ANALYSIS ON THE VARIATION OF RESPIRATORY ORGAN MOTION AND A PRELIMINARY FEASIBILITY STUDY FOR A VOICE COACHING TECHNIQUE TO IMPROVE THE REPRODUCIBILITY OF RESPIRATORY CYCLE BETWEEN TREATMENTS

James C. Li[1], Wen-Shan Liu[1], Hsiang-Chi Kuo[1], Li-Miao Chen[1], David Huang[2], Chi-Wei Hsu[1], His-Chang Chang[1]

Radiation Oncology Department[1], Chung-Shan Medical University Hospital
Medical Physics Department[2], Koo Foundation Sun Yat-Sen Cancer center

Purpose : New advances in radiotherapy technology enable us to attain higher dose delivery to tumor region, resulting in greater tumor control probability, with this sophistication there is more demand to control the uncertainties contributed by organ motion. The organ motion related uncertainties can be mainly classified into three main categories: (i) the blurring of planning images due to internal organ motion during CT scan acquisition; (ii) intrafractional organ motion that affect the dose distribution within a single treatment delivery; (iii) interfractional organ motion that affect the dose distribution between treatments.

For patients with supradiagphragmatic and infradiagphragmatic tumor, respiration is a major factor that causes the displacement of the internal organ. For further understanding the magnitude of the respiratory organ motion, we endeavor to investigate: (i) the geometrical differences in spatial displacement of the tumor and critical organ while in free breathing status and breath holding status; (ii) measures the magnitude of the respiratory organ motion in the cranio-caudal direction; (iii) makes a preliminary feasibility study of the coaching breathing technique to improve the reproducibility of the respiratory cycle and hence reduce the variation of organ motion in between treatment.

Materials and Methods : The data were collected between March 2001 to October 2001 in our department from subjects undergoing radiation therapy of the thoracic and abdominal regions using our spiral CT and real time Respiratory Gating system to measure and analyze the variation of respiratory organ motion. A voice coaching technique is designed to improve the consistency of the respiration cycles.

Results and Conclusions : Our analysis shows a significant variation of tumor and organ geometry between free breathing and breath holding state. The cranio-caudal displacement are 15.5 ± 3.5 mm for diaphragm and 13.7 ± 2.4 mm for pancreas, respectively. For patients in our study, coaching technique may improve the reproducibility for those patient whose breathing cycles is not consistent within intrafraction treatment, but not for those with consistent cycles.

[Therapeut Radiol Oncol 2002; 9(1): 1-12]

Key words: Intrafraction, Interfraction, Respiratory organ motion

Received: 2002, 4, 5. Accepted: 2002, 6, 6.

Address reprint request to: Mr. Hsiang-Chi Kuo, Radiation Oncology Department, Chung-Shan Medical University Hospital, No. 110, Sec. 1, Chien-Kuo N. Road, Taichung, Taiwan

INTRODUCTION

New advances in radiotherapy technology enable us to attain higher dose delivery to tumor region resulting in greater tumor control probability. One major dilemma in the modern radiotherapy technique is the respiration-induced organ motion (Fig. 1). The respiratory organ related uncertainties can be mainly classified into three main categories: (i) the blurring of planning images due to internal organ motion during CT scan acquisition; (ii) intrafractional organ motion that affect the dose distribution within a single treatment delivery; (iii) interfractional organ motion that affect the dose distribution between treatments.

The CT motion artifact causes the blurring of the images making causes difficulties in the delineation of the real tumor and normal tissue. Balter et al. have reported observations of lung and liver volume changes for a sample of patients that illustrates the effects of patient respiration on organ volume [2]. The variation of the tumor volume is commonly accounted for by the use of adequate margins that encompass the tumor volume. ICRU Report 50 defines the gross tumor volume (GTV) as the volume containing demonstrated tumor. The clinical target volume (CTV) is defined to enclose the GTV plus a margin to account for suspected tumor involvement. The planning target volume (PTV) is defined by the CTV plus a margin to accommodate the variation for CTV. In ICRU Report 62, this margin is divided into two components: (a) internal margin (IM) to account for variation in size, shape, and position of the CTV; and (b) set up margin (SM) to account for uncertainties in patient position and beam alignment. It is nontrivial that the delineation of the GTV, CTV and the normal tissue affect the treatment planning evaluation and the treatment outcome as well. Conventionally we rely on CT images taken under free breathing status, it will be interesting to compare the geometrical differences for CT images acquired by breath holding to eliminate the respiratory motion artifact.

