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patients, personalised RT techniques that help to manage rectal motion, such as ART, offer an opportunity to reduce rectal toxicity [14,15].

A comprehensive determination of the rectum motion would facilitate personalised external beam RT boost or rectum-sparing treatments, including online-adaptive RT (ART). It could allow the computation of an accurate planning target volume (PTV) margin to be added around the boost volume or a rectum planning organ-at-risk volume (PRV) for other pelvic RT location. Online-ART can be performed with magnetic resonance imaging (MRI)-guided RT or cone-beam computed tomography (CBCT)-guided online-ART [16–20]. By using daily planning and online tracking of the tumour, MRI-guided RT has the potential to prevent geographic misses and excessive dose to organs-at-risk due to both intra- and inter-fraction tumour and rectum motion [16,17]. CBCT-guided online ART cope with the inter-fraction variations, but does not allow real-time tracking and, thus, cannot compensate for intra-fraction motion, which should be included in the PTV/PRV computation. However, these two technologies require substantial material resources and a dedicated team, making them less available. Therefore, integrating inter-fraction motion in PTV/PRV margin computation is essential for personalised RT when online-ART is unavailable.

Understanding the rectal motion is essential to provide tailored RT treatments. In this study, we analysed three factors that potentially impact the rectum motion on CBCTs performed during RT. First, we wondered if the rectum motion varied along a whole RT session. Second, we evaluated the impact of the presence of a tumour on the intra-fraction and inter-fraction rectum motion. Finally, we evaluated whether the motion of a segment of the rectum was greater according to its distance from the anorectal junction.

## Methods

### *Patient selection*

Patients treated with RT for rectal cancer were prospectively included from January to July 2023. Children, patients with a previous pelvic RT, and patients with peritoneal carcinomatosis were excluded. A second cohort of patients without rectal cancer was created by retrospectively including patients treated for a prostate adenocarcinoma by stereotactic ablative RT (SABR) from December 2022 to September 2023. This monocentric study, conducted in accordance with the Helsinki declarations, was approved by the ethics committee of Cliniques Universitaires Saint-Luc (reference number: B4032022000061). Informed consent was provided by rectum cancer patients.

### *RT procedure and CBCT acquisition*

In rectum cancer patients, a 3-mm slice thickness planning-CT (Aquilion LB, Canon medical systems corporation, Japan) was acquired in a supine position with a comfortably full bladder (300 ml of water 60 min before acquisition) and no rectum preparation. For prostate cancer patients, the planning-CT was also acquired in the supine position with the same bladder filling protocol. These patients had 2-mm slices acquired with additional immobilisation by a vacuum bag (Orfit, Belgium) and a rectum voidance protocol (rectal enema about an hour before CT acquisition if required).

For rectal RT, 25 Gy in 5 daily fractions was prescribed for short-course RT, and 45/54 Gy in 25 daily fractions for long-course RT to the pelvic lymph nodes according to the recommendations of Valentini et al., 2016 [21]. A simultaneous integrated boost was delivered to the primary tumour, extending to the entire adjacent rectal wall. A 7-mm and 10-mm isotropic PTV margin were used for the pelvic and boost volumes, respectively. For prostate stereotactic ablative RT, most patients received 29 Gy in 5 fractions every other day prescribed to the seminal vesicles with a 7-mm isotropic PTV margin. A simultaneous integrated boost of 35 Gy was delivered to the whole prostate with a 5-mm PTV margin. One patient received 36 Gy in 6 weekly fractions. Planning was performed on the Raystation planning system (clinical versions 9B and 12A, RaySearch Laboratories, Stockholm, Sweden). All patients were treated in one institution on two linear accelerators (Halcyon® and Ethos®, Varian a Siemens Healthineers Company, Palo Alto, Calif., USA) using equidistant field intensity modulated RT (IMRT) or volumetric modulated arc therapy (VMAT).

Three CBCTs per session were acquired for image-guided RT (IGRT). For SABR prostate patients, the acquisition of these three CBCTs was part of our institutional standard-of-care due to hypofractionated high-dose delivery. For rectum patients, the second and third CBCTs were obtained solely for the purpose of this analysis. For both groups of patients, the first CBCT (CBCT1) is acquired at the beginning of the session, allowing an initial co-registration with the planning-CT. This co-registration is based on the bony pelvis for rectum patients and radiopaque gold markers for prostate patients. Based on this co-registration, translational table displacements in the three axes can be done before the acquisition of a second CBCT (CBCT2), which was acquired just before RT delivery. A second rigid co-registration with the planning-CT is then performed, to ensure that there is no major intra-fraction variation, and supplementary table displacements are allowed. After the RT treatment, a third CBCT (CBCT3) is finally acquired and co-registered with the second CBCT, in order to evaluate the intrafraction anatomical variations. In this trial, for short-course rectal RT and prostate cancer patients, these three CBCTs were acquired at each session (totalling 15 CBCTs per patient), though there were some missing images in the retrospective prostate cancer group. For long-course rectum RT patients, these three CBCTs were acquired during the five first sessions and then during the first RT session of each following week, totalling 27 CBCTs per patient.

