Technical Innovations & Patient Support in Radiation Oncology 32 (2024) 100284

Contents lists available at ScienceDirect

Technical Innovations & Patient Support in Radiation Oncology

journal homepage: www.sciencedirect.com/journal/technical-innovations-and-patient-support-in-radiation-oncology

Research Article

On the trail of CBCT-guided adaptive rectal boost radiotherapy, does daily delineation require a radiation oncologist?

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ARTICLE INFO

Keywords:
Rectum radiotherapy
CBCT-guided radiotherapy
Rectum boost
Delineation variability
Radiation Therapists

ABSTRACT

Introduction: Dose-escalation radiotherapy for rectal tumours is increasingly considered as a non-operative approach, with online-adaptive radiotherapy (oART) supporting this approach by correcting inter-fraction tumour position errors. However, using cone-beam computed tomography (CBCT)-guided oART requires daily target volume delineation by different operators, leading to inter-operator delineation variability and potential dosimetric issues. This study aims to compare and quantify the inter-operator and inter-professional delineation variability of the rectal boost volume on CBCT, including volumes by an automatically delineated oART treatment planning system.

Materials and methods: A rectal boost volume, defined as the primary tumour extended to the entire adjacent rectal wall, was delineated on 10 CBCTs from 5 patients by 15 operators: 4 expert radiation oncologists (ROs), 4 radiation therapists (RTTs) and 7 non-expert ROs. These contours were compared between the different professional groups. A comparison to the average volume of the group (ROs, RTTs, or non-expert ROs) with the lowest delineation variability was also performed for each individual volume including the volume automatically generated by an oART treatment planning system.

Results: Delineation variability was the highest in the superior (range: 2.3–6.0 mm), and inferior (2.3–12.4 mm) directions, compared to the left (0.2–4.4 mm), right (0.3–2.0 mm), anterior (0.1–2.9 mm), and posterior (0.5–4.0 mm) directions. Non-expert ROs, RTTs, and automatic oART volume showed similar ranges of delineation errors when compared to the expert ROs' volume, which was chosen as reference volume since this professional group showed the lowest variability.

Discussion: Expert ROs showed consistent results. Other professional groups exhibit similar variability, comparable to the automatic oART volume. Therefore, RTTs could safely perform the rectal boost delineation without non-expert ROs supervision in the absence of expert ROs during CBCT-based oART. Moreover, these findings provide quantitative data to compute accurate margins for the rectal boost planning target volume in a CBCT-guided oART workflow.

Abbreviations: AI, Artificial intelligence; (A)RT, (Adaptive) Radiotherapy; CBCT, Cone-beam computed tomography; CTV, Clinical target volume; MRI, Magnetic resonance imaging; OAR, Organ-at-risk; PTV, Planning target volume; RO, Radiation oncologist; RTT, Radiation therapist; W&W, Watch and wait.

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https://doi.org/10.1016/j.tipsro.2024.100284
Received 27 June 2024; Received in revised form 9 October 2024; Accepted 15 October 2024
Available online 22 October 2024

Introduction

Neoadjuvant long-course concomitant radiochemotherapy is currently recommended for treating locally advanced rectal cancer before surgery, improving local recurrence and survival rates [1–3]. This treatment paradigm is shifting towards "Total Neoadjuvant Treatment" (TNT), which combines long-course radiotherapy (RT) with chemotherapy, leading to high rates of complete responses and enabling non-operative "Wait and Watch" (W&W) strategies [1,2,4]. However, only patients achieving a complete clinical response after this TNT are suitable for W&W [4,5]. A model published by Appelt et al. 2013 indicates a RT dose–response relationship in rectal cancer, that RT dose escalation (boost) to the primary tumour could increase complete response rates. [6]. This boost can be performed using external-beam RT, either sequentially or simultaneously [4,7,8]. However, minimising the RT dose to the organs-at-risk, such as the small bowel, the bladder, or the non-tumorous rectum is crucial to prevent superimposed toxicities.

