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Offline Adaptive Radiation Therapy for prostate cancer: using daily CBCT and deformable image fusion for correct replanning

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Offline adaptive radiation therapy for prostate cancer: using daily CBCT and deformable image fusion for correct replanning

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Think green before you print

ABSTRACT

INTRODUCTION

Adaptive radiation therapy (ART) is an established clinical practice, especially for treatments requiring rapid changes due to organs-at-risk (OAR) that might influence the target position. Adapting the procedure to a case-to-case basis involves combining different tools, such as scanning pretreatment images, clinically assessing the need for adaptation, replanning a new treatment, and guaranteeing the final quality of the entire process. Modern radiation therapy equipment enables multiple optimization strategies, both online and offline.

The primary aim of this study is to define an offline ART procedure to correct the replanning of prostate treatments according to objective evaluation criteria.

MATERIALS AND METHOS

The simulation and treatment protocols for prostate patients involve emptying the rectum when needed and ensuring that the bladder is filled with adequate urine volume. To comply with the simulation conditions during the treatment, daily cone-beam computed tomography (CBCT) images are acquired and controlled on a daily basis. The image-guided radiation therapy (IGRT) protocol provides a rigid fusion of the images acquired in the bunker with those collected from the simulation CT. For this study, we selected 23 patients with prostate adenocarcinoma (medium and low risk) treated with 40 fractions, with a daily dose of 2 Gy (80 Gy) at UPMC San Pietro FBF Advanced Radiotherapy Center in Rome, from October 2018 to May 2019.

During the treatment, patients were placed in the supine position, with their arms on their chest and legs restrained by an immobilization device (ProSTEP™ Klarity). The offline ART workflow required pretreatment verifications, registration with the simulation images, and calculation of the rectum and bladder filling variations. The analysis was performed using the Velocity v4.0 software (Varian Medical System, Palo Alto CA). At the end of the Velocity-based software-automated process, the CT and CBCT images were used to generate an aCT (adaptive CT). Organs of interest were contoured on the aCT automatically.

The Dice coefficient and the dispersion and distribution statistical indexes were taken into consideration to ensure accurate qualitative comparison.

RESULTS

Percentage dispersion of the rectum volume values was higher in Group A.

Distribution of rectum volume variation percentage in Group A had an IQR = 5,55% (Q1= -4,06%; Q2= -1,13%; Q3= 1,49%), whereas Group B had an IQR= 4,24% (Q1= -2,50%; Q2= 2,09%; Q3= 1,75%).

Percentage dispersion of the bladder volume values was higher in Group A.

Distribution of bladder volume variation percentage in Group A had an IQR = 9,65% (Q1=-7,34%; Q2= -2,32%; Q3= 2,31%), whereas Group B had an IQR = 12,13% (Q1= -7,18%; Q2= -1,56%; Q3= 4,96%).

The Dice coefficient in Group A showed an average daily superimposition of the bladder of 0,91 ± 0,07, whereas in Group B this was 0,87 ± 0,10. In both groups, the rectum volume had an average Dice coefficient of 0,89 ± 0,09.

CONCLUSIONS

The results show that the Dice coefficient can be useful to establish whether the volume localization can be superimposed to the simulation CT. Based on our practice, we suggest that the offline ART protocol should be verified over the first five therapy fractions, representing an adequate window to assess the need for replanning.

Because this index does not consider the volumes but only the possibility of their geometric superimposition, we recommend checking the mean OAR volumes when using an offline ART workflow. This is particularly important for the bladder, which is more susceptible to this kind of change than variations in its localization.

Dice coefficient rectum $\Delta Dice_R$	Dice coefficient bladder $\Delta Dice_B$	CBCT image acceptance	Volume variation percentage rectum ΔV_R	Volume variation percentage bladder ΔV_B
> 0.83	> 0.93	Replanning not required	<3%	<6%
> 0.50 <0.83	> 0.80 <0.93	Consider replanning	> 3% <6%	>6% <9%
< 0.50	< 0.80	Recommended replanning	>6%	>9%

Keywords: Offline Adaptive Radiotherapy, replanning, Deformable registrations, prostate cancer, IGRT, Cone Beam CT.

INTRODUCTION

In modern external beam radiation therapy, the main challenge when treating prostate cancer are the anatomic and positioning variations of the prostate and of the surrounding OAR [1]. These variations can often hinder the precision of the treatment, thus reducing the efficacy of the therapy [2]. Intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) are commonly used to treat prostate cancer [3] as they allow to irradiate the target with the maximum dose with a high surrounding dose-gradient index [4]. Because of this, the planning target volume (PTV) must be duly localized and identified with images scanned before the treatment. Image-guided radiation therapy (IGRT) uses volumetric images (cone-beam computed tomography, or CBCT) [5] obtained before each fraction or according to different customized protocols [6]. Pretreatment verifications provide information on any anatomical changes in the patient. Volumetric differences of OAR and PTV [7] between simulation and treatment can be progressive, random, or combined [8]. Progressive variations are affected by systemic features of the irradiated structures (e.g., downsizing or shrinking of the treated disease); random variations do not depend on volume changes and are the consequence of a different localization of the disease during the treatment. Combined changes present the same characteristics of both previously described variations. To achieve the best possible outcome in terms of efficiency and accuracy, different strategies can be implemented to monitor OAR and PTV movements. Some strategies provide for an active intervention on the patient for localization of fiducial markers directly on the area to irradiate [9][10], whereas other strategies only plan online and offline corrections of the variations detected daily when verifying the patient's positioning. Should discrepancies be found between the images used for treatment planning and those used for verification, it is possible to re-plan the treatment to guarantee the therapeutic goals are accomplished. The adaptive radiation therapy (ART) procedures include the actions taken to modify patients' therapies if discrepancies are found [11]. Variations occurring during an ongoing fraction requires an online ART strategy. If a predictive statistic is used to define new irradiation criteria this requires an offline ART strategy [12]. When treating prostate patients, both ART strategies can be used to correct the variations [13]. The online technique eliminates any intrafraction geometric uncertainty, compensating the variations in the organs being treated [14]. The offline technique allows to manage the main systemic variations offering a new dose distribution, mediated through target and OAR variations. Adaptive radiotherapy is hence a key instrument for the correct administration of treatments according to current quality criteria. This allows to reduce the target margins according to the specific variations of each patient, considering the changes in the internal organs. Long-term follow-up [15] shows promising results in terms of outcomes and toxicity, highlighting the strong correlation between clinical effects of PTV variations based on the scanned images, and adapted treatments. Most of the reviewed studies focus on ART as a useful tool to define margins from CTV to PTV according to OAR variations [16]. Many studies also note the correlation [17] between the variations and the dose that reaches the target [18]. The scope of our work is to define adequate protocols for international quality standards for prostate radiotherapy, focusing on the OAR and their volume variations during the treatment. This retrospective translational study aims at investigating the acceptable limits of variations in the rectum and bladder when treating medium and high risk prostate carcinoma patients, in case of offline adaptive radiation therapy with deformable image fusion of daily CBCT and simulation CT.

