Organ Motion during Beam Delivery Detected by CyberKnife System in Stereotactic Body Radiation Therapy

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Abstract

Purpose: To evaluate organ motion detected by CyberKnife system during Stereotactic Body Radiation Therapy (SBRT) and to study the factors affecting errors during SBRT by the CyberKnife system

Materials and Methods: 31 patients (41 lesions, total 174 fractions) with lung, upper abdominal, lower abdominal or spine tumors were treated with CyberKnife system. Errors in all 6 directions were recorded in the system in graph form. Errors that exceeded the threshold limit of the system were recorded in our data collection form.

Results: Spine and rectum patients had median maximum delta error of 1.5-2.5 mm and median maximum error in all 3 rotational directions of 1-2 degree. Lung, liver, prostate and cervix patients had median maximum delta error of 3.0-3.8 mm and median maximum error in some rotational directions in excess of 5 degree except in cervix patients.

Conclusion: The spinal and rectal patients had lower magnitude of error than the lung, liver, prostate and cervix patients. The data of median of maximum movement in each axis of each organ group might be beneficial in determining the safety margin for organ motion in treating cancer of that organ group.

Keyword: Stereotactic body radiation therapy, CyberKnife, Organ motion

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Introduction

Movement of tumors and the normal organs during beam delivery of the extracranial lesion can cause a significant degree of uncertainty in target delineation and treatment delivery. As a result, a markedly larger margin may be needed to cover for organ movement, which in turn causes a greater volume of normal tissue to be exposed to radiation and an increased risk of treatment-related toxicity. CyberKnife is an image-guided stereotactic body radiation therapy system that can detect and correct errors due to organ motion by using tracking system [1]. However, its availability in Thailand is still limited. Data regarding tumor movement during radiation treatment, unlike the interfraction motion, were difficult to obtain from the other radiotherapy system and might be useful information when determining the proper treatment margin. The objective of this study was to study the tumor movement during CyberKnife treatment in patients with extracranial lesions.

Materials and Methods

The present study was approved by ethic clearance committee of human rights related to research involving human subjects, Mahidol University; protocol number ID 11-53-15.

Patient Group

All patients with extracranial tumor treated with CyberKnife system at Ramathibodi hospital during November 2010 to December 2011 were included in our study. The general criteria of patients included life expectancy should be more than 6 months, Karnofsky performance status (KPS) more than 70, and age of more than 18 years.

Treatment procedure

Image Guidance System

The image guidance system is a correlation between the position of tumor from CT planning and the position in the treatment room. The in-room image guidance system consists of two kilovoltage X-ray tubes attached to the ceiling of the treatment room and a pair of orthogonally positioned flat-panel images on the floor. Before the treatment started, the patients would be positioned coarsely on the treatment couch. The fine alignment would be conducted by the image-guidance system and the remotely controlled treatment couch, which could correct residual positional errors in 6 directions (3 translation errors, i.e. AP, SI and LR directions and 3 rotational errors, i.e. roll, pitch and yaw) (Figure 1). During treatment, the robot-modulated linear accelerator would give hundreds of small beam from around 69-140 robotic positions, each position with 6 degree of freedom of beam directions since the robot had 6 joints. Before each beam delivery, images would be taken and compared with the planned position. If there were tumor motions, the robot would automatically adjust the position in 6 directions before beam delivery. The positional errors recorded during treatment were used in this study. CyberKnife uses tracking systems based on tumor location. For spinal tumor, it uses the X-sight spine tracking system [(2)]. For soft tissue tumors, internal fiducial marker placement is needed. For pelvic tumor, it tracks internal fiducial marker only. For lung and upper abdominal tumor, it uses Synchrony tracking system [(3)]. Briefly, this system collects data obtained from external marker placed on chest wall or upper abdomen and from internal fiducial marker to predict and correct organ motion during the treatment.

