Original Article PROGRESS in MEDICAL PHYSICS Vol. 26, No. 3, September, 2015
http://dx.doi.org/10.14316/pmp.2015.26.3.127

Dosimetric Evaluation of Amplitude-based Respiratory Gating for Delivery of Volumetric Modulated Arc Therapy

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The purpose of this study is to perform a dosimetric evaluation of amplitude-based respiratory gating for the delivery of volumetric modulated arc therapy (VMAT). We selected two types of breathing patterns, subjectively among patients with respiratory-gated treatment log files. For patients that showed consistent breathing patterns (CBP) relative to the 4D CT respiration patterns, the variability of the breath-holding position during treatment was observed within the thresholds. However, patients with inconsistent breathing patterns (IBP) show differences relative to those with CBP. The relative isodose distribution was evaluated using an EBT3 film by comparing gated delivery to static delivery, and an absolute dose measurement was performed with a 0.6 cm^3 Farmer-type ion chamber. The passing rate percentages under the 3%/3 mm gamma analysis for Patients 1, 2 and 3 were respectively 93.18%, 91.16%, and 95.46% for CBP, and 66.77%, 48.79%, and 40.36% for IBP. Under the more stringent criteria of 2%/2 mm, passing rates for Patients 1, 2 and 3 were respectively 73.05%, 67.14%, and 86.85% for CBP, and 46.53%, 32.73%, and 36.51% for IBP. The ion chamber measurements were within 3.5%, on average, of those calculated by the TPS and within 2.0%, on average, when compared to the static-point dose measurements for all cases of CBP. Inconsistent breathing patterns between 4D CT simulation and treatment may cause considerable dosimetric differences. Therefore, patient training is important to maintain consistent breathing amplitude during CT scan acquisition and treatment delivery.

Key Words: Amplitude-based respiratory gating, Respiratory motion, Volumetric Modulated Arc Therapy (VMAT)

Introduction

Advanced radiotherapy techniques, such as intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) which evolved from intensity modulated radiation therapy, have enhanced treatment outcomes by delivering a conformal radiation dose to the targeted tumors while sparing healthy surrounding tissues from radiation.[1] However, this delivery technique is difficult to apply in the thoracic and abdominal regions because there is limited target delineation accuracy resulting from motion artifacts produced during imaging and increased dose uncertainties that arise from irradiating a moving target with a large number of small fields. Hence, the motion of the target that is due to respiration is a significant and challenging problem for the delivery of radiation therapy.

Gated volumetric modulated arc therapy provides an opportunity to account for respiration-induced motion of the targets. In order to achieve the desired dose distribution during beam delivery of gated VMAT, the dose rate, gantry rotation speed, and multileaf collimator (MLC) leaf moving speed are not only modulated but also intentionally interrupted to synchronize with the patient's respiratory cycle.

This research was supported by a grant (15172MFDS395) from the Ministry of Food and Drug Safety in 2015.
Received 13 August 2015, Revised 31 August 2015, Accepted 8 September 2015
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The geometric accuracy of gated VMAT has been investigated using a dynamic phantom, and the dosimetric accuracy of gated VMAT has shown in a preclinical study that gated VMAT delivery is robust and dosimetrically accurate in a non-clinically released environment.[2-4] These studies investigated the dosimetric fidelity of gated VMAT delivery using log file-based dose reconstruction and ion chamber array measurements.[5,6] In a study performed by Qian et al., artificial regular sinusoidal motion, not a real patents' respiratory motion, was used to verify the experiments, which obviously provides results that are different from an actual clinical situation. As shown in a recent study, the interplay effect has a limited impact on gated RapidArc therapy when evaluated with a linear phantom.[7] On the other hand, reports on the dosimetric evaluation of gated VMAT under actual clinical conditions that focus on amplitude-based respiratory gating for delivery are scarce.

This study uses respiratory data acquired from three clinical patients to investigate the variation in the breathing patterns between a 4D CT simulation and during treatment, and to evaluate the dosimetric influence of amplitude-based respiratory gating for the delivery of VMAT using a one-dimensional respiratory motion phantom under actual clinical conditions.

Materials and Methods

1. RapidArc with Clinac® iX linear accelerator and respiratory motion phantom

This study used a Varian Clinac® iX linear accelerator with RapidArc capabilities and a real-time position management (RPM) system for respiratory gating. RapidArc is a novel planning and delivery technique used in volumetric modulated arc therapy, and it was introduced and commercialized based on Karl Otto's concept of volumetric arc therapy.[8] The RPM system tracks the respiratory cycles of the patient using a reflective plastic box placed on the patient's abdominal surface.

To evaluate the dosimetric influence during gated VMAT delivery, we used a respiratory motion phantom (Quasar, Modus Medical Devices, Inc., London, ON, Canada), as shown in Fig. 1. The motion phantom consists of rotary cam-driven cylindrical inserts that move through a solid perspex chest cavity in the superior-inferior direction with variable speed and amplitude, moving a platform (representing the chest wall) in the anterior-posterior (AP) direction and synchronously moving the insert in the superior-inferior (SI) direction, in order to simulate patient breathing. There are two cams inside the Programmable Drive Unit housing. The cams are used to drive the vertical motion of the chest wall platform. One cam has a sinusoidal profile (circular) and the other has the profile of a typical respiratory cycle. Both profiles have 10 mm peak-to-peak amplitude.