Cone-beam computed tomography (CBCT)-guided online-adaptive RT (oART) is emerging as a valuable technology in rectal cancer treatment. It offers the potential to reduce the planning target volume (PTV) margin by eliminating setup and interfraction anatomical variation uncertainties [9]. CBCT-guided oART incorporates an online treatment planning system (TPS), which daily delineates organs-at-risk and target volumes before generating an adapted plan. Although these delineations are initially automated, about 50 % require time-consuming manual adjustments [9–11]. This procedure is usually performed by a radiation oncologist (RO), though radiation therapists (RTTs) are also integrating into these workflow for rectal RT [9]. Multiple operators, including ROs and RTTs, may handle these delineations throughout treatment, introducing target volume delineation variability, particularly problematic when escalating doses within a larger clinical prophylactic target volume. Currently, the absence of standardised guideline for the rectal boost delineation exacerbates this variability, which could impact dosimetry significantly, potentially leading to a lack of local control due to tumour underdosage or excessive toxicities due to organ-at-risk overdosage [12–15]. Additionally, the duration of the oART process is crucial, particularly in rectal radiotherapy where significant anatomical changes can occur rapidly due to physiological motion of the rectum, often within the span of several minutes, necessitating fast adaptation to ensure treatment accuracy [16]. This underscore the importance of developing workflow that reduce adaptation times.

This study aims to quantify the inter-operator and inter-professional (expert ROs, RTTs, and non-expert ROs) delineation variability of the rectal boost volume on CBCT and to compare these with automatically delineated volumes by an oART TPS. This would provide insights for making the oART process more efficient.

Material and methods

Sampling

CBCT images from five patients who underwent a 5-week concurrent radiochemotherapy regimen for rectal cancer were collected and anonymized. Patients were prospectively selected based on tumour location using a convenience sampling approach to include a diversity of cases reflecting clinical practice. Children and patients with a prior history of pelvic RT were excluded. RT was performed in a supine position with a full bladder (oral water intake of 300 ml, 60 min before acquisition) and without rectum preparation. All patients were treated using two linear accelerators (Halcyon® and Ethos®, Varian a Siemens Healthineers Company, Palo Alto, Calif., USA). CBCTs were acquired using the "pelvis fast" (energy: 125 kV, electric charge: 560 mAs, acquisition time: 21.2 s) or the "pelvis large fast" (energy: 140 kV, electric charge: 672 mAs, acquisition time: 25 s) modes of both linear accelerators. The CBCT slice thickness was set to 2.00 mm for all the patients, with a resolution of 512 x 512 pixels (0.96 x 0.96 mm). Two CBCTs from the first RT session (one acquired before and one after RT delivery) for each patient were used to evaluate delineation uncertainties, yielding a total of 10 CBCTs. For all CBCT images, no corresponding daily magnetic resonance images (MRI) were available.

Procedure and data collection

Fifteen operators participated in this delineation study: four ROs with expertise in pelvic RT, four RTTs, and seven non-expert ROs. All operators were working at the same institution during the study and are actively involved in online adaptive radiotherapy delivery.

The boost clinical target volume (CTV) was defined as the rectal tumour extending to the entire adjacent rectal wall. This definition was based on a preliminary analysis assessing intra- and inter-operator reproducibility between different CTVs (see Appendix). Each of the 10 CBCTs was delineated for boost CTV by all 15 operators using the Raystation Planning system (clinical version 12A, RaySearch Laboratories, Stockholm, Sweden). To guide the delineation, the operators had access to the planning CT with the originally delineated CTV used for the treatment and a T2-weighted MRI with transversal and sagittal reconstructions obtained prior to RT planning.

In order to generate the automatic oART volume, virtual oART sessions were conducted using the oART TPS emulator of the ETHOS®, a linear accelerator dedicated to oART. This TPS integrates an artificial intelligence-based software for automatic organ-at-risk delineation. Based on the anatomy of the day of some of these organs-at-risk, called influencers, a deformable image registration is computed between the planning CT and the CBCT. Then, target volumes are propagated from the planning CT to the CBCT using the vector field from this deformable registration. In this study, the only influencer used for target volume propagation was the rectum. The automatically generated oART rectal boost volumes were collected without manual adaptation and, finally, compared to human volumes.

Data analysis

Inter-operator and inter-professional analysis

The overall delineation variability was evaluated across all directions by generating an average volume from the rectal boost volumes delineated by all human operators. For each operator, the average deviation variability value was reported.

Additionally, the inter-professional delineation variability among expert ROs, RTTs, and non-expert ROs was evaluated and compared. Within each professional group, the individual rectal boost volumes to the group's average volume were compared. Subsequently, the average deviation variability values were compared between each professional group. The average volume of the group (ROs, RTTs, or non-expert ROs) with the lowest delineation variability was considered as the reference for the last part of this analysis.