Patient preparation

One to five gold fiducials were placed percutaneously direct into the tumor under fluoroscopic or CT guidance for lung and upper abdominal cases or transrectal ultrasound guidance for prostate cases. If only 1 fiducial could be track, the system could track only translational error. At least 3 fiducials with the minimum distance of 2 cm and angle of 20 degree from each others were needed to track both translational and rotational errors. At least 1 week after fiducial placement, a custom-made vacuum bag in supine

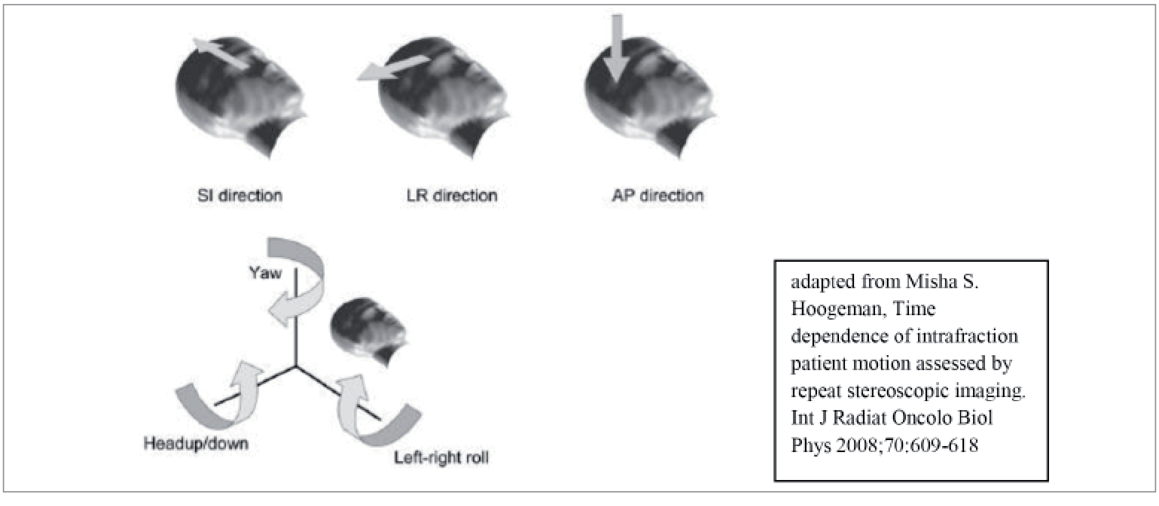

Fig. 1. Definition of the applied coordinated system. The arrows give the direction of a positive change in the patient position or orientation. AP=anterior; LR=left=right; SI=superior-inferior

position of each patient was done for immobilization. Patient then underwent 1.5-mm thickness Computed Tomography (CT) scan for treatment planning. For patients with spinal tumors and some cases of prostate cancer, MRI was also performed for planning. Prostate cancer patients were managed to have partially filled bladder when they underwent CT scan to match with the images from MRI, and also before each treatment fraction. Laxatives were given the night before CT scan and each treatment fraction. Most patients received the treatment in 3-5 fractions. For each fraction, the radiation dose was delivered in multiple small-dose beams according to the individual's plan, ranging from 138 to 367 beams (median of 262 beams).

Data collection

Translational motion was calculated from the distance between centers of the triangle created by three fiducials' positions. The rotation motion was calculated from the difference between planes of the triangle created by three fiducials' positions. For spine cases, the mean movement for all multivoxels was reported. The translation error was recorded into a graph of delta, which is 3D vector motion calculating from the below formula

$$d = \sqrt{dSI^2 + dLR^2 + dAP^2};$$

For rotational errors, the system would record the movement into graph separately for roll, pitch and yaw directions (Fig 2). Data from these graphs were reported. Recorded errors during treatment were automatically adjusted by the robot unless the errors exceeded the threshold limit, when manual adjustment was needed. The thresholds that the system needed manual adjustment of the patient's position were as follows: translation >10 mm in non-synchrony mode and >25 mm in synchrony mode, rotation >1o in roll and pitch, and rotation >3o in yaw. If at least one of these thresholds was reached, the system would stop until the acceptable position from each adjustment was achieved. The positions of the tumor from the image that needed manual adjustment were recorded in our data collection form.

Statistical data analysis

The data of organ motions were calculated separately for each uninterrupted time period. The maximum movement in each axis from all uninterrupted time periods was taken separately. The median of maximum movement in each axis from each group of organ and location of tumor was reported. The data of error were later stratified by 3 groups of organ; lung and liver group, pelvis group and spine group. The pelvis group consisted of patients with tumor of cervix, rectum and prostate.