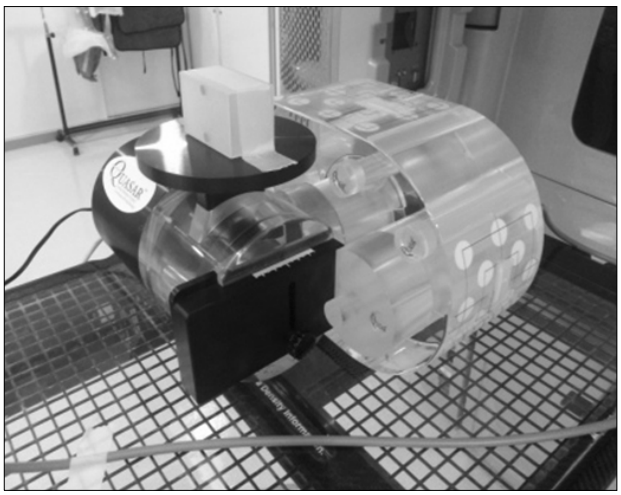

Fig. 1. Experimental setup of the programmable respiratory motion phantom. The insert containing the film or ion chamber moves in the inferior-superior direction, and the top platform moves in the anterior-posterior direction for the RPM block.

We used a dedicated breathing control program. In this system, the patient observes his/her own breathing trace through a goggle monitor screen and follows programmed sinusoidal oscillations that can be adjusted in terms of the frequency. This system can be allowed the patient to familiarize him or herself with a breathing pattern so that he/she can evaluate his or her ability to achieve reproducible respiratory signals.

2. Image acquisition and selection of patient's breathing pattern

In this study, three patients with liver tumor who had been treated with gated VMAT were selected. The details of the characteristics of each patient and their corresponding treatment plans are listed in Tables 1 and 2.

To evaluate the dosimetric influence of the plans for selected cases, a 4D CT of the motion phantom was scanned us-

Table 1. Characteristics of the study patients derived from 4D CT.

Patient	Gender/Age	Tumor information*				Breathing period (s)
		Pathology	Location	GTV (cm^3)	Max liver motion amplitude (mm)	
1	M†/59	HCC‡	S6§	5.85	7.2	3.4
2	M/60	HCC	PVTT‖	68.41	14.1	5.1
3	M/39	HCC	S5 - S8	2,764.86	9.2	5

*Patients are listed in ascending order of target volume. Prescribed percentage is defined to cover 95% PTV. †M: Male, ‡HCC: Hepatocellular Carcinoma, §S6: Segment 6, ‖PVTT: Portal Vein Tumor Thrombosis.

Table 2. Summary of the gated VMAT treatment plans investigated in this study.

Patient	PTV (cm^3)	Energy (MV)	Field	Total monitor unit	Prescribed dose (Gy)	Fractions
1	15.28	6	7 partial-arcs	7,081	57	3
2	124.61	6	2 full-arcs, 1 partial-arc	4,043	40	4
3	3,656.38	6	2 full-arcs	387	45	25