### *Motion evaluation*

All our analyses were conducted offline in a test version of the Raystation planning system dedicated to research, in which all the CBCTs were exported, cleaned of any co-registration information.For the evaluation of the interfraction motion, the CBCT1 was co-registered to the planning-CT, with a bone-based rigid co-registration. For the intra-fraction motion evaluation, we compared the CBCT2 & CBCT3 to the CBCT1. The CBCT2 displacements to align with the planning-CT and the CBCT3 displacements to align with CBCT2, which were made during the clinical RT session, were ignored for these analyses. In other terms, CBCT1, CBCT2, and CBCT3 were acquired in the same frame of reference, and no additional displacements or co-registrations were performed between them.

The rectum was manually delineated on each (CB)CT by one operator for all patients according to the guidelines of Mir et al., 2020 [22]. For rectal RT patients, a separate volume encompassing the circumferential rectal wall was delineated at each CBCT slice where the tumour was visible, using a co-registered planning-MRI. The anal canal wall was also included if the tumour extended inside. Therefore, we compared three groups of rectal structures: (1) the whole rectum of prostate cancer patients in which no tumour was present ($Rectum_{Prostate}$), (2) the whole rectum of rectum cancer patients in which a tumour was present (including the tumoral part, $Rectum_{Rectum}$), and (3) the tumoral rectal wall in rectum cancer patients ($Rectum_{Tumour}$).

The first analysis evaluated rectal motion as a function of time on a single treatment session timescale. For that purpose, we compared the motion of the rectum between CBCT1 and CBCT2 of the day to the motion between CBCT1 and CBCT3. No initial registration was made between CBCTs of the same session. We used the Hausdorff distance 95 % (HD95) and the mean distance-to-agreement (MDTA) to quantify this motion. The HD95 is a surrogate of the maximal distance between overlapping structures, and the MDTA quantifies the average distance between two structures. These values were reported for the three groups of volumes ($Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$).

The second analysis compared rectal motion based on the presence

or absence of a tumour. Intra- and interfraction HD95 values of $Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$ were compared. For interfraction motion evaluation, volumes delineated on CBCT1 were compared with those of the planning-CT after bone-based rigid co-registration. To assess intrafraction motion, volumes delineated on CBCT3 (or, if unavailable, CBCT2) were compared with those of the CBCT1 from the same day without co-registration between CBCTs (Fig. 1).

The third analysis evaluated whether rectum motion amplitude varied with distance from the anorectal junction. Intra- and interfraction motion were quantified for $Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$ at each CBCT slice level using the HD95. Unlike the first analyses comparing three-dimensional volumes, this comparison was made between sequential two-dimensional structures along the entire rectum. As opposed to the first analyses, here, $Rectum_{Tumour}$ slices were excluded from the $Rectum_{Rectum}$. For each of the $Rectum_{Prostate}$, $Rectum_{Rectum}$, or $Rectum_{Tumour}$ slices, the distance from the anorectal junction was calculated by multiplying the CBCT slice thickness by the number of slices separating it from the first section of the rectum.

### *Statistical analysis*

For each analysis (except the first one, aiming to evaluate the existence of a correlation between time and rectum motion), we reported the mean value of HD95 and MDTA over all sessions per patient. The distribution of HD95 and MDTA values was reported as the median [interquartile range] since they had a non-Gaussian distribution. The correlation between time and motion was performed using a linear mixed effect model where time was a fixed effect. Since multiple observations per patient were obtained, a linear mixed model was used with patients as the random factor when analysing the comparison between $Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$, the comparison between intra- and interfraction, and the correlation between distance from the anorectal junction and motion. In order to investigate the difference between categorical variables, post-hoc pairwise comparisons were performed with p-value adjustments for multiple comparison using the Benjamini-Hochberg method. A p-value $< 0.05$ was considered significant. HD95 and MDTA values were obtained using a homemade Python (version 3.10) script on Visual Studio Code (version 1.18.1). All data and statistical analyses were performed on RStudio (R version 4.2.1) using the "tidyverse", "lme4", and "ggpubr" packages.

## Results

### *Patients*

We included 10 rectum cancer and 10 prostate cancer patients (Table 1). In the rectum cancer group, one patient underwent a short-course RT, and nine patients were treated with long-course rectal RT combined with chemotherapy for locally advanced or metastatic rectal adenocarcinoma. Eighty-six sessions with three CBCTs each were performed in the rectum cancer group. In the prostate cancer group, there were 35 sessions with three CBCTs and 11 with two CBCTs each. In the rectum cancer group, liver, lung, and lymph node metastases were found in 2, 1, and 2 patients. One prostate cancer patient had lymph node metastases. All metastatic patients had systemic disease control during RT of the primary tumour. No patient presented symptoms form their metastatic disease nor liver dysfunction.