Information about the amount and nature of the CTV motion is essential for the determination of internal margin size. Data on various types of organ motion are available in the literature. Most of the studies point out that the main dimension of the respiratory organ displacement is in the cranio-caudal direction caused by diaphragmatic movement between respiration cycles [2,9,12]. For the information on the diaphragmatic displacement to be incorporated into margin extension of CTV, we proposed the use of respiration synchronized serial fluoroscope images to evaluate the margins needed for supradiagphragmatic and infradiagphragmatic

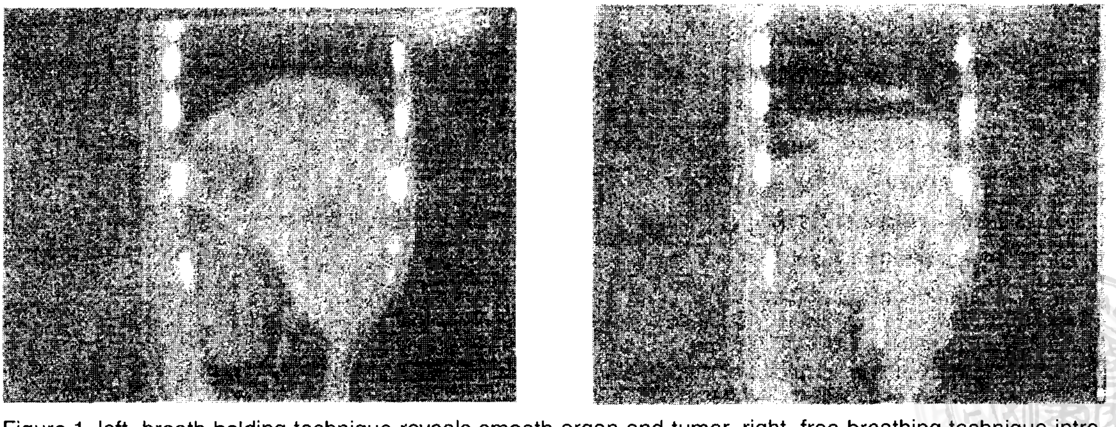

Figure 1. left, breath holding technique reveals smooth organ and tumor, right, free breathing technique introduced jig shape and disconnection boundary.

tumor.

The sophistication of 3 dimensional conformal radiotherapy demand tighter margin around the CTV for normal tissue sparing and for dose escalation purposes. A respiration gating technique has been under studies to treat tumor at least motion phases within intrafractional respiration cycles. However, to safely implement this technique, a consistent respiration cycle should be maintained between treatments. The third objective of this study is to investigate the variation of interfractional respiration cycle and try to reduce this variation through voice coaching technique.

MATERIALS AND METHODS

(A) A spiral CT (GE Hispeed Fx/i) is performed for all supradiphragmatic and infradiaphragmatic cancer in patients with both normal breath and breath hold technique. Both of the CT images are acquired with 5 mm slice thickness and 1.2 pitch. The two sets of CT Scans are exported to a virtual simulation workstation (SomaVision, TM) for further delineation of tumor (GTV only) and critical organ by the same physician. In the treatment planning workspace (virtual-sim), two orthogonal beams (AP and Lat) are set at the geometrical center of the tumor, then the maximum dimension in the X, Y, and Z direction of the tumor and critical organs can be measured from the Beam Eye View (BEV) (Fig. 2). The volume of the interest organ can be obtained during dose volume histogram analysis.

(B) The respiratory synchronized fluoroscope video images were attained with Varian Real-time Position Management (RPM) system

