ONLINE FIRST

This is a provisional PDF only.

Nowotwory
Journal of Oncology

ISSN: 0029-540X

e-ISSN: 2300-2115

Cone beam computed tomography-based online adaptive radiotherapy as a crucial step in increasing the effectiveness of cancer treatment — first clinical experience

Authors: Iwona U. Dębosz-Suwińska, Dawid Bodusz, Barbara Bekman, Aleksandra Napieralska, Agnieszka Namysł-Kaletka, Agata Roch-Zniszczoł, Jerzy Wydmański

DOI: 10.5603/njo.103533

Article type: Research paper (original)

Submitted: 2024-11-14

Accepted: 2025-02-04

Published online: 2025-03-12

How to cite:

Dębosz-Suwińska I U, Bodusz D, Bekman B, et al. Cone beam computed tomography-based online adaptive radiotherapy as a crucial step in increasing the effectiveness of cancer treatment — first clinical experience. NOWOTWORY J Oncol 2025; 75 (Ahead of print).

Original article

Cone beam computed tomography-based online adaptive radiotherapy as a crucial step in increasing the effectiveness of cancer treatment — first clinical experience

Iwona U. Dębosz-Suwińska[1] (https://orcid.org/0000-0002-4554-8905), Dawid Bodusz[1] (https://orcid.org/0000-0003-1938-0325), Barbara Bekman[2] (https://orcid.org/0000-0002-2218-9495), Aleksandra Napieralska[1, 3] (https://orcid.org/0000-0002-7390-9165), Agnieszka Namysł-Kaletka[1] (https://orcid.org/0000-0003-0472-7322), Agata Roch-Zniszczoł[1] (https://orcid.org/0000-0002-3134-7272), Jerzy Wydmański[1] (https://orcid.org/0000-0002-2879-3781)

[1]*Department of Radiotherapy, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice, Poland*

[2]*Treatment Planning Department, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice, Poland*

[3]*Department of Radiotherapy, Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland*

DOI: 10.5603/njo.103533

Introduction. Online adaptive radiotherapy (oART) is an innovative approach that allows a treatment plan to be adjusted accurately and precisely on a daily basis according to changes in tumour and normal tissues during treatment courses.

Material and methods. The publication will focus on the presentation and subsequent stages of treatment planning, as well as their implementation, using the example of a patient with prostate cancer treated at our institution. The patient underwent hypofractionated radiotherapy with a daily fraction dose of 7.25 Gy to a total dose of 36.25 Gy.

Results. The median time required for the adaptation workflow (AT) was 29 min (SD 5 min). The mean bladder volume measured in the cone beam computed tomography (CBCT) images done before treatment was 184 cm³ and ranged from 146 cm³ to 203 cm³. For comparison, the blader volume at baseline computed tomography (CT) was 238 cm³. The mean rectal volume during treatment was 82 cm³ and ranged from 70cm³ to 100 cm³ and was also less than at baseline CT (122 cm³). The observed differences in patient geometry influenced changes in dose distribution in the planning target volume (PTV) and clinical target volume (CTV). In an

extreme case (the fourth fraction of treatment), the patient treated according to the scheduled treatment plan would receive 99% (7.18 Gy) and 98% (7.11 Gy) of the prescribed dose only in 49% of CTV and 48% of PTV, respectively. The adaptation process improved dose distribution to cover 100% of the PTV and CTV to at least 98% and 99% respectively of the prescribed dose during each fraction of treatment.

Conclusions. The example shown presented very high interfractional mobility. The use of oART allowed for adjustment to those changes, ensuring proper coverage of the CTV and PTV with the therapeutic dose during each treatment fraction.

Keywords: online adaptive radiotherapy, Ethos, prostate cancer, radiosurgery

Introduction

Radiotherapy (RT) of pelvic tumours is a challenge due to the variability in the location of the tumour and critical structures. The mobility of the tumour and critical organs (organs at risk — OAR) in the chest and in the abdominal cavity may be affected by the respiratory motion. The change in the position of OAR and the cancerous tumour in the pelvis occurs less dynamically and predictively, spreads over time, and is independent of the patient's will. Therefore, the use of current planning systems that coordinate the location of the tumour with the phase of the respiratory cycle in the case of pelvic cancers is useless. The pattern of anatomical changes differs in head and neck cancers, where regression of the primary tumour and regional lymph nodes can be observed. This causes changes in the thickness of the irradiated block of tissues due to weight loss, and can cause serious discrepancies between prescribed and administered doses [1, 2]. In that group of patients, adaptive radiotherapy (ART) may be the best option. Offline ART is generally performed between fractions, but is very time-consuming and can take up to several days.