**Table 1**
Patient characteristics.

| | Prostate cancer patients | Rectum cancer patients |
|---|---|---|
| **N** | 10 | 10 |
| **Gender** | | |
| Male | 10 | 9 |
| Female | 0 | 1 |
| **Age (mean +/- SD)** | 69.4 +/- 8.2 | 59.5 +/- 14.4 |
| **Pelvic surgery history** | 2 | 1 |
| **Inflammatory bowel disease history** | 0 | 0 |
| **T stage** | | |
| Tx | 1 | 0 |
| T1 | 3 | 0 |
| T2 | 5 | 0 |
| T3 | 1 | 7 |
| T4 | 0 | 3 |
| **N stage** | | |
| N0 | 9 | 1 |
| N1 | 1 | 2 |
| N2 | 0 | 7 |
| **M stage** | | |
| M0 | 9 | 7 |
| M1 | 1 | 3 |
| **Medication during RT** | | |
| Antispasmodic | 0 | 1 |
| Opioid | 0 | 2 |
| **Number of sessions with multiple CBCTs** | 46 | 86 |
| **Number of CBCTs** | 127 | 258 |

CBCT: Cone-beam computed tomography, SD: Standard deviation

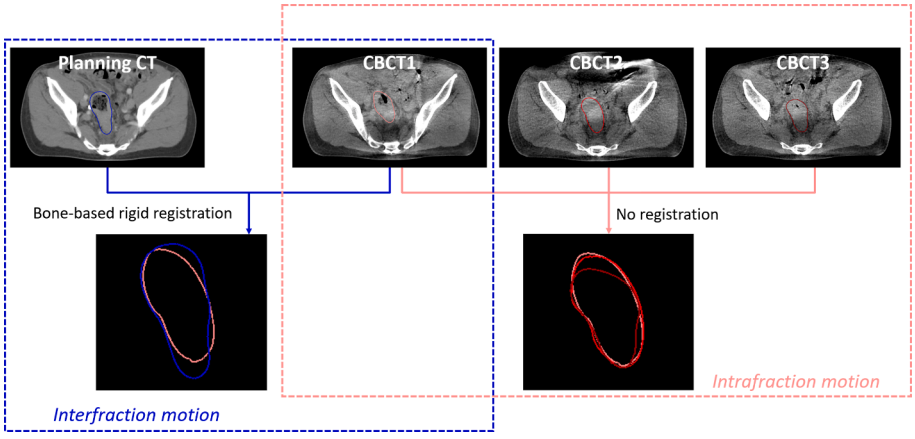


**Fig. 1.** Intrafraction and interfraction rectum motion evaluation. For intrafraction motion evaluation, rectum volumes on the three CBCTs of the session have been compared without any co-registration. For interfraction motion evaluation, rectum volumes on planning-CT and the first CBCT of the session have been compared after a bone-based co-registration between both images. (CB)CT: (Cone-beam) computed tomography.

*The impact of time*

In rectum RT patients, the median time elapsed from CBCT1 to CBCT2 and CBCT3 was 2.6 min [range: 2.2 – 3.3] and 6.9 min [6.0 – 7.9], respectively. For prostate cancer patients, this median time was 3.9 min [2.9 – 5.1] and 10.7 min [10.0 – 12.1], respectively. A significant positive correlation was found between time and increased motion in all groups ($Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$; $p < 0.05$). This correlation was the most pronounced for HD95 of $Rectum_{Prostate}$ ($\beta = 0.61$, Fig. 2).

At the time of the CBCT2, rectal motion was significantly smaller than at CBCT3 for all $Rectum_{Rectum}$ and $Rectum_{Tumour}$, demonstrating a progressive increase of the motion over time (Table 2).

*The impact of tumour presence*

For intrafraction motion assessment, the median HD95 values were 5.9 mm [4.0 – 7.1], 3.7 mm [3.1 – 4.2], and 2.8 mm [2.5 – 3.3], and the median MDTA values were 1.9 mm [1.6 – 2.1], 1.3 mm [1.2 – 1.3], and 1.0 mm [0.9 – 1.2], for the $Rectum_{Prostate}$, the $Rectum_{Rectum}$, and the $Rectum_{Tumour}$, respectively. Intrafraction motion was higher for $Rectum_{Prostate}$, followed by the $Rectum_{Rectum}$, with the $Rectum_{Tumour}$ showing the smallest variations (Fig. 3A).

For interfraction motion, the median HD95 values were 15.7 mm [12.4 – 23.9], 11.3 mm [10.2 – 17.9], and 12.0 mm [9.0 – 13.3], and the median MDTA values were 4.6 mm [4.4 – 5.7], 3.8 mm [2.9 – 4.5], and 3.2 mm [2.5 – 4.0], for the $Rectum_{Prostate}$, the $Rectum_{Rectum}$, and the $Rectum_{Tumour}$, respectively. Similarly, although less significantly than intrafraction motion, interfraction motion was greater for $Rectum_{Prostate}$ and smaller for $Rectum_{Tumour}$ (Fig. 3B).

For all three groups of structures, interfraction motion was significantly higher than intrafraction motion (Fig. 4).

