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FULL PAPER

Assessment with cone-beam computed tomography of intrafractional motion and interfractional position changes of resectable and borderline resectable pancreatic tumours with implanted fiducial marker

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Objective: The volume of targets to which a high radiation dose can be delivered is limited for pancreatic radiotherapy. We assessed changes in movements of pancreatic tumours between simulation and treatment and determined compensatory margins.

Methods: For 23 patients, differences in implanted fiducial marker motion magnitude (MMM) and mean marker position (MMP) between four-dimensional CT and cone-beam CT were measured. Subsequently, residual uncertainty was simulated after no action level (NAL) and extended no action level (eNAL) protocols were adopted.

Results: With no correction, respective 95th percentile of MMM were 4.5 mm, 6.2 mm and 16.0 mm and systematic (random) errors of MMP were 2.8 mm (3.3 mm), 3.2 mm (2.0 mm) and 5.9 mm (4.0 mm) in the left-right (L-R), anteroposterior (A-P) and superoinferior (S-I) directions,

so that large margins were required (L-R, 10.5 mm; A-P, 11.7 mm; and S-I, 24.8 mm). NAL reduced systematic errors of MMP, but resultant margins remained large (L-R, 8.0 mm; A-P, 9.6 mm; and S-I, 18.1 mm). eNAL compensated for time trends and obtained minimal margins (L-R, 6.7 mm; A-P, 6.7 mm; and S-I, 15.2 mm).

Conclusion: Motion magnitude and position of pancreatic tumours during simulation are frequently not representative of that during treatment. eNAL compensated for systematic interfractional position change and would be a practical approach for improving targeting accuracy.

Advances in knowledge: Considerably large margins, especially in the S-I direction, were required to compensate for intrafractional motion and interfractional position changes of the pancreatic tumour. An application of eNAL was an effective strategy to diminish these margins.

INTRODUCTION

For patients with pancreatic cancer, radiotherapy combined with chemotherapy has contributed to improving outcomes.^{1–3} Hirata et al⁴ demonstrated that more favourable histopathological outcomes are related to higher radiation doses. However, the volume of targets to which a high radiation dose can be delivered is limited because pancreatic tumours are surrounded by radiation-sensitive organs at risk.

The International Commission on Radiation Units and Measurements Report 83 defined the internal target

volume (ITV) as the clinical target volume (CTV) plus an internal margin taking into account uncertainty of the position of the CTV within the patient, including breathing-induced motion.⁵ Four-dimensional CT (4DCT) is a standard modality to measure the position and motion of organs; but, 4DCT is often acquired only once during treatment simulation. Previous investigators reported considerable intrafractional motion and interfractional position changes of pancreatic tumours.^{6–9} Consequently, a large CTV–planning target volume (PTV) margin would be required to fully compensate for such uncertainty of movement of pancreatic tumours.

Online correction, supposedly yielding the most accurate patient positioning for modern radiotherapy, can minimize setup error and diminish margins.^{10,11} However, it is often difficult to perform online corrections over a finite period of time in clinical practice because such corrections require daily imaging and online image analysis before irradiation. To reduce margins while reducing both workload and concomitant imaging dose, offline correction protocols (OCPs) constitute one solution. Harris *et al*¹² showed the relationship between the margins and the correction frequencies with online correction protocols, OCPs and no correction protocols. In the report, although the required margin was the smallest with the online correction protocol, the offline correction with the lower imaging frequency and the exposure dose achieved compromise reduction of the margin compared with the no correction protocol.¹² The no action level (NAL) protocol, which is both simple and time efficient, obtains systematic errors of displacement measurements in only a few initial imaging sessions.¹³ The systematic error can then be corrected in the subsequent sessions. To monitor systematic errors and correct them during a treatment course, the extended no action level (eNAL) protocol measures displacements weekly and updates the correction values.¹⁴ Previous investigations have shown that eNAL is more effective than NAL for tumours with time trends or sudden transitions during treatment.^{15,16}

The present study consisted of three steps. The first was to assess, by means of cone-beam CT (CBCT), intrafractional motion and interfractional position changes of pancreatic tumours with an implanted fiducial marker and the second was to provide data on the residual uncertainty after the use of OCPs. Third was to determine compensatory CTV–PTV margins for intrafractional and interfractional changes.

