

Feasibility Study of Adaptive Prostate Cancer Radiotherapy Using Daily kVCT Images on a Ring-Gantry Radiotherapy Machine

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Abstract

Background: For prostate cancer patients undergoing external beam radiotherapy, dose delivery accuracy of radiotherapy is limited due to daily anatomical variations. One alternative, adaptive radiotherapy (ART) based on daily imaging, has been proposed to minimize changes in treatment delivery. **Methods:** We aimed to evaluate kilo-voltage computed tomography (kVCT) image quality from a ring-gantry medical linac (X1 machine) with an integrated fan-beam CT imaging system and assess whether daily kVCT images can be used to plan ART in prostate cancer radiotherapy. We compared the image quality of all kVCT scanning protocols on the X1 and a clinical CT simulator on an image quality phantom. To calculate volumetric modulated arc therapy plan doses, we used CT images for an anthropomorphic phantom from the CT simulator and X1 linac. We retrospectively selected treatment plans and daily imaging data for ten prostate cancer patients who received X1 machine treatments. Using daily kVCT images, we delineated normal organs and target volume contours and created adaptive plans with the original treatment optimization parameters. **Results:** Excluding the air insert, average CT numbers for different density inserts on the image quality phantom varied from -3.5 to 5.7 HU between CT simulator and X1 kVCT images. kVCT images had less than 0.3% variation in mean dose compared to phantom CT simulation images. Daily bladder and rectum volume variation ranged from -352 to +212 cc and from -138.6 to 81.8 cc, respectively. Relative to the original treatment plans, kVCT image-based plan mean doses for the primary PTV, bladder, rectum, and penile bulb were $100.9\% \pm 2.7\%$, $97.8\% \pm 9.2\%$, $98.1\% \pm 9.2\%$, and 96.1%

$\pm 24.7\%$, respectively. **Conclusions:** The kVCT images from the X1 machine demonstrated adequate CT image quality for treatment planning. Most optimized adaptive treatment plans had comparable target coverages and acceptable normal organ dose variations, indicating potential clinical benefits with adaptive treatment planning in the presence of large daily anatomical variations.

Keywords

Adaptive Radiotherapy, Image-Guided Radiotherapy, Prostate Cancer, kVCT

1. Background

Intensity modulated radiotherapy (IMRT) is widely used in modern external beam radiotherapy for prostate cancer [1]. The benefits of IMRT include highly conformal dose to target volumes and rapid dose drop-off outside of target volumes. To ensure accurate dose delivery, these target volumes are aligned to treatment planning positions prior to radiotherapy delivery using image-guided setup techniques with three-dimensional imaging modalities [1] [2]. However, in the case of external beam radiotherapy for prostate cancer patients, the bladder and the rectum are adjacent to the target volumes, and their volume, shape, and relative anatomical positions may vary significantly when daily treatment fractions are given, thereby potentially affecting radiation dosage to patients [3] [4]. These anatomical variations and the resultant uncertainties in dosing highlight the need for a more robust approach. Researchers/clinicians have proposed techniques such as rectal and bladder balloons as a method to minimize bladder and rectal filling variability [5]-[7]. Furthermore, adaptive radiotherapy (ART) techniques, both online and offline, have also been implemented for prostate cancer radiotherapy [8]-[10]. While conventional ART techniques have improved treatment precision and adaptability, novel radiotherapy technologies have presented new opportunities for patient treatment and planning.

Existing ART techniques can create adaptive treatment plans based on a variety of daily imaging modalities including cone-beam computed tomography (CBCT), CT-on-rails, and magnetic resonance imaging (MRI) in MRI-guided radiotherapy systems. As novel radiotherapy machines continue to be developed with new imaging capabilities, ART becomes feasible on more radiotherapy delivery systems. However, before ART can be implemented on new radiotherapy machines, it is necessary to perform thorough evaluations of the imaging subsystem. In recent years, a new radiotherapy machine with hybrid imaging modalities that combines a compact 6-MV linear accelerator (linac) and 16-slice fan-beam kilo-voltage computed tomography (kVCT) with a ring gantry and integrates a positron emission tomography (PET) subsystem to guide radiotherapy delivery in real-time has become available [11] [12] (ReflEXion[®] X1 with SCINTIX[®] therapy, ReflEXion Medical Inc., Hayward, CA). The kVCT system can support daily patient setup

via three-dimensional imaging. Our group previously demonstrated that kVCT image quality had the highest image quality compared to other online CT imaging technologies [13], and we found that X1 kVCT images can be combined with deep learning-based auto-segmentation to develop treatment workflows for cancer patients [13]. However, no group has yet evaluated how these X1 linac-based kVCT images can be used to develop ART plans to better treat prostate cancer patients. We hypothesized that daily kVCT image acquisition on the X1 machine can provide adequate image quality comparable to CT simulation images and could be used for online or offline ART planning. In this study, we sought to evaluate the kVCT image quality and to evaluate the feasibility of using daily kVCT images to treat prostate cancer patients with efficient ART treatment planning workflow techniques.

We found that X1 machine kVCT images had comparable quality to CT simulation images when used for treatment planning. Furthermore, we demonstrate that most adaptive treatment plans generated from these kVCT images had similar target coverages and dose variations to those from CT images. Our findings demonstrate that kVCT-based adaptive treatment plans can deliver accurate doses of radiation despite daily anatomical variations. Our results lay the foundation for the use of adaptive planning with kVCT images to treat prostate cancer patients.

2. Methods

2.1. kVCT Image Quality Evaluation

The fan-beam CT imaging subsystem on the X1 machine provides eight kVCT scanning protocols with a tube peak kilovoltage (kVp) at 120 kV, the pitch ranging from 0.222 to 1.333, and the X-ray tube current ranging from 45 to 400 mA. **Table 1** lists nomenclature and scan parameters of the eight kVCT scanning protocols on the X1 machine. For all scanning protocols, the reconstructed kVCT images have an axial image spacing of 2 mm, axial image resolution of 512×512 pixels,

Table 1. Uniformity index (UI) and low contrast visibility (LCV) test results for the CT simulation image and for kVCT images with each scanning protocol.

Scanning type/protocol	Tube current (mA)	Pitch	UI	LCV
CT simulation	326	0.625	0.10	6.38
LS (Low Dose & Slow Couch)	45	0.222	0.20	5.39
LM (Low Dose & Medium Couch)	100	0.5	−0.25	5.45
LF (Low Dose & Fast Couch)	267	1.333	−0.20	5.40
MS (Medium Dose & Slow Couch)	67	0.222	−0.15	5.94
MM (Medium Dose & Medium Couch)	150	0.5	−0.10	6.26
MF (Medium Dose & Fast Couch)	400	1.333	−0.20	5.99
HS (High Dose & Slow Couch)	133	0.222	0.20	9.19
HM (High Dose & Medium Couch)	300	0.5	−0.20	8.24

and axial image dimension of 50 cm × 50 cm. In this study, we evaluated kVCT image quality as compared to CT images from a clinical CT simulator (GE Discovery CT590 RT CT Simulator, GE Healthcare, Chicago, IL). A commercial image quality phantom (CatPhan 600, The Phantom Laboratory, Inc., Salem, NY) was used for evaluation. The phantom contained a uniformity test module with uniform density and an inhomogeneity module containing seven inhomogeneity inserts with relative density ranging from 0.0 to 2.16. The phantom was scanned on the X1 machine using each of the eight scanning protocols and on the clinical CT simulator with a clinical scan protocol using a kVp of 120 kV, pitch of 0.625, and X-ray tube current of 326 mA.