Finally, the delineation variability was compared between the automatic oART volumes and the human volumes to this reference volume, thus assessing the performance and accuracy of the automated system in relation to the human-delineated volumes.

Delineation variability analysis

The delineation variability values were acquired, for transversal (left, right, anterior, and posterior) directions, by including all the operator's volumes in the same frame of reference (Fig. 1A) and by restricting these to the CBCT slices delineated by all the 15 operators (Fig. 1B). Since no matched MRI was available to delineate the real contours of the tumour on the daily CBCTs, an average volume was generated from the structures created by all human operators, which was then used as the reference volume (Fig. 1C). For the left–right direction, coronal slices were individualised from the average volume and compared them to those from each operator's delineations (Fig. 1D). To focus only the left–right variability and eliminate the influence of

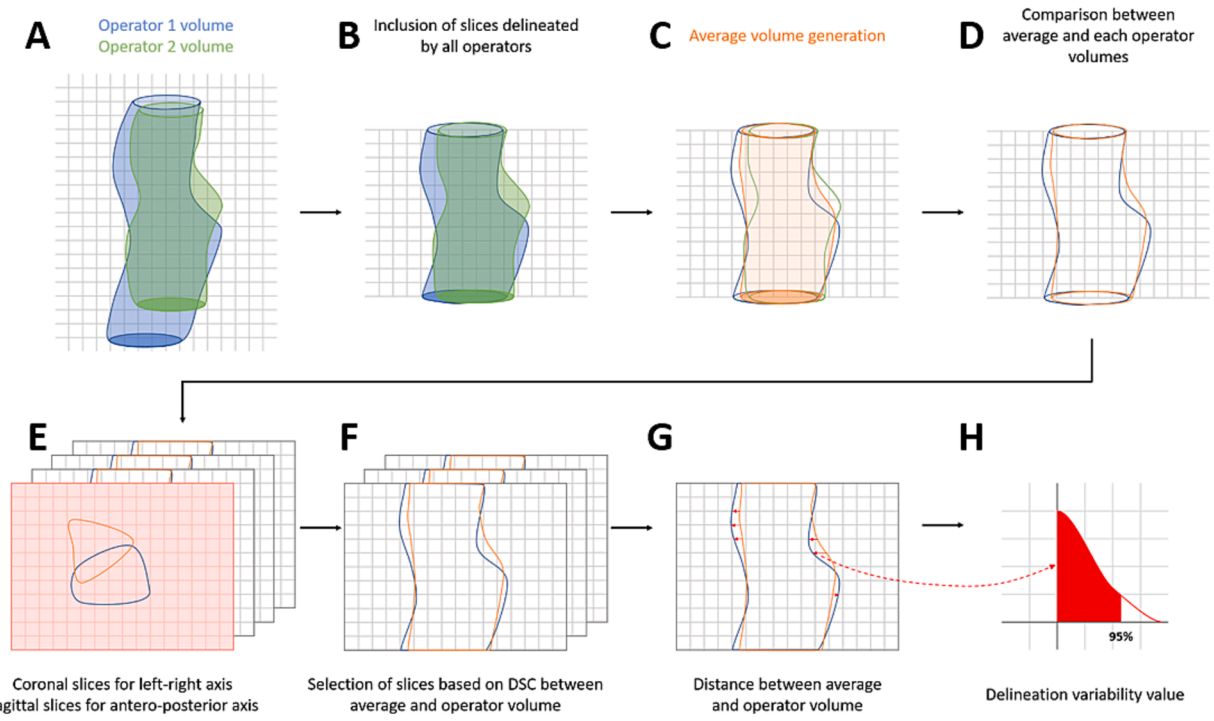

Fig. 1. Delineation variability assessment methodology in left–right and antero-posterior directions. For a better visualisation, the volumes of 2 operators were present here, whereas the analysis was made on the volumes of 15 operators. DSC: Dice similarity coefficient.

antero-posterior variability, the most extreme coronal slices, representing approximately 10 % of the slices, were excluded (Fig. 1E and F). For each selected slice, the left and the right distances between the average and the operator delineations at each voxel level along the supero-inferior axis were measured (Fig. 1G). The absolute values of these distances typically followed a half-normal distribution. Therefore, the percentile 95 value of this distribution was reported for each operator and each CBCT as a measure of delineation variability (Fig. 1H). For the antero-posterior axis, a similar analysis using sagittal slices was conducted.