MATERIALS AND METHODS

The difficulty of faithfully reproducing the radiation treatment of prostate cancer patients (medium and high risk) results from the physiological changes of the OAR, prostate, and seminal vesicles.

IGRT protocol

To guarantee an efficient treatment, the IGRT protocol for the pelvic region provides for a daily scan of kV-CBCT images before each therapy session [19][20]. Images were scanned according to the pelvis protocol [21] in Figure 1.

	Head	Pelvis	Spotlight	Thorax	Image Gently	Pelvis Obese	4D Thorax	4D Spotlight
Voltage [kVp]	100	125	125	125	80	140	125	125
Tube current [mA]	15	60	60	15	20	75	40	40
Pulse duration [ms]	20	20	25	20	10	25	20	20
Frame rate [fps]	15	15	15	15	15	15	7	7
Scan arc [deg]	200	360	200	360	200	360	360	200
Gantry rotation speed [deg/s]	6	6	6	6	6	6	3	3
Scan duration [s]	33	60	33	60	33	60	120	67
Number of projections	500	900	500	900	500	900	840	467
Exposure (mAs)	150	1080	750	270	100	1688	672	373
CTDIw, norm [mGy / 100 mAs]	1.95	1.32	1.34	1.32	0.84	1.64	1.32	1.34
CTDIw (mGy)	2.93	14.3	10.1	3.56	0.84	27.7	8.87	5.00
Fan type	Full fan	Half fan	Full fan	Half fan	Full fan	Half fan	Half fan	Full fan
Default pixel matrix	512 x 512	512 x 512	512 x 512	512 x 512	512 x 512	512 x 512	512 x 512	512 x 512
Slice thickness [mm]	2	2	2	2	2	2	2	2
Ring suppression algorithm	Medium	Medium	Medium	Medium	Medium	Medium	Disabled	Disabled

Figure 1: Techniques on different kV-CBCT imaging scanning protocols

Images are monitored by technicians in online match mode and by the radiation oncologists in offline review [22] mode at the end of the day, and in any case before each following therapy. Online and offline image verification follow the schedule outlined in Table 1. Image registration takes place with a rigid fusion based on bone findings in a field of view (FOV) defined the day before the therapy by the radiation oncologist.

	Online Match	Offline Review
MONDAY	*RO*	*RO*
TUESDAY	*RTT*	*RO*
WEDNESDAY	*RTT*	*RO*
THURSDAY	*RTT*	*RO*
FRIDAY	*RO*	*RO*
#5 FR	*RO*	*RO*

Table 1: Online and offline verification planning according to enforced IGRT protocol (RO = Radiation Oncologist; RTT = Radiation Therapist)

Image assessment guidelines

To allow a univocal CBCT image verification, all staff involved in the image validation process developed set of common guidelines.

These guidelines define a simulation and treatment protocol that provides for emptying the rectum when is needed, filling the bladder with water waiting a defined lag time before CT scan.

Assessing the filling of the bladder and the emptying of the rectum also complies with a shared procedure. In the event of anomalies, resolution methods are implemented. Stools and gas are removed from the rectum with a tube or an enema.

In the event of an empty bladder, patients are asked to drink larger amounts of water and wait a longer time before starting the treatment. No specific indications on the diet or nutritional advice are given to patients, to avoid any issue resulting from a change in habits. In case of differences between the simulation and the positioning images, the presence of a radiation oncologist is always requested at the accelerator control console.

The presence of a health physicist is also requested for the most particular cases. The limits of acceptance of the images depends on the experience of the radiation oncologist, hence they can vary. The CBCT pretreatment images were evaluated and only those approved were taken into consideration for radiation therapy.

This study relied on the experience in evaluating biomedical images of several expert operators, such as duly trained technicians and radiation oncologists, to obtain a correlation between image acceptance and statistical values of the volumes of interest.

Eligibility criteria

A total of 23 patients were selected for this study.

These patients were affected with adenocarcinoma of the prostate (medium and low risk) and received 40 fractions with a daily dose of 2Gy (for a total of 80Gy) at the UPMC San Pietro FBF Advanced Radiotherapy Center in Rome, from October 2018 to May 2019.

During treatment, patients were placed in a supine position, with their arms on their chest and their legs placed on an immobilization device (ProSTEP™ Klarity). A total of 1121 kV-CBCT pretreatment images were scanned, but only 1080 were used for therapy. The remaining ones were discarded due to unsatisfactory rectal and bladder filling.

Offline adaptive radiation therapy

14 patients completed treatment with no need for replanning (Group A); 9 other patients required replanning (Group B).

When necessary, the radiation oncologist requested a replanning based on the CBCT images, considering the OAR variations during treatment, position variation of the prostate and seminal vesicles, and the dose to administer to the patient.

The patients undergoing offline replanning were identified as reference for OAR filling limits of acceptance, while those not undergoing offline replanning were used to determine, using the OAR filling quantitative limits, whether they would have undergone replanning.

The offline ART workflow required pretreatment verifications, registration with the simulation images, and calculating the rectum and bladder filling variations. The analysis of the offline ART was performed using the Velocity v4.0 software (Varian Medical System, Palo Alto CA).

This software allows to compare DICOM images uploaded into it making rigid or deformable registrations (DIR) to extrapolate quantitative data about voxels information and OAR fillings during every radiotherapy treatment fraction.

