

Dose Tracking Accuracy of the Dose on the Treatment Day using Cone-beam Computed Tomography for Radiation Therapy of Prostate Cancer: Pilot Study

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Abstract

Background: The benefit of cone-beam computed tomography (CBCT) is not only for pretreatment setup verification, but also their potential in providing the three-dimensional anatomical information to present the organ deformation and daily actual dose distribution.

Objective: This study aimed to investigate the dose tracking on the treatment day for 5 volumetric modulated arc therapy (VMAT) prostate cancer patients using CBCT-based dose calculation.

Materials and methods: The CBCT HU to electron density calibration curve was firstly generated. Then, the accuracy of CBCT-based dose calculation (D_{CBCT}) was verified by comparing with dose measurements on CIRS pelvic phantom using IC (0.13cc) and Gafchromic EBT3 film. Velocity 3.2.0 deformable image registration (DIR) software was applied to map organ contours from planning CT (PCT) to the fractionated CBCT and modified by the radiation oncologist. Isodose distribution on CBCT images was calculated and variation of the organ volume as well as the dosimetric parameters following the QUANTEC-guideline for the planning target volume (PTV) and organ at risks were collected and analyzed.

Results: Point dose and dose distribution difference in phantom, between the measurements and D_{CBCT} , 2.28% and 87.7% (3%/3mm) gamma passing rate was presented. In clinical investigation, the volume ratio of CBCT/PCT for PTV, bladder and rectum were found to be 1.04, 1.11 and 0.91. D_{CBCT} was found to be deviated from D_{PCT} about -8.26% for $D_{95\%}$ of PTV, 1.12% and 9.12% for D_{mean} and V_{70Gy} of bladder, 6.60%, and 7.10%, for D_{mean} and V_{70Gy} of rectum, respectively.

Conclusion: Dose tracking on treatment day using CBCT-based dose calculation and DIR to guide organ contouring is found to be feasible and adequate to predict the actual dose delivery to the VMAT prostate cancer.

Keywords: CBCT, Dose tracking, Prostate cancer, VMAT

บทคัดย่อ

หลักการและเหตุผล: ระบบภาพนำวิถี cone-beam computed tomography (CBCT) ถูกนำมาใช้ตรวจสอบความถูกต้องของตำแหน่งการรักษา และข้อมูลกายวิภาคแบบสามมิติที่แสดงตำแหน่งและรูปร่างที่เปลี่ยนแปลงไปของอวัยวะยังนำมาใช้คำนวณหาปริมาณรังสีจริงที่ผู้ป่วยได้รับอย่างมีประสิทธิภาพ

วัตถุประสงค์: ศึกษาปริมาณรังสีในผู้ป่วยมะเร็งต่อมลูกหมาก 5 รายได้รับจากการฉายรังสีประจำวันด้วยเทคนิคปรับความเข้มเชิงปริมาตร (VMAT) ด้วยวิธีคำนวณปริมาณรังสีบนภาพ CBCT (D_{CBCT})

วัสดุและวิธีการ: สร้างกราฟความสัมพันธ์ระหว่างค่า HU ของภาพ CBCT กับความหนาแน่นอิเล็กตรอน ตรวจสอบความถูกต้องของ D_{CBCT} โดยเปรียบเทียบกับปริมาณรังสีในหุ่นจำลองเชิงกราน CIRS ด้วยหัววัดรังสี IC (0.13cc) และฟิล์ม Gafchromic EBT3 การศึกษาในผู้ป่วยใช้โปรแกรม Velocity รุ่น 3.2.0 สำหรับ deformable image registration (DIR) เพื่อส่งผ่านขอบเขตอวัยวะที่กำหนดในภาพวางแผนการรักษา (PCT) ไปยังภาพ CBCT และปรับแก้ไขโดยรังสีแพทย์ จากนั้นคำนวณหา D_{CBCT} พร้อมเก็บข้อมูลปริมาตรอวัยวะและพารามิเตอร์แสดงปริมาณรังสีของ PTV และอวัยวะข้างเคียงบนภาพ CBCT