To evaluate delineation variability in the supero-inferior direction, the cranial and caudal limits of the operator volumes were reported. The distance between the average of all cranial limits and the highest slice of each operator volume was reported as the measure of delineation variability in the superior direction for each operator and each CBCT. Similarly, to determine the value in the inferior direction, the distance between the average of all caudal limits and the lowest slice of each operator volume was calculated.

Statistical analysis

For the inter-operator delineation variability evaluation, the mean +/- standard deviation of the delineation variability values of each operator volume compared to the average volume was reported. These values were compared between different professional groups using a two-sided Student's *t*-test. A Bonferroni correction for multiple comparisons was applied when required. A p-value < 0.05 was considered statistically significant. The average volume generation and comparison with individual operators' volume were conducted using a homemade Python script (version 3.10) in Visual Studio Code (version 1.18.1). All data processing and statistical analyses were performed in RStudio (R version 4.2.1) using the "tidyverse" package.

Ethical considerations

This monocentric study was conducted in accordance with the declaration of Helsinki and was approved by the ethics committee of the Cliniques universitaires Saint-Luc (reference number: 2022/24JUI/253).

Results

Patients and tumour characteristics are described in Table 1.

Overall, delineation variability ranged from 0.2 to 4.4 mm on the left, 0.3 to 2.0 mm on the right, 0.1 to 2.9 mm anteriorly, 0.5 to 4.0 mm posteriorly, 2.3 to 6.0 mm superiorly, and 2.3 to 12.4 mm inferiorly among all operators (Fig. 2).

Inter-professional delineation variability for all directions is presented in Fig. 3 and Table 2. Variability was highest among RTTs (2.2 – 4.8 mm), followed by non-experts ROs (1.2 – 4.4 mm), and lowest among experts ROs (1.1–3.2 mm).

When comparing the RTTs group to the expert ROs group, average delineation variability was significantly higher in the right ($p < 0.001$), anterior ($p = 0.002$), and posterior ($p = 0.006$) directions. Comparing non-expert ROs and expert ROs, the delineation variability was only significantly greater in the posterior direction ($p = 0.041$). Comparing non-expert ROs to RTTs, significant difference in delineation variability

Table 1
Demographic characteristics of the included patients.

Characteristics	N = 5
Gender	
Male	4
Female	1
Age range (years)	48–74
Tumour location	
Low rectum	2
Middle rectum	2
High rectum	1
T-stage	
T3	4
T4	1
Radiotherapy	
Short-course	1
Long-course	4

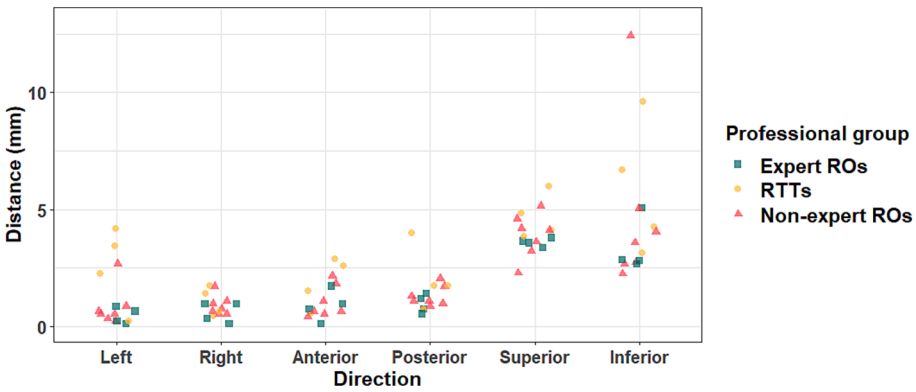

Fig. 2. Inter-operator delineation variability in the six spatial directions compared to an average volume of all operators. ROs: Radiation oncologists, RTTs: Radiation therapists.