Results

Thirty-one patients (41 lesions, total 174 fractions) with lung, upper abdominal, lower abdominal or spinal tumors were included in this study. One patient received the CyberKnife treatment for 2 times. Patient and tumor characteristics categorized by organ and location of tumor were summarized in Table 1. All patients could be tracked for translational error. Fifteen patients (21 tumors) could have rotation tracking and correction. The other 16 patients (20 tumors) had problems including; less than 3 fiducial markers were implanted (5 tumors from both upper and lower lungs), less than 3 fiducial markers could be tracked (5 tumors from lower lung, liver and rectum), or the tumor's rotations were so large that the system couldn't start the treatment unless we shut off the rotation tracking threshold (9 tumors). In the former mentioned 15 patients, there were only 3 patients (2 thoracic spine tumors and 1 rectum tumor) whose rotations were so small that the system didn't need manual adjustment at all.

The magnitude of tumor's motion in both translation and rotation stratified by organ and tumor location is shown in Table 2. The largest median-maximum translational magnitude of 3.8 mm in Delta was detected in lower lung cancer patients while the Delta's magnitude in upper lung, prostate and liver cancer patients was 3.5 mm. The largest median-maximum rotational magnitudes in roll and yaw directions were both also detected in lower lung cancer patients, which were greater than 5 and 4 degrees, respectively. The largest rotational magnitude of greater than 5 degrees in pitch direction was detected in prostate patients. The median total treatment time per fraction (TTT) and number of fraction were 110 minutes (60-305 minutes) and 5 fractions (1-7 fractions), respectively. The median TTT was longest in liver cancer patients, 155 minutes. There were 6 fractions that actual TTT could not be recorded due to machine breakdown during treatment.

Error exceeding threshold of the system in the 13 patients who had rotation tracking and correction is detailed in Table 3. The median and range of maximum

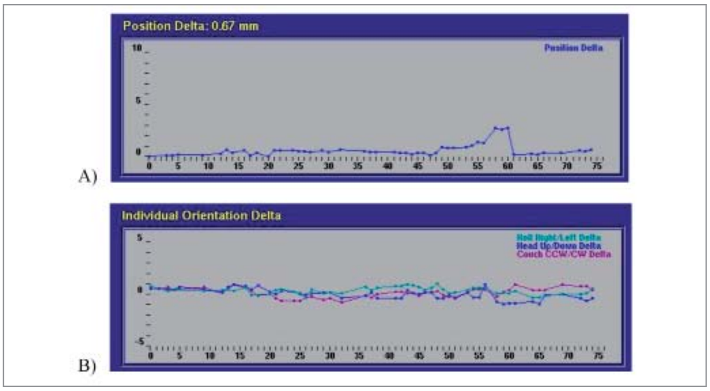

Fig.2. the graph of delta (A) and rotational errors in 3 directions (B) after finishing CyberKnife treatment fraction

motion in 3D vector translation and 3 rotation directions were also stratified by 3 groups of organ. Lung and liver group had median maximum 3D vector motion of 4 mm (2.5-5.0 mm) and the largest median maximum rotation of greater than 5 degree (4.5-greater than 5 degree) in roll direction. However, small number of fractions that could be tracked for rotation in this group (5 from 25 fractions) should be considered. Pelvis group had median maximum 3D vector motion of 3 mm (1-10 mm) and the largest median maximum rotation of 4.5 degree (1-greater than 5 degree) in pitch direction, which could be explained by the change of bladder and/or rectum volume during treatment. Numbers of fractions that had maximum error greater than 5 degrees in pelvis group for roll, pitch and yawn directions were 4, 22 and 1 fractions, respectively. Spine group had median maximum 3D vector motion of 2.5 mm (1.0-5.5 mm) and median maximum rotation of 1 degree in all 3 directions. Only in yaw direction that had maximum-maximum motion of 3 degree. In 13 patients (19 tumors, 87 fractions) that had treatment interruptions and manual adjustment showed numbers of interruptions as following; 705 times in roll direction, 228 times in pitch directions and 3 times in yaw direction (see Table 3). The interruptions due to roll rotational threshold limit were most frequently seen in lumbo-sacral spine patients. The interruptions due to pitch rotational threshold limit were most frequently seen in prostate and cervix patients; 88 and 66 times, respectively. This finding could be explained by the change of bladder and rectum volume during treatment which affected on the position of cervix and prostate, as previously seen in the study of Ahmad et al[4]. After the treatment went on for some period of time, the tumor's rotations of prostate and cervix patients would eventually be so large that the system couldn't continue the treatment unless we shut off the rotation threshold. No translational threshold was reached, so all interruptions were due to rotational threshold. There was no correlation between the magnitude of rotational errors and the duration of each treatment fraction (not shown in graph). Majority of roll and pitch errors that exceeded the threshold limit was within 1-2 degrees range, only 24/705 times (3.4%) in roll direction and 23/228 times (10%) in pitch direction that the errors were more than 2 degrees.