ผลการศึกษา: การวัดปริมาณรังสีแบบจุดและกระจายตัวเทียบกับ D_{CBCT} ในหุ่นจำลอง พบความแตกต่าง 2.28% สำหรับการวัดปริมาณรังสีแบบจุด และ 87.7% ที่ผ่านการวิเคราะห์ด้วยแกมม่า 3%/3mm การศึกษาในผู้ป่วยอัตราส่วนระหว่าง CBCT/PCT สำหรับปริมาตร PTV กระจายปัสสาวะ และลำไส้ตรง คือ 1.04, 1.11 และ 0.91 ตามลำดับ ความแตกต่างของปริมาณรังสีที่ได้จาก D_{CBCT} กับ DPCT เท่ากับ -8.26% สำหรับ $D_{95\%}$ ใน PTV, 1.12% และ 9.12% สำหรับ D_{mean} และ V_{70Gy} ในกระจายปัสสาวะ 6.60% และ 7.10 % สำหรับ D_{mean} และ V_{70Gy} ในลำไส้ตรง ตามลำดับ

ข้อสรุป: การคำนวณปริมาณรังสีลงบนภาพ CBCT และการใช้โปรแกรม DIR ในการกำหนดขอบเขตอวัยวะ สามารถทำได้และมีประสิทธิภาพเพียงพอสำหรับใช้ประเมินปริมาณรังสีที่ผู้ป่วยมะเร็งต่อมลูกหมากได้รับประจำวันด้วยเทคนิค VMAT

Introduction

Currently, radiotherapy prostate cancer patients are mostly treated with the intensity modulated radiotherapy (IMRT), and volumetric modulated arc therapy (VMAT), from their main dosimetric advantage to create highly conformal dose distributions to the planning target volume (PTV) while minimizing the dose given to the organs at risk (OARs)^[1,2].

To enhance the treatment accuracy, the three-dimensional anatomical images obtained from treatment room cone beam computed tomography (CBCT) for image-guided radiation therapy (IGRT), has been introduced to reduce the daily patient positioning uncertainties-maintaining

interfraction set-up reproducibility^[3]. However, for prostate cancer, the problem of organ motion, changeable volume and shape of the prostate gland and nearby organs such as bladder and rectum are resulted in dosimetric change. Thus, the accuracy of daily dose to the PTV and OARs were questioned, and the attempts to determine the actual dose which the patient received in each treatment fraction was mentioned and reported^[4,5]. The CBCT image-guided system which is commonly used for patient positioning verification, also presented their advantage in providing the three-dimensional anatomical information on treatment position. The Hounsfield unit (HU) on CBCT was

found to be a meaningful method for recalculation dose distribution for the patient receiving radiation therapy on that treatment day^[6]. Organ delineation on CBCT can also be performed with reduced time consuming, via the contour deformation which is one of the applications in deformable image registration (DIR) software.

In this study, dose tracking on the treatment day for prostate cancer patients using CBCT-based dose calculation was investigated and reported.

Materials and Methods

VMAT treatment planning technique and acquisition of CBCT data set

Five prostate cancer patients treated with VMAT technique with total prescribed dose 78 Gy in 39 fractions (2 Gy per fraction) were retrospectively investigated. The planning CT (PCT) images for all patients were acquired using Philips Bigbore-16 slice CT simulator (Philips Healthcare, Cleveland, OH) with 3 mm slice thickness and full bladder protocol. The VMAT treatment planning was generated with the Eclipse treatment planning system version 13.6 (Varian Medical Systems, Palo Alto, CA) using 2.5 mm grid size and analytical anisotropic

algorithm. All VMAT treatment plans were evaluated following the QUANTEC guideline^[7]. For CBCT data set, the images were acquired with Truebeam STx accelerator equipped with on-board imaging (OBI) system (Varian Medical System, Palo Alto, CA). In this study, all patients underwent the treatment with CBCT acquisition on the first three days and then once a week using clinical pelvic exposure parameters: 125 kV, 1080 mAs and slice thickness 2.5 mm. For every patient, 10-12 CBCT images were used to recalculate the isodose distribution. The existing plans were transferred to the CBCT without any change of MUs. For organ volume (PTV, bladder volume and rectum volume) on CBCT, the Velocity AI™ version 3.2.0 DIR (Varian Medical Systems, Palo Alto, CA) was used to deform the contour of PTV-prostate bed including the seminal vesicles, and organ at risks-rectum and bladder from the PCT image to every fractionated CBCT image. The deformed contours were then reviewed and modified by radiation oncologist.

