

Effectiveness of oesophageal gastric junction tumour motion with and without a pneumatic abdominal compression belt in the era of precise image-guided radiation therapy

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INTRODUCTION

In China, 6.791 million and 498 thousand new cases and deaths from gastric cancer occur per year, respectively, which are second only to lung cancer; the proportion of stage II/III gastric cancer is as high as 70.8% (1, 2). Previous studies have shown the important role of radiotherapy in the comprehensive treatment of locally advanced oesophageal gastric junction (EGJ) cancer (3, 4). However, the movement range of the stomach is considerable and variable, causes uncertainty in the precise radiation dose given to the target volume and may lead to an increase in the local recurrence rate (5, 6). Previous studies have reported the application of four-dimensional computed tomography (4DCT) and image-guided radiotherapy (IGRT) in the assessment of organ movement without intervention (7-9). The abdominal compression device, a novel and easy to use equipment, can reduce the complex intra- and

ABSTRACT

Background: To investigate the effect of a pneumatic abdominal compression belt (PACB) on suppressing the movement of primary lesions in the oesophageal gastric junction (EGJ). **Materials and Methods:** Titanium clips A and B were placed on the upper and lower edges of the tumour grossly in 10 patients by using gastroscopy before preoperative chemoradiotherapy. Four sets of images of clips were obtained by 4DCT in each patient with and without PACB. Nine sets of CBCT images were obtained from each patient for analysis. Paired t tests and independent t tests were used to test for differences. **Results:** In the crano-caudal (CC) directions, the internal motion of clip B was smaller with PACB than without PACB ($P=0.000$). The interfraction motion of clip B in the left-right (LR), anterior-posterior (AP) and CC directions was smaller with than without PACB ($P=0.002$, 0.002 and 0.005). We determined that 0.9, 0.9 and 0.9 cm ITV margins in the LR, AP and CC directions are suggested for EGJ lesions with PACB to better cover the tumour movements. **Conclusion:** A pneumatic abdominal compression belt can reduce the intra- and interfraction movements of EGJ tumours during preoperative radiotherapy.

interfraction variation in the movement of the abdominal organs during radiotherapy. The purpose of this study was to investigate the effect of a pneumatic abdominal compression belt (PACB) on suppressing the movement of primary lesions in the EGJ with an imaging technique for precise irradiation dose delivery.

MATERIALS AND METHODS

Patients

Ten patients in this study were identified from a prospective clinical study (clinical trials.gov: NCT03427684) in our centre, and the patients received preoperative concurrent chemoradiotherapy for EGJ cancer between February 2018 and September 2018. Before treatment, all patients were diagnosed with adenocarcinoma by histopathology. The distances between the dentate line of the

oesophagus and stomach, the upper edge of the tumour and the lower edge of the tumour from the incisor were measured by gastroscopy. Titanium clips A and B were placed at the upper edge of the tumour and the lower edge of the tumour, respectively. The median distance between the upper edge and the lower edge of the tumour to the incisors was 41 (38-43) cm and 46 (40-52) cm, respectively. The patient characteristics are shown in table 1. A total of 20 titanium clips were placed at the EGJ for observation and analysis (figure 1). Approval for the study was obtained from the human research ethics committee.

Table 1. Patient characteristics.

Case	Sex	Age	Clinical stage	Distance from dentate line to incisors (cm)	Distance from Clip A to incisors (cm)	Distance from Clip B to incisors (cm)
1	Male	62	T3N1M0	39	38	40
2	Female	61	T3N1M0	38	39	43
3	Male	48	T3N1M0	41	38	44
4	Male	53	T3N1M0	42	42	45
5	Male	55	T3N2M0	42	43	47
6	Female	52	T4N2M0	40	41	46
7	Male	70	T4N1M0	42	40	46
8	Male	67	T3N1M0	41	41	52
9	Female	49	T3N1M0	40	42	50
10	Male	43	T3N1M0	40	41	53