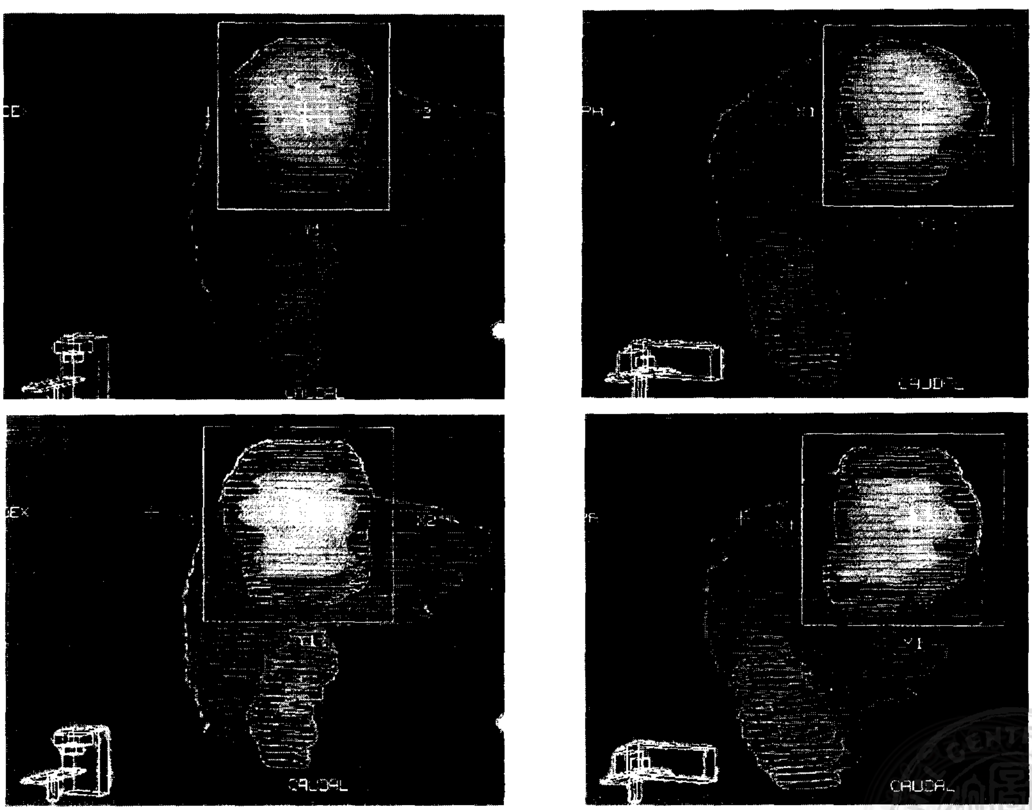

Figure 2. Upper right and upper left, BEV-AP and BEV-Lateral for static images, a non-uniform margin is designed at inferior to superior direction; lower right and lower left, BEV-AP and BEV-Lateral for images with motion artifact, uniform margin is designed at inferior to superior direction.

connected to Ximatron (Varian). The RPM system used an infrared illuminator to highlight infrared reflectors attached to a marker block placed on the patient's abdomen or chest, which is imaged using a CCD camera. The respiration induced periodic motion of the marker is tracked synchronously with the input fluoroscopy signal from the simulator. The synchronous inputs allow a time correction of the internal motion seen on the fluoroscopy images and the external marker motion. Information about the extent of the displacement of the diaphragm in the cranial-caudal direction was obtained by determining the extreme vertical positions of the diaphragm apex within 30 seconds fluoroscopy acquisition (Fig.3). For patients who have undergone post-operation radiotherapy for pancreas, catheters were embedded during operation, the motion extent of pancreas can be observed with the same method from the movement of the catheter.

(C) After the synchronous correlation between fluoroscopy signal from diaphragm and the video signal from marker motion has been checked, the interfractional reproducibility of the respiratory cycle are evaluated during every day radiotherapy on treatment room with RPM system. To improve the consistency of the respiration cycle, a coaching technique is introduced with two steps. First, collects and analyses patients' respiration cycles from RPM system to attain patients' typical exhalation and inhalation time under normal breathing condition. Second, record a voice instruction of "exhale" and "inhale" with time period mimicked patient's respiration patterns. The recorded voice instruction are played during day by day radiation treatment to coach patient's respiration cycle between interfractional treatment.

RESULTS

(A) The geometrical differences in spatial placement of the tumor and critical organ while in free breathing and breath holding status:

Among the 27 patients who were scanned

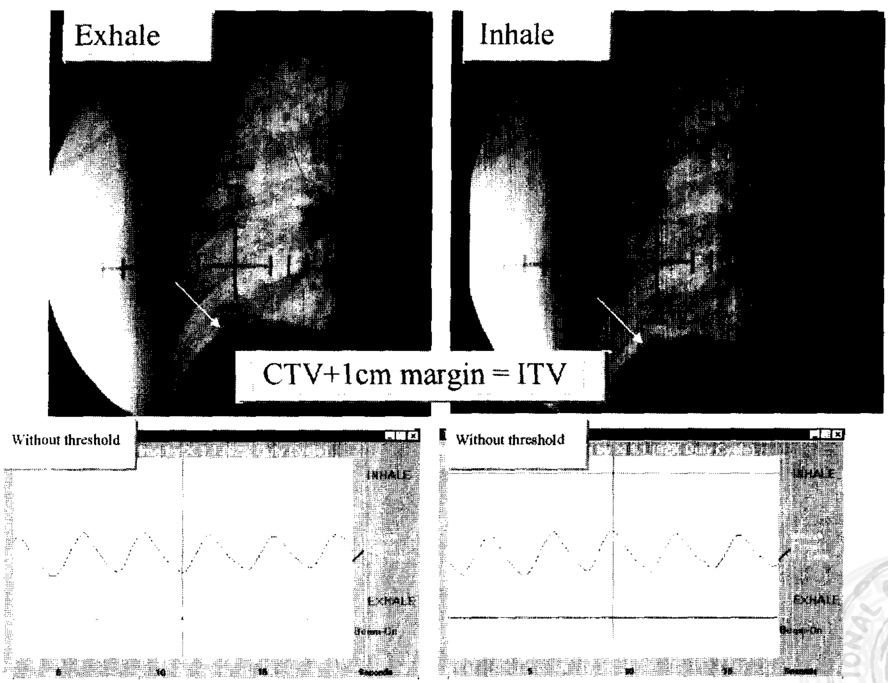

Figure 3. A real time play mode of the synchronized fluoroscopic images to evaluate the displacement of the diaphragm during respiratory cycles.

with two breathing status, 9 organs were delineated to compare the differences of the dimensional change on 3 main axis and volume differences (Table 1). With the breath holding scan as standard images, we found that volume differences in most organs are around 10% except the intestine which is mobile in nature and is more difficult to maintain in static images. The motion artifact on CT images would introduce a geometrical uncertainty on the definition of target and the critical organ, the average variation is less than 5 mm in all dimensions but has a wide range which can be as large as 3 cm.