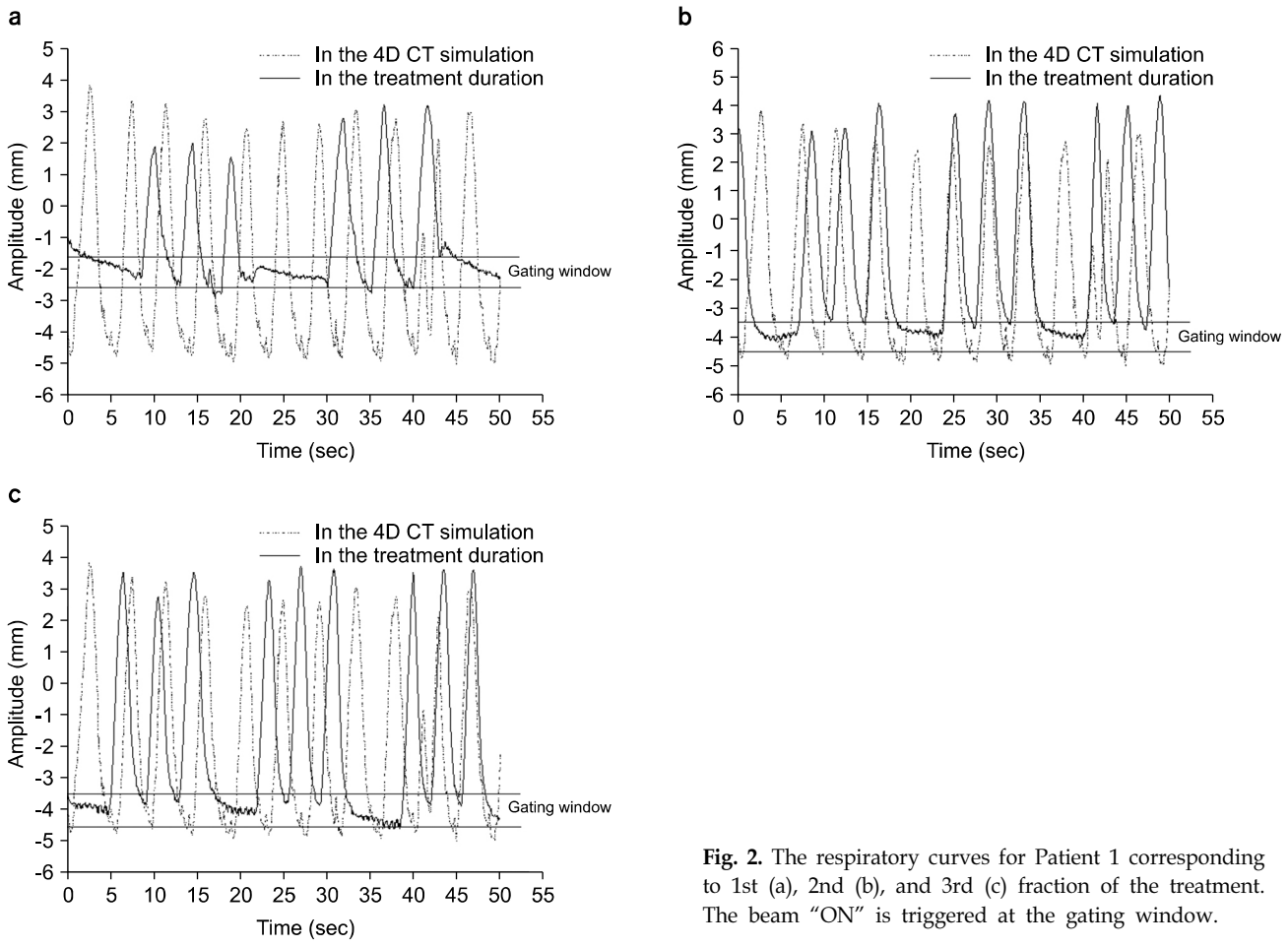

Fig. 2. The respiratory curves for Patient 1 corresponding to 1st (a), 2nd (b), and 3rd (c) fraction of the treatment. The beam "ON" is triggered at the gating window.

ing a GE LightSpeed 16-slice CT scanner that was integrated with the Varian real-time position management (RPM) system. The phantom was scanned with 1.25 mm slice thickness in order to capture objects at the highest resolution. The execution of the 4D CT simulation on the phantom was based on the selected patient's respiratory trace data sets.

Once the scan was completed, reconstructed CT images and RPM chest wall motion data were sent to a GE Advantage (General Electric Company, Waukesha, WI) computer for sorting. After the phases of all patients image set were sorted from 40% to 60% for use in gated VMAT, the image sets were forwarded to the treatment planning system to generate the treatment plan.

We analyzed the breathing patterns that are caused by programmable motion control software during patient treatment and compared them to those of the 4D CT simulation. Fig. 2 shows the respiratory curves for Patient 1 corresponding to all fractions of the treatment. Fig. 3 shows the analyzed patients breath-holding position from marker signals for entire treatment fractions. We selected two types of breathing patterns subjectively from the log files of the gated VMAT of the patients. For patients with a consistent breathing pattern (CBP) relative to the 4D CT respiration data, the variability of the breath-holding position during treatment was observed within thresholds defined from 4D CT image sets for phases of 40% and 50%. Since all patients image set were sorted from 40%