2.2. kVCT Image Inhomogeneity Insert Quality Evaluation

For the inhomogeneity inserts, the kVCT images from the X1 machine and the CT simulation images were evaluated in terms of image uniformity, low contrast visibility, and Hounsfield unit (HU) consistency. To evaluate image uniformity in the uniformity test module region, we used the uniformity index (UI) [14]:

$$UI = 100 \frac{\overline{HU}_{periphery} - \overline{HU}_{center}}{\overline{HU}_{center} + 1000},$$

where $\overline{HU}_{periphery}$ and $\overline{HU}_{center}$ are average HU in peripheral and central regions of the uniformity test module, respectively. For commercial CT scanners, fluctuation of CT numbers should not exceed ± 5 HU [15], corresponding of ± 0.5 variation in UI. Visibility of low contrast inserts were evaluated with the low contrast visibility (LCV) metric, defined as [16]:

$$LCV = 2 \frac{\overline{HU}_P - \overline{HU}_L}{\sigma_P + \sigma_L},$$

where $\overline{HU}_P$ and $\overline{HU}_L$ are average HU for two inserts with close HU values: polystyrene and low-density polyethylene (LDPE), respectively, and σ_P and σ_L are the standard deviations of HU for the polystyrene and LDPE inserts, respectively. Both the UI and LCV were calculated with in-house software that utilized a publicly available image analysis software library [17].

2.3. CIRS Thoracic Phantom Generation and Testing

We generated HU-to-density tables for each kVCT scanning protocol based on the average CT numbers of the inhomogeneity inserts used for kVCT image dose calculations. To validate dose calculation results with the HU-to-density tables for kVCT images, we used a commercial anthropomorphic thoracic phantom (CIRS Thorax phantom Model 002LFC, Computerized Imaging Reference Systems, Inc., Norfolk, VA) that included bilateral low-density regions that mimic the left and right lungs and a middle high-density region that mimics the vertebral column (Figure 1). A cylindrical planning target volume (PTV) of 3 cm in diameter and 4.5 cm in length was delineated between the lung volumes and anterior to the vertebral column. This phantom was scanned on the CT simulator using a tho-

racic simulation protocol and on the X1 machine using all available kVCT scanning protocols. Using the CT simulation images, we generated a treatment plan with two 6 MV volumetric modulated arc therapy (VMAT) photon fields to deliver 30 Gy in 10 fractions to the target volume. We then applied the same plan to each individual kVCT image data set per kVCT scanning protocol with the same isocenter location. Three-dimensional dose distributions were calculated in all the treatment plans using the same dose calculation algorithm (the Anisotropic Analytical Algorithm, Varian Medical Systems, Palo Alto, CA), with a scanner- and protocol-specific HU-to-density table for the image used in each treatment plan. We compared the treatment plans of different CT images in terms of dose to the PTV and critical organs.

2.4. Patient Cohort for Adaptive Treatment Planning

First, we performed a retrospective review of all patients treated on the X1 machine at our institution since 2021. We included the first ten prostate cancer patients who received a course of image-guided radiotherapy with at least fifteen treatment fractions between 2021 and 2023. Patient characteristics are listed in **Table 2**. The average age was 69 ± 9 years old (range: 54 - 80). Five of the ten patients had radical prostatectomy and received post-operative radiotherapy, while the other five had intact prostates and received definitive external beam radiotherapy on the X1 machine. Each patient had a CT simulation on the 16-slice CT simulator (Optima 560, GE Healthcare, Chicago, IL) to the pelvic region in a supine position with a slice thickness of 2.5 mm and field-of-view dimension of 50×50 cm. Patients were asked to maintain a full bladder during CT simulation by drinking a fixed amount of water (28 ounces) half an hour prior to CT simulation. Patients were also asked to empty their rectums through bowel movements shortly before the CT simulation appointment.

Table 2. Characteristics of prostate cancer patients in this study. STD: standard deviation.

Characteristics/parameter		Average $\pm$ STD (range)
Age/years-old		69 ± 9 (54 - 80)
Status	Post-prostatectomy	5 (50%)
	Intact prostate	5 (50%)
Prescription	45 Gy	8 (80%)
	60 Gy	1 (10%)
	70 Gy	1 (10%)
PTV volume/cm ³		726.0 ± 281.4 (160.0 - 1182)
Beam-on time/sec		97 (456 - 718)

2.5. Structure Delineation

The CT simulation images were sent to a commercial radiotherapy treatment

planning system (TPS) (Eclipse v16.1, Varian Medical Systems, Inc., Palo Alto, CA), on which normal organs and target volumes were delineated. The normal organs included the bladder, rectum, penile bulb, sigmoid colon, small intestine, and femoral heads. The gross target volumes (GTVs)/clinical target volumes (CTVs) included the prostate gland and seminal vesicles for patients with intact prostate, prostate fossa for patients with prostatectomy, and pelvic lymph nodes. Margins of 3 - 5 mm were added to the CTVs to form PTVs. The target volume that included the prostate gland or prostate fossa, with or without lymph nodes, was regarded as the primary target. The images and the structure set were then sent to the X1 TPS for plan generation.

2.6. X1 Machine Treatment Plan Optimization

The X1 machine has been described previously [18]. Briefly, radiation was delivered with a flattening filter-free 6 MV photon beam modulated by a 64-leaf binary multi-leaf collimator (MLC) and a pair of 2 cm primary jaws to collimate the beam in the longitudinal direction. The couch remained stationary while radiation is administered with a rotational gantry, and the couch moved incrementally with a step size of 2.1 mm while the beam was off. For post-prostatectomy patients, an initial treatment plan was generated with a prescription dose of 45 Gy in 25 equal treatment fractions to the prostate fossa and pelvic lymph nodes, followed by a boost treatment plan with a prescription dose of 19.8 to 21.6 Gy in 11 to 12 equal treatment fractions to the prostate fossa. Among patients with intact prostates, one patient had a treatment plan with a prescription dose of 60 Gy, 55 Gy, and 42 Gy to the prostate, seminal vesicles, and pelvic lymph nodes, respectively, in 20 equal treatment fractions; one patient had a treatment plan with a prescription dose of 70 Gy in 28 treatment fractions to the prostate and seminal vesicles; and three patients had an initial treatment plan with a prescription plan of 45 Gy in 25 treatment fractions to the prostate, seminal vesicles, and pelvic lymph nodes, followed by either permanent prostate seed implant (one patient) or by external beam radiotherapy boost with a prescription dose of 34.2 Gy in 19 treatment fractions (two patients). In plan optimization, a smoothing penalty of 10 and a treatment time penalty of 1000 were applied to all treatment plans while structure-specific optimization parameters were individually tuned based on interim optimization results in an iterative optimization process. In all X1 treatment plans, the optimization parameters were set for a goal of covering 95% of the primary PTV with the prescription dose.