This kind of imaging analysis allows to evaluate offline adaptive radiotherapy strategies in case of using LINAC without possibilities to make online adaptive radiotherapy strategies, and also makes possible to predict cut-off values to be used in further treatments, or to establish what kind of variations make to a treatment if is necessary to replan.

The simulation CT scans with their respective PTV and OAR contours were exported from the ARIA v15.2 (Varian Medical System) treatment planning system (TPS) with the daily CBCT and the according rigid registrations performed at the bunker workstation during treatments.

All data were imported in the Velocity software to generate adapted images containing information from the CT and the CBCT for each individual patient.

Deformable image registration (DIR) and adaptive CT

The deformable image registrations (DIR) used for this study were processed using the patients' simulation CT scans and the kV-CBCT pretreatment images scanned in the bunker. The registration used as reference to create the deformable images was the rigid registration approved for the radiation therapy23.

This registration allowed to correct the (translational and rotational) setup error as it was used online before the therapy.

To create the DIR on velocity, first step was selecting rigid registration of interest (between CT Sim and daily CBCT used for treatment), then was launched the automatic registration called "*Assessment- plan Generator- Actor*".

During this process, the Radiation therapist used a VOI including rectum, bladder and prostate to adapt images and to generate DIR. The last step was checking vectors generated from registration, to assure that there were no errors.

The obtained DIR also allowed to correlate the systemic error to the random error24. At the end of the automatic process generated by the Velocity software, the combined CT and CBCT images, named aCT (adaptive CT), were available25.

The aCT provides information on the CBCT size and location, but with the characteristic of resolution, contrast, and noise deriving from the simulation CT. The possibility to use the aCT Hounsfield units to calculate the OAR and PTV dosage is currently the object of another study.

Automatic contouring

Organs of interest contouring on the CBCT was conducted automatically when creating the aCT. To guarantee an efficient automatic contouring the images were reviewed, the deformable registrations were assessed based on the rigid registrations, and the contours of the new OAR were approved.

In no case it was necessary to manually intervene and modify the automatic contouring.

Coefficient of similarity between two volumes

The CBCT study and aCT creation with the volumes of interest allowed to establish how much the new OAR deriving from the pretreatment images differ from the same volumes contoured during the simulation [26][27].

Using Velocity software, it was possible to generate quantitative data during a timeline from aCT regarding bladder and rectum fillings for each treatment session. Using these data has made possible to extrapolate graphs to understand variations from baseline (Simulation CT).

To achieve an effective qualitative comparison, we considered the Dice coefficient [28] that measures to what extent two similar structures are superimposed or how much volume they have in common. The result is a scale number between 0 and 1, where:

0 = the two structures share no superimposition or have different volumes;

1 = the two structures have identical and superimposed volumes.

The formula used to calculate the Dice coefficient is:

$$\mathrm{DSC}\ (\mathrm{A}, \mathrm{B}) = \frac{2|\mathrm{A} \cap \mathrm{B}|}{|\mathrm{A}| + |\mathrm{B}|}$$

A: Contour volume on CT

B: Contour volume on aCT

∩: Superimposition of the two contours [29]

RESULTS

The results of the OAR volume variations studied during the set-up verifications on prostatic patients were divided in two groups. Group A included patients who did not require replanning, and Group B included patients who required it.

GRUPPO A				
	Bladder		Rectum	
	Media ± SD	Dice ± SD	Media ± SD	Dice ± SD
#1	8.43% ± 0.05	0.95 ± 0.04	2.01% ± 0.02	0.94 ± 0.05
#2	6.37% ± 0.06	0.94 ± 0.04	6.82% ± 0.03	0.88 ± 0.09
#3	9.76% ± 0.05	0.94 ± 0.03	2.26% ± 0.02	0.78 ± 0.12
#4	8.20% ± 0.10	0.93 ± 0.05	2.72% ± 0.02	0.77 ± 0.17
#5	6.10% ± 0.07	0.69 ± 0.23	3.84% ± 0.05	0.89 ± 0.08
#6	8.65% ± 0.05	0.95 ± 0.04	5.29% ± 0.06	0.80 ± 0.17
#7	5.70% ± 0.08	0.96 ± 0.02	2.65% ± 0.04	0.93 ± 0.05
#8	3.95% ± 0.05	0.94 ± 0.06	3.47% ± 0.02	0.78 ± 0.16
#9	4.60% ± 0.06	0.96 ± 0.02	2.67% ± 0.05	0.90 ± 0.05
#10	6.41%± 0.05	0.95 ± 0.04	3.15% ± 0.03	0.93 ± 0.06
#11	5.03%± 0.03	0.96 ± 0.03	2.65%± 0.02	0.92 ± 0.05
#12	3.24%± 0.03	0.91± 0.09	3.11%± 0.03	0.89± 0.11
#13	3.74%± 0.03	0.93± 0.08	1.97%± 0.02	0.89± 0.10
#14	4.29%± 0.03	0.96 ± 0.02	3.66%± 0.02	0.94 ± 0.04

Table 2: Mean values and Dice coefficient of rectum and bladder volume variation in Group A patients