**Table 2**
Evolution of intrafraction rectal wall motion from the CBCT1 to the CBCT2 and to the CBCT3.

| Volumes | Metric | CBCT2 | CBCT3 | p-value |
|---|---|---|---|---|
| $Rectum_{Prostate}$ | HD95 (mm) | 3.7 [2.4 – 6.5] | 5.1 [4.4 – 7.3] | 0.32 |
| | MDTA (mm) | 1.4 [1.0 – 1.9] | 1.8 [1.6 – 2.0] | 0.13 |
| $Rectum_{Rectum}$ | HD95 (mm) | 2.7 [2.5 – 3.3] | 3.3 [2.9 – 4.0] | 0.027 |
| | MDTA (mm) | 1.0 [1.0 – 1.1] | 1.2 [1.1 – 1.3] | 0.006 |
| $Rectum_{Tumour}$ | HD95 (mm) | 2.3 [2.1 – 2.5] | 2.6 [2.3 – 3.2] | 0.037 |
| | MDTA (mm) | 0.9 [0.8 – 0.9] | 1.0 [0.9 – 1.1] | 0.010 |

For $Rectum_{Rectum}$ and $Rectum_{Tumour}$, the motion of the rectum was significantly higher at the time of the CBCT3 than the CBCT2. The motion was quantified by reporting the HD95 and MDTA (median [interquartile range], in mm) between CBCT1 volumes and CBCT2/CBCT3 volumes.
Wilcoxon paired test, p-value $< 0.05$ is significant.
CBCT: Cone-beam computed tomography, HD95: Hausdorff distance 95%, MDTA: mean distance-to-agreement.

*The impact of distance from the anorectal junction*

Linear mixed effect models demonstrated a significant correlation between an increased distance from the anorectal junction and an increase in intrafraction motion of the rectum ($p < 0.001$, Fig. 5A). Similar results were demonstrated for the interfraction motion analysis ($p < 0.001$, Fig. 5B). The fixed-effect regression coefficients between interfraction rectum motion and distance from the anorectal junction were the highest for $Rectum_{Prostate}$, followed by $Rectum_{Rectum}$, and, then $Rectum_{Tumour}$ (HD95 fixed-effect regression coefficient $\beta = 1.81$, 0.97, and 0.77, and MDTA $\beta = 0.85$, 0.24, and 0.19, respectively) so was the correlation with interfraction motion (HD95 $\beta = 0.55$, 0.27 and 0.31, and MDTA $\beta = 0.17$, 0.06 and 0.08, respectively).

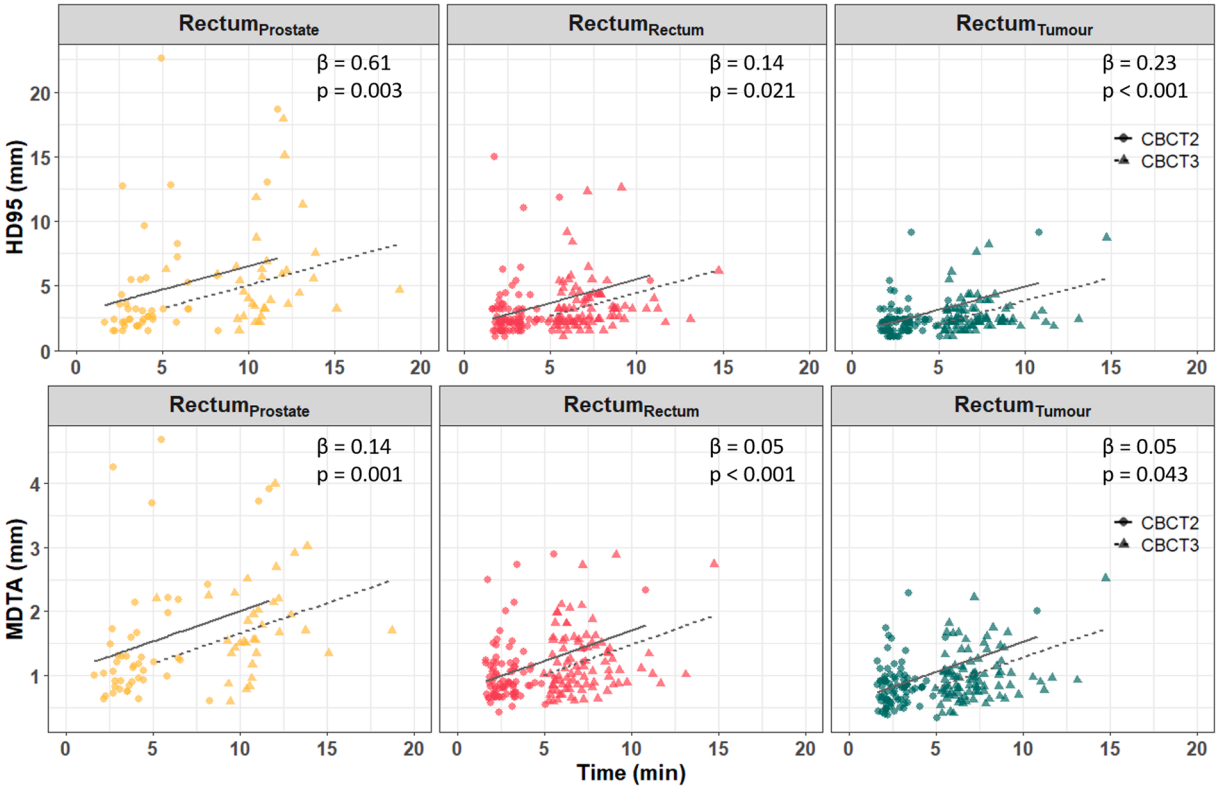


**Fig. 2.** Rectum motion increased with time. All three groups of structures ($Rectum_{Prostate}$, $Rectum_{Rectum}$, and $Rectum_{Tumour}$) demonstrated a significantly motion increase during the duration of a radiotherapy session. This was assessed by the HD95 and MDTA between the same structures delineated on each cone-beam computed tomography of a session. Grey line: linear regression line. Linear mixed-effect model, p-value $< 0.05$ is significant. HD95: Hausdorff distance 95 %, MDTA: Mean distance-to-agreement.