Online adaptive radiotherapy (oART) is an innovative approach to RT that allows one to adjust the treatment plan in real time to fit daily anatomy, and account for interfraction variations using image-based monitoring (cone beam computed tomography — CBCT) of anatomical and geometrical changes.

This approach aims to deliver radiation accurately and precisely, so it could limit the irradiated volume by decreasing the margins for clinical target volume (CTV) to create a smaller planning target volume (PTV), and decrease the toxicity related to the irradiation of OAR [3–5].

The development of image-guided radiotherapy that improves oncologic outcomes and reduces toxicity is the technology world’s answer to new challenges in the treatment of cancer

patients. and remains a hot topic in the radiation oncology field. The author describes one of these technologies, which provides online adaptive therapy. The potential advantages of this CBCT-based procedure are highlighted, with a discussion of a chosen clinical case.

Materials and methods

Treatment preparation

The first steps in preparing for online adaptive radiotherapy treatment are the same as conventional image-guided radiotherapy (IGRT). The workflow to prepare the oART treatment plan is presented in Figure 1.

Immobilization

All patients must be positioned on their backs.The vacuum mattresses with supports are used not only for proper and reproducible patient positioning during each therapeutic session but also to facilitate mapping the patient's position from computed tomography used for treatment planning purposes.

Computed tomography/magnetic resonance imaging

After immobilization, computer tomography (CT) and magnetic resonance imaging (MRI) scans of the irradiated area are performed in the dedicated treatment position. The preparation for imaging is similar for all patients with prostate cancer, and includes instructions related to filling the bladder and intestine. Patients are recommended to eat an easily digestible diet 2–3 days before treatment imaging and treatment delivery. On the day of CT, patients should have an empty rectum and a full bladder. A radiographer explains the preparation of the bowel and bladder required for the scan. To obtain optimal conditions, every patient is asked to empty his bladder, drink 250ml of water and hold it in his bladder for as long as he can. If there was no stool on the morning of the examination, the doctor can administer a glycerin suppository or enema that helps to empty the rectum faeces.

CT/MRI fusion, target volume and OAR delineation

As a standard, a fusion of CT and magnetic resonance imaging is used to define and delineate the CTV (prostate gland and base of seminal vesicles). The institutional treatment protocol always requires considering the base of seminal vesicles in the treatment volume – despite the lack of tumour infiltration. The main OAR are the bladder, rectum, testes, bowels, urethra and femoral neck. The constraints with the fractionation schedule of 7.25 Gy to a total

dose of 36.25 Gy are as follows: (rectum: V18 Gy < 50%, V29 Gy < 20%, V32.6 Gy < 10%, V36.25 Gy < 5%, $D_{max} \leq 38$ Gy; bladder: V18 Gy < 55%, V29 Gy < 25%, V32.6 Gy < 15%, V36.25 Gy < 10%, $D_{max} \leq 38$ Gy; bowel: V20.7 Gy < 30 cm^3, $D_{max} < 28.5$ Gy; femoral head: V25 Gy < 45%; testes: $D_{max} < 2$ Gy; body and urethra: $D_{max} \leq 43.5$ Gy).

The Ethos treatment planning system (TPS) has a module dedicated to contouring, but it is more convenient for us to use the functionality of the Eclipse system. The PTV is derived from the CTV by adding the additional margin directly to the Ethos TPS. Planning target volume margins commonly used in stereotactic radiotherapy for patients with prostate cancer are applied. This margin is set at 3 mm on the rectal side and 5 mm in all other directions.