Discussion

There are many previous studies about organ motion during beam delivery. Shitaro et al [5] evaluated real-time tumor-tracking system for gated therapy, and found that the system significantly improved the accuracy of targets in motion. In 4 patients with lung cancer, the range of tumor marker movement during irradiation reduced from 9.6-38.4 mm without gating to 2.5-5.3 mm with the use of the tumor tracking radiotherapy. Shimizu et al [6] reported that real time tumor tracking could reduce uncertainty due to setup error and internal organ motion in prostate cancer treatment from 6.9 mm to 1.6 mm. Balter et al [7] stated that motions of the prostate in the anterior-posterior(AP) and superior-inferior(SI) directions were significantly larger than in the left-right(LR) direction. Although significant prostate displacement could occur between treatments, the typical range of movement seen along a major axis was less than 5 mm.

The strong point of this study was the evaluation of intrafraction error, which was the error detected during beam delivery, unlike the other studies of

Table 1. Patient and tumor characteristics categorized by organ and location of tumor

Organ	Location	No. of pt	No. of tumor	age (y)		sex (n)		KPS		GTV (ml)		no. of Fx (fraction)		TTT (min)	
				median	range	male	female	90-100	70-80	median	range	median	range	median	range
spine	cervical	2	3	23	21-25	2	0	2	0	1.5	0.6-2.7	5	5	90	75-135
	thoracic	6	7	57	21-69	2	4	5	1	8.6	0.3-21	5	5	115	60-420
	lumbarsacral	6	8	58	21-76	3	3	2	4	4.5	0.6-120	5	2-5	120	55-211
rectum		2	2	40	37-43	1	1	2	0	149	139-159	5.5	5-6	70	60-105
prostate		10	10	71.5	53-82	10	0	10	0	41	16-55	5	3-7	110	60-305
cervix		1	1	41	41	0	1	1	0	19	19	5	5	126	85-127
lung	upper	1	3	77	77	0	1	1	0	7.8	5.8-14	1	1	105	85-115
	lower	3	4	77	34-81	1	0	2	1	12.2	3.4-223	3	2-5	125	85-170
liver		3	3	76	72-79	0	3	0	3	215.4	75-344	3	2-4	155	95-245

**According to the study of Maxim et al (22), a transverse plane bisecting the carina was used to separate the upper from lower thorax for lung cancer cases.*
***no.=number, pt=patient, KPS = Kanofsky Performance Status, GTV=gross target volume, Fx=fraction, TTT=total treatment time per fraction*