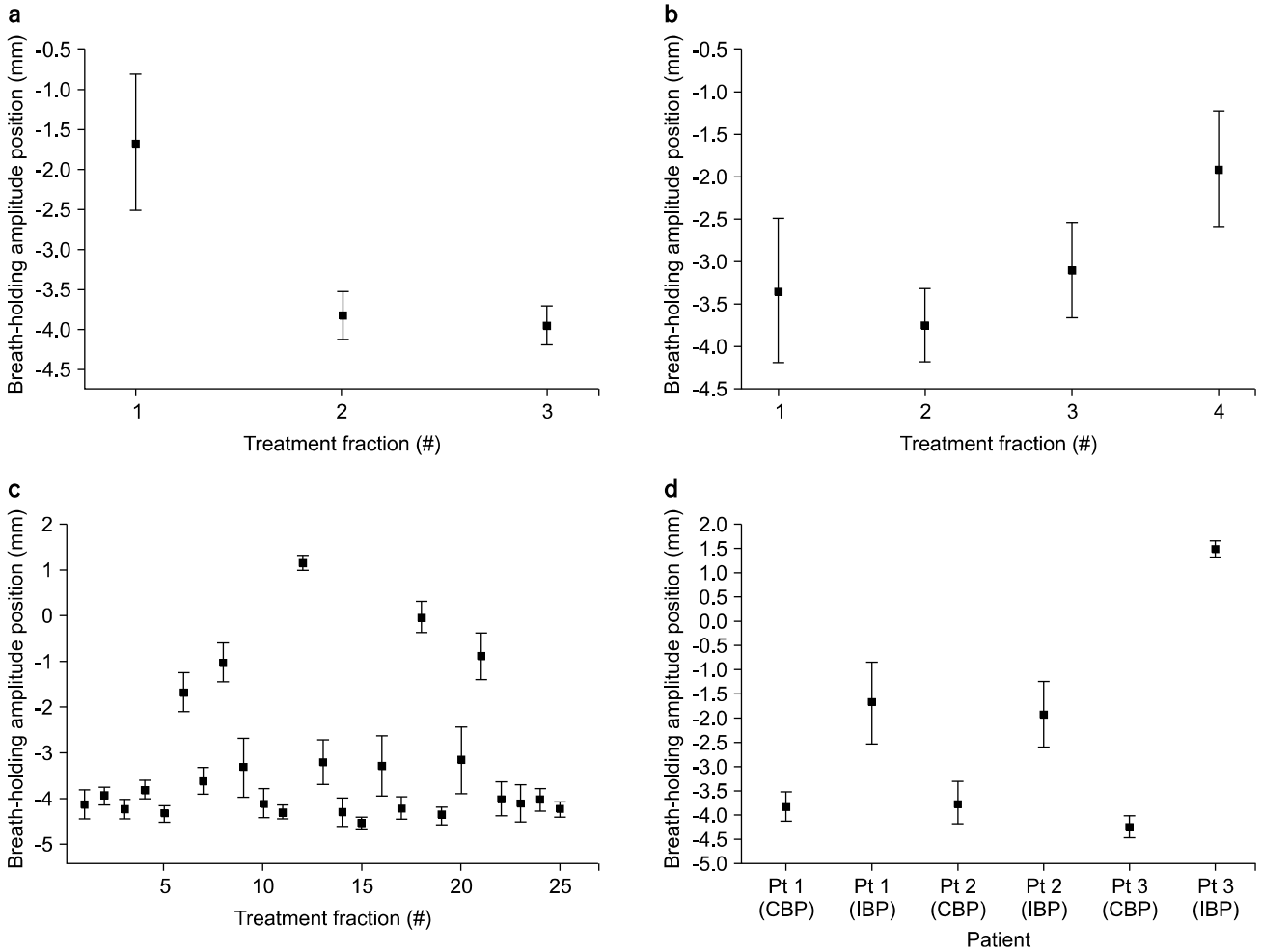

Fig. 3. The breath-holding position from marker signals are shown specifically for Patients 1 (a), 2 (b), and 3 (c). The error bars represent the amplitude standard deviations determined over the duration of the treatment. Subjectively selected patients' breathing patterns (d) are shown.

to 60% for use in gated VMAT, we should know the marker position at phase of 40% and 50% from 4D CT image set. However, for inconsistent breathing patterns (IBP), the variability of the breath-holding position during treatment deviated from the thresholds. The actual patients were successfully treated without problems associated with baseline shift. But, there was a change in the respiratory amplitude size between the inter-fractional treatments. In this study, we have investigated the dosimetric difference between the two cases under assumed that delivery deviated from the thresholds as IBP. The error bars represent the variation of amplitude position during gated VMAT.

Table 3 shows a comparison of the total delivery time and of the breath-holding characteristics of each of the breathing patterns that correspond to gated VMAT delivery during treatment. As expected, for patients with CBP, the variability of the breath-holding position during treatment was observed to be within the thresholds for each patient, as shown in Fig. 3. For IBP, the changes in the amplitude of the breathing position show aspects different from those of CBP. In the case of Patient 3, the mean amplitude of the breathing position deviated substantially from the range of the thresholds.

3. Treatment planning

The treatment was planned using the Eclipse treatment planning system (TPS, Version 8.6; Varian Medical Systems). A spherical target of 3.6 cm in diameter was created as the planning target volume (PTV), and it was manually generated for all trials in order to eliminate the influence of dose exposure out of the field of the motion phantom. To validate the influence of patient respiration during beam delivery, three plans were created that kept the same configurations as those used in the original gated VMAT plans. For each dose delivery plan, the dose coverage values of the PTV received at least 95% of the prescribed dose. The plans were transferred to a treatment machine, and the phantom was set up to simulate cranio-caudal motion perpendicular to the field of arc rotation.

4. Gafchromic EBT3

The delivery and distribution of the doses were verified using the GAFCHROMIC EBT3 (International Specialty Products, Wayne, NJ) self-developing film with sheet dimensions of 20.3×25.4 cm^2. To create the calibration curve, eighteen pieces of 4×4 cm^2 in size were irradiated using a 6 MV beam in order to deliver dose levels ranging from 0 Gy to 3 Gy, with intervals of 0.3 Gy, and ranging from 3 Gy to 24 Gy, with intervals of 3 Gy. An Epson Expression 10000XL photo flatbed color scanner (Epson America, Inc., CA) was used to read all the films, and to minimize the effect of the lateral dependence artifacts (the non-uniform response of the readout that is due to the light of the scanner lamp scattering as a result of striking the particles in the active layer of the film) a 25.5×20.5 cm^2 cardboard template was fitted to the scanner to position the films at a reproducible central location of the scan surface which could be considered to be uniform.