Treatment planning in oART is a process that dynamically adjusts radiation doses to changes in the patient's anatomy. The very first step in preparing the oART plan in Ethos TPS is like the standard IGRT planning. In each case, the base plan (the reference one) must be prepared offline. Therefore, all clinical goals and their priorities, for targets and organs at risk, must be added to the requirements specified in the templates or determined on an ongoing basis. Once a goal is reached, Ethos will continue to optimize that goal, taking into account other goals and the complexity of the plan. The results of the calculations are several proposed dose distributions created using volumetric modulated arc therapy (VMAT) and intensity modulated radiotherapy (IMRT) techniques. The user selects the level of complexity of these plans. Volumetric modulated arc therapy plans are usually inferior to IMRT plans (poorer target coverage, more hotspots, higher D_{max}). Ethos also takes longer to calculate a VMAT than an IMRT plan, and the time constraint is significant in online adaptation. After accepting the treatment plan, it must be verified in the MOBIUS system.

Treatment delivery

The patients are placed in the dedicated immobilization system with supports on the Ethos therapeutic table. Then, CBCT is performed before each session. The HyperSight imaging solution enables the acquisition of CBCT images in only six seconds, resulting in a high-quality image. The HyperSight image reconstruction algorithms, combined with the expanded field of view (FOV), also provide improved visualization of the target volume and surrounding OAR. Once the CBCT is accepted, the adaptation procedure is performed to adjust the structure contours from the reference plan to the current position and geometry. The OAR in the pelvic region are propagated only using AI algorithms. Targets can be propagated in two methods, i.e. adjusted as a result of deformable fusion or copied from a reference image. After the propagation stage, both the contours of the OAR and the targets undergo

verification with the possibility of editing them. Then the treatment plans are created while the patient is still on the therapeutic table (online re-planning). The dose distribution is automatically calculated on the constraints defined in the REFERENCE plan dose optimiser for the volume dose assumption. The RT technique remains the same as originally selected in the reference plan (IMRT or VMAT and their complexity in the plan).

The physician evaluates two treatment plans — both scheduled and adapted — in the new geometry of the patient. In the SCHEDULED treatment plan, the dose distribution calculations account for the new OAR and CTV contours, but recalculate using the same beam geometry control points as in the reference plan. This means that the original plan is recalculated according to the patient's specific anatomy in each fraction. In the adapted treatment plan, ADAPTED, optimisation and dose distribution recalculations are performed with new control points (Fig. 1, 2). This means that the original plan is adjusted to the specific anatomy in each fraction. The physician must assess whether the adapted plan is better or worse than the scheduled plan compared to the reference in terms of dose distribution and meeting of the plan constraints. If the scheduled treatment plan is selected, the patient can begin RT immediately, without requiring the signature of the physician. If the adapted plan is chosen, both the physician and the physicist must sign for approval (after verification in the Mobius software). Timing is critical in the adaptation process due to the possible intrafraction motion of the target and OAR (bladder and rectum filling is critical).

Results

Our publication focuses on presentation, subsequent stages of treatment planning and its implementation, using the example of a patient with prostate cancer.

Characteristics of the patient and prescription of treatment

The patient was diagnosed at the age of 68 with intermediate risk localised prostate cancer (T1cN0M0, adenocarcinoma 3) and a maximum prostate specific antigen (PSA) of 13.93 ng/mL. He was also diagnosed with multiple sclerosis (MS) and Parkinson’s disease (PD). His symptoms before RT included problems with sexual, bowel and bladder function. The patient was qualified for hypofractionated radiotherapy with a daily fraction dose of 7.25 Gy to a total dose of 36.25 Gy. Taking into account the patient’s comorbidities and potential difficulties related to the reproducibility of OAR, a treatment based on the Ethos therapeutic accelerator was proposed.

Interfraction changes

Due to comorbidities, despite repeating the treatment preparation protocol, the patient had difficulty achieving proper urinary bladder volume, and, at the same time, a small rectum volume (due to retained stool and gases). On consecutive days of treatment, we observed differences in pelvic organ anatomy (volume and position) compared to the CT performed for treatment planning purposes (Fig. 3). For this specific patient, in each fraction, the volume of the bladder and rectum was less than at baseline CT (Tab. I).