Accuracy verification of CBCT-based dose calculation

Using CBCT-based dose calculation to represent treatment dose, quality of

the CBCT image following the AAPM Task Group 179 guideline^[8] was assessed with the Catphan[®] 600 phantom (CatPhan[®], Phantom Laboratory, Salem, NY). A calibration of CBCT HU to electron density for inhomogeneity correction was also created using CIRS-062A CBCT electron density phantom (CIRS Tissue Simulation and Phantom Technology, Norfolk, VA, USA)

To verify the accuracy of dose calculation on CBCT, prostate VMAT treatment plan was created on CIRS pelvic phantom using PCT-based and CBCT-based dose calculation (**Figure 1**) for comparing with the measurement dose. The point dose at the treatment isocenter was measured using a CC13 ionization chamber (IBA Dosimetry, Schwarzenbruck, Germany)

and a Gafchromic EBT3 film (Ashland ISP Advanced Materials, NJ, USA) was placed at 0.3 cm above the isocenter (**Figure 2**) to measure dose distribution. Point dose difference and dose distribution gamma analysis (10% threshold) between CBCT-based dose calculation and measurement as well as the calculation on CBCT and PCT were determined and analyzed.

Variation of the organ volumes and dosimetric parameters evaluation

Dosimetric parameters presented on the treatment day from a total number of 55 CBCT images from 5 prostate cancer patients (10-12 images per patient) were collected. For each patient, dose differences between the PCT and CBCT were

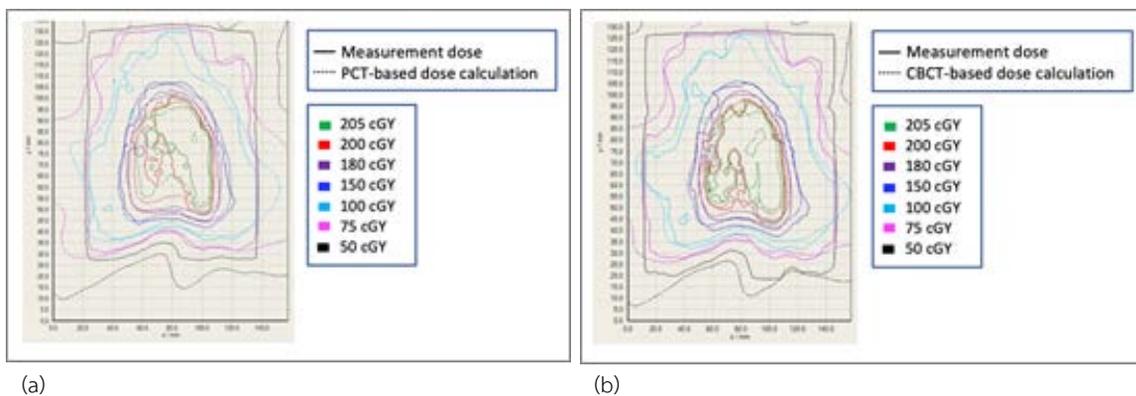


Figure 1. The isodose distribution of prostate VMAT plan on CIRS pelvic phantom, comparison between the measurements doses with (a) PCT-based dose calculation and (b) CBCT-dose calculation using the EclipseTM treatment planning system.



(a)

(b)

Figure 2. The position of (a) ionization chamber and (b) Gafchromic EBT3 film on the CIRS pelvic phantom for point dose and dose distribution measurement.

evaluated using dosimetric results from dose volume histogram (DVH); $D_{2\%}$, $D_{95\%}$ and $D_{98\%}$ for PTV; $D_{2\%}$, D_{mean} , V_{40Gy} , V_{65Gy} and V_{70Gy} for both bladder and rectum for the analysis. Moreover, the volume changes in PTV, bladder and rectum on each CBCT image during the treatment course were also compared to the PCT and the significance of the comparison results was evaluated using the independent t-test on Statistical Package for the Social Sciences (SPSS) version 18. (IBM SPSS Statistics)

Results

CBCT image quality

From quality assessment, the CBCT

image from TrueBeam STx OBI system presented the excellent and acceptable results as described in AAPM Task Group 179. The image uniformity and HU accuracy was within 1%, 5-line pair/cm, and 0.7 cm of low contrast resolution were detected for spatial accuracy at 1% contrast object.