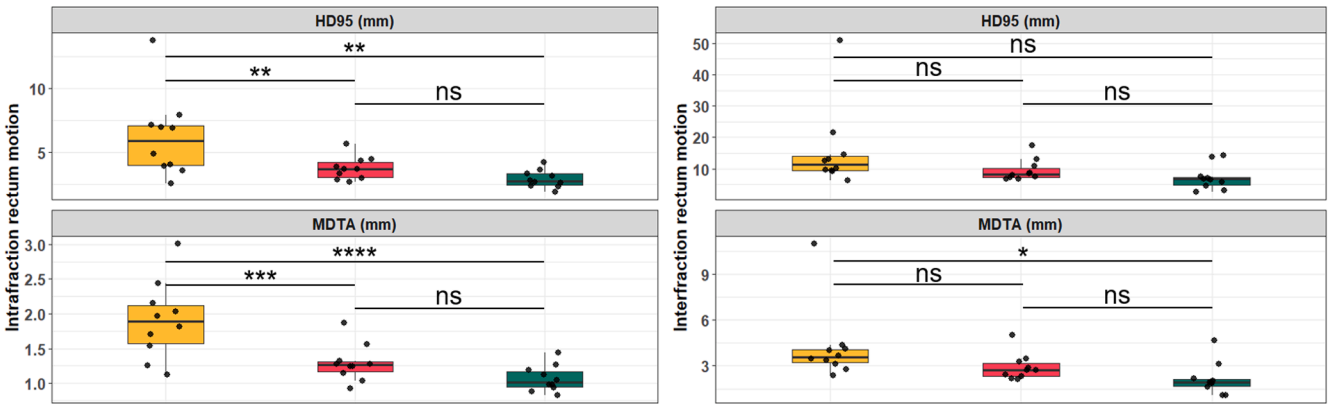


**Fig. 3.** Intrafraction (A) and interfraction (B) motion of the rectal wall in prostate SABR patients, the rectum in rectum RT patients, and the tumoral rectal wall in rectum RT patients. Scales in the ordinate axes are different between intrafraction and interfraction motion. Linear mixed-effect model, p-value $< 0.05$ is significant. ns: not significant, *$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, *** $p < 0.0001$. HD95: Hausdorff distance 95 %, MDTA: Mean distance-to-agreement, ns: Not significant, RT: Radiotherapy, SABR: Stereotactic ablative radiotherapy.