Impact of OAR variability on the dose distribution in the plan

The observed differences in patient geometry also influenced changes in dose distribution in the PTV and CTV (Fig. 4, 5). The goal of the prepared treatment plan was to obtain, during each fraction of radiotherapy in 100% of the CTV, at least 99% of the prescribed dose (that is 7.18 Gy of the prescribed 7.25 Gy) and in 100% of the PTV at least 98% of the prescribed dose (that is 7.11 Gy of the prescribed 7.25 Gy). In an extreme case (the fourth fraction of treatment), the patient treated according to the scheduled treatment plan would receive 99% (7.18 Gy) and 98% (7.11 Gy) of the prescribed dose only in 49% of CTV and 48% of PTV, respectively (Tab. II). This means that only half of the prostate on the fourth day of treatment would receive the desired curable radiation dose. The differences in the dose distribution in the CTV and PTV in subsequent treatment fractions for the scheduled and adapted plan are presented in Table 2. The adaptation process improved dose distribution to cover 100% of the PTV to at least 98% of the prescribed dose during each fraction of treatment.

Intrafraction changes

As the adaptive process requires time, there is always concern about intrafraction variability. The average time required for adaptation in the case of the patient presented was 29 minutes, with a standard deviation of 5 minutes. The irradiation time alone, defined as the execution of the treatment plan, did not exceed 8 minutes (measured from the acceptance of the plan to post-irradiation completion of the CBCT). For this patient, no significant changes in the shape or volume of the organs at risk were observed during a single treatment session (Tab. III). However, internal organ verification using CBCT after adaptation and before irradiation seems justified due to replanning time, ensuring treatment precision.

Discussion

In adaptive radiotherapy, treatment plans are adjusted based on anatomical changes such as organ deformation, weight loss and tumour shrinkage. It can be provided online (adjustments made during treatment sessions) or offline (adjustments made between treatment sessions). Advances in technology and artificial intelligence have made online adaptive radiotherapy possible in a relatively short time. This technique has been studied at various tumour sites, such as the head and neck, lung, cervix, prostate, rectum and bladder, demonstrating accurate and precise target coverage and protection of organs at risk [6–8]. This leads to the avoidance of the "cold spot" (Fig. 4, 5), considering that the dose deficit is strongly correlated with a high risk of local relapse. The magnitude of the dose deficit and the size of the cold subvolume within the gross tumor volume (GTV) have an independent negative impact on real tumour control [9].

Peng et al. [10] showed the interfraction variations and their dosimetric effects in patients with prostate cancer. The authors demonstrated that the current standard repositioning using prostate alignment might be adequate only for two-thirds of fractions. They stressed that for the other better online correction strategies, such as online replanning, are needed.

The patient presented was such an example. As expected, we observed high interfraction mobility; however, intrafraction mobility turned out to be minimal (Tab. III). For oART, due to the time of the adaptation process, we always need to keep in mind the intrafraction variation [11]. It is very important to emphasise the issue of appropriate preparation for each treatment session. To reduce intrafraction mobility, patients should be asked to refrain from drinking large amounts of fluids and not drink coffee or tea prior to the treatment session. Since the treatment itself lasts about 4 minutes, it is preferable to perform CBCT just before irradiation. This procedure will allow to observe intrafraction variation and, in rare cases of clinically relevant changes, withdraw from treatment. When purchasing the next CBCT after the entire adaptation process, the suitability of the margins can be verified, and the target coverage is ensured.

Conclusions

Adaptive techniques are new, demanding, but also promising tools used in radiotherapy, increasing the opportunity to improve the tolerance and long-term results of radiation treatment.

Article information and declarations

Data availability statement

The datasets generated and analyzed during the current study are not publicly available due to the right of personal data protection but can be made available by the corresponding authors upon reasonable request.

Ethics statement

The treatment was according to protocols of Radiotherpy Department and in agreement with Helsinki Declaration. The research was approved by the Committee of Research Ethics of Maria Sklodowska-Curie National Research Institute of Oncology nr 60/2024.

Authors contributions

Iwona U. Dębosz-Suwińska — writing: original draft preparation.

Dawid Bodusz — visualization.

Barbara Bekman — writing: review & editing.

Aleksandra Napieralska — writing: review & editing.

Agnieszka Namysł-Kaletka — methodology.