GRUPPO B				
	Bladder PRE		Bladder POST	
	Media ± SD	Dice ± SD	Media ± SD	Dice ± SD
#1	15.09% ±0.06	0.92 ± 0.05	2.90% ± 0.03	0.95 ± 0.04
#2	5.91% ±0.06	0.90 ± 0.07	5.38% ± 0.05	0.94 ± 0.04
#3	7.71% ±0.03	0.95 ± 0.03	4.70% ± 0.05	0.95 ± 0.03
#4	3.12% ±0.04	0.85 ± 0.12	6.02% ± 0.07	0.92 ± 0.03
#5	9.54% ±0.14	0.94 ± 0.05	8.80% ± 0.13	0.93 ± 0.08
#6	5.23% ±0.05	0.91 ± 0.08	4.72% ± 0.05	0.93 ± 0.06
#7	6.61% ±0.03	0.95 ± 0.03	4.50% ± 0.05	0.95 ± 0.03
#8	3.22% ±0.04	0.95 ± 0.12	2.12% ± 0.08	0.93 ± 0.03
#9	5.32% ±0.05	0.95 ± 0.03	3.12% ± 0.06	0.95 ± 0.06
	Rectum PRE		Rectum POST	
	Media ± SD	Dice ± SD	Media ± SD	Dice ± SD
#1	3.45% ± 0.03	0.91 ± 0.07	2.17% ± 0.02	0.90 ± 0.11
#2	3.50% ± 0.05	0.86 ± 0.10	2.63% ± 0.05	0.87 ± 0.13
#3	2.02% ± 0.02	0.90 ± 0.11	2.73% ± 0.02	0.77 ± 0.20
#4	2.07% ± 0.02	0.83 ± 0.11	3.57% ± 0.02	0.69 ± 0.17
#5	2.62% ± 0.03	0.89 ± 0.12	5.79% ± 0.03	0.87 ± 0.15
#6	2.62% ± 0.03	0.89 ± 0.12	5.79% ± 0.03	0.87 ± 0.15
#7	2.32% ± 0.02	0.90 ± 0.11	2.43% ± 0.02	0.77 ± 0.20
#8	2.37% ± 0.03	0.83 ± 0.07	2.40% ± 0.02	0.90 ± 0.07
#9	3.57% ± 0.03	0.85 ± 0.06	2.10% ± 0.02	0.87 ± 0.05

Table 3: Mean values and Dice coefficient of rectum and bladder volume variation in Group B patients.

Radiation oncologists did not require replanning Group A patients (Table 2), therefore mean values can be used as limit of acceptance of images.

The mean values listed in Table 3 show the rectum and bladder variation percentages before and after replanning. An evident decrease of the bladder volume variation percentage was detected in one case only. All remaining cases showed no significant difference before and after replanning.

Results on dispersion, distribution, and volume of both patient groups are outlined in the following subsections for rectum, bladder, and Dice coefficient.

Rectum

Percentage dispersion of the rectum volume was higher in Group A. Distribution of rectum volume variation percentage in Group A had an IQR = IQR = 5,55% (Q1=-4.06%; Q3= 1.49%), whereas Group B had an IQR = 4,24% (Q1= -2,50%; Q3= 1,75%).

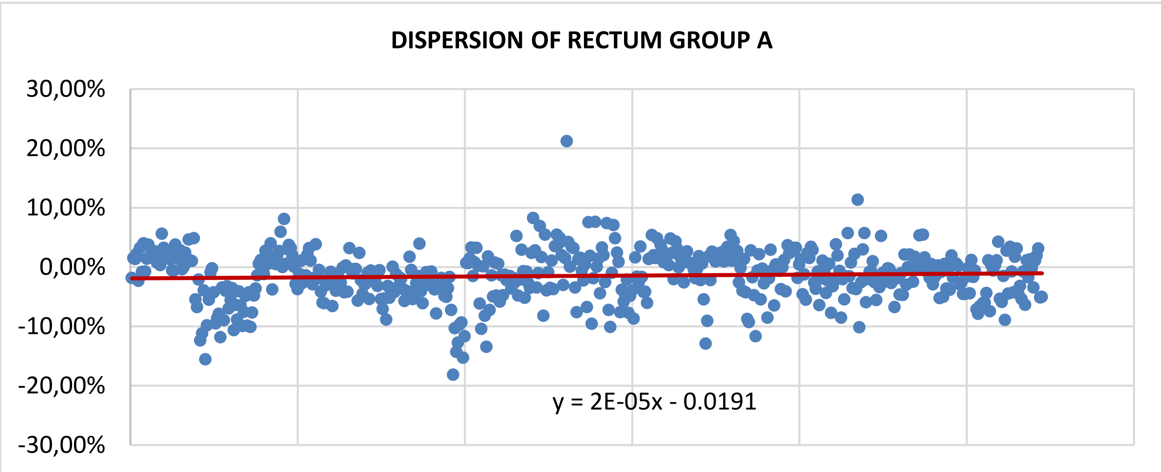

Figure 2: Dispersion of rectum volume variation percentages in Group A patient's trend line in red.

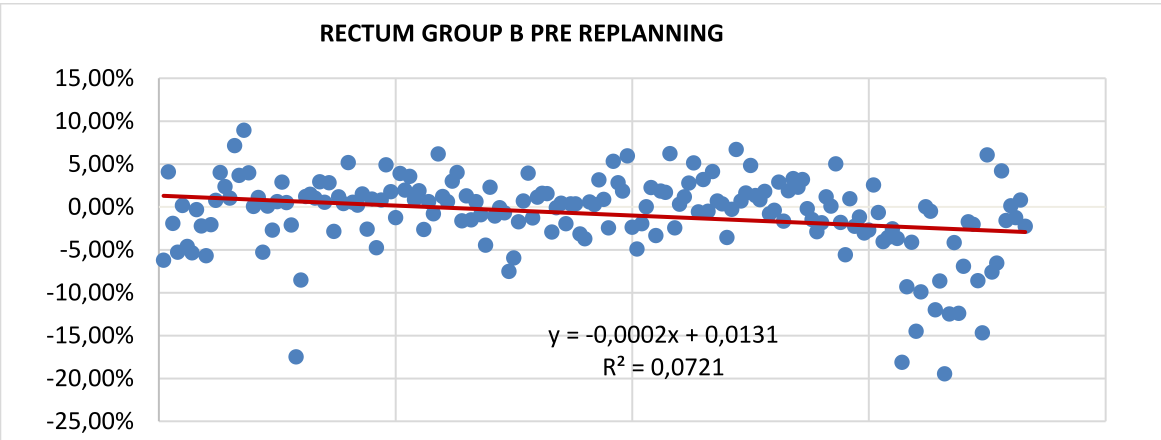

Figure 3: Dispersion of rectum volume variation percentages in Group B patient's trend line in red