5. Dose delivery and measurements

The EBT3 films were cut to 15 by 6.5 cm in size to fit the cassette, and a personal computer was used to communicate with the motion phantom using a software application that downloads respiratory waveforms of patients to the phantom, thereby simulating the breathing. The treatment was delivered

Table 3. Characteristics of respiration determined over the treatment duration for individual patients.

Patient		Total delivery time	Total Breath-holding time	Number of breath-holding	Mean breath-holding tpb‡ (s)	Breath-holding amplitude position (mm)	
						Mean	Std
1	(CBP*)	30 min 05 s	12 min 22 s	79	9.4	−3.82	0.30
	(IBP†)	30 min 02 s	11 min 57 s	83	8.3	−1.67	0.85
2	(CBP)	24 min 44 s	8 min 48 s	56	9.4	−3.75	0.43
	(IBP)	21 min 28 s	8 min 23 s	47	10.7	−1.91	0.68
3	(CBP)	10 min 48 s	3 min 13 s	39	4.9	−4.21	0.23
	(IBP)	9 min 14 s	3 min 10 s	26	7.3	1.50	0.17

*CBP: Correct Breathing Pattern, †IBP: Incorrect Breathing Pattern, ‡tpb: time per breath-holding.

to the phantom on two separate occasions: first it was delivered using a gated VMAT, and then reference stationary measurements were taken. The results of both were then compared.

The absolute doses were measured with a 0.6 cm^3 Farmer-type ion chamber (PTW Type 30013). The ion chamber was placed in a movable insert of the motion phantom, and the measurements for the stationary phantom without beam gating were used as a standard for comparison against other measurements. Three measurements were taken for all configurations of the ion chamber, and the average was used to present the results in this study.

