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Reproducibility and stability of voluntary deep inspiration breath hold and free breath in breast radiotherapy based on real-time 3-dimensional optical surface imaging system

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Abstract

Background The aim of this study was to evaluate the inter-fraction reproducibility and intra-fraction stability of breast radiotherapy using voluntary deep-inspiration breath hold (DIBH) and free breathing (FB) based on an optical surface imaging system (OSIS).

Methods Seventeen patients (510 breath-hold sessions) treated using a field-in-field (FiF) technique and twenty patients (600 breath-free sessions) treated with a volume-modulated arc therapy (VMAT) technique were included in this retrospective study. All the patients were positioned with the guidance of CBCT and OSIS, and also monitored with OSIS throughout the whole treatment session. Eight setup variations in three directions were extracted from the treatment reports of OSIS for all sessions and were subsequently manually introduced to treatment plans, resulting in a total of 296 perturbed plans. All perturbed plans were recalculated, and the dose volume histograms (DVH) for the target and organs at risk (OAR) were analyzed.

Results The OSIS and CBCT for both DIBH and FB treatments showed a good agreement of less than 0.30 cm in each direction. The intra-fraction respiratory motion data during DIBH were −0.06 ± 0.07 cm, 0.12 ± 0.15 cm, and 0.12 ± 0.12 cm in the lateral, longitudinal, and vertical directions, respectively; for FB, the respiratory motion data were −0.02 ± 0.12 cm, 0.08 ± 0.18 cm, and 0.14 ± 0.20 cm, respectively. For the target, DIBH plans were more sensitive to setup errors; the mean deviations in D_{95} for CTV were 39.78 Gy–40.17 Gy for DIBH and 38.46 Gy–40.52 Gy for FB, respectively. For the OARs, the mean deviations of V_{10}, V_{20}, and D_{mean} to the heart; V_5, V_{20}, and D_{mean} to the ipsilateral lung; and D_{mean} to the breast were lower for the FB plan compared with the DIBH plan.

Conclusion Based on OSIS, our results indicate that both DIBH and FB can provide good reproducibility in the inter-fractions and stability in the intra-fractions. When the patient respiratory motion is large, the FB technology has greater possibility for the undercoverage of the target volume, while DIBH technology is more likely to result in increases in dose to OARs (the lung, heart, and contralateral breast).

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Keywords Surface guided radiotherapy, Deep inspiration breath hold, Volumetric modulated arc therapy, Breast cancer

Background

Breast cancer is one of the most common cancers in women worldwide. This is also reflected in China, where it accounted for 16.72% (306,000) of all cancers in women in 2016 [1]. However, breast cancer has a high 5-year overall survival rate of 90% due to advances in prevention, early diagnosis, and multidisciplinary therapy. Radiotherapy (RT) is an integral part of the multidisciplinary management of breast cancer [2–5].

For left sided breast cancer, deep inspiration breath hold (DIBH) with field in field (FiF) and volumetric modulated arc therapy (VMAT) techniques have become a standard method in radiotherapy modality [6–10]. FiF strategy refers to two open opposing tangential radiation fields with several segments (usually two to four) with a multileaf collimator (MLC) instead of wedges and VMAT refers to two round-trip arcs with plenty of segments than FiF. Many studies have been published in recent years to demonstrate the advantages of DIBH radiotherapy in breast cancer treatments, showing a reduced irradiation dose for nearby organs at risk (OAR) and maintaining a better target dose coverage, due to an increased distance between the target and the heart [11, 12]. Moreover, VMAT resulted in even better target coverage, sparing OARs for complex targets, such as concave-shaped breasts and breast cancer with supraclavicular lymph nodes metastasis [9, 10].