Table 2. Magnitude of tumor translation and rotation

Organ	Location	no. of pt	no. of tumor	no. of Fx	maximum delta (mm)		maximum rotation (degree)									Reason
							roll			pitch			yaw			
					median	range	median	range	interrup	median	range	interrup	median	range	interrup	
spine	cervical	2	3	15	2	1-3	1.4	1.1-2.2	116	1.3	1.1-1.8	14	2	1.0-3.3	3	
	thoracic	6	7	35	2.5	1-6	1.4	1.0-2.7	146	1	1-2.9	36	1	1-3	none	too small
	LS	6	8	35	2.5	1-4	1.7	1.0-5.7	395	1	1-3	12	1	1.0-2.5	none	too small
rectum		2	2	11	1.5	1.0-2.5	1	1-1	none	1	1-1	none	1	1-2	none	too small
prostate		10	10	48	3.5	2-10	2.3	1-5+	23	5+	1-5+	88	2	1-5+	none	too large
cervix		1	1	5	3	2.5-3.5	2	2.0-2.5	18	3.5	3-5	66	2.5	1-3	none	too large
lung	upper	1	3	3	3.5	3.5-4.5	u	u	u	u	u	u	u	u	u	track < 3
	lower	3	4	13	3.8	2.5-5.0	5+	4.5-5+	none	3	2.5-5.0	none	4	2.0-4.5	none	too large
liver		3	3	9	3.5	3-5	u	u	u	u	u	u	u	u	u	track < 3

u = unable to track rotation (see reason in the right-most column), 5+ = value greater than 5, pt=patient, Fx=fraction, no.=number,
interrup = interruption during treatment because error exceeded threshold
too small = rotations were so small that the system didn't need manual adjustment at all.
too large = rotations were so large that the system couldn't start or continue the treatment unless we shut off the rotation tracking threshold
track < 3 = less than 3 fiducial markers could be tracked by the system

intrafraction error, which usually evaluated the difference between the CBCT taken prior to and after treatment (see below). The limitation of this study was small number of patients and fractions.

For lung cancer, there are studies of Franks [8], Guckenberger [9], and Olivier et al [10] using cone-beam computed tomography (CBCT) to evaluate intrafraction tumor motion while treating with SBRT. The data of these 3 studies and ours are shown in Table 4. The first one determined the intrafraction error by the displacement of target between maximum exhale phase and maximum inhale phase. The other two used the CBCT prior to and after treatment to determine the intrafraction error. Our study used tumor tracking method with Synchrony system. The mean/median TTT was much greater in our study because of the different machine; we used CyberKnife system while others used Linear-accelerator with multi-leaf collimator (MLC) for beam delivery. Our result reported in median of maximum motion from each fraction was greater than the mean vector of other studies. The maximum motion of our study was less than other studies (5 mm vs 7.2 mm). The mean and SD of vector motion from Olivier et al study [10] were smaller than our study and the other two studies, most likely due to the use of abdominal compression device in all cases. Limitation in our study was small number of tumors (7 tumors) and fractions (total 16 fractions). Our study could not track the rotational error in all 7 lung tumors; 5 tumors had less than 3 fiducial markers implanted, 1 tumor had less than 3 fiducial markers tracked, and the other one had so large rotation that the system couldn't start the treatment unless we shut of the rotation tracking.

For liver cancer, Case et al. [11] reported the mean absolute intrafaction change in vector position for 3 mm and P90 of 5.4 mm in 29 patients using CBCT prior-to and after treatment. About half of the CBCT in this study was obtained from patient with abdominal compression. Our study reported median of each fraction maximum vector translation of 3.5 mm (range 3-5 mm). All 3 liver tumors could not be tracked for rotation because only 2 fiducials were detected by the system.

For prostate cancer, Kitamura et al.[12] described prostate motion as determined by fluoroscopic detection of internal prostatic fiducial marker. In 10 patients, the amplitude of 3D motion range between 0.1 to 2.7 mm in the supine position and 0.4 to 2.4 mm in the prone position, each position was tracked for 2 minutes. Wouldoughby et al.[13] found that using the 8 minute tracking session with Calypso system, average 3D difference of 1.5 mm (SD=0.9 mm) was reported. Two of the 11 patients showed displacement of greater than 1 cm in AP direction. Hsi et al.[14] evaluated 1,237 fractions of treatment for 48 prostate cancer patients, the largest average shifts from treatment isocenter was 5.6 mm (+/- 4 mm) in AP direction. The average treatment time was 12.8 minutes (+/- 3.2 min). The results of those studies showed that the largest motion was in AP direction. The median of maximal vector motion of our study was 3.5 mm (range 2-10 mm) and highest magnitude of maximum rotation error in pitch direction. Our study had greater median total treatment time of 110 minutes, which caused greater effect of bladder and rectum filling, resulting in highest magnitude of error in pitch direction.