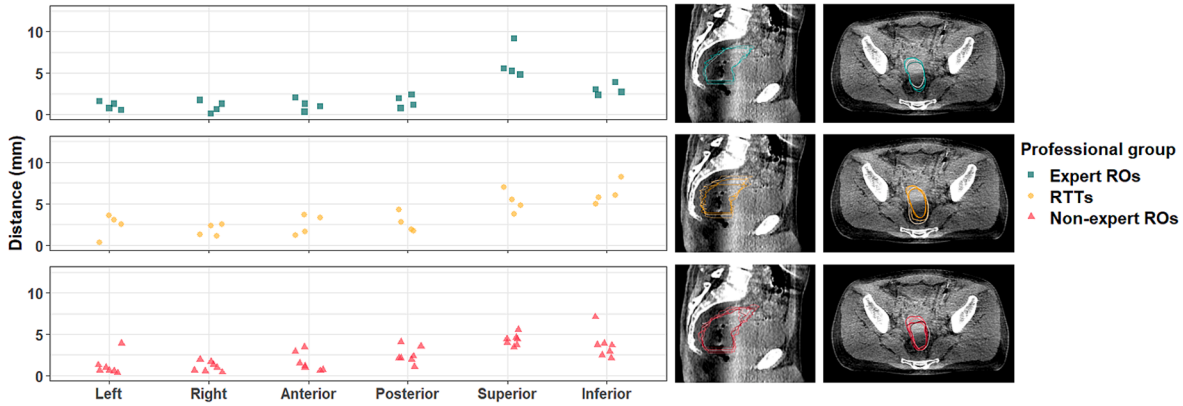

Fig. 3. Inter-profession delineation variability in all directions. Each dot represents the mean value of the 10 rectal boost volumes delineated on CBCTs for one operator. ROs: Radiation oncologists, RTTs: Radiation therapists.

Table 2
Inter-profession delineation variability values in all directions.

Direction	Expert ROs	RTTs	Non-expert ROs
Left	1.3 +/- 1.2	4.6 +/- 8.9	1.4 +/- 1.6
Right	1.1 +/- 1.0	2.2 +/- 1.6	1.2 +/- 0.9
Anterior	1.3 +/- 1.3	2.9 +/- 2.8	1.8 +/- 0.7
Posterior	1.6 +/- 1.6	3.1 +/- 2.3	2.7 +/- 2.6
Superior	3.2 +/- 2.8	4.3 +/- 2.8	3.7 +/- 2.9
Inferior	2.9 +/- 2.3	4.8 +/- 4.7	4.4 +/- 4.8

Each value is expressed in millimetres and is the mean of delineation errors from all volumes delineated by each operator of the professional group +/- standard deviation.
ROs: Radiation oncologists, RTTs: Radiation therapists.

was only observed in the right direction ($p < 0.001$).

When comparing individual contours from all groups (including automatic oART volume) with those from the expert group as reference volume, differences ranged from 0.6 to 5.0 mm on the left, 0.6 to 2.1 mm on the right, 0.8 to 3.0 mm anteriorly, 1.3 to 5.0 mm posteriorly, 2.6 to 5.8 mm superiorly, and 2.4 to 12.7 mm inferiorly (Fig. 4). There were no significant differences between the average delineation variability of the different professional groups in any direction ($p > 0.05$), nor with the automatic oART volumes ($p > 0.05$).

Discussion

In this study, the delineation variability of a rectal boost volume was assessed among individual operators, and different professional groups, including 4 expert ROs, 4 RTTs, 7 non-expert ROs, and volumes automatically delineated by an oART TPS. Evaluating delineation variability on CBCTs is a first step towards performing CBCT-guided online-ART and incorporating this delineation error in a population-based PTV margin for rectal boost RT.

Current guidelines for rectal RT planning do not specify recommendations for boost volume, and multiple boost volume definitions are reported in literature [4,15,17–20]. Based on preliminary analysis (see Appendix), a CTV that encompasses the entire rectal wall on transversal slices containing the tumour was adopted, as it demonstrated the lowest delineation variability. This variability has significant dosimetric implications, potentially leading to insufficient tumour control due to underdosage or increased toxicity from overdosage to organs-at-risk [12–14]. However, the designation of "CTV" could be incorrect in regard of the International Commission on Radiation Units and Measurements (ICRU) report No. 83 definition [21]. Indeed, this structure extending to the circumferential rectal wall is actually part of both the CTV (microscopic tumour infiltration) and PTV (delineation error) concepts.