2.7. kVCT Scans

kVCT scans were performed using the integrated fan-beam kVCT system on the X1 machine after patients were aligned on the treatment couch according to skin marks. We used the medium dose/fast couch kVCT scanning protocol and adjusted the couch position translationally and rotationally according to the kVCT image registration with the planning CT images. Following this, patients were

then treated with radiation.

2.8. ART Treatment Plan Preparation

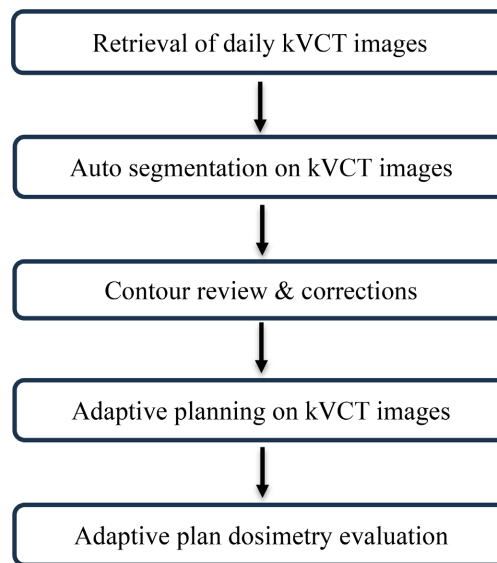


Figure 1. Schematic diagram of the workflow for adaptive treatment plan generation and analysis in this study.

For the initial treatment plan during the first part of the treatment course, we generated ART treatment plans using kVCT images from one fraction from every five consecutive treatment fractions (corresponding to the evaluation of one fraction per week). **Figure 1** shows the workflow for adaptive treatment plan generation and analysis in this study.

Pre-treatment kVCT images were retrieved from treatment archives and sent to a commercial auto-segmentation system (RT_Mind AI, MedicalMind Ltd., Beijing, China) using a convolutional neural network (CNN) algorithm for automatic delineation of structures in the pelvic region, including the bowel bag, rectum, sigmoid colon, bladder, and prostate gland [18]. The auto-segmentation results were sent to the Eclipse TPS for review and manual correction of AI-generated contours by experience planners. A radiation oncologist reviewed and approved contours used for each adaptive treatment plan. The same sets of normal organs and GTV/CTVs were delineated using pre-treatment kVCT images, and PTVs were created with the same setup margins. The kVCT images and associated structure set were transferred to the X1 treatment planning station for the creation of offline ART treatment plans. All ART treatment plans used the same jaw size of 2 cm and had the same prescription as in the original treatment plan. Similarly, the same normalization criteria were applied to the ART treatment plans. To improve the efficiency of ART treatment planning, the same optimization parameters from the original treatment plan were applied to each subsequent ART treatment plan. Due to the difference in the number of treatment fractions for each patient, a total of 48 ART treatment plans based on kVCT images were created and optimized:

five ART treatment plans created for eight patients (40 total) and four ART treatment plans created for the remaining two patients (8 total). Bladder and rectum volume variations were evaluated in all ART treatment plans. Mean doses to the primary PTV and major critical organs were examined and compared with those in the original treatment plans. Pearson's correlation coefficient was calculated between the daily bladder volume and the mean bladder dose in the adaptive plans, where the correlation was deemed strong when the absolute value of the correlation coefficient was greater than 0.7.

3. Results

3.1. kVCT Image Quality Evaluation

To determine whether kVCT images could be used for adaptive planning, we first compared kVCT image quality to that in CT simulation images. To simulate the different densities of tissues commonly imaged in the human body, we used a commercial image quality phantom with seven inhomogeneity inserts (CatPhan 600). We performed the eight kVCT scanning protocols on these phantom inserts and found that the UI ranged from -0.25 to 0.20 , and the LCV ranged from 5.40 to 9.19 for all kVCT scanning protocols (**Table 1**). In comparison, CT simulation images acquired from the phantom inserts using a clinical scan protocol had UI and LCV values of 0.10 and 6.38 , respectively. We found that all UI results were within tolerance for commercial CT scanners [14]. Next, to evaluate how well X1 kVCT images were able to provide quantitative tissue density, we compared the differences in average CT numbers and found that excluding the air insert, average CT numbers ranged from -3.5 to 5.7 HU between the CT simulator and the X1 kVCT images (**Figure 2**, Supplemental **Table S1**). Furthermore, when we evaluated the differences between scanning protocols for kVCT images, we found that CT number variations ranged between 1.8 to 3.5 HU for all inhomogeneity inserts. CT number standard deviations for the different density inserts extended from 5.7 to 7.7 HU with the CT simulator image, and from 5.8 to 8.3 HU in the kVCT images from high-dose protocols.

Based on our findings, we then used a commercial anthropomorphic thoracic phantom (CIRS) to mimic the lungs and vertebral column and validate kVCT dose calculation results. **Figure 3(A)** shows the dose color wash with dose calculated on the planning CT of the CIRS anthropomorphic thorax phantom with contours for the PTV and normal organs, while **Figure 3(B)** shows the dose color wash with dose calculated on a kVCT image using the low dose & fast couch (LF) scanning protocol. The mean PTV dose in the treatment plan based on CT simulation images was 31.14 Gy and ranged from 31.21 to 31.24 Gy based on dose calculations using kVCT images with different scan protocols from the X1 machine (**Figure 3(C)**, Supplemental **Table S2**; relative difference: 0.2% - 0.3%). Compared to the mean doses for the left lung, right lung, and spine using CT simulation image dose calculation, mean doses to those organs based on kVCT dose calculation had a relative difference of 0.2% to 0.3% (**Figure 3(C)**, Supplemental **Table S2**).