Agata Roch-Zniszczoł — visualization.

Jerzy Wydmański — supervision.

Funding

None.

Acknowledgments

None.

Conflict of interest

The authors declare no conflict of interest.

Supplementary material

None.

Iwona U. Dębosz-Suwińska

Department of Radiotherapy

Maria Sklodowska-Curie National Research Institute of Oncology
Wybrzeże Armii Krajowej 15
44–102 Gliwice, Poland
e-mail: iwona.debosz-suwinska@gliwice.nio.gov.pl

Received: 14 Nov 2024
Accepted: 04 Feb 2025
Early publication date: 12 Mar 2025

References

1. Miszczyk L, Wydmański J. Evaluation of delivered dose changes during radiotherapy. Acta Oncol. 1999; 38(2): 197–201, doi: 10.1080/028418699431618, indexed in Pubmed: 10227441.
2. Barker JL, Garden AS, Ang KK, et al. Quantification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT/linear accelerator system. Int J Radiat Oncol Biol Phys. 2004; 59(4): 960–970, doi: 10.1016/j.ijrobp.2003.12.024, indexed in Pubmed: 15234029.
3. Åström LM, Behrens CP, Calmels L, et al. Online adaptive radiotherapy of urinary bladder cancer with full re-optimization to the anatomy of the day: Initial experience and dosimetric benefits. Radiother Oncol. 2022; 171: 37–42, doi: 10.1016/j.radonc.2022.03.014, indexed in Pubmed: 35358605.
4. Maciejewski B. Tumor and normal tissue radiation side effects. Nowotwory. Journal of Oncology. 2022; 72(4): 242–246, doi: 10.5603/njo.2022.0037.
5. Christiansen RL, Dysager L, Hansen CR, et al. Online adaptive radiotherapy potentially reduces toxicity for high-risk prostate cancer treatment. Radiother Oncol. 2022; 167: 165–171, doi: 10.1016/j.radonc.2021.12.013, indexed in Pubmed: 34923034.
6. Li XA, Liu F, Tai An, et al. Development of an online adaptive solution to account for inter- and intra-fractional variations. Radiother Oncol. 2011; 100(3): 370–374, doi: 10.1016/j.radonc.2011.08.027, indexed in Pubmed: 21924781.
7. Yock AD, Ahmed M, Ayala-Peacock D, et al. Initial analysis of the dosimetric benefit and clinical resource cost of CBCT-based online adaptive radiotherapy for patients with cancers of the cervix or rectum. J Appl Clin Med Phys. 2021; 22(10): 210–221, doi: 10.1002/acm2.13425, indexed in Pubmed: 34529332.

8. Moazzezi M, Rose B, Kisling K, et al. Prospects for daily online adaptive radiotherapy via ethos for prostate cancer patients without nodal involvement using unedited CBCT auto-segmentation. J Appl Clin Med Phys. 2021; 22(10): 82–93, doi: 10.1002/acm2.13399, indexed in Pubmed: 34432932.
9. Hawrylewicz L, Maciejewski B, Trott K, et al. Overall and GTV subvolumes tumour control probability (TCP) for head and neck cancer treated by 3D-IMRT with inhomogeneous dose distribution. Nowotwory. Journal of Oncology. 2020; 70(4): 127–134, doi: 10.5603/njo.2020.0027.
10. Peng C, Ahunbay E, Chen G, et al. Characterizing interfraction variations and their dosimetric effects in prostate cancer radiotherapy. Int J Radiat Oncol Biol Phys. 2011; 79(3): 909–914, doi: 10.1016/j.ijrobp.2010.05.008, indexed in Pubmed: 20732764.
11. Khouya A, Pöttgen C, Hoffmann C, et al. Adaptation time as a determinant of the dosimetric effectiveness of online adaptive radiotherapy for bladder cancer. Cancers (Basel). 2023; 15(23), doi: 10.3390/cancers15235629, indexed in Pubmed: 38067333.