(B) Displacement of the respiratory organ motion in the cranial-caudal direction:

With the serial fluoroscopic images and the record/play mode on RPM system, the motion extent which is useful in the determination of internal margin (IM, according to ICRU report 60 terminology) can be measured. The average

Table1. Geometrical variation of CT images of normal breath compare to breath holding technique.

Organ	Patient #	Geometrical dimension	Mean variation ± SD	Range
GTV1	9	X axis	4.7 ± 6.6mm	-3~22mm
		Y axis	1.8 ± 5.1mm	-9~12mm
		Z axis	-4 ± 8.5mm	-27~6mm
		volume	9.7 ± 2%	5.1~14.5%
GTV2	4	X axis	0.8 ± 5.2mm	-9~5mm
		Y axis	4.3 ± 4.6mm	-10~2mm
		Z axis	0.6 ± 6mm	0~9mm
		volume	9.9 ± 1%	8.2~10.8%
Liver	12	X axis	-0.08 ± 4.8mm	-8~12mm
		Y axis	0.75 ± 3.4mm	-6~5mm
		Z axis	2.4 ± 9mm	-19~7mm
		volume	9.7% ± 0.4%	9~10.3%
Rt. Kidney	11	X axis	2.4 ± 3.4mm	-4~10mm
		Y axis	-0.3 ± 3.3mm	-7~5mm
		Z axis	1.5 ± 4mm	-4~10mm
		volume	9.9 ± 4%	-6.1~10.4%
Lt. Kidney	11	X axis	1.6 ± 2.4mm	-2~7mm
		Y axis	-1.5 ± 4.1mm	-4~5mm
		Z axis	2 ± 4.5mm	-6~7mm
		volume	9.9 ± 0.5%	8.8~10.5%
Intestine	3	X axis	6.7 ± 6.6mm	1~16mm
		Y axis	13 ± 12.8mm	2~31mm
		Z axis	3.3 ± 4.6mm	-3~8mm
		volume	13.4 ± 1.9%	11.6~16.1%
Gastric	1	X axis	-8mm	
		Y axis	4mm	
		Z axis	-15mm	
		volume	8.6%	
Stomach	1	X axis	2mm	
		Y axis	-7mm	
		Z axis	-15mm	
		volume	9.3%	
Lt. Lung	1	X axis	-2mm	
		Y axis	-2mm	
		Z axis	-19mm	
		volume	9.3%	

displacement of the diaphragm among our 27 patients is 15.5 mm, ranging from 9 to 20 mm with a standard deviation of 3.5 mm (Fig. 4, Table 2). Only one patient is available for the analysis for pancreatic displacement during respiratory cycle, we obtained a mean value of 13.7 mm (Table 3).

(C) Preliminary feasibility study of the coaching breathing technique:

The correlation of the synchronous diaphragm motion and marker motion were checked for every patient in this study. The results show they are quite consistent (Fig. 5). The consistency of these two motions (one is external marker movement, the other is internal diaphragm movement) approved for further investigation. eight patients show 0.8 mm mean variation at inhalation (peak) position and 1.5 mm mean variation at exhalation (trough) position (Fig. 6, Table 4). Regarding the reproducibility of the respiration induced position displacement, our voice coaching technique do

Table 2. Comparison of diaphragm motion studies. PTT: peak to trough.

	Patient #		Normal breath PTT(mm) Avg ± SD	Range	Deep breath PTT(mm) Avg ± SD	Range
Wade	10	Standing	16 ± 2		103 ± 22	
	10	Supine	17 ± 3		99 ± 16	
Weiss	30	Standing	8 ± 4			
	30	Supine	13 ± 5			
Korin	15	Supine	13		39	
Davies	9	Supine	12 ± 7	7~28	43 ± 10	25~56
Hanley	5	Supine	26.4	18.8~38.2		
Balter	12		9.1 ± 2.4			
This study	27	Supine	15.5 ± 3.5	9~20		

Table3. Comparison of pancreas motion studies. Our results are taken from the same patient with and without voice coaching technique. (see figure 7)

	Patient #		Normal breath Avg ± SD PTT(mm)	Range	Deep breath PTT(mm) Avg ± SD	Voice coach PTT(mm) Range	Avg ± SD
Suramo	50	Supine	20	10~30	43	20~80	
Bryan		Supine	18				
	36	Prone	19				
	36		22				
This study	1	Supine	13.7 ± 2.6				13.7 ± 2.1