METHODS AND MATERIALS

Patients

This study included 23 patients (12 males and 11 females) undergoing pre-operative radiotherapy for either resectable or borderline resectable pancreatic cancer according to the MD Anderson Classification¹⁷ and was approved by the ethics committee. Written informed consent was obtained from each patient. 11 patients had a tumour in the pancreatic head, 11 patients had a tumour in the pancreatic body and 1 patient had a tumour in the pancreatic tail. A fiducial marker (thickness, 0.5 mm; length, 5 mm) (Visicoil, Core Oncology, Santa Barbara, CA) was implanted endoscopically to visualize the position of the pancreatic tumour on the verification images obtained during treatments. For simulation, patients were advised not to eat or drink for 3 h beforehand to avoid unexpected displacement of pancreas due to bulky stomach and were immobilized with a vacuum pillow (Blue Bag, Medical Intelligence, Schwabmuenchen, Germany) in a supine position with the arms raised. Free-breathing 4DCT (CT dose index volume, 77–111 mGy) was acquired using a LightSpeed16 instrument (GE Medical Systems, Waukesha, WI) with the rotation time of 0.5 s to evaluate magnitude of respiratory motion of the target. We instructed patients not to breathe deeply. In case an irregular respiratory pattern was visually judged, the acquisition of 4DCT was stopped and the acquisition was started again.

The slight exhale and inhale breath-holding CT was also acquired because the evaluation of magnitude of respiratory motion by 4DCT was affected by artefact at high frequency (90%).¹⁸ The isocentre was determined on the exhale breath-holding CT, and anterior and bilateral skin marks, which indicated the isocentre by means of the wall-mounted lasers of CT simulation, were placed on patients. The parameters for CT acquisitions were 2.5-mm slice thickness, 512 × 512 pixels matrix and 50-cm field of view. 4DCT images, which consisted of 10 respiratory phase images, were generated by means of the phase-based method using the Advantage Sim workstation (GE Medical Systems). For 4DCT, the mean marker position (MMP) represented the geometric centre between the exhale and inhale phases and the marker motion magnitude (MMM) represented its distance.

The CTV was delineated by means of the treatment planning system (Eclipse; Varian Medical Systems, Palo Alto, CA) to cover the primary pancreatic tumour, retropancreatic regions and some margins. The ITV was generated to encompass the CTVs for each respiratory phase image of the 4DCT and the slight exhale and inhale breath-holding CT. The PTV was created by adding an isotropic margin of 5–10 mm to the ITV depending on the distance between the CTV and the organs at risk such as the stomach and duodenum. Treatment plans were generated using three-dimensional conformal radiotherapy technique with the prescription dose of 50 Gy for PTV (2 Gy/fraction). We used the simultaneous boost technique for delivering a 10 Gy (0.4 Gy/fraction) radiation boost to the roots of the celiac and superior mesenteric arteries, which have been recognized as high-risk areas of perineural invasion.⁴

Acquisition of cone-beam CT

Patients were immobilized on the treatment couch in the same way as for CT simulations. Patient positioning was performed by alignment of skin marks and lasers in the treatment room in the three directions. Thereafter, daily CBCT acquisition (18 mGy) was performed for 10 patients. The parameters for CBCT acquisition were 1-mm slice thickness, 512 × 512 matrix and 45-cm field of view. For 13 patients, the acquisition of CBCT was intended on the first and fifth sessions; then, it was intended on every second day during treatment course. An orthogonal pair of kilovoltage (kV) X-ray images were obtained for remaining sessions. For the latter 13 patients, from second to fourth sessions, 4DCT images were acquired after treatment in the same manner as CT simulation.

The irradiation dose was delivered after bony registration. The bony structures near the PTV in the CBCT were registered with the CT image in the simulation, and the bony structures near the PTV in the kV X-ray images were registered with the digitally reconstructed radiograph created from the simulation CT image. The kV images were used only for patient positioning and not for subsequent analysis because the intrafractional motion and interfractional position changes could not be evaluated by these images.

Since the duration of CBCT (about 1 min) covers many respiratory cycles, the outline form of the marker was mostly rhombus, as shown in [Figure 1](#). For the CBCT, the MMP stood

for the mean position between the upper and lower edge of the marker outline, and the MMM for its distance because the centre of the edge indicated the positions of the centre of the marker at the maximum respiration excursion during acquisition time.