Accuracy of CBCT-based dose calculation

To calculate the daily dose distribution accurately, a calibration of CBCT HU to electron density for inhomogeneity was generated as shown in **Figure 3**. Moreover, when the calculated point dose was compared with the measurements, percentage of dose difference at the

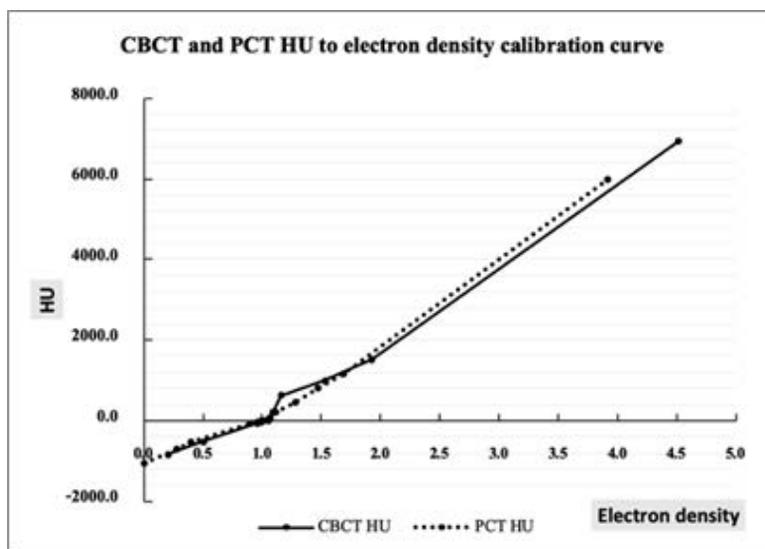


Figure 3. The generated CBCT HU and PCT HU to electron density calibration curve in this investigation.

treatment isocenter, 2.03% and 2.28% were seen for the PCT-based and CBCT-based dose calculation, respectively. The accuracy of dose distribution was evaluated, the percent gamma passing rate of CBCT and PCT were obtained at 87.69 and 91.23, respectively, for 3%/3mm gamma criteria and that both of them increased when the gamma criteria strength was lower as shown in **Table 1**. For the comparison between the CBCT and PCT isodose distribution, 99.9-100% passing rate in all gamma criteria was exhibited as also presented in Table 1.

Variation of the organ volumes

The variation of PTV and OARs

volumes in each patient, found on the daily CBCT images was shown in **Table 2**. For PTV, ratio of the volume averaged from 55 CBCT of all patients to the PCT was 1.04, 1.11 for bladder and 0.91 for rectum. Small variation of volume change for PTV was observed. This was in contrast with the bladder, as seen from **Figure 4**, CBCT/PCT volume ratio for bladder, especially in patient no.3 exhibited the higher variation of data, even the same full bladder protocol was controlled for the entire treatment. For rectum, the volume presented on CBCT were found to be smaller than PCT, and showed more consistent from fraction to fraction.

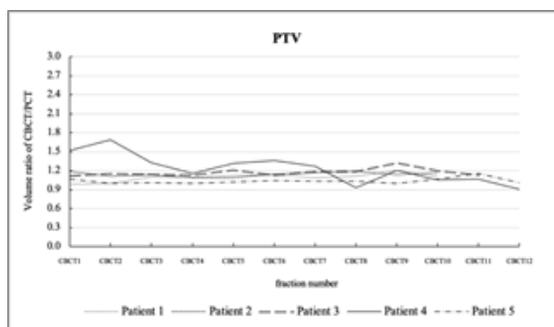
Table 1. Percentage of gamma passing rate at different gamma criteria for dose distribution calculated between CBCT (D_{CBCT}) and PCT (D_{PCT}) comparison with the measurement dose.

Gamma criteria	The percentage of gamma pass rate		
	D_{CBCT} vs $D_{Measurement}$	D_{PCT} vs $D_{Measurement}$	D_{CBCT} vs D_{PCT}
3%/3 mm	87.69	91.23	99.9
3%/4 mm	93.63	94.17	100
3%/5 mm	96.22	95.99	100
4%/3 mm	91.09	93.30	100
4%/4 mm	95.59	95.29	100
4%/5 mm	97.60	96.68	100
5%/3 mm	93.82	94.50	100
5%/4 mm	97.20	96.17	100
5%/5 mm	98.81	97.24	100

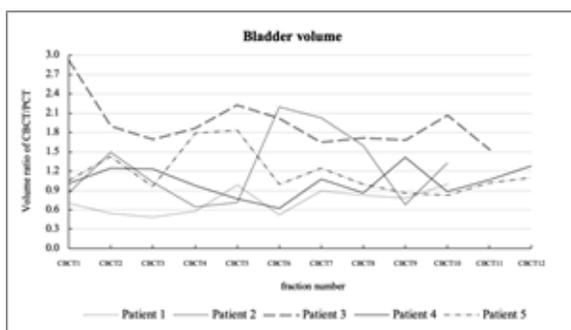
Table 2. The ratio and percentage difference of average PTV and OARs volume on CBCT/PCT.