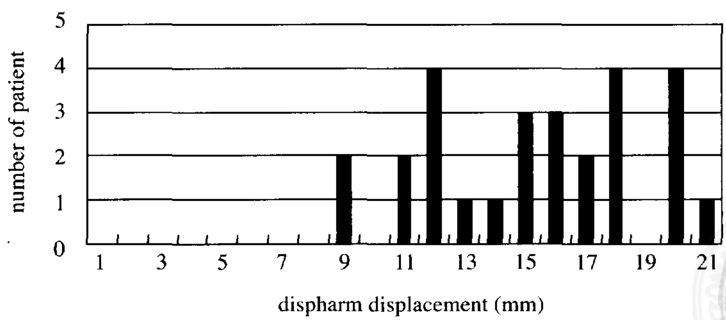

Figure 4. The distribution of diaphragm displacement extent measured from 27 patients.

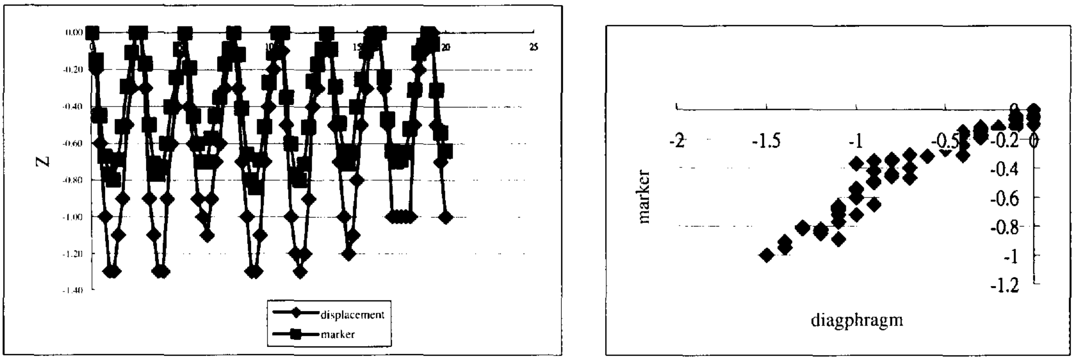

Figure 5. The correlation between the movement of diaphragm and marker are quite consistent (left) and quite linear (right).

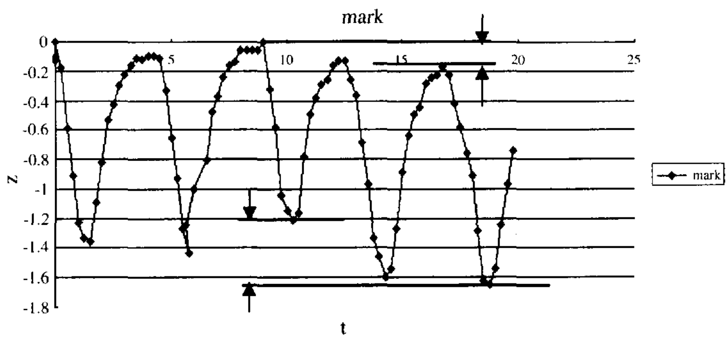

Figure 6. Arrows indicate the deviations of peak and trough positions at inhalation and exhalation which are results of respiration inconsistent.

Table 4. Evaluation of interfractional respiratory consistency from the variation of the inhalation peak position and exhalation trough position between treatments (see Fig. 6).

Patient#	# of study	Mean variation of inhalation peak amplitude ± SD Ave ± SD (mm)	Mean variation of exhalation peak amplitude ± SD Ave ± SD (mm)
P1	19	1 ± 0.9	2.5 ± 1.4
P2	8	1 ± 0.05	2 ± 0.9
P3	8	1 ± 0.5	0.7 ± 0.2
P4	16	0.8 ± 0.6	2 ± 1.6
P5	8	0.4 ± 0.3	0.7 ± 0.4
P6	8	0.8 ± 0.9	0.8 ± 1.1
P7	3	0.5 ± 1.7	2 ± 0.9
P8	3	0.8 ± 0.2	1 ± 0.5
Average		0.8	1.5

improve the consistency for the patient whose original respiration is not quite stable, but for patients with consistent respiration cycle, our technique did not help to further improve the results (Table 5).

DISCUSSIONS

Standard deviation of the geometrical dimensional differences between static images and images with motion artifact ranged from 3

Table5. Comparison of respiratory motion consistency between treatment with and without voice coaching.