Patient positioning and respiratory movement are major concerns in dose delivery in FB and DIBH radiotherapy for breast cancer. This is because dose delivery deviation is mainly due to inaccuracy in patient positioning and patient respiratory movement throughout treatment, respectively. Regarding patient position, we can employ many additional imaging techniques, such as cone beam computed tomography (CBCT) and kilovoltage (kV) and megavoltage (MV) panel images to ensure accurate positioning. However, the disadvantages of such additional imaging are the associated extra radiation dose and the difficulty in monitoring patient respiratory motion for the whole treatment time. In recent years, optical surface imaging has provided the potential to monitor patient movement in real time during treatment and to help breast cancer patients with pre-treatment positioning without the delivery of ionizing radiation [13, 14]. Thus, surface-guided radiotherapy (SGRT) has been developed, which uses a 3-dimensional (3D) model of the skin surface for intrafraction patient positioning and monitoring for respiratory motion. The AlignRT system (Vision RT, London, UK) has been evaluated in this study.

Previous studies have only assessed setup errors with surface imaging system for a single technique [13, 14]. To our knowledge, studies comparing FB and DIBH in breast radiotherapy using the SGRT technique and the dosimetric effect of patient respiratory motion are rare. Therefore, in this paper, we aimed to evaluate the following: (1) the inter-fraction clinical performance of pre-treatment positioning (setup errors) of the AlignRT system as compared with the XVI system and to evaluate the reproducibility of FB and DIBH treatments; (2) the intra-fraction respiratory motion data acquired by SGRT in breast patients with FB and DIBH and to evaluate the stability of FB and DIBH treatments; (3) the dosimetric effect of intra-fraction respiratory motion acquired by SGRT in breast patients with FB and DIBH.

Methods

Patient selection and contouring

Between February 2022 and October 2023, 17 patients with left-sided breast cancer treated with surface-guided voluntary DIBH and 20 patients with left-sided or right-sided breast cancer treated by surface guided FB at the Department of Radiation Oncology, Sichuan Cancer Hospital, were recruited for the retrospective study. This retrospective study was approved by the Ethics Committee of our hospital (Approval Number No. SCCHEC-02-2021-026). The mean age and median age were 57.6 ± 12.2 yrs and 55.2 yrs, respectively. Patient characteristics and radiotherapy prescription are summarized in Table 1.

The patients were immobilized with a WingStep (IT-V, Innsbruck, Austria) breast board in the supine position with their arms above their head. CT scans with a 3 mm slice thickness were acquired with a 16-slice Brilliance Big Bore CT (Philips Medical Systems, Cleveland, OH, USA). The CT scans were performed in free breathing (FB) and breath hold (BH) positions or with FB alone for their use in DIBH or FB treatment, respectively. After the CT scan, imaging datasets were imported to MIM Version 7.0.5 (MIM Software Inc.) for contouring. The clinical target volume (CTV) and organ at risks (OARs) were delineated on each DIBH and FB scan by experienced radiation oncologists of the breast department. For the DIBH group, the clinical target volume (CTV_{DIBH}) encompassed the whole breast, excluding chest wall muscles, ribs, and pectoralis muscles, while for the FB

Table 1 Patient characteristics and radiotherapy prescription of the study

Parameters	No. (%)
Age (yrs.)	
Mean ± SD	57.6 ± 12.2
Median (range)	55.2 (50–68)
Tumors site	
Left	27 (73%)
Right	10 (27%)
Tumor stage	
pT1	23 (62.2%)
pT2	8 (21.6%)
pT3	5 (15.5%)
pT4	1 (2.7%)
Number of patients	
DIBH	17 (45.9%)
FB	20 (54.1%)
Nodal status	
pN0	26 (70.3%)
pN1	9 (24.3%)
pN2	1 (2.7%)
pN3	1 (2.7%)
Fractionation	
Hypo-fractionated (2.67 Gy/15 F)	17 (45.9%)
Hypo-fractionated with simultaneously integrated boost (2.67 Gy and 3.2 Gy/15 F)	20 (54.1%)

group, CTV_{FB} encompassed the whole breast and supraclavicular fossa region, and gross tumor volume (GTV) included the tumor bed, visible surgical clips, and anatomical distortion. The planning target volume (PTV_{FB} and PTV_{DIBH}) was generated as an isotropic expansion of the CTV_{FB} and CTV_{DIBH} with a 3 mm margin in all directions, while PGTV was generated as an isotropic expansion of the GTV with a 5 mm margin in all directions. The OARs of this study were contoured on the CT image, which included the lung, heart, spinal cord, breast, liver, thyroid, esophagus, and trachea. Patients were treated either with hypo-fractionated therapy with simultaneously integrated boost (2.67 Gy for PTV_{FB} and 3.2 Gy for PGTV in 15 fraction) for FB or hypo-fractionated therapy for DIBH (2.67 Gy for PTV_{DIBH} in 15 fractions).

