

Introduction: There is evidence that the prostate moves relatively independently of the bony pelvis, and requires more accurate localization techniques.¹ At University of California Davis (UC Davis) Radiation Oncology Department, ultrasound was replaced with kilovoltage (kV) Cone-Beam Computed Tomography (CBCT) in 2005 and Calypso system in 2009 for prostate localization. The kV CBCT coupled with Image-Guided Radiation Therapy (IGRT) is a relatively new technique, which provides volumetric imaging with high spatial resolution and sufficient soft tissue contrast.² The Calypso system, which uses implanted electromagnetic transponders and thus is free from extra dose to patients unlike CBCT, detects the slightest tumor movement and enables the patient to be repositioned if necessary. Several institutions previously reported daily setup variations in a cohort of Intensity-Modulated Radiation Therapy (IMRT)-treated prostate cancer patients using kV CBCT and Calypso system. However, there is no prior comparison study of prostate localization in the two systems, particularly with volumetric imaging data supporting the patient alignment method. The goal of this study is to assess the differences in daily setup offsets for prostate cancer patients by comparing kV CBCT and Calypso system. A phantom is added to validate the results.

Method and Materials: Twenty one patients having three electromagnetic transponders (median age: 68 years; median dose: 79.2 Gy; median fraction: 44) participated in this study. Patients were initially aligned to skin tattoos made at CT simulation, and appropriate shifts to isocenter were made. A kV CBCT scan was obtained prior to every treatment fraction. Following CBCT, the Calypso array panel was placed and offsets from coordinates of the three beacons relative to isocenter were recorded in translational directions (lateral, longitudinal and vertical). The three beacons and surrounding soft tissue structures (bladder and rectum) seen on the CBCT image were then automatically registered to those of the planning CT image. After CBCT image registration was performed, offsets in rotation were set to zero and those in translation were recorded for comparison with Calypso offsets.

Seven hundred and forty six CBCT images and Calypso data pairs were analyzed, with three orthogonal offsets (lateral, longitudinal and vertical) recorded from each system. A Kolmogorov-Smirnov (K-S) test was performed to determine whether the two datasets came from the same distribution using GraphPad Prism 5 (Version 5.04, GraphPad Software Inc, San Diego, CA). In addition, an unpaired t-test and an F-test were performed to determine if the means of the offset distributions were significantly different and to analyze differences in the variances of the distributions, respectively. The 746 CBCT and Calypso data pairs were also compared by subtracting Calypso offsets from CBCT offsets in each direction (right, inferior and posterior directions are positive) and the offset differences in each direction were grouped in 1mm increments and recorded. Then the PTV margins necessary to account for positional uncertainties of the target and internal organs and setup uncertainties were determined from the systematic error (Σ) and random error (σ) using the van Herk formula of $2*\Sigma + 0.7*\sigma$. The 3D shift vectors were determined from offsets in three directions for CBCT and Calypso system using a formula of $(X^2 + Y^2 + Z^2)^{1/2}$ where X, Y and Z are offsets in lateral, longitudinal and vertical directions, respectively and compared with different PTV margins.

A Calypso daily quality assurance (QA) phantom (size: 10 cm × 10 cm × 13 cm) (Calypso Medical Technologies, Inc., Seattle, WA) having three beacons was used for phantom study to determine differences in the CBCT and Calypso system without the influence of the patient. The same setup procedures were performed and localization offsets were determined by both systems for 10 fractions. Ten CBCT images and Calypso datasets were analyzed using the same analysis as for the patient data.

Results: Fig. 1 (a) and (b) display setup offset distributions relative to three beacons and soft tissue for the two systems. The mean setup offsets determined by CBCT were 0.57 ± 3.64 mm, 1.44 ± 3.95 mm and -0.37 ± 4.15 mm in the lateral, longitudinal and vertical directions, respectively; where positive localization offsets represented right, inferior and posterior couch shifts. Similarly, corresponding setup offsets in Calypso were -0.49 ± 3.33 mm, -1.81 ± 4.04 mm and -0.15 ± 4.28 mm. Table 1 contains the p values for the K-S-, t- and F-tests. The K-S test shows that the CBCT and Calypso data did not come from the same distribution ($p < 0.0001$) in all three directions. The mean and variance of the offset distributions were significantly different ($p < 0.05$) in the lateral directions while opposite results ($p > 0.05$) were observed in the vertical direction. In the longitudinal direction, the mean was significantly different whereas the variance was not significantly different.

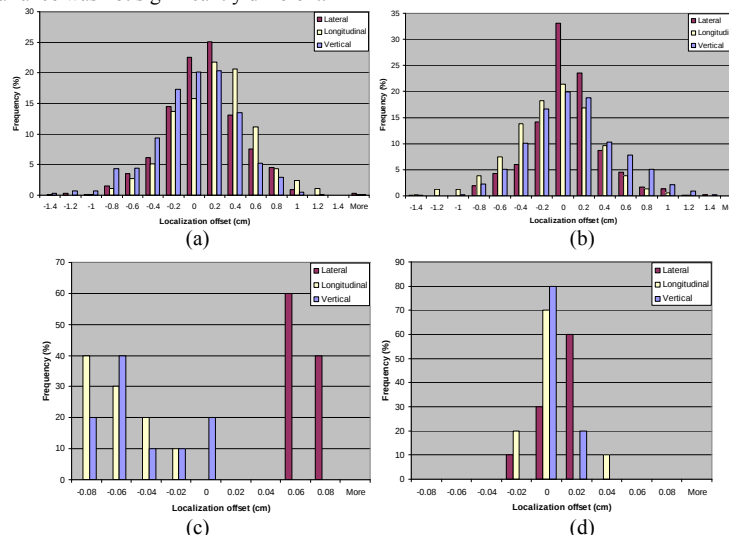


Fig. 1 Setup offset distribution in lateral, longitudinal and vertical directions in (a) CBCT and (b) Calypso for the 21 patients, and (c) CBCT and (d) Calypso for the QA phantom. Right, inferior and posterior directions are positive.