Patient#	# of study	Mean variation of inhalation peak amplitude ± SD Ave ± SD (mm)		Mean variation of exhalation peak amplitude ± SD Ave ± SD (mm)	
		Free breath	Voice coaching	Free breath	Voice coaching
P1	8	0.4 ± 0.3	0.8 ± 0.5	0.7 ± 0.4	1.8 ± 1.5
P2	8	0.8 ± 0.9	0.4 ± 0.3	0.8 ± 1.1	1.7 ± 0.9
P3	19	1 ± 0.9		2.5 ± 1.4	
	10		0.5 ± 0.2		2.1 ± 0.7

to 9 mm in our data. Most of the time the organ delineated (especially the tumor) from images with motion artifact tends to over estimate the organ size since the boundary are blurred by motion. The system error causes the oversize of aperture design during treatment planning and would deliver unnecessary dose to the normal tissue close to tumor. In addition, the 5 mm SD in dimension would need 8 mm more safe margin (to have any point on the surface of the CTV to be within 95% of the time requires a margin of 1.65 SD) to maintain well coverage of the tumor, which will worsen the dose delivered to organ at risk [1]. To tighten the margin and spare more critical organ, we suggest that CT images within thorax or abdomen should be acquired with breath holding technique to prevent the systemic error from motion artifact.

In Korin's study for upper abdominal organs, they concluded that there is little dilation present in the abdominal organs. Their results show that the motion of upper abdominal organs is primarily translational in nature and occurs along the S/I (cranial-caudal) direction (The average ratio of the amplitude of S/I motion of the diaphragm versus A/P motion of the abdomen wall was determined to be 5.1 ± 1.9 for normal breathing and 5.0 ± 2.7 for deep breathing) [4]. To manage the respiratory organ motion for modern's radiotherapy technique, a powerful tool to identify the extent of respiratory organ motion in S/I direction is needed.

The RPM system not only provide the positional extent of diaphragm in S/I direction, but also the corresponding respiration cycle during the respiratory movement. This information is necessary for design of a non-uniform margin for the internal margin according to ICRU report 62. After carefully verifying the patients in this study, the synchronization is quite good between fluoroscopic images and the reflector marker signal (Fig. 5). Our results show that the average diaphragm displacement is 15.5 ± 3.5 mm, which is similar to those results reported in the literatures [7]. With this remarkable variation, the intrafractional respiration has long been a dilemma in radiotherapy technique to give a well coverage of the tumor during treatment and spare the normal tissue at the same time. Haken et al. has shown the potential benefits of eliminating planning target volume expansions for patient breathing in the treatment of liver tumors [11]. The others have presented in their studies that the respiration-induced motion increase the dose delivered to normal tissue and hence the toxicity as well [6].

A lot of effort has been spent to control or correct the interfractional respiratory organ motion, two of the strategies are the use of active breathing control apparatus [13] and the respiratory gating system [5,10]. The ABC (active breathing contral) device stops the flow of air into or out of the lungs when the lungs are at a specific volume and flow direction. The gating system utilized the RPM system mention in this study to gate the irradiation within a least motion phase of acceptable duty cycle. No matter which method is used, the efficacy of the

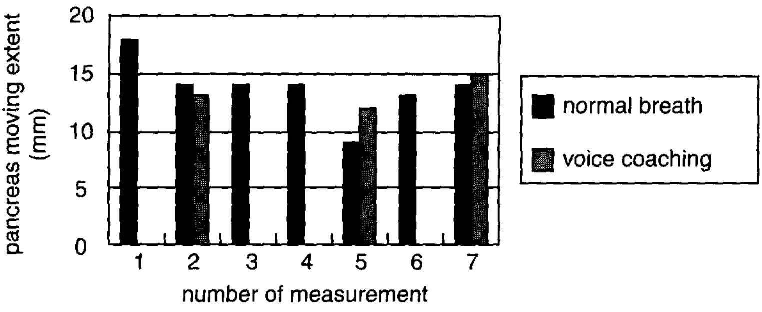

Figure 7. The variation of the moving extent for pancreas with and without voice coaching.