SGRT workflow

The AlignRT system (Vision RT, London, UK) employs a combination of light projectors, and the position of the patient is monitored with three cameras that generate a 3D map of the patient's topography. Moreover, the system consists of software and a computer workstation, does not require the use of body film, and produces no irradiation during the imaging process. DIBH and FB patients were set up and monitored throughout treatment using AlignRT in real-time mode. In real-time mode, AlignRT displays three axis linear translations (vertical, lateral and longitudinal), the root mean square of the linear translations (RMS), and three axis rotations (yaw, pitch, and roll) (Fig. 1). The tolerance of linear translations and rotations is set to 3 mm and 3˚ based on manufacture recommend, respectively.

For both DIBH and FB treatments, the SGRT workflow consists of initial setup in the AlignRT system, and preparation before DIBH and FB treatment and daily treatment (Fig. 2). The workflow of DIBH is the same as that published by our group in other, previous studies [15, 16]. First, for the DIBH and FB treatments, import the DIBH and FB body contour into the Align RT workstation, delineate the surface-monitoring region for the initial setup position. Second, the AlignRT and CBCT are used for daily patient setup and to assess the agreement of AlignRT with CBCT. Based on the system prompt for setup errors, manually adjust the rotational direction by ≤ 3°, and then perform linear translation by ≤ 3 mm. Third, acquire the CBCT images and record the deviations from the XVI workstation. Then, shift the couch based on CBCT registration and capture the present surface image as a reference image. Finally, turn on the gating switch in the Align RT workstation and activate the Elekta Response controller to monitor patient respiratory motion during beam delivery.

Figure 3 shows the result of a typical breath-hold session with DIBH treatment and a free breath session with FB treatment, as tracked in the AlignRT system in a vertical direction and as printed from the system's session reports, respectively. The shaded areas of Fig. 3 (A) indicate automatically gated beam hold when predetermined tolerance limits (± 3 mm) are exceeded.

Treatment planning

All clinical treatment plans were generated using Pinnacle TPS (version 9.10, Philips Radiation Oncology Systems, Fitchburg, WI, USA). Intensity modulation was performed using the direct machine parameter optimization (DMPO) algorithm. The collapsed cone (CC) algorithm was applied for final dose calculations, with a grid size of 3.0 mm. For the DIBH group, all plans used the tangential field-in-field (TFiF) technique, and treatments were performed with an Elekta Infinity linear accelerator (Elekta, Stockholm, Sweden) using 6 MV photons. Moreover, to be eligible for DIBH treatment, patients must be able to hold their breath for at least 25 s and demonstrate a stable breath-hold position. The Infinity linear accelerator is equipped with a multileaf collimator, which has 40 leaf pairs of 0.5 cm thickness. The TFiF treatment plan