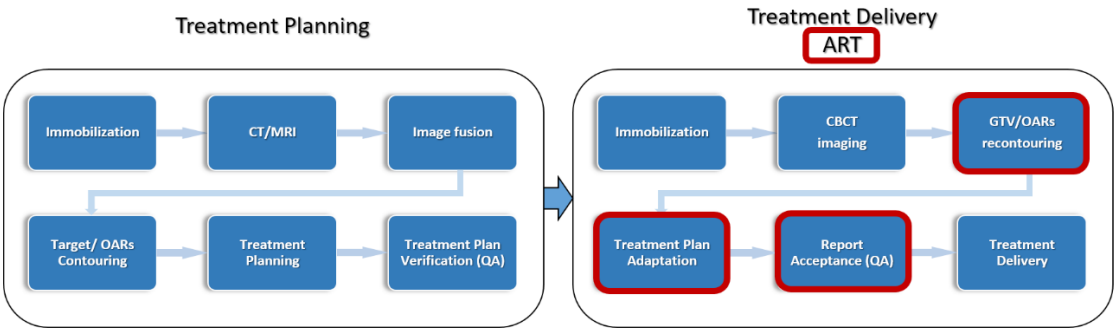

Figure 1. The schematic diagram of the workflow for the preparation and treatment for the online adaptive radiotherapy; ART — adaptive radiotherapy; CBCT — cone beam computed tomography; CT — computer tomography; GTV — gross tumor volume; MRI — magnetic resonance imagining; OAR — organs at risk; QA — quality assurance

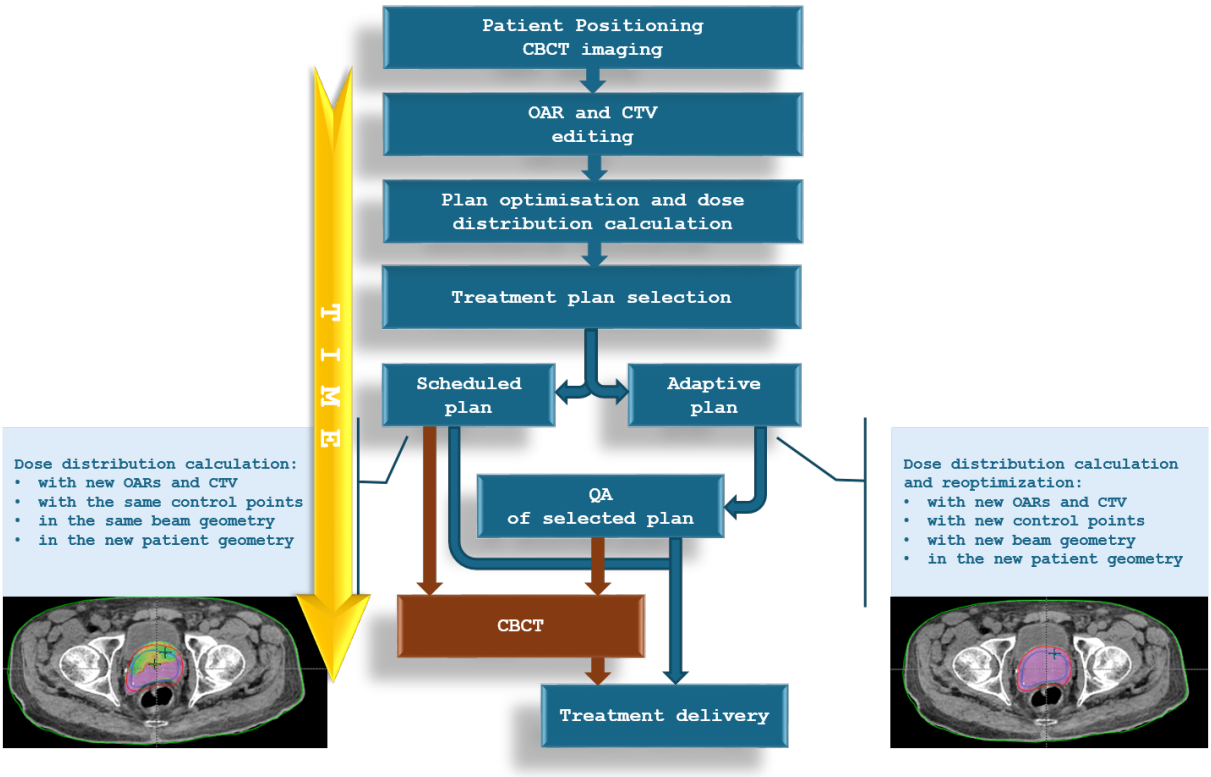

Figure 2. Schematic diagram of the workflow for the online adaptive radiotherapy; CBCT — cone beam computed tomography; CTV — clinical target volume; OAR — organs at risk; QA — quality assurance