On the basis of the CBCT and 4DCT images during treatment, the displacement of the MMP between simulation and treatment was a measure of the interfractional position change (ΔMMP). For this study, ΔMMP s of NAL and eNAL were retrospectively analyzed and compared with uncorrected ΔMMP . For both the NAL and eNAL protocols, ΔMMP was not corrected for the first three sessions. For NAL, the correction value which was equal to the mean of ΔMMP for the initial three sessions was used for correction of each ΔMMP from the fourth until the final session. For eNAL, the initial correction was the same as for NAL; thereafter, ΔMMP was measured weekly to offline update the correction vector for application in the next week based on linear regression analysis of uncorrected ΔMMP .¹⁴

Data analysis

The following statistical values were calculated: Σ as the standard deviation of systematic errors (Σ_{mmp}) and σ as the root mean square of random errors (σ_{mmp}). For this study, the systematic errors are derived from the mean ΔMMP of each patient, and the random errors are derived from the standard deviation of ΔMMP of every patient. By using these values, the CTV-PTV margin was calculated according to the British Institute of Radiology margin formula:¹⁹

$$\text{CTV-PTV margin} = 2.5 \sqrt{\Sigma_{\text{bone}}^2 + \Sigma_{\text{mmp}}^2} + a + \frac{b}{2} + \beta \left(\sqrt{\sigma_{\text{bone}}^2 + \sigma_{\text{mmp}}^2 + \sigma_p^2} - \sigma_p \right), \quad (1)$$

where Σ_{bone} (1 mm) and σ_{bone} (1 mm) are defined as the residual error after bone alignment which is related to the positioning accuracy of the CBCT, a is the linear treatment planning beam algorithm error and is assumed to be 0 in this study, b is

Figure 1. A sagittal view on cone-beam CT of the implanted fiducial marker for Patient 13: the mean positions between the upper and lower edges of the marker outline (black circle) and the length of the arrows (white arrows) indicate the mean marker position (MMP) and marker motion magnitude (MMM), respectively.

the linear breathing error and is defined as the 95th percentile of MMM encompassing 95% intrafractional motion change during treatment for all patient, σ_p (6.8 mm) is the width of the penumbra for 10×10 -cm field size with 6-MV beam at 10-cm depth²⁰ and β is the planning parameter to take account for different treatment beam configurations [1.04 mm for the left-right (L-R) and anteroposterior (A-P) directions and 1.64 mm for the superiorinferior (S-I) direction].⁷

To evaluate interfractional displacement during a treatment course, a linear regression line was obtained by means of a linear fit through all measured ΔMMP s with no correction. The time trend was determined as the difference between the marker positions in the last and first fractions consistent with the linear regression line. Pearson's correlation coefficient (SPSS v. 16; IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) was performed for the statistical measure of the strength of a linear relationship between the ΔMMP s and the time after the start of the treatment. A p -value < 0.05 was considered to indicate statistical significance.

RESULTS

In total, 448 images (409 CBCT and 39 4DCT images) during treatment course were acquired for 23 patients and retrospectively analyzed in this study. The respective means [95% confidence interval ($\text{CI}_{95\%}$)] of MMM in the L-R, A-P and S-I directions during simulation were 1.5 mm (1.1–1.9 mm), 2.1 mm (1.7–2.5 mm) and 8.2 mm (6.8–9.6 mm) and during treatment they were 2.3 mm (2.2–2.5 mm), 3.1 mm (3.0–3.2 mm) and 9.5 mm (9.2–9.8 mm). MMM was thus larger in the S-I direction than in other directions and varied widely from patient to patient (Figure 2). For a total of 448 fractions, the means ($\text{CI}_{95\%}$) of ΔMMM were 1.3 mm (1.2–1.4 mm), 1.7 mm (1.6–1.7 mm) and 2.6 mm (2.4–2.7 mm) in the L-R, A-P and S-I directions, respectively. It was found that $\Delta\text{MMM} \geq 3$ mm was 7.0%, 18.4% and 36.2%, and $\Delta\text{MMM} \geq 5$ mm was 0.2%, 2.0% and 12.4% in the L-R, A-P and S-I directions, respectively. For the cohort of 13 patients, the difference between the means ($\text{CI}_{95\%}$) of ΔMMM using the 4DCT [39 images; 0.9 mm (0.8–1.0 mm), 1.1 mm (1.0–1.2 mm) and 2.3 mm (2.2–2.4 mm) in the L-R, A-P and S-I directions, respectively] and using the CBCT [156 images; 1.3 mm (1.2–1.4 mm), 1.4 mm (1.3–1.5 mm) and 2.2 mm (2.0–2.4 mm) in the L-R, A-P and S-I directions, respectively] was < 1 mm in the all directions.