For spine cancer in our study, the maximum rotational errors in pitch and yaw direction were the largest in cervical spine tumor. The roll rotational error was highest in LS level. This finding could be explained by the nature of cervical spine that tends to have motion easier than the thoracic and lumbro-sacral spine. Lijun et al [15] also found that cervical spine targets exhibited the highest incidence of nonrandom target motion along all 6 directions. In our study, the cervical spine patients were a lot younger than thoracic and lumbosacral spine patients. Younger age might be a factor that associated with small 3D translational errors in our cervical spine patients.

Conclusion

This study reported median of maximum movement in each axis. The spinal and rectal patients had median maximum delta and rotational error of 1.5-2.5 mm and 1-2 degrees, respectively. The lung, liver, prostate and cervical patients had median maximum delta and rotational error of 2.5-3.8 mm and 2 to greater than 5 degrees, respectively. The data of median of maximum movement in each axis of each organ group might be benefit in determining the safety margin for organ motion in treating cancer of that organ group. Further study for margin calculation was needed, which must be cautious about the difference in image-guidance system and beam delivery between different treatment systems. Rotational threshold limit of CyberKnife system may be too sensitive, leading to a lot of interruptions and also much longer total treatment time in each fraction.

Table 3: Error exceeding threshold of the system in the 13 patients who had rotation tracking and correction

Pt. No.	Organ	Location	no. of tumor	no. of Fx	maximum rotation (degree)								
					Roll			pitch			yaw		
					median	range	interrup	median	range	interrup	median	range	interrup
1	cervix		1	5	1.6	1.2-1.7	18	2.4	1.6-3.4	66			
2	prostate		1	4	1.5	1.4-1.9	13	2.7	2.2-3.8	38			
3	spine	thoracic	1	5	1.7	1.6-2.2	38	1.1	1.1-1.1	1			
3	spine	thoracic	2	5	1.4	1.3-1.4	18						
4	spine	lumbar	1	5	2.1	1.8-5.7	114	1.2	1.1-1.2	6			
4	spine	lumbar	2	5	2	1.7-2.6	75	1.1	1.1-1.1	1			
4	spine	lumbar	3	5	1.9	1.6-2.7	67	1.3	1.3-1.3	2			
5	spine	cervical	1	5	1.3	1.1-2.2	21	1.4	1.3-1.8	4			
5	spine	thoracic	2	5	1.3	1.2-1.4	9						
5	spine	lumbar	3	5	1.6	1.3-1.8	39						
6	spine	thoracic	1	5	2.4	1.9-2.6	39	1.5	1.5-1.5	3			
7	spine	lumbar	1	5	1.2	1.1-1.8	14	1.2	1.1-1.2	3			
8	prostate		1	3	1.6	1.2-1.7	10	2.2	1.9-2.4	50			
9	spine	sacrum	1	3	2.3	1.9-2.6	29						
10	spine	cervical	1	5	1.6	1.2-2.0	53	1.2	1.1-1.7	9			
10	spine	cervical	2	5	1.4	1.2-1.8	42	1.2	1.2-1.2	1	3.2	3.1-3.3	3
11	spine	lumbar	1	5	1.6	1.2-1.7	44						
12	spine	lumbar	1	2	1.6	1.5-1.6	13						
13	spine	thoracic	1	5	2	1.5-2.7	49	1.4	1.3-2.9	44			
13	spine	lumbar	2	5									
	sum		20	92			705			228		3	

pt=patient, Fx=fraction, no.=number, interrup=interruption during treatment because error exceeded threshold
Blank=threshold was not reach. No translational threshold was reached.