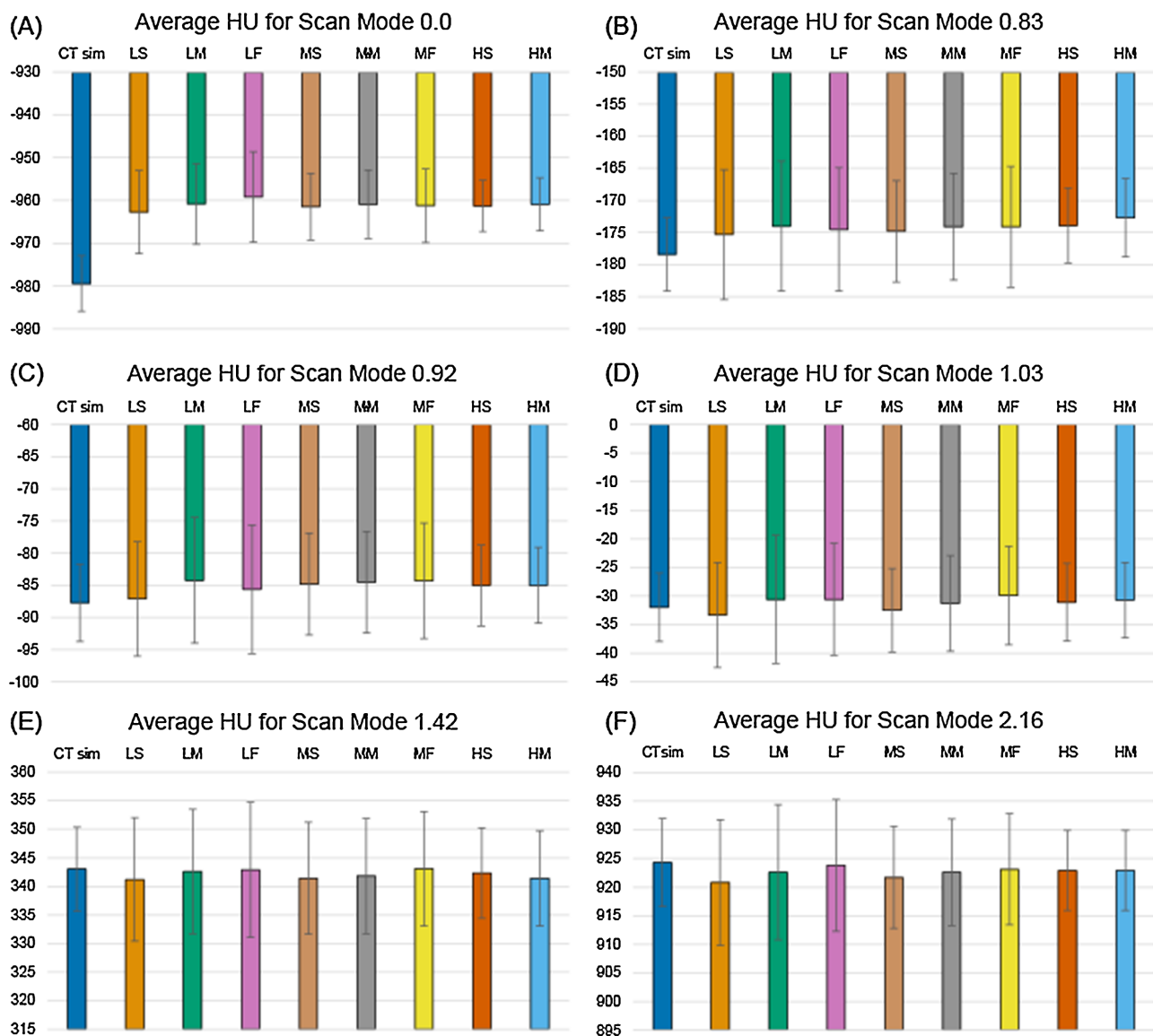


Figure 2. Average HU and standard deviations for inhomogeneity inserts in the CT simulation image and kVCT images with each scanning protocol ((A) relative density 0.0, (B) relative density 0.83, (C) relative density 0.92, (D) relative density 1.03, E. relative density 1.42, F. relative density 2.16). Detailed data tables are provided in the supplemental materials.

3.2. Adaptive Treatment Planning

We included ten prostate cancer patients who received at least 15 treatment fractions of image-guided radiotherapy. Therapists asked these patients to drink 28 ounces of water half an hour before CT simulation and to empty their rectums through bowel movements before CT simulation, and we evaluated bladder and rectum volume variations in kVCT images (**Figure 4**). For these ten patients, the bladder volume in the planning CT simulation ranged from 67.5 to 609.7 cm³ whereas in kVCT images, the bladder volume fell between 27.1 to 536.6 cm³. Relative to the CT simulation images, the relative bladder volume in the kVCT images extended from 21.2% to 256.0%, and the change in bladder volume varied between -352.3 cm³ to 211.7 cm³. Seven patients had a maximum bladder volume

variation of over 50% in the evaluated kVCT images. The rectum volume in planning CT simulation images exhibited a range of 37.7 to 193.0 cm³ while in the kVCT images, the rectum volume was distributed between 37.2 to 163.6 cm³.