The gamma (γ) index that was proposed by Low et al. to

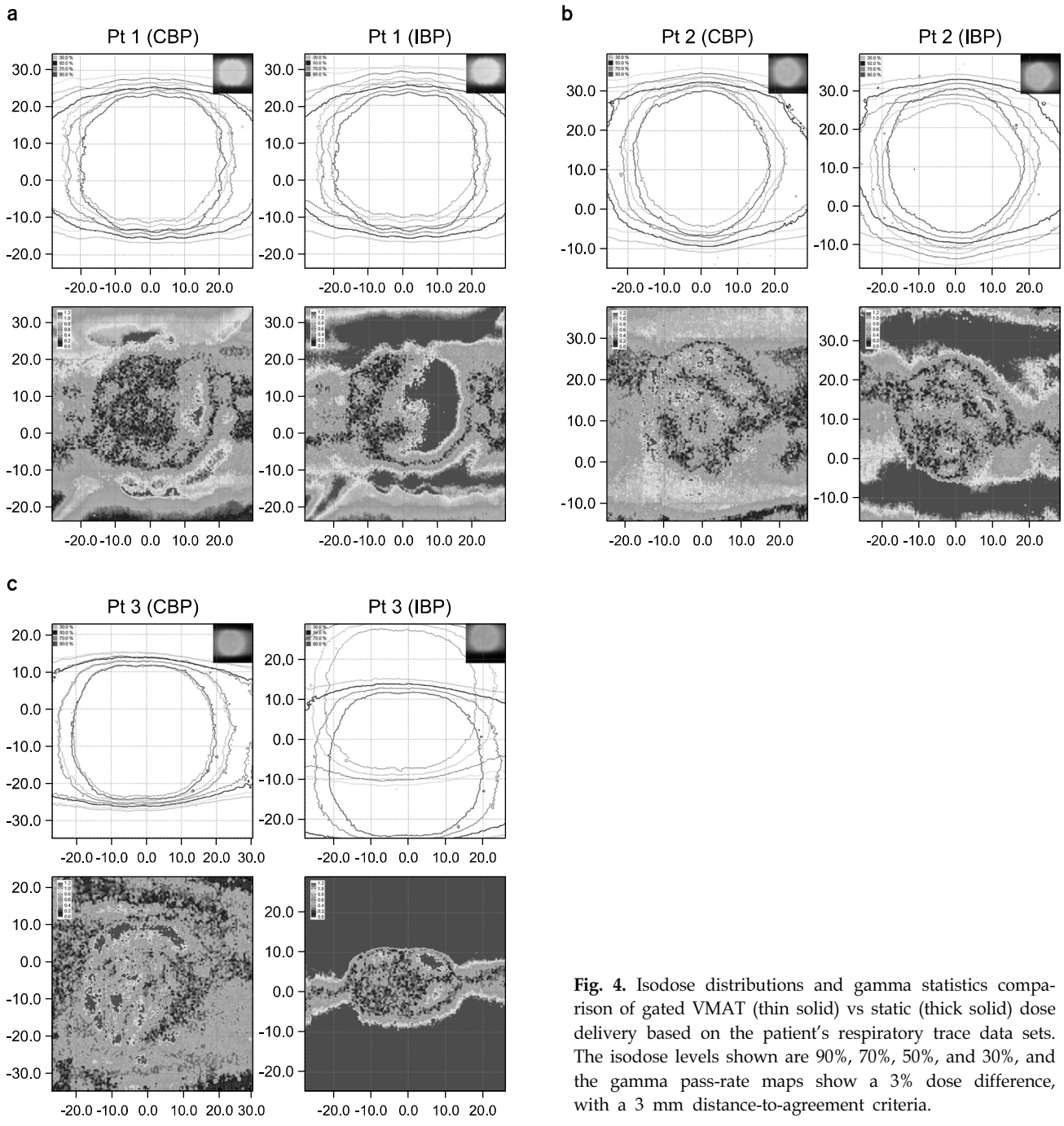

Fig. 4. Isodose distributions and gamma statistics comparison of gated VMAT (thin solid) vs static (thick solid) dose delivery based on the patient's respiratory trace data sets. The isodose levels shown are 90%, 70%, 50%, and 30%, and the gamma pass-rate maps show a 3% dose difference, with a 3 mm distance-to-agreement criteria.

quantitatively evaluate the dose distributions was used to perform a quantitative comparison of the dose distributions.[9,10] The isodose comparison and gamma statistics analysis, with a 3%/3 mm and 2%/2 mm gamma index in global area of field, were performed with the FILMQA™ software version 2.2.0113 (International Specialty Products, Wayne, NJ).

Results

We evaluated the dose accuracy of the gated VMAT on the linear phantom by comparing the isodose distributions, gamma statistics, and ion chamber measurements.

1. Film measurement

A film-to-film comparison has an advantage in that it isolates the effects of gating by not having to consider either positioning errors or any confounding effects from the dose calculation engine in the TPS. For this reason, the evaluation method presented here uses a film-to-film comparison of the dose distributions.

The dose delivery for the respiratory motion phantom with respect to the three adapted patient plans resulted in varying degrees of dose conformity. For all plans, the gamma analysis (3%, 3 mm) of the film measurements for static delivery, compared to the TPS calculated dose maps, indicates that the average percentage of agreement was of over 99.0%. Fig. 4 shows the comparison in isodose distributions and gamma statistics of static and gated VMAT dose delivery for individual patients where dose deterioration is evident when comparing isodose distributions. The passing rate percentage under the 3%/3 mm gamma analysis for Patients 1, 2 and 3 were respectively 93.18%, 91.16%, and 95.46% for CBP, and 66.77%, 48.79%,