The respective means of the ΔMMP (μMMP) in the L-R, A-P and S-I directions were -2.2 mm, 0.4 mm and 1.9 mm for no correction and NAL reduced μMMP (-0.4 mm, 0.4 mm and 1.4 mm in the L-R, A-P and S-I directions, respectively). μMMP with eNAL were < 1 mm in the three directions (-0.1 mm, 0 and 0.6 mm in the L-R, A-P and S-I directions, respectively). Figure 3 shows cumulative frequencies of systematic errors of MMP for each patient in the three directions for each protocol. ≥ 5 mm for no correction were observed in 5, 2 and 10 patients in the L-R, A-P and S-I directions, respectively. For NAL, systematic errors for two patients exceeded 5 mm in the S-I direction only, whereas for eNAL, the largest systematic error was only 3.0 mm in the all directions.

Figure 2. Marker motion magnitude (MMM) during simulation (dashed lines) and during treatments (box plots) in the left-right (L-R) (top), anteroposterior (A-P) (middle) and superoinferior (S-I) (bottom) directions.

The time trend during the treatment course in the three directions is shown in Figure 4. The positive values of time trend indicate that the position of the marker moves to the left, anterior or inferior directions from the first session to the last. The means ($CI_{95\%}$) of the time trend were -0.2 mm (-2.2 – 1.8 mm), 0.1 mm (-1.2 – 1.4 mm) and 2.3 mm (0.2 – 4.4 mm) in the L-R, A-P and S-I directions, respectively. For 8, 5 and 10 patients out of 23 patients, a significant difference was observed in the time trend from 0 mm/day ($p < 0.05$) in the L-R, A-P and S-I directions, respectively.

Table 1 summarizes the statistical values for the margin calculation to compensate for intrafractional motion and interfractional position changes of the pancreatic tumours. As for systematic errors of interfractional position change, Σ_{mmp} of no correction showed large values, especially in the S-I direction, for which it was 5.9 mm. NAL reduced Σ_{mmp} , resulting in 2.2 mm, 1.4 mm and 2.7 mm in the L-R, A-P and S-I directions, respectively, while the application of eNAL produced the smallest residual systematic errors (approximately 1 mm in all directions). In contrast, σ_{mmp} for NAL (4.0 mm, L-R; 2.3 mm, A-P and; 5.1 mm, S-I) as well as that for eNAL (4.0 mm, L-R; 2.5 mm, A-P; 5.4 mm, S-I) were higher in all directions than the corresponding values for no correction (3.3 mm, L-R; 2.0 mm, A-P; and 4.0 mm, S-I). As for intrafractional motion change, the respective values for b -values

were 4.5 mm, 6.2 mm and 16.0 mm, in the L-R, A-P and S-I directions. The CTV-PTV margins were obtained, resulting in 10.5 mm, 11.7 mm and 24.8 mm in the L-R, A-P and S-I directions with no correction protocol. These margins were reduced by NAL, but the reduction was not satisfactorily. With eNAL, the margins were reduced than with NAL, resulting in 6.7 mm, 6.7 mm and 15.2 mm in the L-R, A-P and S-I directions.

DISCUSSION

In this study, substantial intrafractional motion and interfractional changes in the position of the pancreas were observed, including daily variations in motion magnitude due to respiratory motion (Figure 2), systematic displacement of the tumour between simulation and treatment (Figure 3) and time trend during treatment (Figure 4). Previous investigators also reported on the movement of the pancreas during treatment by means of various imaging techniques such as orthogonal X-ray images and iterative CT scans.^{9,21,22} These studies concluded that CT scans during simulation cannot accurately predict the movement of pancreatic tumours and that intrafractional motion and interfractional position changes were not insignificant. However, findings of these studies are not representative of those obtained during a treatment course of several weeks and cannot refer to or discuss margins that compensate for geometric uncertainty of the pancreatic tumours.