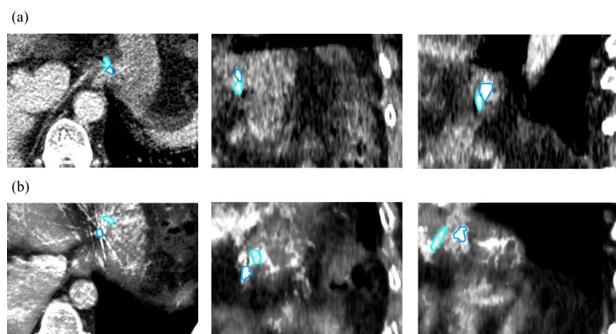


Figure 1. (a) Clips on a fused 4DCT image; (b) Clips on a fused CBCT image.

Positioning methods

All patients were placed in a supine position, they were asked to breathe quietly, and laid on a vacuum cushion for computed tomography (CT) simulation and treatment. The patients fasted for more than 4 hours before the CT simulation or radiotherapy. 4DCT scanning was performed with or without a PACB. The PACB device consists of a pressure band with scales, a pressure gauge and an inflation compression device (Body Pro-Lok ONE, Orange City, Iowa). The patients laid on the vacuum cushion, the pressure band was tied to the abdomen of the patient, and the scale measurements were recorded at the same time. The superior edge of the band was at the inferior border of the patient's ribs (figure 2). The inflation compression device can inflate and pressurize the abdominal belt to 2 kPa.



Figure 2. PACB device, the pressure band with scales.

Image processing method

(1) Intrafraction image acquisition and fusion: All patients underwent 4DCT simulation. A real-time respiratory monitoring device (RPM) system was used to acquire images in different respiratory phases. In each patient, 10 sets of 4DCT images from 0% - 90% of the respiratory phase were automatically reconstructed by the CT image processing system, and all images were transferred to the MIM maestro system (MIM Software Inc., Cleveland, Ohio). The positional data of the two titanium clips located at the EGJ in all phases with or without a PACB were analysed.

(2) Interfraction image acquisition and fusion: In our study, 5 patients completed the whole treatment with a PACB, while the other 5 patients completed treatment without a PACB. All patients underwent cone-beam computed tomography (CBCT) scans for the first 5 fractions and 7th, 12th, 17th and 22nd fractions. The obtained CBCT images were transmitted to the MIM system, and each patient's CBCT images and positioning CT images were registered according to the bone anatomical markers by experienced physicists to eliminate positioning errors. The positional data of the two titanium clips located at the EGJ in all fractions were analysed.

Data assessment

The intrafraction data were assessed on the 4DCT image. The positional change of titanium clips A and B at the EGJ represents the intrafraction motion of the tumour. The titanium clip position in the 0% breath phase was defined as the original geometric centre (intrap0), and the X-axis, Y-axis and Z-axis values of the distance between the geometric centre of the titanium clips and intrap0 were recorded in different image sets. The interfraction data were assessed by CBCT imaging. The titanium clip position in CT simulation is defined as the original geometric centre (interp0), and the X-axis, Y-axis and Z-axis values of the distance between the geometric centre of the titanium clips and interp0 were recorded in different image sets.

According to the method proposed by Van Herk,

the system error (Σ) and the random error (δ) of the intra- and interfraction movement were calculated, respectively, and the internal target volume (ITV) margin was defined⁽¹⁰⁾.

Statistical methods

SPSS 22 software (IBM, Armonk, New York) was used to perform paired t tests for intrafraction movements on the x-, y- and z-axes and independent sample t tests for the interfraction data. One-way ANOVA was used to compare the movements between the intra- and interfraction data.