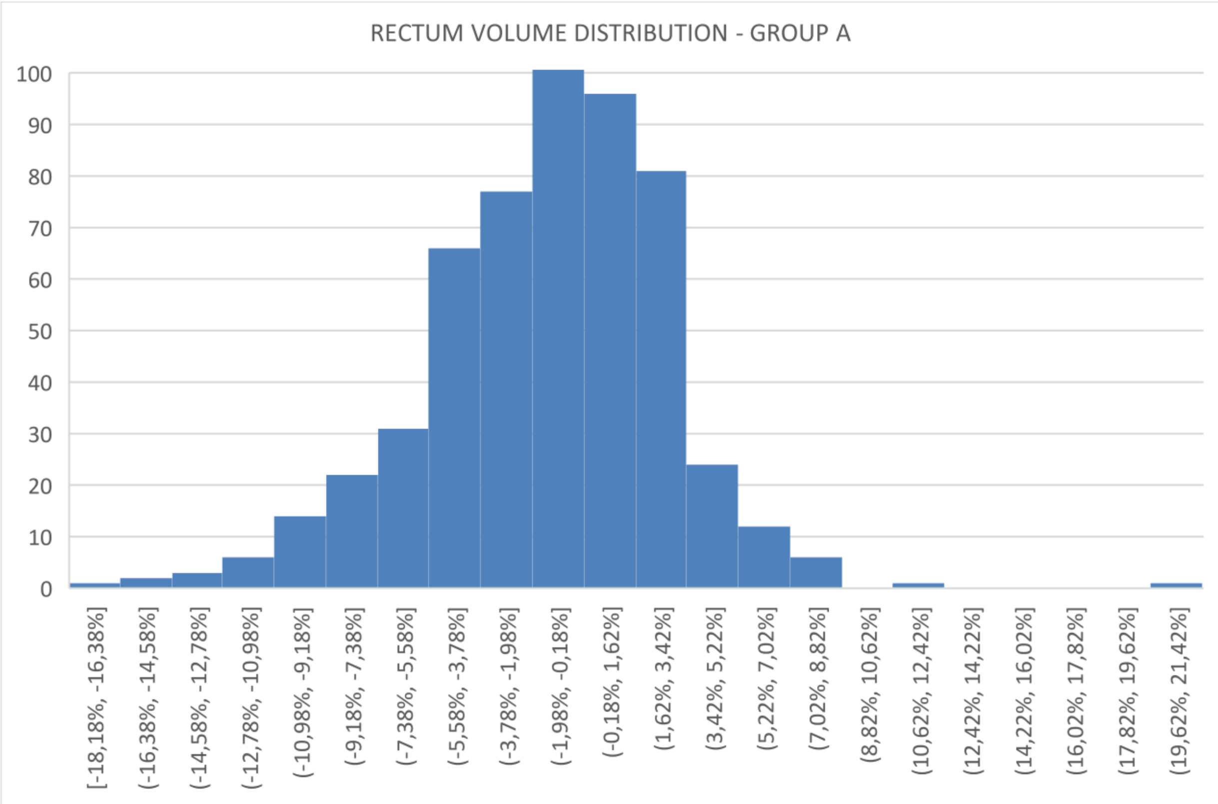

Figure 4: Percentage distribution of volume changes in rectum for group A patient's

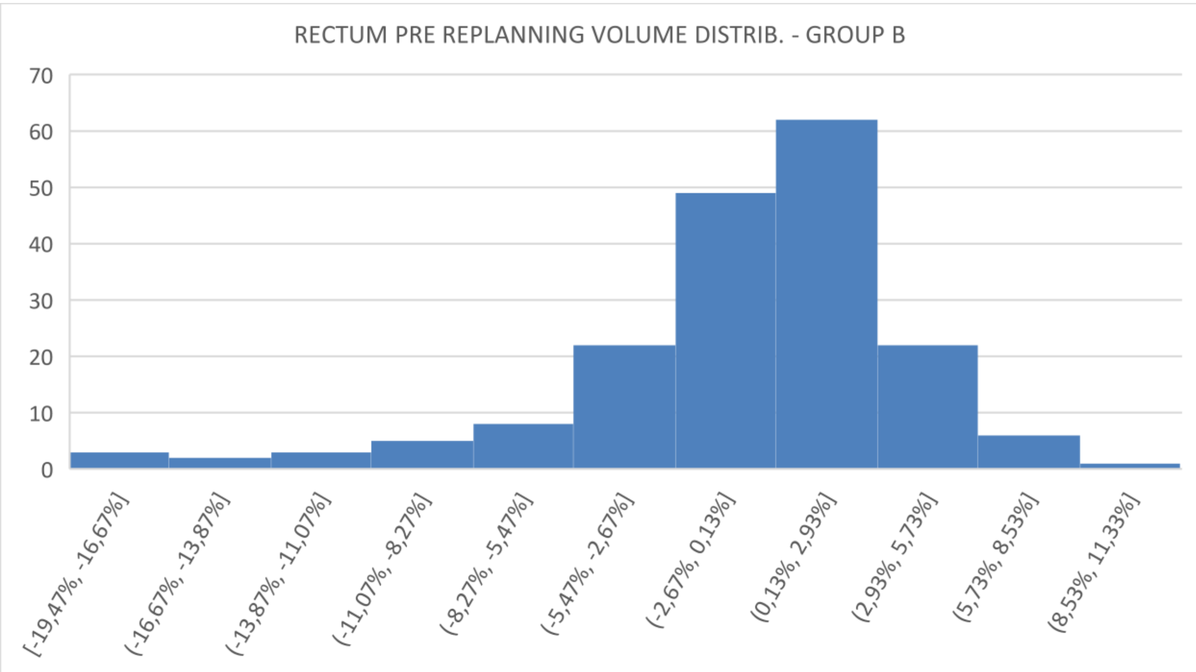

Figure 5: Percentage distribution for rectum volume changes in Group B patient's

Bladder

Percentage dispersion of the bladder volume was higher in Group A.

Distribution of bladder volume variation percentages in Group A had an IQR=11.80% (Q1=-10.12%; Q2=-5.49%; Q3=1.67%), whereas Group B had an IQR=9.07% (Q1=-3.57%; Q2=0.95%; Q3=5.51%).