Table 1 Mean $\pm$ SD localization offsets and p values for the K-S-, t- and F-tests performed on CBCT and Calypso localization offset distributions for the patients and Calypso QA phantom. Right, inferior and posterior directions are positive.

Patients				
	# of data	Lateral (mm)	Longitudinal (mm)	Vertical (mm)
CBCT	746	0.57 ± 3.64	1.44 ± 3.95	-0.37 ± 4.15
Calypso	746	-0.49 ± 3.33	-1.81 ± 4.04	-0.15 ± 4.28
	Test	Lateral	Longitudinal	Vertical
P value	K-S	< 0.0001	< 0.0001	< 0.0001
	t-test	< 0.0001	< 0.0001	0.3240
	F-test	0.0153	0.5305	0.3870
Phantom				
	# of data	Lateral (mm)	Longitudinal (mm)	Vertical (mm)
CBCT	10	0.64 ± 0.08	-0.66 ± 0.25	-0.50 ± 0.30
Calypso	10	0.03 ± 0.13	-0.05 ± 0.17	0.00 ± 0.07
	Test	Lateral	Longitudinal	Vertical
P value	K-S	< 0.05	< 0.05	< 0.05
	t-test	< 0.0001	< 0.0001	< 0.0001
	F-test	0.2550	0.2759	0.0001

The results from the phantom study are shown in Fig. 1 (c), (d) and Table 1. The mean setup offsets determined by CBCT were 0.64 ± 0.08 mm, -0.66 ± 0.25 mm and -0.50 ± 0.30 mm in the lateral, longitudinal and vertical directions, respectively; whereas those in Calypso were 0.03 ± 0.13 mm, -0.05 ± 0.17 mm, 0.00 ± 0.07 mm. As with the patient data, the CBCT and Calypso data did not come from the same distribution ($p < 0.05$). The means of the offset distributions were found to be significantly different ($p < 0.05$) in all directions, whereas the variances were found significantly different ($p < 0.05$) only in the vertical direction.

For the patients, the offset differences between CBCT and Calypso system were between ± 5 mm for 60.72 %, 48.66 %, 53.08 % of total days in the lateral, longitudinal and vertical directions, respectively. For the Calypso QA phantom, the offset differences were between 0.4 and 0.8 mm, between -1.2 and 0.0 mm and between -0.8 and 0.4 mm for 100 % of total days in the lateral, longitudinal and vertical directions, respectively.

The setup offsets separated into systematic and random components for patients are shown in Table 2, with the calculated PTV margins for the two systems. Systematic and random errors were on the order of 2 to 3 mm. PTV margins calculated from the van Herk formula were 7.8 mm in the lateral and longitudinal directions and 8.4 mm vertically for CBCT, and for Calypso, 6.7 mm, 7.9 mm and 8.1 mm in the lateral, longitudinal and vertical directions, respectively. For CBCT, the number of days that the shift vector exceeded a 3-, 5-, 7-, 8- and 10-mm PTV margin was 667, 469, 278, 190 and 74, respectively; thus, 89.41, 62.87, 37.27, 25.47 and 9.92 % of total days where the CTV was outside the PTV were observed by imaging every day (Table 3). The corresponding number of days for Calypso was 612 (82.04 %), 459 (61.53 %), 289 (38.74 %), 214 (28.69 %) and 89 (11.93 %) (Table 3).

Table 2 Systematic error, random error and PTV margins determined by CBCT and Calypso for patients

		CBCT			Calypso		
	Direction (mm)	Lat	Long	Vert	Lat	Long	Vert
Error value	Systematic (Σ)	3.1	2.9	3.2	2.5	3.0	2.9
	Random (σ)	2.4	2.7	2.9	2.4	2.9	3.3
	PTV Margin ($2\Sigma + 0.7\sigma$)	7.8	7.8	8.4	6.7	7.9	8.1

Table 3 Number of days that 3D shift vector exceeds different PTV margins for CBCT and Calypso for patients

3D shift vector	# of days (%)	
	CBCT	Calypso
>3 mm	667 (89.41)	612 (82.04)
> 5mm	469 (62.87)	459 (61.53)
>7 mm	278 (37.27)	289 (38.74)
> 8 mm	190 (25.47)	214 (28.69)
> 10 mm	74 (9.92)	89 (11.93)

Conclusion: KV CBCT and Calypso system have been used in the UC Davis Department of Radiation Oncology for prostate localization since 2005 and 2009, respectively, and a comparison of localization offsets between the two systems was presented in this study. Both patient and phantom studies showed that localization offset distributions between the two systems were statistically significantly different from one another, but localization offset differences from the phantom study between the two systems were less than 1 mm (in absolute value) for 100 % of the total days in the lateral and vertical directions and for 90 % longitudinally. PTV margins (when considered in the absence of imaging) calculated from the CBCT data are up to 1.12 times larger than those determined by Calypso and the 3D shift vector larger than a uniform 7-mm PTV margin was observed for 37.27 % (CBCT) and 38.74 % (Calypso) of the total days. The two systems have their own advantages for clinical necessity and thus, they can be used conjunctively for accurate prostate localization.

References:

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- ² Xu F, Wang J, Bai S, *et al*. Detection of intrafractional tumor position error in radiotherapy utilizing cone beam computed tomography. *Radiother Oncol* 2008;89(3):311-319.