Such as other reports in the literature, these analyses indicate that delineation errors were lower in transversal directions compared to supero-inferior axis [22–24], a direct consequence of the boost volume definition. In the transversal directions, the limit was the rectal wall, which was clearly identifiable on CBCT images. In contrast, the supero-inferior boundaries, defined by the tumour's upper and lower poles, were more difficult to identify on CBCTs. Also, this greater variability is partly due to the lower resolution of the CBCT in the supero-inferior direction (2.00 mm) compared to left–right and antero-posterior directions (0.96 mm). Several strategies could be implemented to mitigate this issue and minimise delineation errors during the oART workflow. MRI-guided online-ART enables direct visualisation of the tumour,

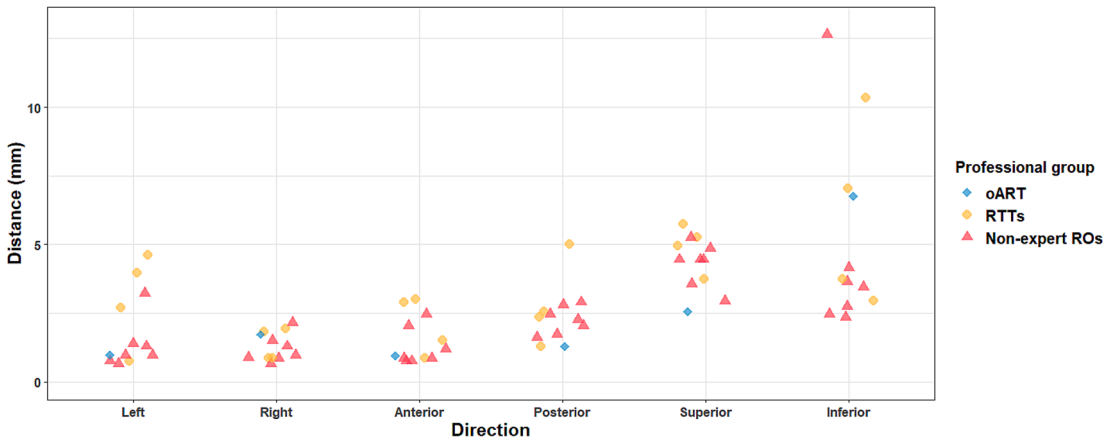

Fig. 4. Delineation variability of automatic oART volume, RTTs, and non-expert ROs volumes compared to the Expert ROs' average volume. oART: online-adaptive radiotherapy, ROs: Radiation oncologists, RTTs: Radiation therapists.

improving inter-operator agreement in delineating the macroscopic tumoral volume compared to CT [25]. By this way, boosting only the GTV is feasible and allows reduction of the high-dose volume compared to the broader CTV used in this study [26]. For CBCT-guided oART, implanting radio-opaque markers at the tumour's upper and lower poles during an endoscopic procedure before RT planning could serve as guide for online delineation on CBCT [27,28]. However, MR-Linac are sparse, such as the routine implementation of radio-opaque markers. Furthermore, those radio-opaque markers could also cause artefacts that interfere with accurate MRI-based tumour response evaluation. This leaves tall the majority of the RT centers with a delineation variability that should be integrated in the PTV margins.

The contours from the RTT group did not significantly differ from those of the non-expert ROs group and the automatic oART ones. This is of major importance regarding the rising role of RTTs in the new era of ART and raises questions about the necessity of further corrections by non-expert ROs after initial adjustments by RTTs. RTTs are increasingly implicated in CBCT-guided online-ART, and workflows involving RTTs from start to finish are already in place [9,29,30]. Interventions such as developing consensus guidelines, using multimodal imaging, and conducting training sessions could further reduce delineation variability [23,31,32]. On an individual basis, a substantial delineation variability exists inside different professional groups. For example, some RTTs demonstrated lower variability than others when compared to the expert ROs group. This suggests that each subject could be assessed individually to determine whether the autonomy required to perform this task on a routine clinical basis has been achieved or, alternatively, whether further training is required. Furthermore, the results presented here showed that the automatic oART delineation of the boost volume is effective, providing contours comparable to those of RTTs and non-expert ROs even without manual correction. This could eliminate the most time-consuming step in CBCT-guided oART—the manual editing of volumes—thereby enhancing workflow efficiency [10,11]. These findings align with other studies that evaluate artificial intelligence-based segmentation of organs-at-risk and target volumes in various locations. While these volumes often still require expert manual adjustments, the time saving is significant [24,33,34]. In rectum oART, Ferreira Silvério at al. 2024, reported that using a deep learning model for auto-contouring in an MRI-guided workflow can provide target volumes that require no or only small adjustments in the majority of cases (70 %), substantially reducing contouring time from an average of 7 min 34 s in their conventional workflow to 3 min 8 s [24].