Table 4. Comparion of intrafraction motion in lung cancer treating with SBRT

Study	no. of tumor	With AC	vector(mm)			TTT(min)	
			mean	SD	max	mean	SD
Franks et al.	10	0	3.3	2.5		35	
Guckenberger et al.	27	17	2.8	1.6	7.2	21	5
Olivier et al.	8	8	1.5	0.9		22	9
			med-max	range	Median	range	
our study	7	0	4	2.5-5.0	123	85-170	

AC=abdominal compression

Reference

1. Adler JR, Murphy MJ, Chang SD, Hancock SL. Image-guided robotic radiosurgery. *Neurosurgery* 1999;44:1299-1306.
2. Ho AK, Fu D, Cotrutz C, Hancock SL, Chang SD, Gibbs SD, et al. A study of the accuracy of CyberKnife spinal radiosurgery using skeletal structure tracking. *Neurosurgery* 2007;60:147-156
3. Ozhasoglu C, Saw CB, Chen H, Burton S, Komanduri K, Yue NJ, et al. Synchrony – CyberKnife respiratory compensation technology. *Med Dosim*.2008 summer;33:117-123
4. Ahmad R, Hoogeman MS, Bonda M, Dhawtal V, Quint S, Pree ID. Increasing treatment accuracy for cervical cancer patients using correlations between bladder-Filling change and cervix-uterus displacement: Proof of principle. *Radio Onco* 2011;98:340-346
5. Shirato H, Shimizu S, Kunieda T, Kitamura K, Herk MV, Kagei K, et al. Physical aspects of a real-time tumor-tracking system for gated radiotherapy. *Int J Radiat Oncol Biol Phys* 2000;48:1187-1195.
6. Shimizu S, Shirato H, Kitamura K, Shinohara N, Harabayashi T, Tsukamoto T, et al. Use of an implanted marker and real-time tracking of the marker for the positioning of prostate and bladder cancers. *Int J Radiat Oncol Biol Phys* 2000;48:1591-1597.
7. Balter JM, Sandler HM, Lam K, Bree RL, Lichter AS, Haken RKT. Measurement of prostate movement over the course of routine radiotherapy using implanted markers. *Int J Radiat Oncol Biol Phy* 1995;31:113-118.
8. Franks KN, Purdie TG, Bezjak A, Moseley D, Pearson S, Jaffray DA, et al. Quantifying Inter and Intra-Fraction Tumor Motion using Respiration-Correlated Cone Beam CT Lung Stereotactic Body Radiotherapy (SBRT). *Int J Radiat Oncol Biol Phys* 2007;69:S489-490
9. Guckenberger M, Meyer J, Wilbert J, Richter A, Baier K, Mueller G, et al. Intra-fractional uncertainties in cone-beam CT based image-guided radiotherapy (IGRT) of pulmonary tumors. *Radio Onco* 2007;83:57-64
10. Olivier K, Chung H, Jin H, Yang H, Kim S. Intra-Fraction Patient Displacement During Image-Guided Stereotactic Body Radiation Therapy (IGSBRT) for Lung Treatment. *Int J Radiat Oncol Biol Phys* 2006;66:S489
11. Case RB, Sonke JJ, Moseley DJ, Kim J, Brock KK, and Laura D. Inter- and Intrafraction Varibility in Liver Position in Non–Breath-Hold Stereotactic Body Radiotherapy. *Int J Radiat Oncol Biol Phys* 2009;75:302-308
12. Kitamura K, Shirato H, Seppenwoolde Y, Onimaru R, Oda M, Fujita K, et al. Three-Dimensional Intrafractional Movement of Prostate Measured during Real-Time Tumor-Tracking Radiotherapy In Supine and Prone Treatment Positions. *Int J Radiat Oncol Biol Phys* 2009;53:1117-1123
13. Willoughby TR, Kupelian PA, Pouliot J, Shinohara K, Aubin M, Roach M, et al. Target Localization and Real-Time Tracking Using the Calypso 4D Localization System in Patients with Localized Prostate Cancer. *Int J Radiat Oncol Biol Phys* 2006;65:528-534
14. Hsi RA, Vali F, Parsai H, Garver E, MadsenB, Pham1 H, et al. Evaluation of Interfraction and Intrafraction Prostate Motion during the Treatment of Prostate Cancer using the Calypso 4D Localization System. *Int J Radiat Oncol Biol Phys* 2008;72:S300
15. Lijun MA, Sahgal A, Hossain S, Chuang C, Descovich M, Haung K, et al. Nonrandom intrafraction target motions and general strategy for correction of spine stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2009;4:1261-1265.