Figure 3. Cumulative frequency of systematic errors in pancreatic tumour position with no correction (stars) and with no action level (NAL) (circles) and extended no action level (eNAL) (dots) in the left-right (L-R) (top), anteroposterior (A-P) (middle) and superoinferior (S-I) (bottom) directions.

In recent years, CBCT has been increasingly used in the field of image-guided radiotherapy. Lens et al⁶ compared the magnitude of respiratory-induced motion of pancreatic tumours on a single 4DCT with the motion on daily CBCT during a 3–5-week fractionated radiotherapy scheme. In the report, the difference was ≥ 5 mm for 17% of the 401 fractions in the S–I direction, while no fractions had a difference ≥ 5 mm in the L–R and A–P directions. Similar results were obtained in our study and supported their data that the magnitude of the pancreatic motion varied from day to day, especially in the S–I direction, and it was difficult to expect the pancreatic motion with only one 4DCT at simulation.⁶ Horst et al²³ quantified interfractional position variation of pancreatic tumours using fiducial markers and CBCT images for 13 patients and found that Σ_{mmp} was 3.9 mm, 3.6 mm and 5.5 mm and σ_{mmp} was 3.6 mm, 2.4 mm and 4.7 mm in the L–R, A–P and S–I directions, respectively. Similar results

Figure 4. The time trend during treatment calculated from the linear regression line based on uncorrected displacement of the mean marker position between simulation and treatment in the left-right (top), anteroposterior (middle) and superoinferior (bottom) directions.

were demonstrated in our study that the pancreas moves considerably with respect to bony anatomy from day to day. CTV–PTV margins accounting for intrafractional motion and interfractional position changes for 13 patients (4–10 CBCT images per patient) were reported by Whitfield et al,⁷ and they also reported respective required margins in the L–R, A–P and S–I directions were 12 mm, 12 mm and 23 mm. In this study, a plastic or metal biliary stent was used as a surrogate fiducial marker for 6 out of these 13 patients; but, the position of a biliary stent had a poor correlation with pancreatic tumour position. The strong points of our study included that intrafractional motion and interfractional position changes were assessed by means of fiducial markers for all patients, and a larger number of images (15–28 images per patient) and patients than the previous reports were analyzed. Although our results supported the findings reported by Whitfield et al,⁷ that is

Table 1. Clinical target volume (CTV)–planning target volume (PTV) margins for geometric uncertainty in marker motion magnitude and mean marker position (MMP)

Parameters for margin calculation	L–R (mm)	A–P (mm)	S–I (mm)
Systematic errors			
Residual error after bone alignment (Σ_{bone})	1	1	1
Interfractional position change (Σ_{mmp})			
No correction	2.8	3.2	5.9
NAL	2.2	1.4	2.7
eNAL	0.8	0.8	1.3
Linear			
Treatment planning beam algorithm error (a)	0	0	0
Breathing motion error (b)	4.5	6.2	16.0
Random errors			
Planning parameter (β)	1.04	1.04	1.64
Beam penumbra width (σ_p)	6.8	6.8	6.8
Residual error after bone alignment (σ_{bone})	1	1	1
Interfractional position change (σ_{mmp})			
No correction	3.3	2.0	4.0
NAL	4.0	2.3	5.1
eNAL	4.0	2.5	5.4
CTV–PTV margins			
BIR margin formula: $2.5\sqrt{\Sigma_{\text{bone}}^2 + \Sigma_{\text{mmp}}^2} + a + \frac{b}{2} + \beta(\sqrt{\sigma_{\text{bone}}^2 + \sigma_{\text{mmp}}^2 + \sigma_p^2} - \sigma_p)$			
No correction	10.5	11.7	24.8
NAL	8.0	9.6	18.1
eNAL	6.7	6.7	15.2

A–P; anteroposterior; BIR, British Institute of Radiology; eNAL, extended no action level; L–R, left–right; NAL, no action level; S–I, superoinferior.