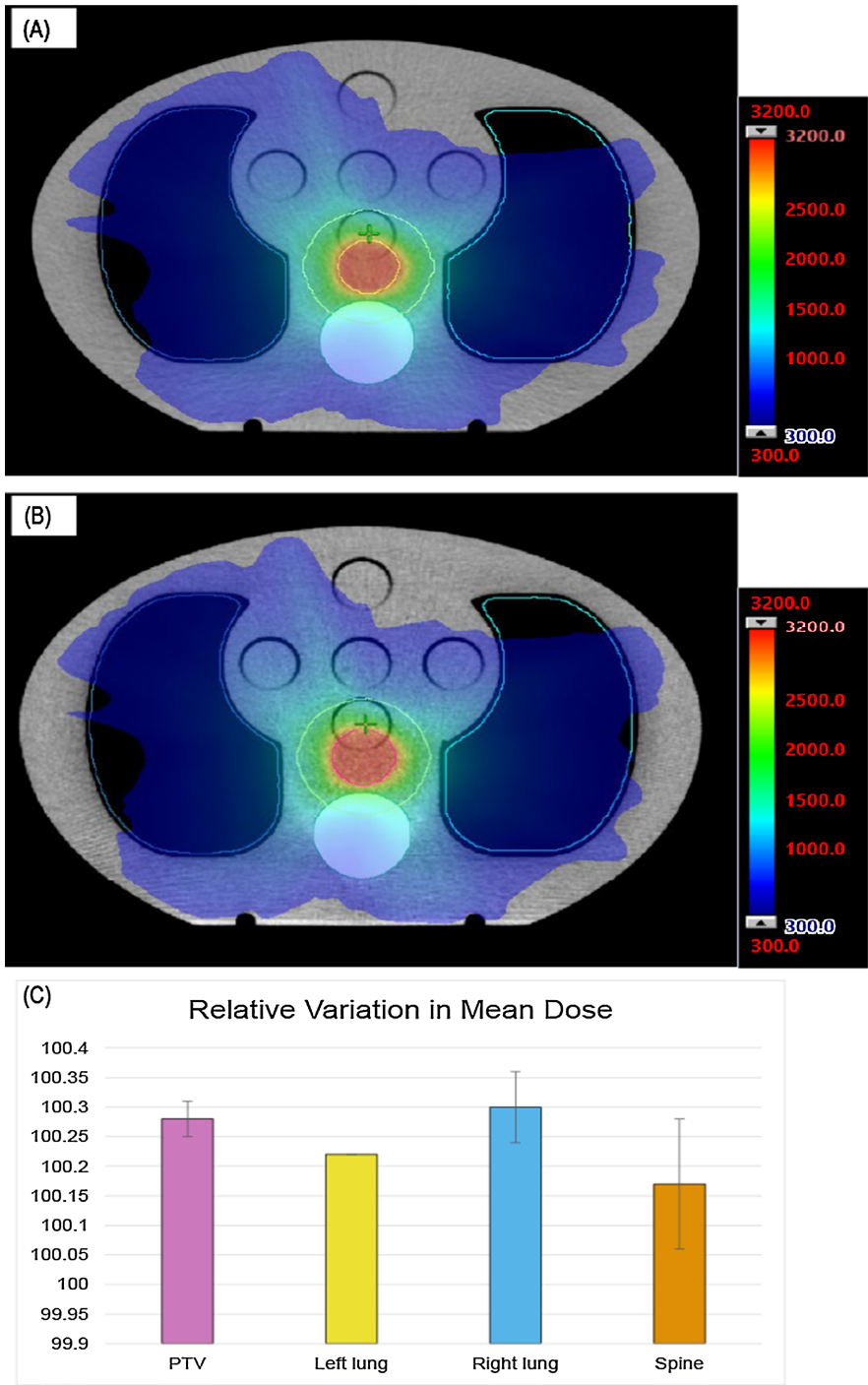


Figure 3. Cross section of the CIRS thorax phantom and dose color wash based on (A) the CT simulation image and (B) a kVCT image using the low dose & fast couch speed scanning protocol. (C) Variation of mean dose to the target and normal organs for the CIRS thorax phantom with different X1 kVCT images relative to plan dose based on the CT simulation image.

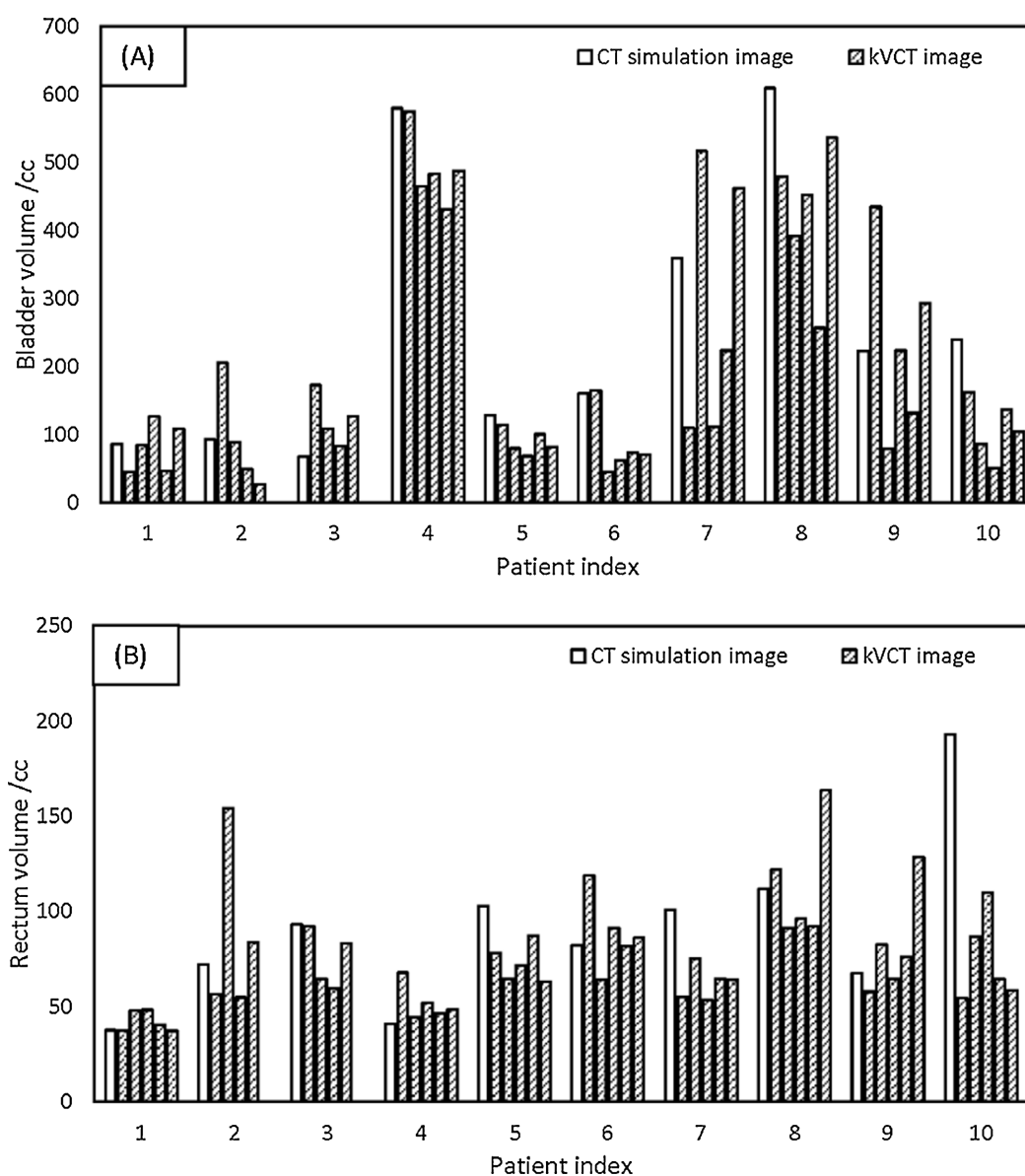


Figure 4. Weekly (A) bladder volume and (B) rectum volume variations for each patient.

Relative to the rectum volume in CT simulation images, the rectum volume in daily kVCT images showed a variation from 28.2% to 213.2%, and the change in rectum volume ranged between -138.6 cm^3 to 81.8 cm^3 .

Based on these findings, we created and optimized 48 ART treatment plans for the ten patients (Figure 5). When we compared the optimized ART treatment plans to the original treatment plans of each patient, we found that the mean dose variations to the primary PTV, bladder, rectum, and penile bulb ranged from 96.4% to 108.9%, 80.9% to 117.3%, 76.9% to 118.6%, and 42.6% to 144.4%, respectively. When we averaged the mean dose to each structure was over all ART treatment plans for each patient, the mean dose extended from 98.4% to 107.7% for the primary PTV, 87.7% to 109.5% for the bladder, 92.5% to 103.2% for the rectum, and 62.8% to 114.6% for the penile bulb (Figure 6).