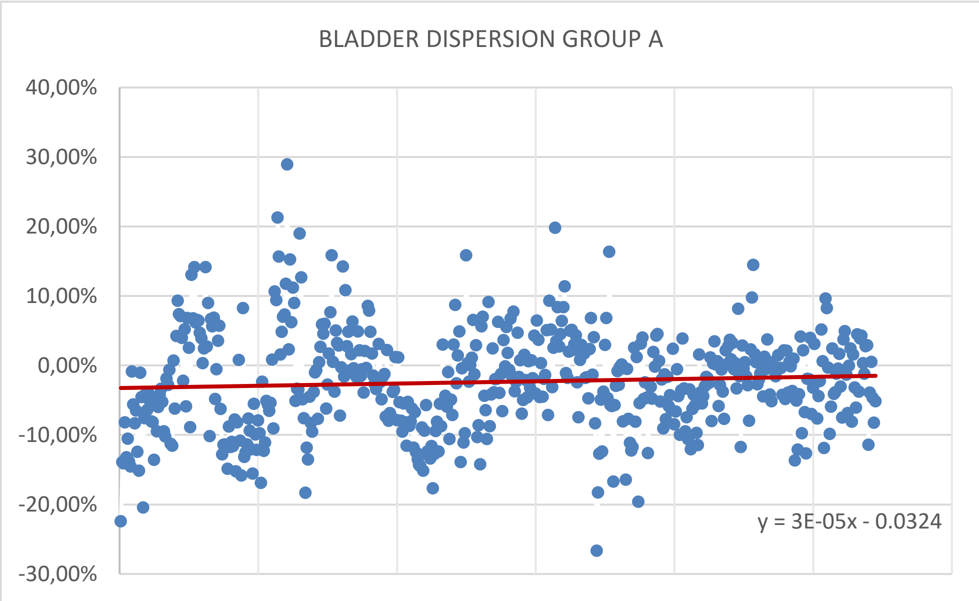

Figure 6: Dispersion of bladder volume variation percentages in Group A, trend line showed in red.

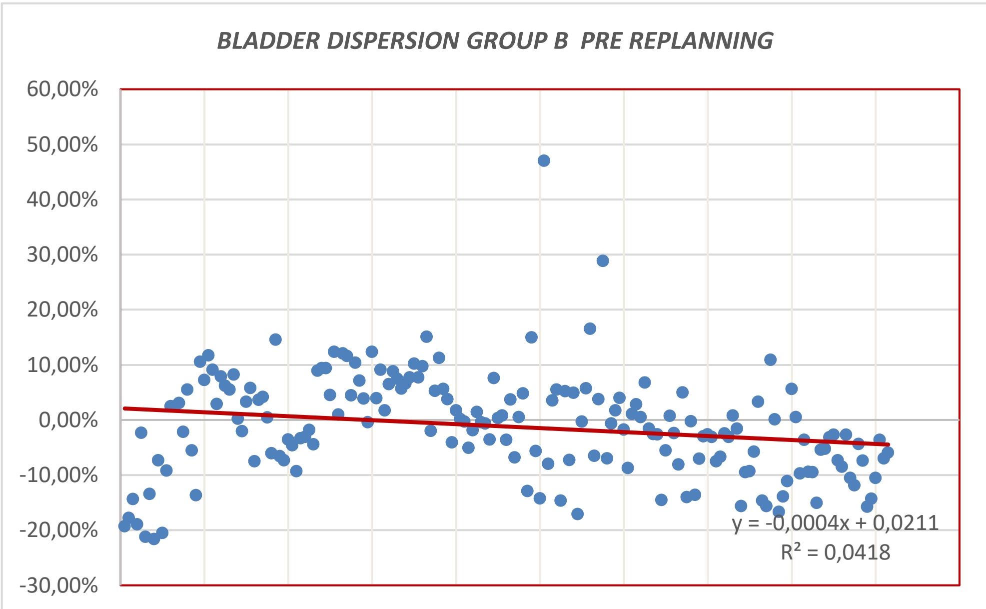

Figure 7: Dispersion of bladder volume variation percentages in Group B, trend line showed in red