Organ volume(cc)	PCT	CBCT	Ratio (CBCT/PCT)	%Difference	p-value*
PTV	130.62	136.37±58.84	1.04	4.40	0.750
Bladder	227.91	253.31±82.14	1.11	11.14	0.664
Rectum	52.23	47.55±15.87	0.91	-8.96	0.691

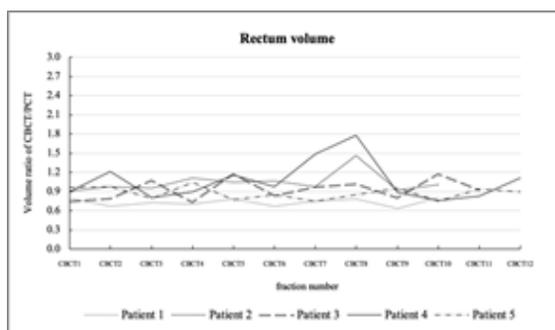
p-value <0.05 is significant difference



(a)



(b)



(c)

Figure 4. The volume ratio of CBCT/PCT for (a) PTV, (b) bladder and (c) rectum.

Dosimetric parameters evaluation

The results of percentage difference of dosimetric parameters between dose tracking on the treatment day using CBCT-based dose calculation and PCT in each patient was shown in **Table 3**. For PTV, all patients presented about 1% higher of $D_{2\%}$, 15% lower of $D_{95\%}$ and 24% lower of $D_{98\%}$. For bladder and rectum, the varied results of both the lower and higher of the D_{mean} , V_{40Gy} , V_{65Gy} and V_{70Gy} among the patients were presented. However, the average+SD of the dosimetric parameter change between

CBCT and PCT as summarized in **Table 4**, showed the significant lower of $D_{2\%}$, $D_{95\%}$, $D_{98\%}$ for PTV from D_{CBCT} , while no significant of dosimetric results was observed in bladder and rectum.

Discussion

There are several studies suggested that the application of CBCT is not only for patient positioning but also for the actual dose assessment for patient receiving dose in each treatment fraction. Yoo et al.^[6] and Tuntipumiamorn et al.^[9] demonstrated the potential of using the

Table 3.