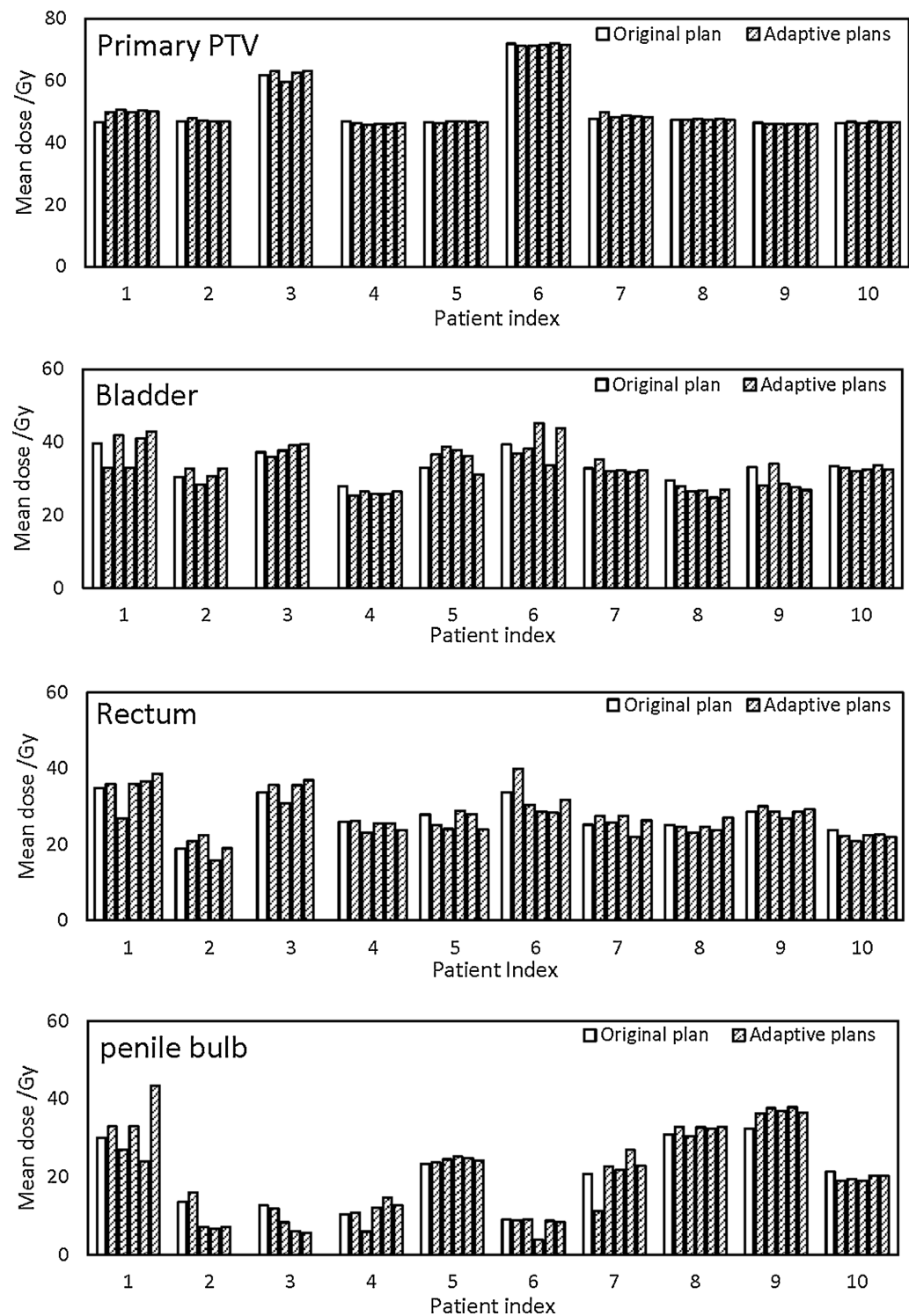


Figure 5. Mean dose to the primary PTV and major critical organs in the original treatment plan and adaptive treatment plans. Data for the adaptive plans are plotted in sequential order of the treatment fractions for each patient.

We next compared the mean and standard deviations of representative dosimetric parameters in ART treatment plans relative to those in original treatment

plans (**Figure 7**, Supplementary **Table S3**). In ART plans, the average primary PTV coverage by the prescribed dose was $96.0\% \pm 1.7\%$, compared to $95.7\% \pm 1.9\%$ in original treatment plans. In contrast, the mean dose in the original treatment plans for the primary PTV, bladder, rectum, and penile bulb were $100.9\% \pm 2.7\%$, $97.8\% \pm 9.2\%$, $98.1\% \pm 9.2\%$, and $96.1\% \pm 24.7\%$, respectively. Strong correlations (Pearson correlation coefficient > 0.7 or < -0.7) between the daily bladder volume and mean bladder dose in the adaptive plans were found in only one patient, where the mean bladder dose ranged from 24.8 to 27.9 Gy in the adaptive plans.

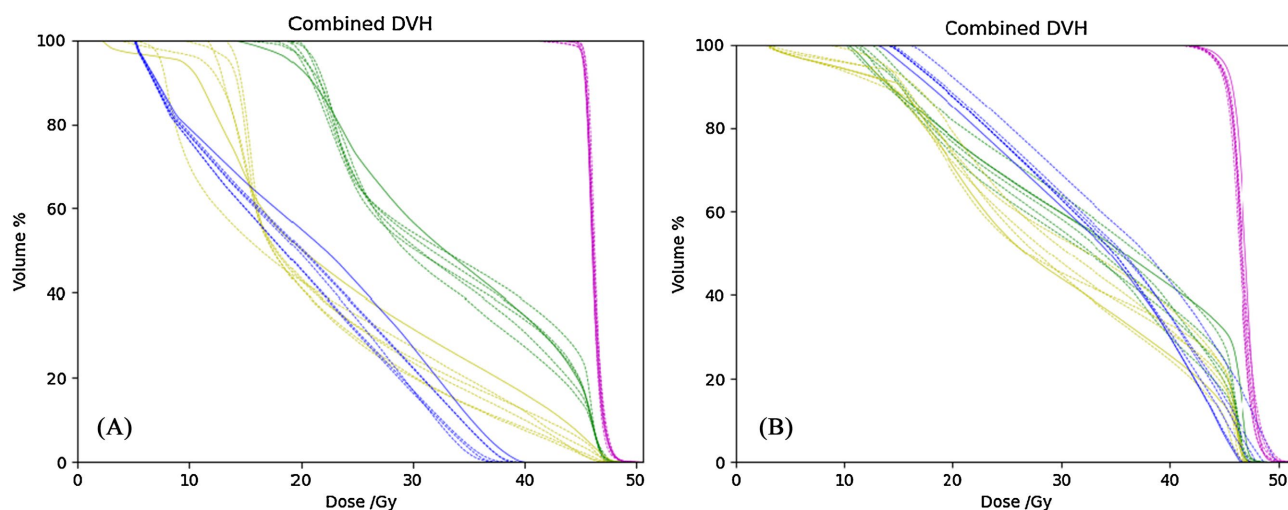


Figure 6. Representative combined DVH for (A) a patient treated to the prostate and (B) a patient treated to the prostate bed. The solid curves are those from the treatment plan and the dotted curves are those from adaptive treatment plans based on daily kVCT images. Magenta: primary PTV; blue: penile bulb; green: bladder; yellow: rectum.