RESULTS

1. Intrafraction movements: There are 10 sets of 4DCT images of each titanium clip for patients with or without a PACB. The intrafraction movements of clip A with a PACB device were similar in the left-right (LR) and anterior-posterior (AP) directions ($P = 0.482, 0.103$), as those without PACB, but were smaller in the cranio-caudal (CC) directions ($P=0.001$). The intrafraction movements of clip B with PACB were smaller in the LR, AP and CC directions than those without PACB ($P = 0.000, 0.000$ and 0.000). Whether with or without PACB, the intrafraction movement of clip B in the LR, AP or CC directions was significantly greater than that of clip A ($P < 0.05$) (table 2) (figure 3).

Table 2. Movements of the clips marking the oesophageal gastric junction.

		Intra-fraction ($\pm SD$) (cm)			Inter-fraction ($\pm SD$) (cm)		
		Without	PACB	P	Without	PACB	P
LR	Clip A	0.0(± 0.0)	0.0(± 0.0)	0.482	0.6(± 0.6)	0.5(± 0.3)	0.168
	Clip B	0.2(± 0.1)	0.1(± 0.1)	0.000	0.7(± 0.8)	0.2(± 0.2)	0.002
	P	0.000	0.000		0.280	0.047	
AP	Clip A	0.1(± 0.0)	0.0(± 0.1)	0.103	0.4(± 0.2)	0.4(± 0.3)	0.838
	Clip B	0.2(± 0.1)	0.1(± 0.1)	0.000	0.7(± 0.7)	0.2(± 0.2)	0.002
	P	0.003	0.002		0.000	0.050	
CC	Clip A	0.1(± 0.1)	0.0(± 0.1)	0.001	0.4(± 0.3)	0.3(± 0.4)	0.461
	Clip B	0.5(± 0.3)	0.1(± 0.1)	0.000	0.5(± 0.4)	0.2(± 0.2)	0.005
	P	0.000	0.002		0.298	0.053	

PACB: pneumatic abdominal compression belt; LR: left-right direction; AP: anterior-posterior direction; CC: cranio-caudal direction

2. Interfraction movements: Each patient had 1 set of CT simulation images and 9 sets of CBCT images with or without a PACB. The interfraction movement of clip A with PACB was similar in the LR, AP and CC directions as that without PACB ($P = 0.168, 0.838$ and 0.461). The interfraction movement of clip B with a PACB device was smaller in the LR, AP and CC directions ($P = 0.002, 0.002$ and 0.005). The interfraction movement of clip B was greater than that of clip A in the AP direction without PACB ($P = 0.000$) (table 2) (figure 3).

3. ITV margin: The system error (Σ) and random error (δ) of the intra- and interfraction movement were calculated by the vector value of the movements in each direction. To better cover the intra- and

interfraction movement, according to Hugo's formula, the external margins of clip A without a PACB should be 1.9, 1.4 and 1.5 cm in the LR, AP and CC directions, respectively, and the external margins with a PACB should be 1.4, 1.2 and 1.0 cm, with reductions of 26.3%, 14.3% and 33.3%, respectively. The external margins of clip B should be 0.9, 0.9, and 0.9 cm and 2.8, 2.7, and 2.9 cm in the LR, AP and CC directions with or without a PACB, with reductions of 67.9%, 66.7% and 69.0%, respectively⁽⁸⁾.