to say, a larger margin was required, especially in the S–I direction, larger margins were required compared with their findings. It is possible that the large margins are attributed to the physical aspect of pancreatic tumours investigated in this study, which are either resectable or borderline resectable tumours, because these tumours are supposed to be more unstable than locally advanced unresectable tumours invading and living in surrounding tissues. The present study indicated that asymmetrical CTV–PTV margins (10 mm in the L–R and A–P directions and 20 mm in the S–I direction), which are widely used for pancreatic radiotherapy,^{7,8} were insufficient to adequately irradiate resectable or borderline resectable pancreatic tumours with a high probability of success with only bony registration. In this study, bony registrations were adopted for the irradiation instead of the fiducial registration for the following reasons: (1) the daily distance between the pancreas and bony structure was found to be substantially large, but the distance between the region of radiation boost (the celiac and superior mesenteric) and the bony structure did not differ a lot, as described by Wysocka *et al*,⁹ (2) the prescription dose to the roots of the region of the celiac and superior mesenteric arteries is 2.4 Gy/fraction, while the prescription dose to the PTV is 2 Gy/fraction; and (3) the gross tumour can be extirpated by

subsequent surgery, but it is difficult to extirpate the areas of perineural invasion.

Even though our study dealt with the relatively large number of patients in this area for estimating CTV–PTV margins, our data could not support in-depth analysis of the effect of the marker migration and the location of the tumour (head, body or tail). The difference between the fast 4DCT scan and the slow CBCT scan may affect the results of MMM and MMP. MMM and MMP on the CBCT image were calculated on the basis of the blurred marker outline, which indicated the maximum peak-to-peak distance during image acquisition, while those on the 4DCT were derived from the respiration excursion at one respiratory cycle. This methodology may be affected by an irregular breathing or the daily variation of the respiratory cycle of a patient during CBCT acquisition. In this study, for the cohort of 13 patients, the difference between the means of measured ΔMMM using the 4DCT and using the CBCT was <1 mm in all directions, and therefore we consider that this uncertainty caused by the irregular breathing was limited. The methodology presented by Lens *et al*⁶ may be suitable for assessing changes in pancreatic motion with an irregular respiratory cycle. In their study, each projection data of CBCT were analyzed, and the

tumour motion was determined as the mean peak-to-peak motion of respiratory motion during CBCT acquisition. Fluoroscopy as used in the real-time tumour-tracking technique enables an evaluation of MMM and MMP during dose delivery, while CBCT acquisition has to be performed before dose delivery.²⁴ The partial volume effect also affects the results of MMM and MMP, especially in the S–I direction, by means of 4DCT (2.5-mm slice thickness) and CBCT (1-mm slice thickness). This effect may overestimate the marker size and affect the accuracy of the MMM and MMP. Moreover, in this study, the MMP was determined as the geometrical centre of the marker outline of the CBCT or the exhale and inhale phase 4DCT images; but, the mean position of the moving target was closer to the exhale phase than the inhale phase. This could lead to an overestimate of the MMP if the MMP displacement is taken into account without further corrections on time weighting. Despite these limitations, our quantitative data provide an important contribution to the unclear area of study for delivering an adequate dose to pancreatic tumours.

To the best of our knowledge, this study is the first report on implementation of OCPs for pancreatic tumours. NAL could reduce the effect of systematic interfractional position change, which was related to the dominant factor for margin calculation, and previous investigations have shown the effect of NAL for various treatment sites.^{12,25} However, a large margin in the S–I direction was still required in our study owing to the large time trend. eNAL achieved further reduction in Σ_{mmp} than in NAL, indicating that weekly corrections could effectively reduce systematic errors for patients with time trend. The large interfractional position changes including time trend may be explained by the relative fullness of surrounding organs

(stomach and bowels), weight loss or gradual changes in muscle tension.²⁶ Although OCPs can diminish the systematic interfractional position changes, intrafractional motion cannot be corrected. To achieve further reduction of margins than the use of OCPs, respiratory-gating dose delivery technique will be a solution. Ge et al²⁷ demonstrated a tight margin with a 3 mm margin for CTV–PTV expansion and an additional 2.5-mm safety margin for gating accuracy for patients with abdominal cancer. However, this approach is technical and resource dependent, and conformal radiotherapy under free breathing is still an option to treat pancreatic cancer. In clinical practice, a way for further margin optimization on the basis of patient-specific linear breathing error (*b*) instead of a population-based method will be a proper approach for avoiding extrairradiation to the normal tissues because the magnitude of pancreatic tumour varied widely from patient to patient.

CONCLUSION

Our results demonstrated that the CTV–PTV margin used conventionally could not fully compensate for pancreatic motion during radiotherapy owing to respiratory motion, systematic displacement and large time trend of the tumour. The eNAL compensated for systematic displacement of the tumour with smaller workload than online protocol and would be a practical approach for improving targeting accuracy.

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