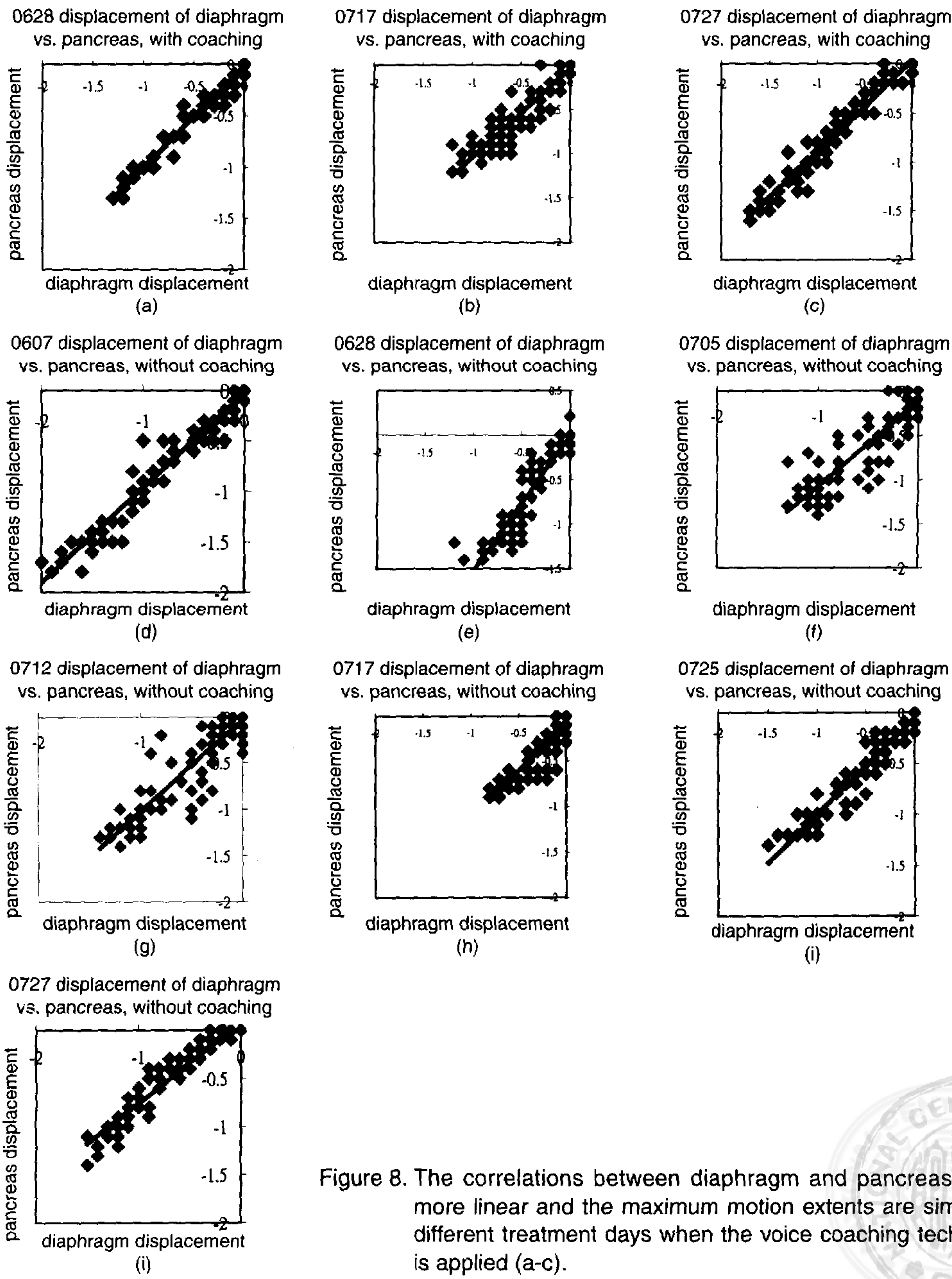

Figure 8. The correlations between diaphragm and pancreas show more linear and the maximum motion extents are similar at different treatment days when the voice coaching technique is applied (a-c).

treatment rely on careful control throughout the whole course, that's why the consistency of the respiratory cycle between treatment has to be checked. Our studies show 1-2 mm variation of the inhalation (peak) and exhalation (trough) positions. This variation only correspond to the marker (which is in A/P direction), the variation of the respiratory amplitude in S/I direction must be bigger. The one in our study to monitor the catheter in pancreas extent shows a standard deviation of 2.6 mm, ranging from 4mm to 18 mm (Fig. 7). Through voice coaching technique, the correlations between diaphragm and pancreas show more linear and the maximum motion extents are similar at different treatment days (Fig. 8).

Since the deviation of the respiratory motion between treatment could be large, the other important issue is to manage the interfractional respiratory organ motion. In this preliminary study we try to regulate patient's respiration through voice coaching technique. The one in pancreas' study we successfully reduced the intrafractional extent of pancreatic movement. On the other study to monitor the respiratory consistency through the observation of the marker's position extent from day to day, the voice coaching technique do show benefit for some patients but not all the patients. We assume that this technique may improve the reproducibility for those patient whose breathing cycles is not consistent within intrafractional treatment, but not those with consistent cycles. Further investigation is needed and improvement has to be made in the implementation of this technique.

The objective of this study is to improve and enhance the functioning or efficacy of a respiratory gating system that is design to eliminate or reduce the effect of respiratory organ motion. This RPM synchronize irradiation with patients respiration at the least motion extent and would ideally decrease the treatment margin. We have been shown at one study that 50% duty cycle selection would decrease the motion extent at about one third to half [3]. In addition, planning with CT images in breath holding status could use a non-uniform margin around (Fig. 2) compare to a uniform margin in aperture design for free breathing CT images. We also showed in another study that a non-uniform margin for respiratory motion extent can decrease 5% to 20% mean dose of normal liver [8] in intrahepatic tumor. This respiration management system is a reasonable design to provide a non-invasive way to freeze and trace the respiratory induced organ motion to improve therapeutic gain (static CT images, synchronized fluoroscopic images and synchronized irradiation). Although this system is easy to manipulate, the workload is double at CT, fluroscope image acquisition and everyday treatment if gating irradiation is performed routinely. The main difficulty of the gating technique is the inssurance of the consistency in the interfractional respiration and its induced motion extent. In this preliminary feasibility study of the voice coaching technique, we have shown the possibility of this technique. For further step in clinical practice, we could do a weekly fluroscope image verification like weekly portal film. In the increasing trend in radiation treatment through IMRT, dynamic treatment combined with gating technique is a more complex situation that we need to deal with.