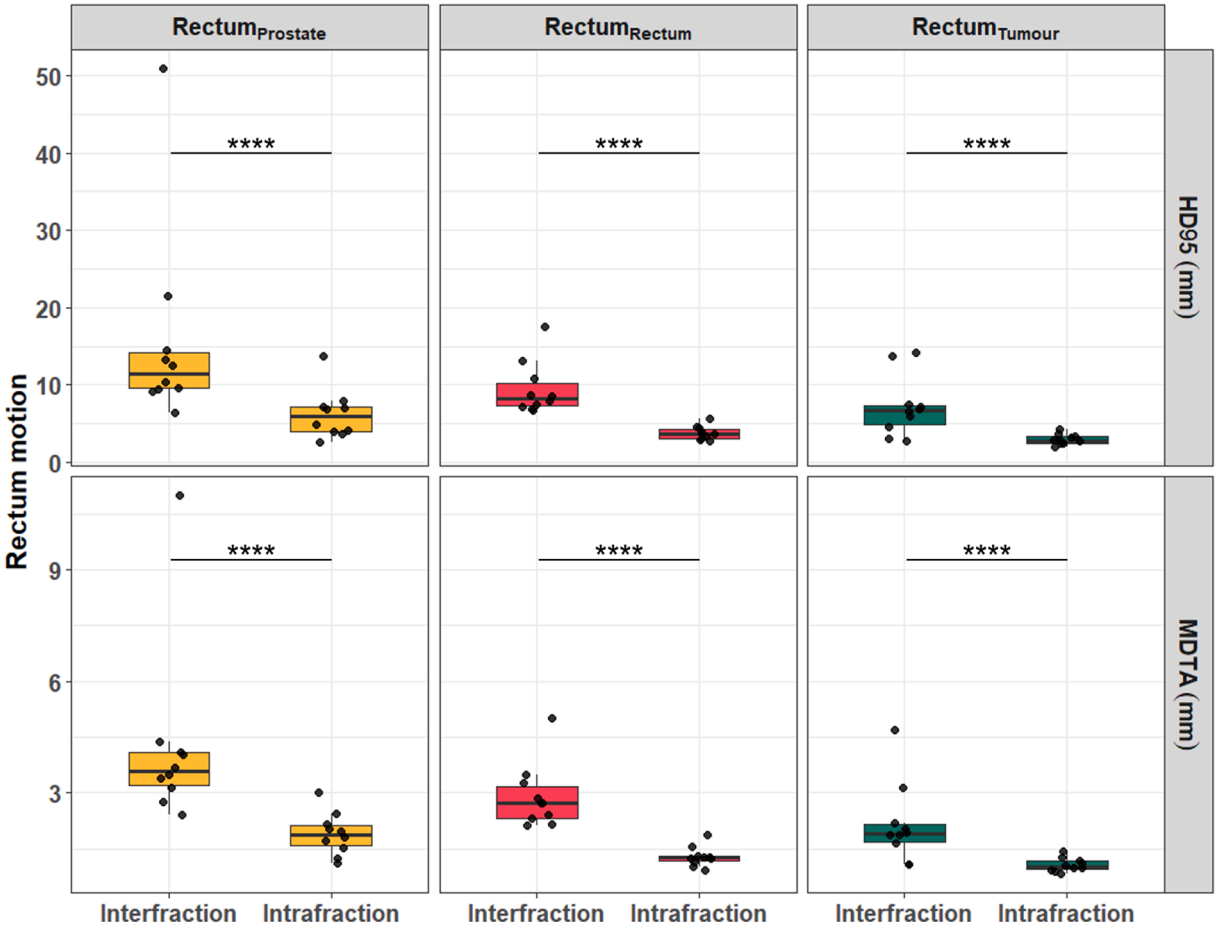


**Fig. 4.** Comparison of the interfraction and intrafraction motion of the rectum for the three groups of structures. Linear mixed-effect model, p-value $< 0.05$ is significant. **** $p < 0.0001$. HD95: Hausdorff distance 95 %, MDTA: Mean distance-to-agreement.

## Discussion

IGRT enhances the accuracy of RT delivery, potentially reducing toxicity and enabling dose escalation [23]. Daily CBCTs remain one of the most common IGRT strategies in pelvic cancer. However, comprehensive IGRT knowledge is necessary before implementing more complex techniques like online-ART. CBCT-guided or MRI-guided RT is promising but not yet widespread due to the need for substantial technical, financial, and human resources [24,25]. In this study conducted on a total of 385 CBCTs, we analysed three factors impacting rectal motion during RT: session duration, tumour presence, and distance from the anorectal junction.

We found a positive correlation between rectum motion and RT session duration. Rectum intrafraction motion was significantly greater at CBCT3 than at CBCT2 in $Rectum_{Rectum}$ and $Rectum_{Tumour}$. This was also observed in a cine-MRI study by Kleijnen et al., 2016, including 16

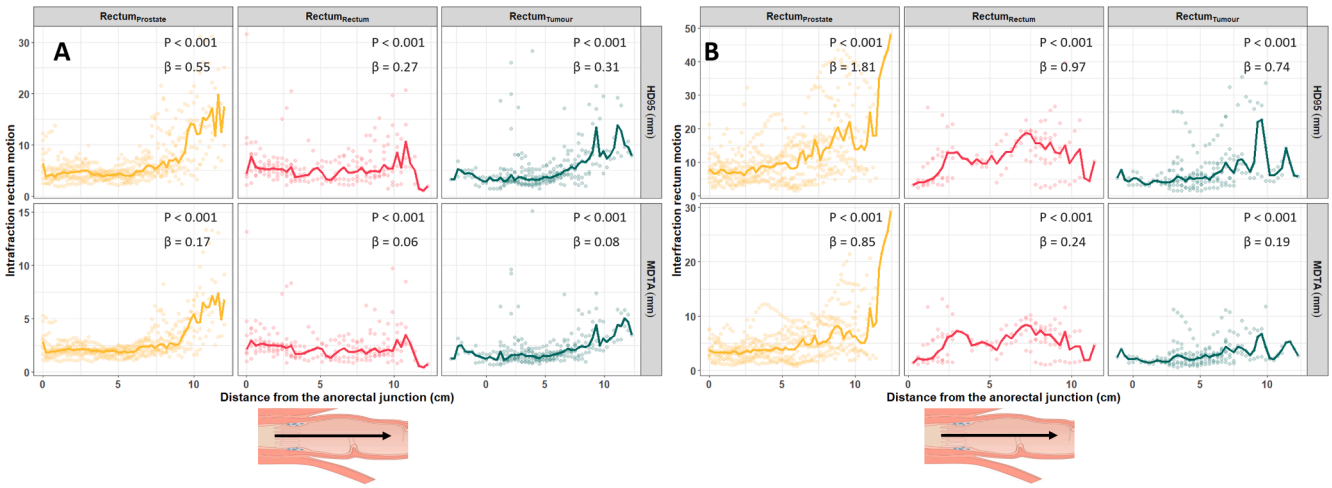


**Fig. 5.** Intrafraction (A) and interfraction (B) rectum motion increased with the distance from the anorectal junction for the $Rectum_{Prostate}$, and $Rectum_{Tumour}$. This was assessed by the HD95% and MDTA between the same structures delineated on CBCT. This correlation was higher for interfraction motion and for prostate cancer patients based on the fixed-effect regression coefficient β. Scales in the ordinate axes are different between intrafraction and interfraction motion. Coloured line: median value at each slice of the CBCTs, Grey line: linear regression line. Linear mixed-effect model, p-value $< 0.05$ is significant. CBCT: Cone-beam computed tomography, HD95: Hausdorff distance 95 %, MDTA: Mean distance-to-agreement. (Rectum image .
adapted from "Slagter, R. (n.d.). Drawing external and internal anal sphincter. AnatomyTOOL. https://anatomytool.org/content/slagter-drawing-external-and-internal-anal-sphincter-no-labels")