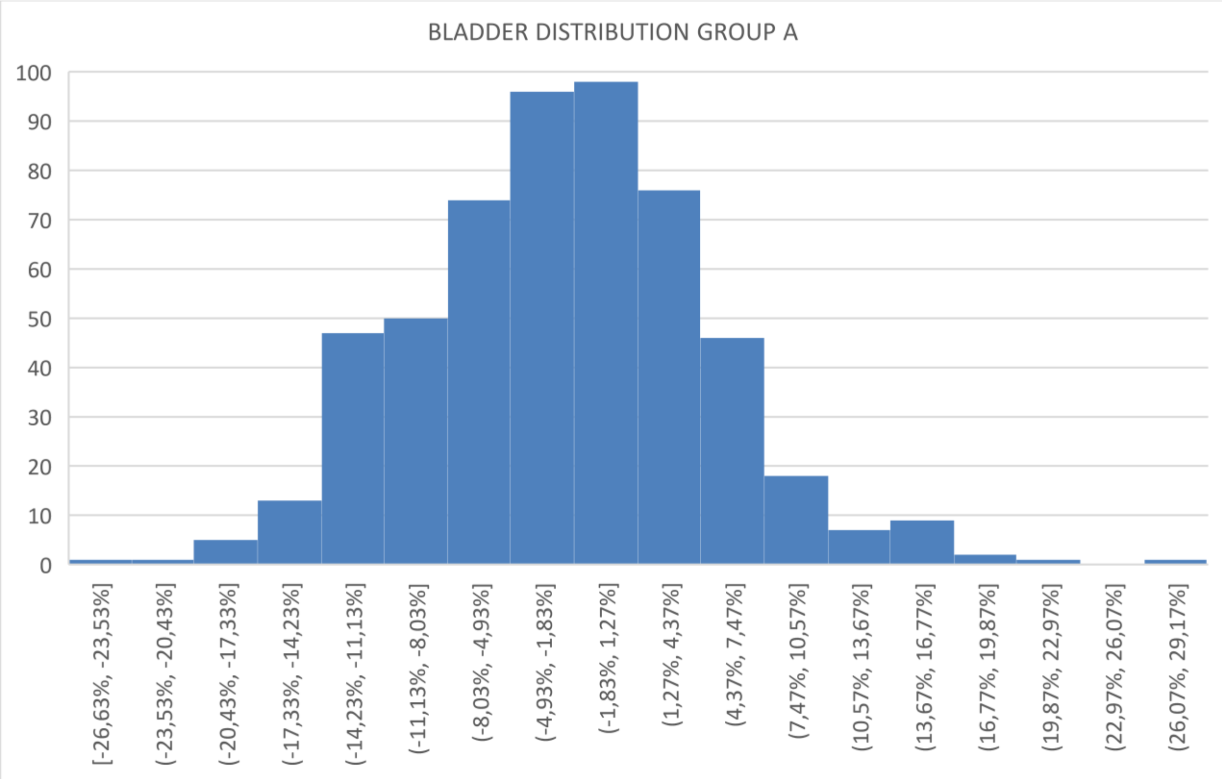

Figure 8: Percentage distribution of volume changes in bladder – Group A

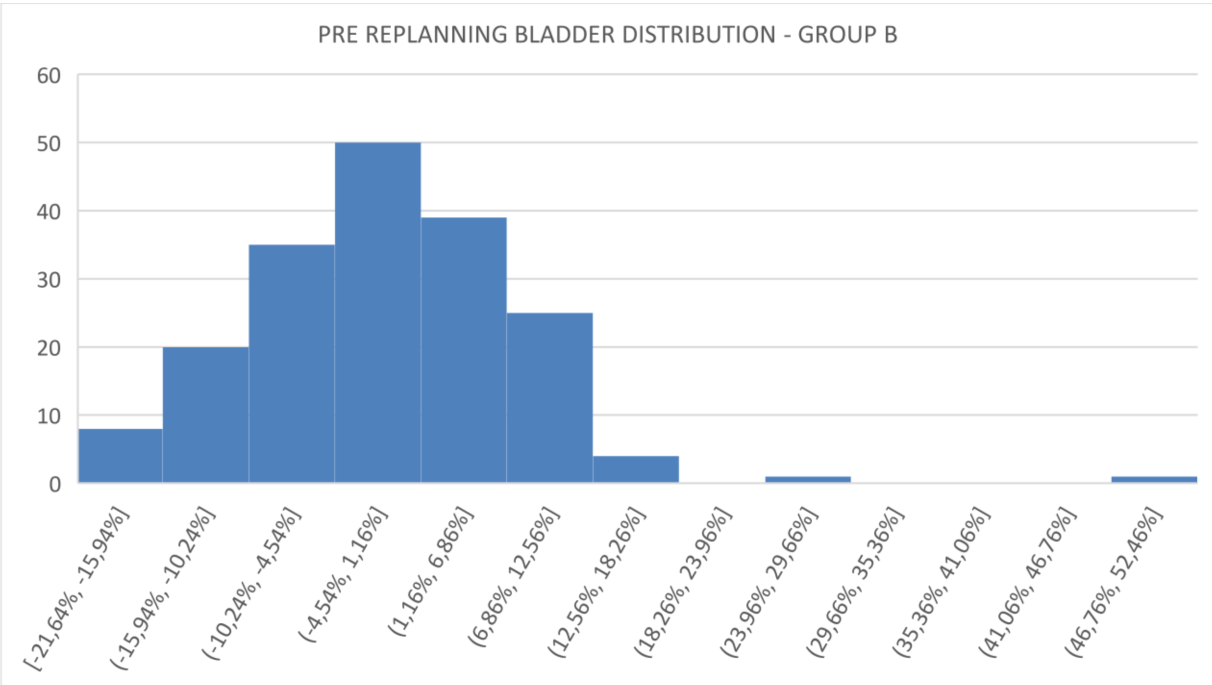

Figure 9: Percentage distribution of bladder volume changes – Group B

DICE coefficient

The study also addressed the geometrical variations of volume displacement. The Dice coefficient in Group A showed an average daily superimposition of the bladder of 0.92±0.13. The same superimposition in Group B reached a mean value of 0.93±0.07. In both groups, the rectum volume had a mean Dice coefficient of 0.85±0.14.).