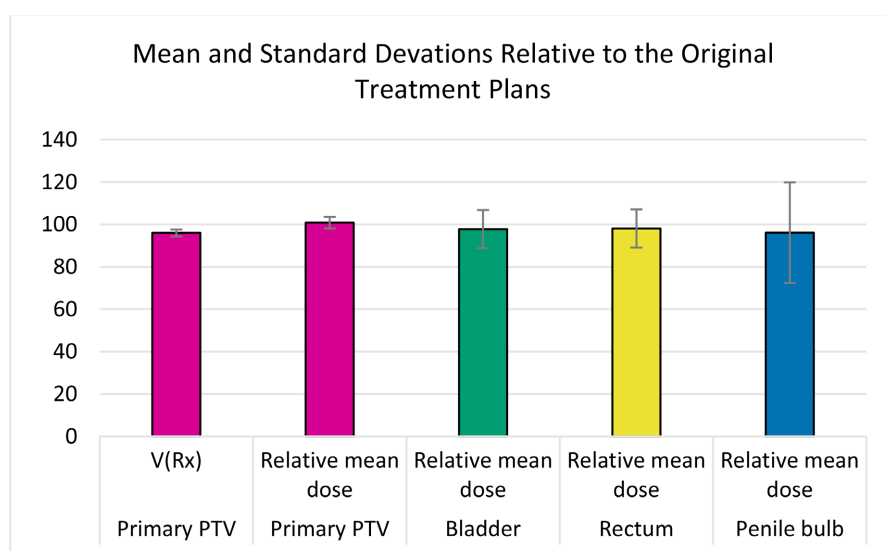


Figure 7. Mean and standard deviations of the primary PTV coverage by the prescription dose (V(Rx)) and mean dose relative to those in the original treatment plans for the primary PTV (magenta), bladder (green), rectum (yellow), and penile bulb (blue) in the ART treatment plans.

4. Discussion

To our knowledge, this is the first study to characterize X1 kVCT image quality and evaluate the feasibility of kVCT images for ART treatment planning of prostate cancer patients. We found that kVCT images showed adequate CT number uniformity and noise, and that dose calculation results based on HU-to-density tables for kVCT images did not have any clinically significant differences from those on a clinical CT simulator. Using optimization parameters in the original treatment plan, our ART plans based on daily kVCT images adequately covered PTV and spared normal organs despite significant bladder and rectum volume variations. Although this study focused on ART in the treatment of prostate cancer, the same technique can be applied to other disease sites including head & neck cancer.

In external beam radiotherapy of pelvic malignancies such as prostate cancer, a full bladder for treatment planning CT simulations and daily treatments may decrease gastrointestinal toxicity as the bowel is moved farther away from the pelvic region, thereby reducing radiation to the bowel. However, increased bladder volume at the time of CT simulation could be associated with increased bladder volume variation during the radiotherapy course [19] [20]. A study by Grün *et al.* revealed that fluctuations in bladder volume correlated with increased risk of acute genitourinary toxicity [5], indicating that the original treatment plan may not be appropriate throughout the treatment course. Our results in **Figure 4** confirmed significant bladder volume heterogeneity between patients even though we tried to regulate water intake prior to daily treatment appointments. No strong correlation was found between the daily bladder volume and the mean bladder dose for most patients, suggesting that the adaptive planning technique achieved consistent bladder dose despite significant bladder volume differences. In addition, significant changes in rectal anatomical positions may also occur during prostate cancer radiotherapy [4]. Although daily patient setup positions can be corrected by volumetric imaging, replanning may be necessary to minimize dosimetric variations to targets and critical organs as a result of the differences in relative organ positions and bladder and rectal filling. Of note, this study did not evaluate daily volume fluctuations to the small bowel since daily kVCT scans only included the inferior portion of the small bowel volume, and the full bladder minimized small bowel involvement in this patient cohort.

Both online and offline ART techniques have been proposed as methods to account for the daily anatomical variations in external beam radiotherapy to treat prostate cancer [8]-[10]. Online ART treatment plans have already been generated using CBCT images, MRI images, or CT-on-rail systems [9] [20] [21]. Compared to other linac systems, the X1 machine is one of the few existing linac systems with an integrated fan-beam CT imaging system on the same ring gantry as the linac. In contrast to MR-guided ART treatment planning systems, X1 machine kVCT images provide direct electron density data. Together, the X1 machine offers high-resolution, true 3D volumetric imaging that allows for precise anatomical locali-

zation and dose calculation, potentially improving dose delivery accuracy and dose conformity. The fan-beam kVCT images from X1 machine have improved image quality compared to conventional CBCT imaging, thereby allowing artificial intelligence-based modern auto-segmentation algorithms to efficiently generate contours [18]. Whereas our previous study focused on potential advantages of kVCT images for auto-segmentation, this current study demonstrates the feasibility of using kVCT images for adaptive radiotherapy.

In this study, the same plan optimization template was applied to all ART plans of a given patient to improve the efficiency of ART planning. Large dosimetric variations occurred to some OARs in a few ART plans (Figure 4), reflecting the need for clinician review and revision of ART planning results and optimization parameters. At the same time, relatively small dosimetric variations were present in most cases when ART plans were adjusted according to the same plan optimization parameters, suggesting that original plan optimization parameters can be used to efficiently plan the beginning of ART (Figure 5). Our representative DVH plots implied that consistent DVH results could be achieved with the same plan optimization template in adaptive planning (Figure 6). However, if a treatment course only had a few treatment fractions, dosimetric variations in a single ART plan more significantly impacted the total dose delivered. As a result, each ART plan should be thoroughly reviewed to avoid significant dose variations. Of note, mean dose data was primarily evaluated in this study while in clinical treatment planning, a comprehensive set of dosimetric metrics were commonly used to establish plan quality for a given prescription scheme. However, other dosimetric metrics were not used in this study because: 1) different types of prescriptions for patients in this study resulted in heterogeneous DVH parameters in plan evaluation; and 2) while most dosimetric metrics are typically evaluated against the total dose in a treatment course, boost treatment plans were not included in this study.

Since daily pre-treatment kVCT imaging was performed with patients already in treatment positions on the X1 machine, daily kVCT images can be used to cost-effectively plan as extra CT simulation is not needed on a dedicated CT simulator. Furthermore, although kVCT imaging introduced extra radiation doses to the patient, the adaptive planning workflow as discussed in this study did not increase imaging dose to the patient because kVCT imaging is already an integral part of daily image-guided radiotherapy workflow. For kVCT scans to the pelvis, the volume CT dose index ($CTDI_{vol}$) was measured in the range of 16.3 to 49.0 mGy [22], which is in the same magnitude as cone-beam CT scans on C-arm linacs [23].