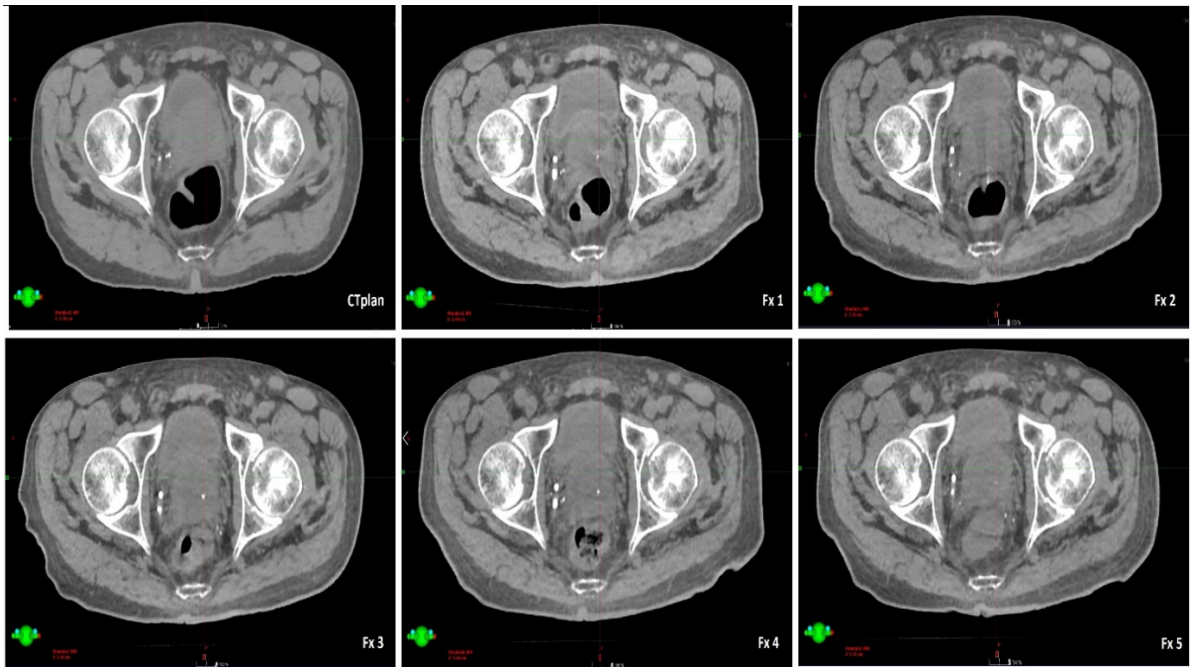

Figure 3. Changes in the anatomy of the treatment volume on the day of computer tomography and on each day of treatment

Figure 4. Example of dose distribution in planning target volume between the adapted and scheduled treatment plan during the first and fifth treatment fractions