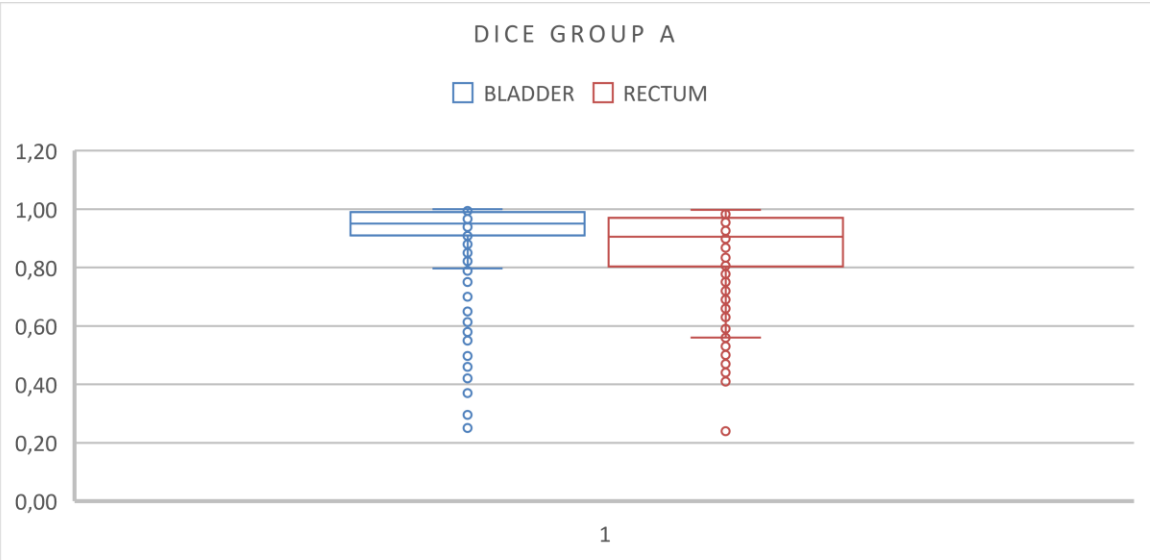

Figure 10: Box plot of the rectum and bladder Dice index in Group A patient's

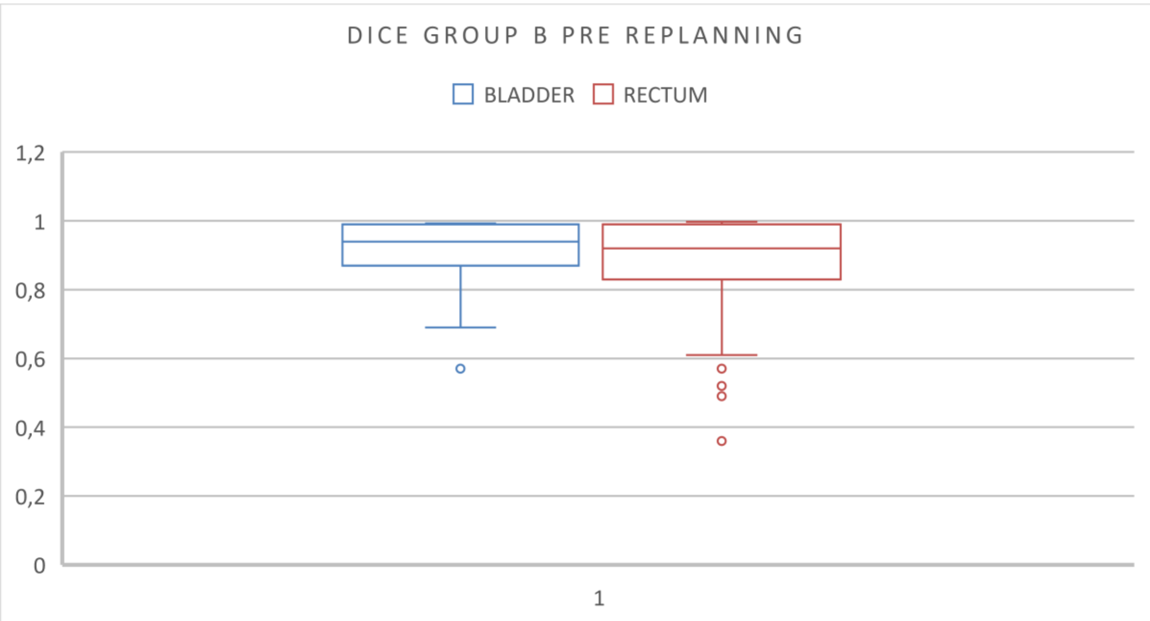

Figure 11: Box plot of the rectum and bladder Dice index in Group B patient's

DISCUSSION

Online adaptive radiation therapy mainly focuses on the daily assessment of PTV and of its variations in position, shape, and volume. By studying the OAR mainly involved in the daily CBCT assessment (rectum and bladder), we were able to identify the quantitative parameters based on the qualitative data used to accept or refuse pretreatment images.

The analysis shows that the bladder is the OAR that mostly influences the movement of the prostate and of the seminal vesicles during treatment, and therefore, because of its daily volume variations, it ends up determining when replanning is required.

The rectum is less impacted by the daily volume variations, also due to the correction procedures defined by the IGRT protocol, although it is most affected by the daily displacements. In the aCT of both groups, the rectum had an average Dice coefficient of 0.86, lower than the one of the bladder which was 0,92, while the volume variation percentages were smaller in the rectum (Group A: Min=-18.18%; Max=21.19%; Group B: Min=-17.49%; Max=8.93%) compared to the bladder (Group A: Min=-21.64%; Max=28.85%; Group B: Min=-21.64%; Max=47.00%).

The rectum volume dispersion percentage was higher in Group A (IQR=5.55%) than in Group B (IQR=4.24%). The bladder volume dispersion percentage was higher in Group A (IQR= 9.65%) than in Group B (IQR=12.13%).

These data contribute to stress the validity of replanning, according to the images scanned during patient set-up by the radiation oncologist.

Despite the rectum volume filling correction procedures are fundamental to obtain minimal variations between the therapy sessions, its position is not guaranteed. The average rectum Dice coefficient in group A was 0.87±0.10 (Min=0.24; Max=1.00) and 0.89 for group B (Min=0.27; Max=1.00).

Bladder filling is the most critical issue to monitor. Although it is true that it is hard to always obtain the same volume, also using a shared protocol, the position of the bladder can be more easily reproduced that the rectum.

The Group A Dice coefficient showed an average daily superimposition of the bladder of 0.91±0.13. The same superimposition for Group B reached an average of 0.92±0.08.

The data collected show an efficacy, albeit minimum, of offline adaptive radiation therapy with respect to consecutive treatment not replanned based on the patient's OAR volume variations.

CONCLUSIONS

The replanning assessment is based on high and modern quality standards. Due to the lack of appropriate infrastructure for online adaptive radiation therapy for high quality treatment, such as last generation hybrid equipment, process must be enforced that analyze the available data, including pretreatment images, according to limits of acceptance of volume variations as clear and objective as possible. In the presence of daily IGRT for the prostate, the criteria that better summons the limits of acceptance of the conditions of the rectum and bladder in the kV-CBCT images, while monitoring the positioning, is the Dice coefficient of similarity. The results show that the Dice coefficient can be useful to establish the possible superimposition of the localization of the volume and of the simulation CT. Therefore, when implementing the offline ART protocol, this should be verified at least every 5 fractions of the therapy, for the actual need for replanning to be assessed in due time.

Because this index does not take into consideration the volumes, but only the possibility of their geometric superimposition, we recommend checking also the mean OAR volumes when using an offline ART workflow. This particularly applies to the bladder, which is more susceptible to this kind of changes, rather than to variations of its localization.

From the tests performed it can be concluded that in the presence of bladder volume variation rates below 6%, treatment replanning is not required. On the contrary, for rates higher than 9%, it is recommended to implement replanning strategies. These statistical rates can support but not replace the clinical assessment of the radiation oncologist.

Rectum volume variation percentage	Bladder volume variation percentage	CBCT image acceptance
$\Delta VR < 3\%$	$\Delta VB < 6\%$	Replanning not required
$3\% < \Delta VR < 6\%$	$6\% < \Delta VB < 9\%$	Consider replanning
$\Delta VR > 6\%$	$\Delta VB > 9\%$	Recommended replanning

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