REFERENCES

1. Antolak JA, Rosen II: Planning target volumes for radiotherapy: How much margin is needed? Int J Radiat Oncol Biol Phys 1999; 44: 1165-1170.
2. Balter JM, Ten Haken RK, Lawrence TS, et al.: Uncertainties in CT-based radiation therapy treatment planning associated with patient breathing. Int J Radiat Oncol Biol Phys 1996; 36: 167-174.
3. Chung KS, Kuo HS, Huang David: A

numerical simulation method for incorporating respiratory organ motion into 3D dose calculations using serial imaging data. 2002, July, AAPM annual meeting

4. Korin HW, Ehman RL, Riederer SJ, et al.: Respiratory Kinematics of the upper abdominal organs: a quantitative study. Magnet Resonan Med 1992; 23: 172-178.
5. Kubo HD, Hill BC: Respiration gated radiotherapy treatment: a technical study. Phys Med Biol 1996; 41: 83-91.
6. Kutcher GJ, Mageras GS, Leibel SA: Control, correction, and modeling of setup errors and organ motion. Semi Radiat Oncolo 1995; 5: 134-145.
7. Langen KM, Jones DTL: Organ motion and its management. Int J Radiat Oncol Biol Phys 2001; 50: 265-278.
8. Li JC: State of the art: respiratory gating for more accurate radiotherapy delivery. C J Radiologic Tech. 2001, 257-262.
9. Moerland MA, van den Bergh ACM, Bhagwandien R: The influence of respiration induced motion of the kidneys on the accuracy of radiotherapy treatment planning, a magnetic resonance imaging study. Radiother Oncol 1994; 30: 150-154.
10. Ohara K, Okumura T, Akisada M, et al.: Irradiation synchronized with respiration gate. Int J Radiat Oncol Biol Phys 1989; 17: 853-857.
11. Ten Haken RK, Balter JM, Marsh LH: Potential benefits of eliminating planning target volume expansions for patient breathing in the treatment of liver tumors. Int J Radiat Oncol Biol Phys 1997; 38: 613-617.
12. Willett CG, Linggood RM, Stracher MA: The effect of the respiratory cycle on mediastinal and lung dimensions in Hodgkin's disease. Cancer 1987; 60: 1232-1237.
13. Wong J, Sharpe M, Jaffray D: The use of active breathing control (ABC) to minimize breathing motion in conformal therapy. XIIth ICCR 1997; 27-30.

呼吸器官運動之變異性分析及呼吸導引技術之可行性研究

李必忍[1] 劉文山[1] 郭祥吉[1] 陳理妙[1] 黃英強[2] 徐啟偉[1] 張席昌[1]

[1] 中山醫學大學附設醫院 放射腫瘤科
[2] 辜公亮基金會和信治癌中心醫院 醫學物理科

目的：放射治療的進步允許腫瘤劑量的提昇，從而促進更高的腫瘤控制率，然而其複雜性也需相對的嚴格控制器官運動造成之不確定度。器官運動造成之不確定度主要可分為（一）體內器官運動形成電腦斷層影像之假影；（二）器官運動影響治療中之劑量分布；（三）器官運動影響分次治療間之劑量。對橫隔膜上下之腫瘤，呼吸是影響體內器官運動之主要因素。為了進一步瞭解呼吸造成器官運動之大小，本文探討（一）自由呼吸與閉氣呼吸腫瘤與重要器官之形狀大小差異；（二）呼吸器官在頭尾方向之位移大小；（三）研究以呼吸導引技術改善治療間呼吸週期與器官運動之變異。

材料與方法：本實驗資料來源為西元 2001 年 3 月至 10 月間於本院從事胸腹部放射治療之病患，使用材料與方法包括螺旋式電腦斷層掃瞄機各取兩組影像及運用立即式呼吸同步透視影像觀察體內器官運動。

結果與討論：本分析顯示自由呼吸影像與閉氣影像差別甚大。橫膈膜在頭尾方向之位移可達 15.5 ± 3.5 mm ，胰臟則有 13.7 ± 2.4 mm 。本實驗顯示呼吸導引技術可改善某些呼吸不穩定患者之呼吸週期，從而能有效的尋求進一步控制其體內呼吸器官運動，至於某些病患其呼吸原本即以規律者，呼吸導引對其反而不利。

[放射治療與腫瘤學 2002; 9(1): 1-12]

關鍵詞：治療中、治療間、呼吸器官運動