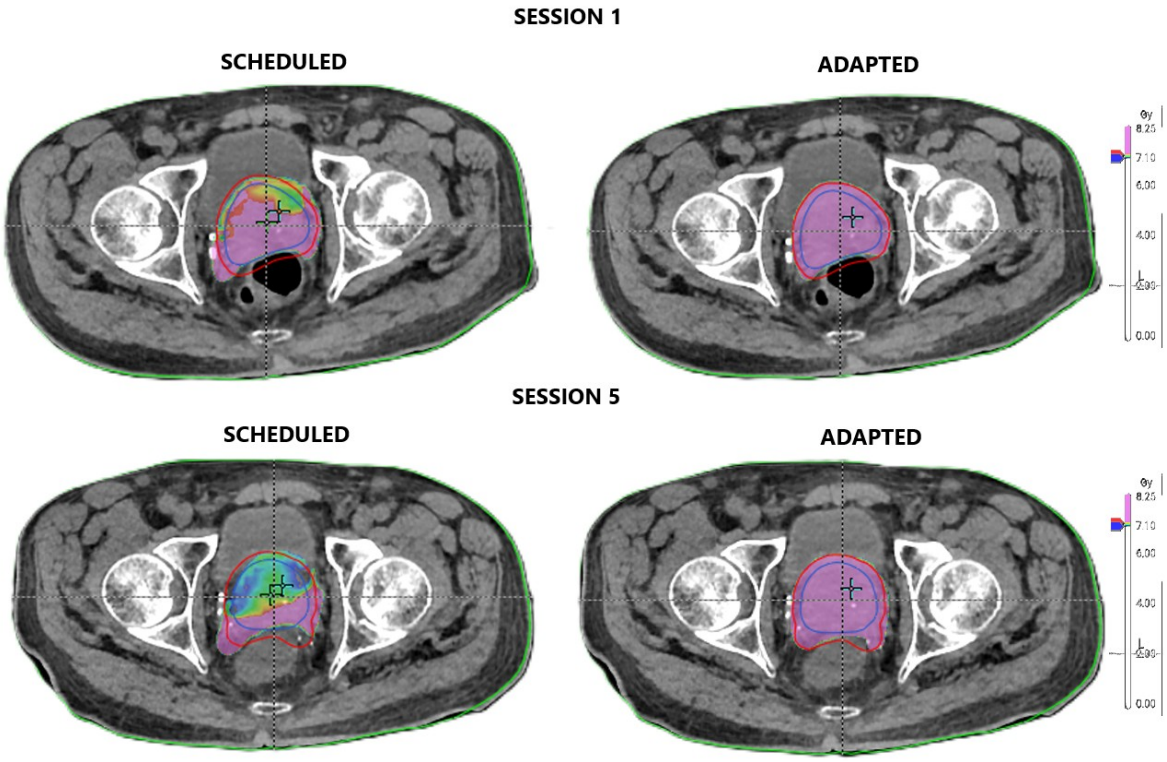

Figure 5. Difference in dose distribution in the planning target volume (98%) between the scheduled plan (**A**) and the adapted plan (**B**) during the first and fifth treatment fraction

Table I. Changes in the volume (cm^3) of the urinary bladder and rectum during each treatment fraction compared to the volumes measured on the computer tomography (CT) done for the treatment planning purposes

Fx	**Volume [cm^3]**				**Volume changes [cm^3]**	
	Bladder		**Rectum**		**Bladder**	**Rectum**
	CT_{plan}	CBCT	CT_{plan}	CBCT	CT_{plan}–CBCT	CT_{plan}–CBCT
1	237.55	202.90	122.2	77.57	–34.7	–44.6
2	237.55	196.82	122.2	78.72	–40.7	–43.5
3	237.55	199.49	122.2	69.70	–38.1	–52.5
4	237.55	146.12	122.2	100.32	–91.4	–21.9
5	237.55	172.70	122.2	74.71	–64.9	–47.5

CBCT — cone beam computed tomography; CT_{plan} — computed tomography done for the treatment planning purposes

Table II. Observed changes in the dose distribution in the irradiated volume (CTV-V100% > 99%, PTV-V100% > 98%) in subsequent treatment fractions in the scheduled and adapted plan

Fx	CTV (V100% > 99%)		PTV (V100% > 98%)	
	schedule d	adapte d	schedule d	adapte d
1	88.9	99,3	78.0	93.5
2	75.0	99,7	65.1	95.2
3	60.1	99,3	55.3	95.4
4	49.0	99,9	48.3	97.4
5	55.8	100	54.0	97.2

CTV — clinical target volume; PTV — planning target volume

Table III. Volume (cm^3) of the urinary bladder and rectum before and after treatment for all sessions

Fx	Bladder volume [cm^3]		Rectum volume [cm^3]	
	before treatment	after treatment	before treatment	after treatment
1	201.6	206.3	76.6	79.0
2	197.0	197.0	69.2	70.8
3	199.0	217.7	67.4	67.4
4	144.9	177.8	50.2	50.5
5	171.5	180.1	78.3	78.0