This study, however, had some limitations, including the small number of patients and CBCTs included and the already discussed definition of the rectal boost volume that was used. Another limitation is that the conditions under which the operators delineated the volumes did not reflect those of an actual oART session. The delineation exercise was made on a different TPS than the one dedicated to oART. Also, no time constraints were applied, although, in real clinical conditions, the RT session duration would be limited to minimise patient discomfort and significant intrafraction anatomical changes. Given the lack of daily MRI images and, consequently, the absence of a truly reliable reference volume, this study was only able to evaluated the delineation variability among several operators, but not the accuracy of their volumes compared to a groundtruth.

Conclusions

The delineation variability was evaluated and quantified for rectal boost volume contouring, defined as the entire rectal wall on transversal slices where the tumour is present. Inter-operator variability was more pronounced in the supero-inferior axis compared to the transversal directions (left, right, anterior, and posterior). Delineation variability was lower in the group of expert ROs. Compared to expert ROs' average volume, no significant differences in delineation variability were found between RTTs, non-expert ROs and a volume automatically delineated by an oART-dedicated treatment planning system. Consequently, during CBCT-guided oART, RTTs can effectively oversee rectal boost delineation in the absence of expert ROs. However, it would be beneficial to validate this autonomy through additional training and individual assessment in order to approach the volumes of expert ROs. This study also provides essential quantitative data for the implementation of CBCT-guided rectal boost oART, including a PTV margin computation that accounts for daily delineation errors. Additionally, these findings offer deeper insights into optimising oART workflows, in which several professional groups are now in frontline.

Informed patient consent

The author(s) confirm that written informed consent has been obtained from the involved patient(s) 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.

Funding statement

Julien Pierrard was funded by Fonds De La Recherche Scientifique–FNRS, grant number FC 50079 and by Varian, a Siemens Healthineers Company.

Loïc Vander Veken was funded by Fonds De La Recherche Scientifique–FNRS, grant number FC 33411.

Other authors were funded by the Cliniques Universitaires Saint-Luc.

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.

Acknowledgement

None

Appendix:. Rectal boost volume definition

Appendix methods.

Regarding the boost clinical target volume (CTV), no clear consensus exists in literature, with some teams boosting only the GTV (CTV_{tumour}), others boosting the GTV plus a numeric or anatomic margin [1–4]. In our institution, the boost clinical target volume used in clinical practice is defined as the primary tumour extended to the entire rectum wall on each CT slice where the tumour is visualised ($CTV_{rectal\ wall}$). In this preliminary analysis, the intra- and inter-operator delineation variability between $CTV_{rectal\ wall}$ and CTV_{tumour} was compared. To assess intra-operator variability, one operator (JP) delineated both CTV_{tumour} and $CTV_{rectal\ wall}$ on each of the 10 selected CBCTs and repeated the same procedure one month later. For the inter-operator variability, JP volumes (the first set of CTV_{tumour} and $CTV_{rectal\ wall}$ volumes delineated for the intra-operator variability analysis) were compared with CTV_{tumour} and $CTV_{rectal\ wall}$ delineated by a second operator (GVO). Volumes were compared using the Dice similarity coefficient (DSC), which is the ratio between the intersection area of two structures (A and B) multiplied by two and the sum of the area of both structures (Eq. A (1).

$$DSC = \frac{2 \times (A \cap B)}{A + B} \tag{A1}$$

The rectal boost volume that the remaining participating operators had to delineate was the volume ($CTV_{rectal\ wall}$ or CTV_{tumour}) with the lowest intra- and inter-operator delineation variability (highest DSC).

Median values [interquartile range] of the DSC were compared using Wilcoxon signed-rank test.

Appendix results.

The median DSC between $CTV_{rectal\ wall}$ volumes delineated by the same operator (0.86 [0.85 – 0.90]) was significantly higher than for the CTV_{tumour} (0.81 [0.78 – 0.84], $p = 0.002$), suggesting a higher intra-operator delineation variability for the CTV_{tumour}. Inter-operator delineation variability was also higher for the CTV_{tumour} (median DSC: 0.79 [0.75 – 0.81]) compared to the $CTV_{rectal\ wall}$ (0.86 [0.83 – 0.88], $p = 0.002$). Based on this, the different operators were asked to delineate a $CTV_{rectal\ wall}$ as the rectal boost volume.

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