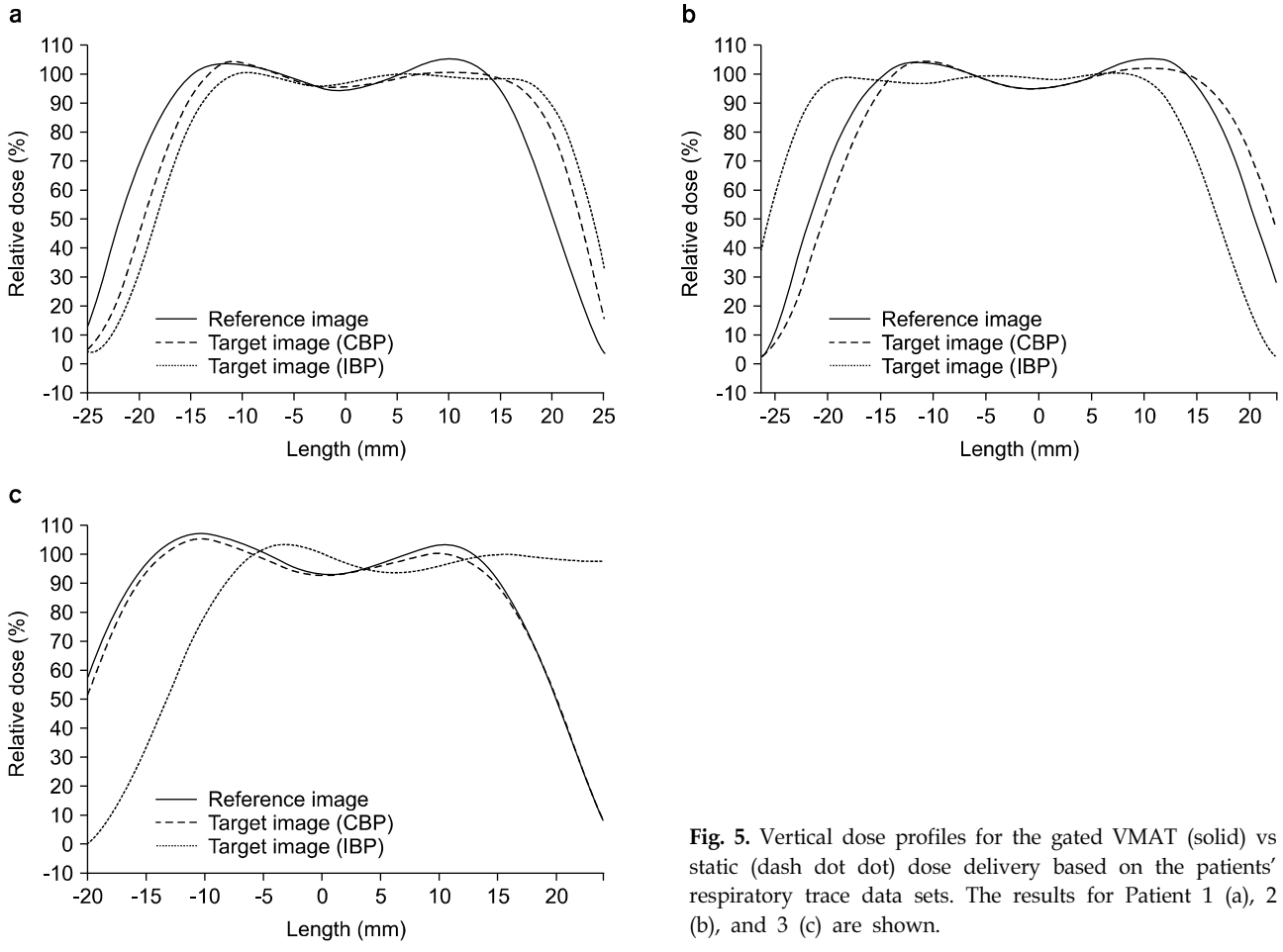

Fig. 5. Vertical dose profiles for the gated VMAT (solid) vs static (dash dot dot) dose delivery based on the patients' respiratory trace data sets. The results for Patient 1 (a), 2 (b), and 3 (c) are shown.

Table 4. Percentage difference in dose from the ion chamber measurements.

Patient	Compared to static (%)	Compared to TPS (%)	Difference between static delivery and TPS (%)
1 (CBP*)	2.12±0.21	3.65±0.21	1.6
(IBP†)	6.51±0.73	7.94±0.71	
2 (CBP)	2.48±0.12	3.98±0.12	2.3
(IBP)	8.23±0.41	9.86±0.40	
3 (CBP)	1.52±0.96	2.88±0.94	1.4
(IBP)	55.54±0.66	56.23±0.65	

*CBP: Consistent Breathing Pattern, †IBP: Inconsistent Breathing Pattern.

and 40.36% for IBP. Under the more stringent criteria of 2%/2mm, passing rates for Patients 1, 2 and 3 were respectively 73.05%, 67.14%, and 86.85% for CBP, and 46.53%, 32.73%, and 36.51% for IBP. The vertical dose profiles show that the shift in the central axis of the gated patient plan trials were measured to be 2, 2, 1 mm and 4, 3, 16 mm for CBP and IBP, respectively, away from the isocenter in the plane of motion, as shown in Fig. 5.

2. Ion chamber measurements

The ion chamber measurements of the gated deliveries were compared to the point doses calculated with the TPS and to the static point dose measurements, and the results are summarized in Table 4. The ion chamber measurements were within 3.5%, on average, of the values calculated using TPS and within 2.0%, on average, when compared to the static point dose measurements for all cases of CBP. For the IBP, we found that the dose discrepancies were more than twice as large as those measured in CBP, as compared to the planned dose. In the case of Patient 3, the percentage difference in dose from the ion chamber measurements can be seen to have a significant difference.

Discussion

The patient always moves to some extent during treatment, and this affects the quality of the delivered dose. Although our studies were based on a phantom that achieved realistic patient motion in one dimension, such is not perfectly identical to organ movement yet the results of the measurements are valid. Our studies are based on motion signals acquired from external markers where patient respiratory signals obtained from image acquisition are applied to dose deliveries.

With respect to the clinical plans for the patient, varied results were observed. For the film and ion chamber measurements, our results indicated that the dose distributions and gamma passing rates were closely correlated with the range of the deviation from the thresholds that serve as a reference. Consequently, inconsistent breathing patterns between 4D CT simulation and treatment duration may result in considerable dosimetric differences with both film and ion chamber measurements.

The results of the analysis of the amplitude of the breath-holding position during treatment are based on motion signals acquired from external markers and were found to be significant. The maximum and minimum fluctuations associated with measurements of intra-fraction motion signals are of less than ±0.85 mm and ±0.17 mm, which are shown as vertical error bars in the plots of Fig. 3. In the case of Patient 3, the variation of the mean motion signals measured across the inter-fraction is 6.04 mm, which is the mean amplitude of the breathing position that deviated largely from the amplitude of the CBP breathing position. This patient tended to have a consistent breathing holding position, but less consistent breathing amplitude compared to those who have the 4D CT breathing pattern.