Dosimetric parameter	Patient 1			Patient 2			Patient 3			Patient 4			Patient 5		
	PCT	DCBCT	%Diff	PCT	DCBCT	%Diff	PCT	DCBCT	%Diff	PCT	DCBCT	%Diff	PCT	DCBCT	%Diff
PTV															
D2% (Gy)	81.54	82.57±0.21	1.27%	81.63	82.88±0.44	1.53%	82.50	82.76±0.22	0.31%	80.89	81.85±0.31	1.07%	81.34	82.58±0.25	1.51%
D95% (Gy)	76.00	64.65±6.29	-14.94%	77.00	67.90±1.54	-11.82%	77.780	72.54±2.36	-6.74%	78.81	77.68±1.24	-1.43%	77.66	73.11±3.36	-5.85%
D98% (Gy)	74.67	58.44±8.24	-23.07%	75.56	63.58±2.48	-15.86%	77.010	68.50±4.00	-11.05%	78.67	76.47±2.49	-2.83%	76.36	65.89±6.41	-13.73%
Bladder															
D2% (Gy)	79.88	80.38±0.74	0.63%	80.02	81.49±0.87	1.84%	79.63	80.34±1.67	0.90%	78.14	77.17±1.72	-1.25%	80.25	81.04±0.37	0.98%
Dmean (Gy)	25.54	30.32±6.59	18.71%	54.68	57.29±6.59	4.78%	44.42	43.48±25.26	-2.12%	21.61	18.89±3.12	-12.59%	39.13	37.66±5.95	-3.77%
V40Gy (cc)	93.85	77.11±4.68	-17.83%	109.27	135.13±41.65	23.69%	78.07	105.98±5.22	35.76%	65.30	54.38±11.79	-16.72%	65.71	69.01±7.10	5.02%
V65Gy (cc)	62.13	51.22±3.51	-17.56%	46.91	58.19±4.05	24.05%	41.00	58.65±4.88	43.05%	29.72	24.49±9.43	-17.58%	35.07	41.17±6.60	17.40%
V70Gy (cc)	56.17	46.03±3.36	-18.05%	36.58	47.46±3.00	29.75%	27.99	40.26±4.77	43.85%	22.89	17.55±9.97	-23.55%	30.58	37.32±6.48	22.07%
Rectum															
D2% (Gy)	77.90	78.31±0.89	0.52%	78.06	77.97±2.82	-0.11%	79.03	78.77±2.50	-0.33%	78.65	79.15±0.98	0.64%	78.35	80.95±0.83	3.32%
Dmean (Gy)	32.28	35.54±2.51	10.07%	48.64	45.86±3.98	-5.71%	43.57	42.20±4.40	-3.14%	30.00	32.63±3.23	8.75%	32.77	43.35±4.68	32.27%
V40Gy (cc)	21.63	17.74±1.36	-17.98%	26.38	26.76±4.76	1.46%	35.38	37.76±17.00	6.73%	19.96	24.08±8.94	20.66%	14.53	18.12±2.66	24.73%
V65Gy (cc)	9.29	6.40±1.02	-31.16%	6.52	4.92±2.08	-23.36%	13.14	12.03±4.40	-8.46%	11.23	13.59±7.10	20.98%	5.41	10.42±1.63	92.75%
V70Gy (cc)	7.06	4.55±0.90	-35.51%	4.72	3.57±1.76	-24.26%	8.73	7.82±4.06	-10.42%	9.34	11.35±6.58	21.63%	3.93	8.92±1.50	127.05%

Note: %Diff mean the percentage difference between CBCT based-dose calculation and planning dose

Table 4. Average+SD of dosimetric parameter from 5 VMAT patients between planning dose (D_{PCT}) and CBCT-base dose calculation (D_{CBCT}).

Dosimetric parameter	DPCT	DCBCT	%Difference	p-value*
PTV				
$D_{2\%}$	82.58±0.59 Gy	82.51±0.44 Gy	-0.08%	0.023
$D_{95\%}$	77.59±1.01 Gy	71.18±5.03 Gy	-8.26%	0.045
$D_{98\%}$	76.45±1.52 Gy	66.37±6.97 Gy	-13.19%	0.030
Bladder				
$D_{2\%}$	79.58±0.84 Gy	80.08±1.70 Gy	0.63%	0.571
D_{mean}	37.08±13.60 Gy	37.54±14.36 Gy	1.24%	0.959
V_{40Gy}	82.44±18.99 cc	88.33±32.23 cc	7.14%	0.734
V_{65Gy}	42.97±12.49 cc	46.74±14.31 cc	8.77%	0.668
V_{70Gy}	33.76±13.56 cc	36.84±12.21 cc	9.12%	0.716
Rectum				
$D_{2\%}$	78.40±0.45 Gy	79.03±1.16 Gy	0.80%	0.291
D_{mean}	37.45±8.17 Gy	39.92±5.58 Gy	6.60%	0.593
V_{40Gy}	23.58±7.84 cc	24.89±8.17 cc	5.56%	0.801
V_{65Gy}	9.10±3.23 cc	9.47±3.69 cc	4.07%	0.869
V_{70Gy}	6.76±2.39 cc	7.24±3.19 cc	7.10%	0.792

* p-value <0.05 is significant difference

$$\% \text{ Dose difference} = (D_{CBCT} - D_{PCT}) / DPCT * 100$$

CBCT and its accuracy for dose calculation in clinical used. In this study, our results also showed the appropriate quality of CBCT image as suggested by AAPM Task Group 179 and with acceptable accuracy level for dose calculation.

There are two main approaches to calculate dose on the treatment day. Firstly, treatment dose was obtained by recalculating dose on CBCT images using the image registration application that warping PCT HU into the daily CBCT. Zhang et al.^[10] reported the accuracy of the dose calculation based on the deformed HU from PCT to CBCT performed on static phantom. With 2%, 2 mm criteria, average the gamma passing rate between CBCT-based dose and planning dose were 98.36%. In clinical, the accuracy of deformed CT HU into CBCT image might be influenced by patient's organs movement and resulted in the image registration accuracy. Another method is using the generated CBCT HU to electron density calibration curve for D_{CBCT} calculation. The study from Yeng et al.^[12] showed that the uncertainty less than 1% of dose difference between TPS calculation and point dose measurement was obtained when using directly generated CBCT HU to electron density for dose calculation.