patients with a rectal tumour. They reported an average tumour motion within one minute of 2.3 mm (assessed by a metric similar to HD95). Most motion variation occurred between 1 and 18 min after reference image acquisition [26]. This is important for CBCT-guided online ART, where average session durations (patient on couch) were 26 min for rectal and 17.5 min for prostate cancer RT [18,27]. Reducing session time should be a key goal for pelvic online-ART to minimise rectum motion uncertainties and, therefore, PTV/PRV margins. Intrafraction motion was significantly lower than interfraction motion. This finding supports the use of online-ART that eliminates interfraction uncertainties and, thus, could reduce PTV/PRV margins compared to conventional RT. In the previously cited study of Kleijnen et al., 2016, a significant reduction of the PTV margin was achieved when only intrafraction tumour motion was considered, particularly with shorter session duration. This was no more applicable if the session duration was higher than 18 min [26]. PTV margins for interfraction motion compensation often exceed 1 cm but can be reduced to 5–8 mm using CBCT- or MRI-guided online-ART, eliminating interfraction motion [18,28–30].

To our knowledge, this is the first study comparing rectum motion between patients with ($Rectum_{Rectum}$, and $Rectum_{Tumour}$) and without a rectal tumour ($Rectum_{Prostate}$). Our results indicate that tumour presence decreases the rectum motion. Both intra- and interfraction rectum motions were higher for $Rectum_{Prostate}$ compared to $Rectum_{Rectum}$. These results should lead radiation oncologists to adapt their strategies of rectum motion management to the type of RT treatment, especially considering emerging RT treatments including prostate SABR and rectum dose escalation for organ preservation purpose [10–12,31]. For example, margins can be used to limit rectal toxicity for prostate SABR patients (i.e. PRV) or to ensure correct target volume coverage in rectum patients (i.e. PTV). Our results suggest therefore that the uncertainties linked to rectal motion are lower for rectum cancer compared to prostate cancer patient and, thus, the rectum PTV used for rectum cancer patient should be smaller than the rectum PRV in prostate SABR patients.

The main limitations of our study are related to the heterogeneity between prostate cancer and rectum cancer patients. First, the preparation differed between the prostate SABR and the rectum RT groups. In the rectum RT group, no rectal preparation was recommended to avoid additional rectal irritation, while in the prostate SABR group, a strict rectum voidance protocol (bowel movement one hour before the RT session, using an enema if necessary) was required to minimise uncertainties linked to rectal volume variations during RT delivery. The impact of laxatives, enemas, and other preparation strategies (probiotics, adapted diet, or mechanical rectal evacuation) on interfraction motion remains debated, while for intrafraction motion, data are scarce [32,33]. If there was an impact to consider, rectal emptying strategies would tend to reduce the variability of rectal volume and, consequently, its motion. In a study of Hoogeman et al., 2015, the rectum volume observed in the planning-CT was correlated with its interfraction variation, suggesting that voidance strategies could reduce interfraction motion [34]. Similarly, the use of enema during prostate RT has the potential to limit prostate interfraction motion [35]. Additionally, in a different context, MRI studies have evaluated strategies to optimise image acquisition. Among these, enemas may improve or, at worst, have no impact on rectum motion artefacts [36,37]. Extrapolating these data to our analysis's context, enemas and, more generally, rectal emptying protocols seem to have only a limited impact on rectal motion and, at worst, would tend to reduce rectal movement in our $Rectum_{Prostate}$ patients. Therefore, our conclusion about greater rectal motion in patients with prostate cancer compared to those with rectal cancer seems reinforced. Though, these results might be contra-intuitive for the prostate cohort, since rectal voidance protocols were built to reduce rectum, and thereby prostate motion during (stereotactic) radiotherapy. However, caution should be paid to the fact that this trial compared a rectal patient cohort to a prostate patient cohort. It did not focus on prostate cancer patients only and therefore did not compare cohorts of prostate SABR patients, and more specifically one with and one without voidance protocol. No conclusion can thus be made in that extend. Man should keep in mind that these results do not discriminated rectal voidance protocols recommended for prostate (stereotactic) radiotherapy. Second, CBCT2s were acquired later in prostate cancer patients compared to rectum cancer patients (median: 2.6 versus 3.9 min, respectively), as were CBCTs3 (median: 6.9 versus 10.7 min), potentially overestimating the rectum motion in prostate SABR patients. This was due to a longer IGRT time, requiring a validation of a radiation oncologists in prostate cancer patients, while, in rectum cancer patients, the whole treatment was performed by the radiation therapists. Additionally, the dose per fraction and the delivered monitor units were higher in prostate cancer patients, leading to a higher RT session duration. We did not try to replicate the timing between CBCTs of prostate cancer patients in the