While we and other groups have verified X1-derived kVCT image quality and potential benefits of kVCT images in auto segmentation using machine learning algorithms [18] [22], the current X1 system still has several limitations that prevent it from being used clinically for online ART at this stage. Online ART workflows involve multiple steps including image acquisition, contouring, plan generation, plan quality assurance, and treatment delivery. While image acquisition only takes three to five minutes due to the fast fan-beam kVCT scans through the

X1 system, other steps require a longer period of time. Since the auto-segmentation system is a stand-alone system, multiple manual steps (ranging from 15 to 25 minutes) are necessary to transfer online imaging data to the auto-segmentation system for processing and to send contouring results to a TPS for review and manual contour corrections. Next, it may take over 20 minutes to optimize an adaptive treatment plan on the X1 TPS. An efficient method for quality assurance (QA) of ART treatment plans is also necessary to improve this workflow.

Several limitations exist for the current study. The number of patients is relatively small due to slow accrual of prostate cancer patients treated on the X1 machine. For the same reason, we included patients with heterogeneous prescriptions, making it difficult to use commonly reported dosimetric metrics. Target coverage and normal organ dose variations were observed in adaptive treatment plans with application of the same optimization templates, indicating the need for individualized plan optimization parameters. However, given lack of an efficient adaptive plan generation workflow, the proposed workflow used in the current study represents a compromise between planning efficiency and plan quality, and results from this study demonstrated the expected plan quality with this adaptive planning technique.

We demonstrated the feasibility of using X1 linac machine-based kVCT images to develop adaptive treatment plans for patients with prostate cancer. We found that kVCT images are currently best suited for online evaluation of anatomical changes and offline ART treatment planning for different disease sites. The development of efficient software solutions in ART plan optimization and efficient plan QA techniques including independent dose calculation systems will help researchers and clinicians fully realize the potential of the X1 machine hardware for online ART for a variety of disease sites. Ultimately, a combination of advanced imaging (such as through the X1 system), adaptive planning (using kVCT images and efficient ART planning algorithms), and real-time patient data analysis may lay the foundation for precise and adaptive RT treatments.

5. Conclusions

The kVCT images from the X1 machine showed adequate CT image quality for ART treatment planning. Significant anatomical variations existed in daily treatments of patients with prostate cancer. By using optimization parameters in the original treatment plan, we were able to find comparable target coverage and acceptable normal organ dose variations in ART treatment plans, indicating that patient-specific optimization templates could be used for efficient ART treatment planning.

Declarations

Statement on Ethics Approval and Consent

This study was conducted in accordance with the Declaration of Helsinki. This research project was carried out according to our institutions' guidelines and with

permission to access the patients' data and was approved by IRB 200039. Written informed consent was received from all patients.

Author Contributions

The authors contributed to the paper as follows: study design: CH, OO, and AM; data collection: CH; data analysis: CH, OO; manuscript preparation: CH; manuscript review: OO, AM, TW, and AL. All authors reviewed the results and approved the final version of the manuscript.

Funding Declaration

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Data Availability Statement

The data that support the findings of this study are not openly available and are available from the corresponding author upon reasonable request. Data are located in controlled access data storage at the corresponding author's institution.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

IMRT	intensity modulated radiotherapy
ART	adaptive radiotherapy
kVCT	kilovoltage computed tomography
PET	positron emission tomography
kVp	peak kilovoltage
UI	uniformity index
LCV	low contrast visibility
HU	Hounsfield unit
LDPE	low-density polyethylene
PTV	planning target volume
VMAT	volumetric modulated arc therapy
GTV	gross target volume
CTV	clinical target volume
MLC	multi-leaf collimator
CNN	convoluted neural network
CBCT	cone-beam computed tomography
MRI	magnetic resonance imaging
QA	quality assurance

Supplementary Tables

Table S1. Average HU and standard deviations for inhomogeneity inserts in the CT simulation image and kVCT images with each scanning protocol.

Scan mode	Relative density						
	0.0	0.83	0.92	1.03	1.18	1.42	2.16
Average HU $\pm$ standard deviation							
CT sim	-979.4 ± 6.5	-178.4 ± 5.7	-87.7 ± 6.0	-32.0 ± 6.0	123.7 ± 6.1	343.0 ± 7.4	924.3 ± 7.7
LS	-962.7 ± 9.7	-175.3 ± 10.1	-87.1 ± 8.9	-33.3 ± 9.2	122.9 ± 8.9	341.2 ± 10.8	920.8 ± 11.0
LM	-960.8 ± 9.4	-174.0 ± 10.1	-84.2 ± 9.8	-30.6 ± 11.2	124.7 ± 10.5	342.6 ± 10.9	922.6 ± 11.8
LF	-959.2 ± 10.5	-174.5 ± 9.6	-85.6 ± 10.0	-30.6 ± 9.8	124.7 ± 11.0	342.9 ± 11.8	923.8 ± 11.5
MS	-961.5 ± 7.8	-174.8 ± 7.9	-84.8 ± 7.9	-32.5 ± 7.3	123.5 ± 8.0	341.4 ± 9.8	921.7 ± 8.9
MM	-960.9 ± 8.0	-174.1 ± 8.3	-84.5 ± 7.9	-31.3 ± 8.4	124.1 ± 8.8	341.8 ± 10.1	922.6 ± 9.3
MF	-961.2 ± 8.6	-174.1 ± 9.4	-84.3 ± 9.0	-29.9 ± 8.6	123.9 ± 8.5	343.1 ± 10.0	923.1 ± 9.7
HS	-961.3 ± 6.0	-173.9 ± 5.8	-85.0 ± 6.3	-31.1 ± 6.8	123.1 ± 7.0	342.3 ± 7.9	922.9 ± 7.0
HM	-960.9 ± 6.2	-172.7 ± 6.1	-85.0 ± 5.9	-30.7 ± 6.6	123.7 ± 6.2	341.4 ± 8.3	922.9 ± 7.0

Table S2. Variation of mean dose to the target and normal organs for the CIRS thorax phantom with different X1 kVCT images relative to plan dose based on the CT simulation image.

Structure	Relative variation in mean dose
PTV	$100.28 \pm 0.03\%$ (100.2% - 100.3%)
Left lung	$100.22 \pm 0.00\%$ (100.2% - 100.2%)
Right lung	$100.30 \pm 0.06\%$ (100.2% - 100.3%)
Spine	$100.17 \pm 0.11\%$ (100.0% - 100.3%)

Table S3. Mean and standard deviations of the primary PTV coverage by the prescription dose ($V(R_x)$) and mean dose relative to those in the original treatment plans for the primary PTV, bladder, rectum, and penile bulb in the ART treatment plans.

Structure	Dosimetric parameter	Average $\pm$ standard deviation
Primary PTV	$V(R_x)$	$96.0\% \pm 1.7\%$
Primary PTV	Relative mean dose	$100.9\% \pm 2.7\%$
Bladder	Relative mean dose	$97.8\% \pm 9.2\%$
Rectum	Relative mean dose	$98.1\% \pm 9.2\%$
Penile bulb	Relative mean dose	$96.1\% \pm 24.7\%$