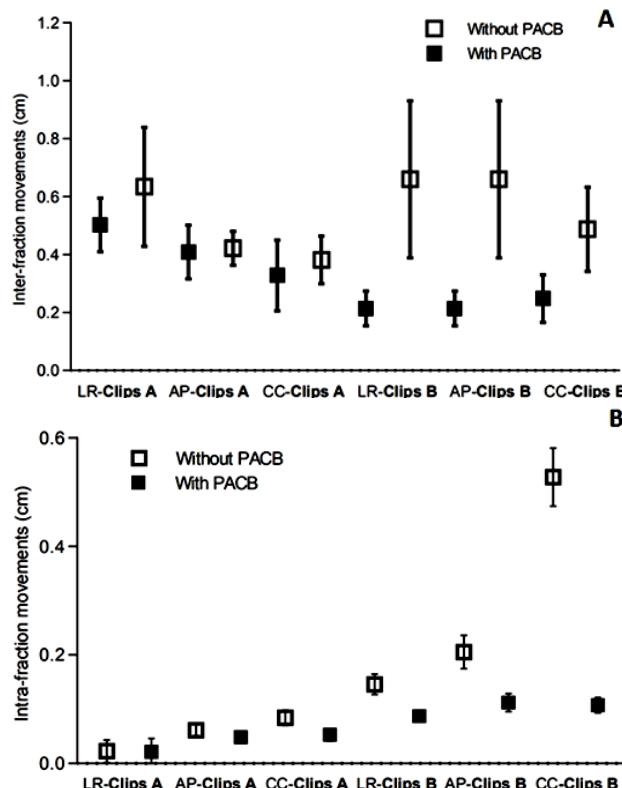


Figure 3. (a) Distribution of the clip intrafraction movements; (b) distribution of the clip interfraction movements (Box: absolute value; Bar: standard deviation; PACB: pneumatic abdominal compression belt; LR: left-right direction; AP: anterior-posterior direction; CC: cranio-caudal direction).

DISCUSSION

The factors that need to be taken into account for the ITV margin include the respiratory movement, gastrointestinal peristalsis and gastric volume. The accuracy of the external margin will directly affect the accuracy of the dose delivery and the safety of the normal tissue⁽¹⁰⁾. The present study comprehensively evaluated the target volume movement with or without PACB using the 4DCT and IGRT techniques. We investigated not only the movement pattern of the radiotherapy target volume for gastric cancer but also the effectiveness of PACB. We provide data to support an extension of the ITV margin and accurate dose delivery.

Previous studies have explored the intra- and interfraction movement patterns and ranges of gastric structures and gastric tumours. Watanabe's

study analysed the gastric motility of patients with gastric lymphoma who received radiotherapy. The results showed that 41.0, 50.8 and 30.3 mm extensions should be added in the LR, AP and CC directions, respectively, to cover the whole gastric area (7). For patients receiving postoperative radiotherapy for gastric cancer, studies have analysed the motility of the remnant stomach. The study involved 15 patients and showed that the motility in the LR, AP and CC directions was 9, 5, and 6 mm, respectively. The ITV margin should be extended by 19.2, 7.8, and 13.5 mm in the corresponding directions, and the motility of the remnant stomach was less than that of the whole stomach (9). The range of gastric movements is wide, and many studies have further explored the motion of gastric tumours. Jin *et al.* used the method of measuring tumour metal markers to analyse the interfraction movement of oesophageal tumours, including some EGJ tumours.

The results showed that the average movement of proximal gastric tumours in the LR, AP and CC directions was 5.4, 1.9 and 4.9 mm, respectively (11). Wang *et al.* measured the movements in patients with EGJ adenocarcinoma during chemo-radiotherapy. The results showed that the absolute values of the movements in the LR, AP and CC directions were 2.88 ± 1.69 mm, 2.90 ± 1.87 mm and 6.77 ± 3.09 mm, respectively (12). Our previous studies explored the range of movement of EGJ adenocarcinomas during preoperative radiotherapy. The results showed that in the LR, AP and CC directions, the intrafraction motion was 0.92 ± 0.95 mm, 2.27 ± 2.73 mm, and 9.95 ± 5.48 mm, respectively, and the motion in the CC direction was the largest ($P = 0.000$). In the LR, AP and CC directions, the interfraction motion was 6.56 ± 4.19 mm, 5.69 ± 3.29 mm, and 6.49 ± 4.37 mm, respectively. The motion was greater in the LR and CC directions than in the AP direction ($P = 0.031$, 0.044). To ensure that 90% of the tumour volume receives 95% of the prescription dose, the LR, AP and CC directions should be extended by 19.4, 14.6 and 27.2 mm for EGJ lesions, respectively (5).