A key issue for gated VMAT with external respiratory monitors is the accuracy of such monitors in predicting the position of internal organ targets. The internal/external correlation can be disturbed or lost completely due to transient changes in breathing. For respiratory gating, minimizing the variation in patient breathing within a treatment fraction and from fraction to fraction, i.e., increasing the reproducibility of patient breathing, is important. For these reasons, patient training is important to allow for the patient to familiarize him or herself with a breathing technique so that he/she can evaluate his or her ability to achieve reproducible respiratory signals that generate the same conditions as those during CT scan acquisition and treatment delivery.

For this study, we used a dedicated breathing control program. However, for the 4D CT simulation and for the treatment duration, Patient 3 did not improve the regularity of the

breathing amplitude. In a clinical situation, there is the possibility for variation of the absolute position of external markers if, say, the patient had a large meal and is very bloated and thus has a very different external signal from the RPM. Consequently, the results of treatment showed dosimetrically larger errors. We suggest that it's necessary to confirm whether external marker movement values correspond to 4D CT treatment or not. Also, special staff efforts such as by therapists training, coaching, and advising patients is important.

There are several sources of uncertainty in the film analysis such as the response at high-dose levels, sensitivity to scanner orientation and post-irradiation coloration, energy and dose rate dependence, and orientation dependence with respect to the side of the film. In the study performed by Casanova Borca et al., most of the characteristics of the EBT3 film were found to be similar to those of the EBT2 film.[11] A study of the colorization process revealed fast stabilization of the film that occurred within two hours. The color variation for unit doses has also been investigated, indicating that the red channel has a greater response for up to 10 Gy while the green channel is preferable at higher dose levels. The analysis of the variation in the energy levels and dose rates shows no significant differences between the two films. The EBT3 film shows a different response that depends on whether the film has a portrait or landscape orientation, but negligible differences where found when the film as placed face up or face down. In addition, the Eclipse AAA algorithm is not very accurate for regions of electronic disequilibrium, such as at the field edges.[12] This could also explain why some of discrepancies are seen in the film/TPS comparison.

Only two fractions for each patient were studied, and the influence of the entire treatment fractionation was not included. However, as the results of the study showed, the results of other adapted patient plans could be intuitively anticipated. Therefore such circumstances should not have an influence on our conclusions.

Conclusion

We have investigated a dosimetric evaluation of gated VMAT using a phantom that achieved realistic patient motion in one dimension. The results of this study show that variations in the amplitudes of patient breathing during treatment arise from inconsistent breathing patterns, and these variations are of great clinical significance. Therefore, an effort to maintain consistent patient breathing patterns is important in order to increase the reproducibility of the patterns, to produce the same conditions as those during CT scan acquisition and treatment delivery. Care must be taken when monitoring a patient's respiratory pattern to determine whether or not the patient achieves reproducible respiratory signals that generate the same conditions as those during CT scan acquisition and treatment delivery.

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진폭 기반 호흡연동 체적변조회전방사선치료의 선량학적 평가

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본 연구의 목적은 진폭 기반 호흡연동 체적변조회전방사선치료의 선량학적인 평가를 하고자 한다. 이 치료를 받은 환자의 호흡 Log 파일을 획득하여 분석하였으며, 4D CT 호흡 형태의 40%~60% 위상 영상 구간 진폭을 기준으로 치료 Log 파일 호흡 진폭의 구간이 4D CT의 진폭 구간과 일치하는 호흡 형태(CBP)와 일치하지 않는 호흡 형태(IBP)로 구분하였다. 상대적인 등선량 분포는 EBT3 필름을 사용하여 측정하였으며, 절대 선량 측정은 PTW 0.6 cm^3 이온전리함을 이용하여 측정하였다. 감마 인덱스 3%/3 mm을 적용한 환자 1, 2, 3의 CBP 호흡인 경우 각각 93.18%, 91.16%, 95.46%이며, 환자 1, 2, 3의 IBP 호흡인 경우 각각 66.77%, 48.79%, 40.36%으로 분석되었다. 또한 감마 인덱스 2%/2 mm을 적용한 환자 1, 2, 3의 CBP 호흡인 경우 각각 73.05%, 67.14%, 86.85%이며, IBP 호흡인 경우 각각 46.53%, 32.73%, 36.51%으로 분석되었다. 모든 CBP호흡인 경우의 이온전리함 측정값은 치료계획 시스템에서 계산된 값과 평균 3.5% 이내로 일치하였으며, 정적인 팬톰 조사와의 차이는 평균 2.0% 이내로 일치하였다. 환자 3의 IBP 호흡인 경우 이온전리함 측정값과 계산된 값과의 차이가 평균 56%로 큰 차이를 보였다. 이는 4D CT의 진폭 구간과 치료시의 진폭 구간의 차이가 크기 때문인 것으로 사료되며, 4D CT 모의 치료시와 환자 치료시의 진폭의 크기를 일정하게 유지하는 것이 중요하다고 판단된다.

중심단어: 호흡연동, 호흡 움직임, 체적변조회전방사선치료