prospective cohort of rectum cancer patients because of logistical implications (prolonged treatment slot, absence of patient benefit, and patient discomfort…) and to reproduce clinical conditions where multiple CBCTs are not acquired in rectum cancer patients. Third, three patients in the rectum RT group have taken opioids or antispasmodic medications during RT, which can potentially reduce gastrointestinal motion, while none of the prostate group patient were treated with those drugs. Constipation is a well-known adverse effect of opioid drugs and is related to prolonged colonic transit time, suggesting a reduction in rectal movement. However, the specific effect on the rectal segment remains debated [38–40]. Similarly, the effect of antispasmodic drugs on rectum motility seems to be limited [41]. Fourth, three and one patients had visceral metastases in the rectum and prostate cancer groups, respectively. None of them had peritoneal carcinomatosis or metastatic-induced liver failure, two conditions that can impact gastrointestinal peristaltism [42,43]. However, whether other metastases can have a systemic impact on rectal motion is unknown; this deserves further investigation. Fifth, both the whole RT treatment duration and the volume of irradiated patients are smaller for prostate cancer patients compared to rectum cancer patients. Alexander et al., 2023 have demonstrated that the rectum volume variation and prostate intrafraction motion is similar in prostate cancer patient treated by either 5- or 20-fractions suggesting that the entire duration of the RT treatment have no impact rectum motion [44]. In rectum cancer patients, the rectum volume is stable or tends to decrease along the RT course, but extrapolation of these results to inter/intrafraction rectal motion variation has not been demonstrated [45,46]. Since bowel irradiation increases bowel mobility, reduces intestinal transit time, and is associated to diarrhoea, our results about a higher rectal motion in prostate cancer compared to rectal cancer patients seems to be reinforced [47–50]. To obtain definitive confirmation that rectum motion is reduced in rectal cancer patients compared to prostate cancer patients, further investigations that control these factors of heterogeneity are required.

Both intra- and interfraction motion of the $Rectum_{Tumour}$ increased with distance from the anorectal junction, consistent with Chong et al., 2011. They evaluated the interfraction motion of the rectum in 16 patients treated for a rectal adenocarcinoma based on an anatomical rectum division based in upper (0—–5 cm from inferior border of L5), mid (5.1 – 10 cm), and lower rectum (>10 cm). The upper rectum motion was significantly higher than that of the mid and the lower rectum. They recommended a PTV margin that accounts for setup and interfraction uncertainties, with to 1.76 cm in the anterior direction for the upper rectum [45]. Similar findings suggesting a higher interfraction motion of the upper rectum were demonstrated in other studies [51–53]. Our results found also an increased intrafraction motion with distance from the anorectal junction in the $Rectum_{prostate}$ group, but, surprisingly, not in the $Rectum_{Rectum}$ group. This was possibly due to our methodology that excluded the tumours from the whole rectum structure for the $Rectum_{Rectum}$ group.

This study has other limitations, such as the retrospective image collection in prostate SABR patients and the small number of patients. The high number of CBCTs included in this analysis could, however, ensure the robustness of the results for each patient. Also, the metrics used for motion quantification, HD95 and MDTA, are sensitive to the delineation variation of rectal structures. To reduce this impact, all volumes were delineated by one single operator. Additionally, we quantified only three factors that influence rectal motion, which should be integrated in the PTV/PRV margin or the IGRT workflows to guide personalised RT strategies, including CBCT-guided online-ART. However, additional factors impacting rectum motion should also be included for PTV/PRV margin computation, including patient's [54–56], treatment position [55], and changes during the treatment course [28,46,51,54]. Further analyses should certainly also focus on these factors.

## Conclusions

In this study, we evaluated the rectum motion in patients with and without rectal cancer. Using a linear mixed model, longer RT sessions were significantly correlated ($p < 0.05$) with an increased intrafraction motion, regardless of tumour presence. Intra- and interfraction rectum motion were smaller in rectal cancer patients in comparison to prostate cancer patients. Interfraction motion was consistently larger than intrafraction across all our analyses. Additionally, we observed a significant association between the rectum motion and the distance to the anorectal junction: the greater the distance from the anorectal junction, the greater the rectum motion ($p < 0.001$). The fixed-effect regression coefficient was higher for prostate cancer patients than for rectum cancer patients, and higher for interfraction compared to intrafraction motion. This corroborates the previous results of a greater rectum motion in prostate cancer patients compared to rectum cancer patients and, thus, suggests a fixing effect of the tumour.

These insights contribute to improve personalised pelvic RT, for which rectal motion should not be managed in the same way for prostate and rectum cancer patients. Finally, our results underscore the need for online adaptive radiotherapy development, certainly in the light of the daily interfraction variations we observed, providing short adaptive treatment sessions.

## Informed patient consent

The authors confirm that written informed consent has been obtained from the prospectively included patients or if appropriate from the parent, guardian, power of attorney of the involved patients; and, they have given approval for this information to be published in this case series. Medical and image data use from retrospective patients, who did not object to their use for research purposes, was approved by the ethics committee of Cliniques Universitaires Saint-Luc.

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## CRediT authorship contribution statement

**Julien Pierrard:** Conceptualization, Methodology, Software, Formal analysis, Data curation, Writing – original draft, Visualization. **Sofie Heylen:** Data curation. **Ad Vandermeulen:** Data curation. **Geneviève Van Ooteghem:** Data curation, Writing – review & editing, Supervision.

## Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Julien Pierrard: PhD project was partially funded by Varian, a Siemens Healthineers Company. Sopfie Heylen: None. Ad Vandermeulen: None. Geneviève Van Ooteghem: None].

## Data Availability

Data will be share upon acceptable request.

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