In the present study, the characteristics and range of intra- and interfraction motion without a PACB are similar to those in previous studies. Present techniques, such as deep breath-holding, breathing gating and real-time tracking, can be used to reduce organ movement. However, the motility of gastrointestinal organs is difficult to control. The technique of abdominal compression is simple, compliant and easy to implement. In an early study, Lax *et al.* exerted slight constant pressure on the abdomen, reducing the motion range of liver cancer from 15-25 mm to 5-10 mm (13). Wunderink *et al.* performed a similar method to reduce the median motion of 12 liver tumours by 62% (14). Since then, the effectiveness of this method has been confirmed by a number of research studies (15-17). In recent

years, radiotherapy body position fixation devices have been developed rapidly. Lovelock *et al.* evaluated the role of a pneumatic compression band in reducing the CC motion of markers implanted in liver, adrenal and pancreatic tumours with fluoroscopic imaging methods. The author adjusted the air pressure in the pressure band until the superior-inferior movement of the marker was less than 5 mm under fluoroscopy. The average movement was 11.4 mm (5-20 mm) without using the compression band, which was larger than the 4.4 mm (1-8 mm) with compression (18). Kimberley's study used a similar compression device to reduce the effect of respiratory movement on renal motility (19). This study found that the abdominal compression device can reduce the intrafractional motion of the left kidney in the CC direction from 8 mm (2-18 mm) to 4 mm (2-10 mm) ($P = 0.047$) and that of the right kidney from 10 mm (4-16 mm) to 6 mm (2-10 mm) ($P = 0.051$). Rapheal's research method of reducing the postoperative anastomotic motility of gastric cancer is similar to this study. The results suggest that abdominal compression can reduce the average respiratory deviation from 5.92 mm to 4.15 mm and the average respiratory deviation in the CC direction from 11.3 mm to 7.2 mm (20).

Van Gelder's study is different from most of the other results. Among the 14 patients in this study, not all patients had reduced internal movements of their abdominal organs due to the compression device. The author thinks this may be related to individual differences (21). All previous studies discussed interfraction movements. However, in the process of clinical implementation, both intra- and interfraction movements must be considered. In our study, we discussed the effect of an abdominal compression device on intra- and interfractionation. The results of this study were similar to those of previous studies, which confirmed that the abdominal compression device was effective for intra- and interfraction movements. The intra- and interfraction movements were significantly decreased in all directions. In particular, PACB is more effective on the distal part of an EGJ tumour. The external margins in the LR, AP and CC directions were reduced by 67.9%, 66.7% and 69.0%, respectively, which makes dose delivery more precise for distal gastric cancer.

There are still limitations in this study. First, due to image registration, image quality and other factors, there are errors in the image fusion and CBCT for the observation of the interfraction measurements, which may affect the accuracy of the results. Second, the 4DCT and CBCT images cannot determine the motility and pattern of gastrointestinal peristalsis. Third, there were only 10 patients in this study, so the sample size may not be sufficient, and there may be bias. We believe that the ideal solution for the accurate implementation of dose delivery is to monitor and track the location and movement of tumours in real time. A certain range of ITVs cannot

completely solve the problem of individualized differences. With new developments in technology and equipment, it is hoped that there will be more simple and accurate methods to solve the problem of target motion in radiotherapy in the future.

CONCLUSIONS

In conclusion, the movement of oesophagogastric junction tumours is considerable during preoperative radiotherapy. An abdominal compression device is simple and feasible and can reduce the intra- and interfraction movement of EGJ tumours during preoperative radiotherapy and can improve the delivery accuracy of radiotherapy.

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Conflicts of interests: None to declare.

Ethical considerations: This work was registered as clinical trial at (clinical trials.gov: NCT03427684) and approved by institutional ethical committee.

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