Nevertheless, the accuracy of D_{CBCT} may be affected by the scatter dose from high density, the image artifact and distortion as well as the limited field size which is shown to be inferior when compared to the PCT.

Accuracy of CBCT-based dose calculation in this study agreed with the other reports^[11-13] that 2-3% of dose difference between CBCT-based and PCT-based calculation were presented. Furthermore, in this study the dose distribution was further investigated by comparing with dose measurements from film. More than 90% (4%/3mm) gamma passing rate was found which indicated the accuracy level obtained from dose calculation on CBCT.

Changes in the location and volume of the prostate and organ at risks during the course of radiation therapy result in the dosimetric consequence which may impact the tumor control and normal tissue complication. From our results, due to a small number of data, no statistically significant difference of volumetric and dosimetric parameters between the PCT and CBCT was detected. However, the tendency of the CBCT dose coverage at $D_{95\%}$ of PTV about 8% lower than the prescribed dose and lower near maximum

dose ($D_{2\%}$) from our investigation was similar to the study from Hüttenrauch et al.^[14] About the OARs, due to a change of volume and shape in bladder, especially for patient number 3, bladder dose was shown to be largely increased when compared with the PCT. Pearson et al.^[4], also found that about 25% of rectum volume moved to high dose region during the treatment fraction and the average percentage difference of $V_{70\text{Gy}}$ of bladder and rectum were increased more than 5%.^[4-5] In our study, 2/5 of the patients also presented higher results of $V_{65\text{Gy}}$ and $V_{70\text{Gy}}$ for rectum, especially in patient no.5 which the rectum position on the treatment day was moved to the high dose region as shown in **Figure 5**, and resulted in 93% higher of $V_{65\text{Gy}}$ and 127% higher of $V_{70\text{Gy}}$ for this patient. This information insisted the importance of

the online adaptive radiation therapy to compensate the lacking of dose in PTV and avoid high dose to the moveable organ along the treatment course.

Conclusion

Dose tracking on the treatment day using CBCT-based dose calculation and DIR to guide organ contouring is found to be feasible in clinical used. The dosimetric information from CBCT showed a potential for supporting the adaptive work procedure for prostate cancer patients. The present method also showed the excellent capability in evaluating the daily applied dose to bladder and rectum. It will be beneficial data for radiation oncologist to assess the treatment quality and maintain the optimal management for individual patient.

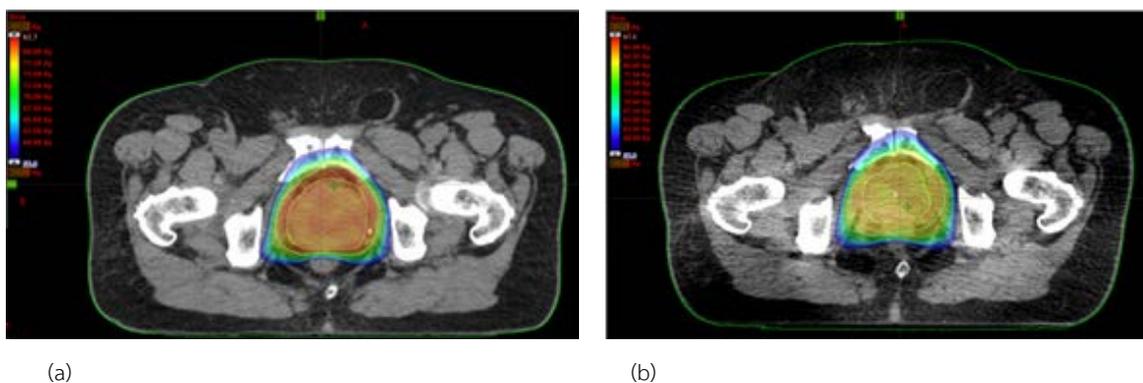


Figure 5. The dose distribution of VMAT prostate plan (a) PCT-based dose calculation and (b) CBCT-based dose calculation in patient no.5.

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