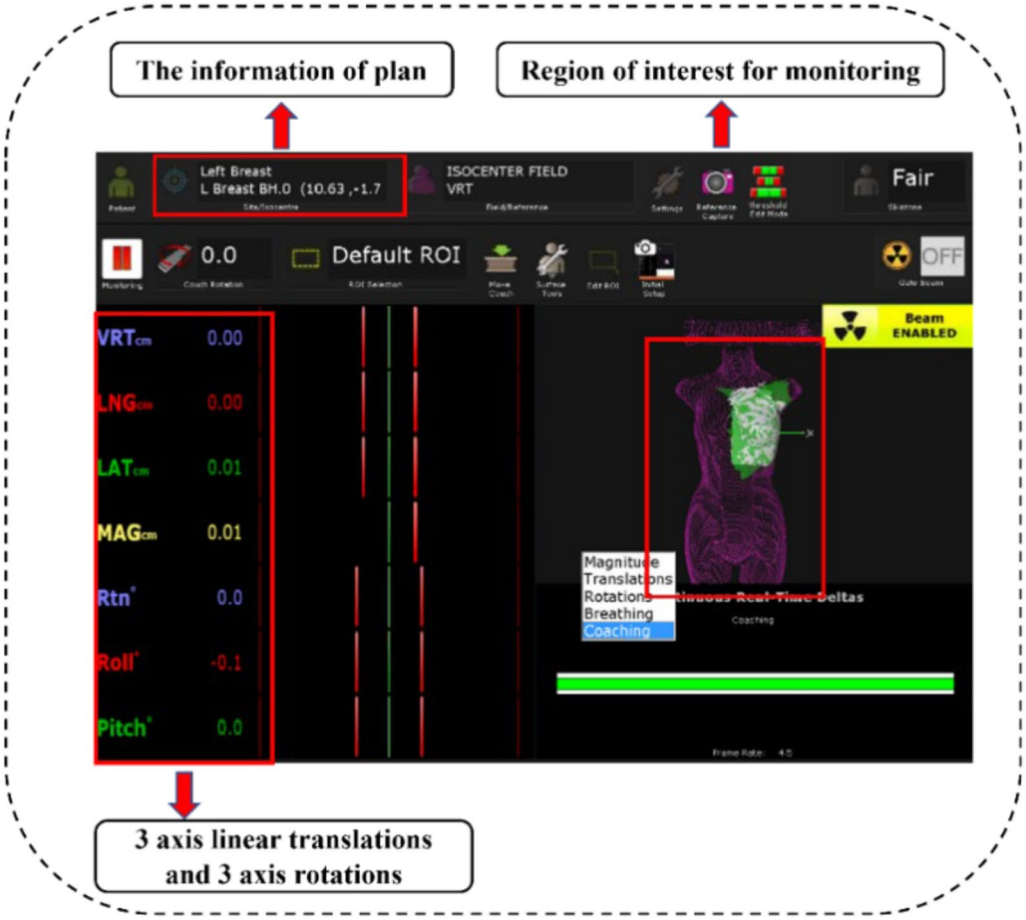

Fig. 1 An example of the AlignRT monitoring screen during treatment

consists of two opposing tangential fields with gantry angles between 300˚ and 315˚ for the medial beam and 120˚ and 135˚ for the lateral beam, with two or three sub-segments included. For the FB group, all plans had two arcs, with an angle ranging from 181˚ to 30˚ for the right-side breast cancer patients and from 330˚ to 179˚ for the left-side breast cancer patients, respectively. The mean deviation and standard deviation in three directions of DIBH and FB were acquired from the AlignRT system during beam-on time. Then, eight setup variations with respect to the ± 95% confidence interval of deviation distribution (the mean deviation of three directions ± (1.96*standard deviation)) were introduced for each reference DIBH and FB plan to generate eight new plans, shifting the isocenter from its reference position in three directions. If the original isocenter is (x, y, z), the mean and standard deviations are a ± a1, b ± b1 and c ± c1 in three directions, respectively, the new eight plans as detailed in Table 2. A total of 296 perturbed plans were recalculated with these new isocenters and without changing any optimized parameters compared with the original plan ($plan_{org}$), four groups of plans, $DIBH_{min}$, $DIBH_{max}$, FB_{min} and FB_{max}, were selected according to the maximum and minimum deviations of dosimetric parameters.

The dose constraints for the PTV were 1) $D_{95} \geq 100\%$ of the prescribed dose, and 2) $D_2 \leq 110\%$ of the prescribed dose. For the OAR, both the DIBH and FB plans met the dose volume limits, as detailed in Table 3 [17, 18].

Evaluation of dosimetric data

The dosimetric quality of the treatments was measured using a dose-volume histogram (DVH). For CTV, the target coverage (D_{95}, D_{98}, D_{99}, D_{mean}, D_{50}, and D_2) and the conformity index (CI) were reported [19–21].

CI was defined as

$$CI = (TV_{PV})^2/(TV \times PV) \quad (1)$$

where PV is the volume covered by the prescription isodose. The CI values range between 0 and 1, and a CI close to 1 represents better conformity. Furthermore,

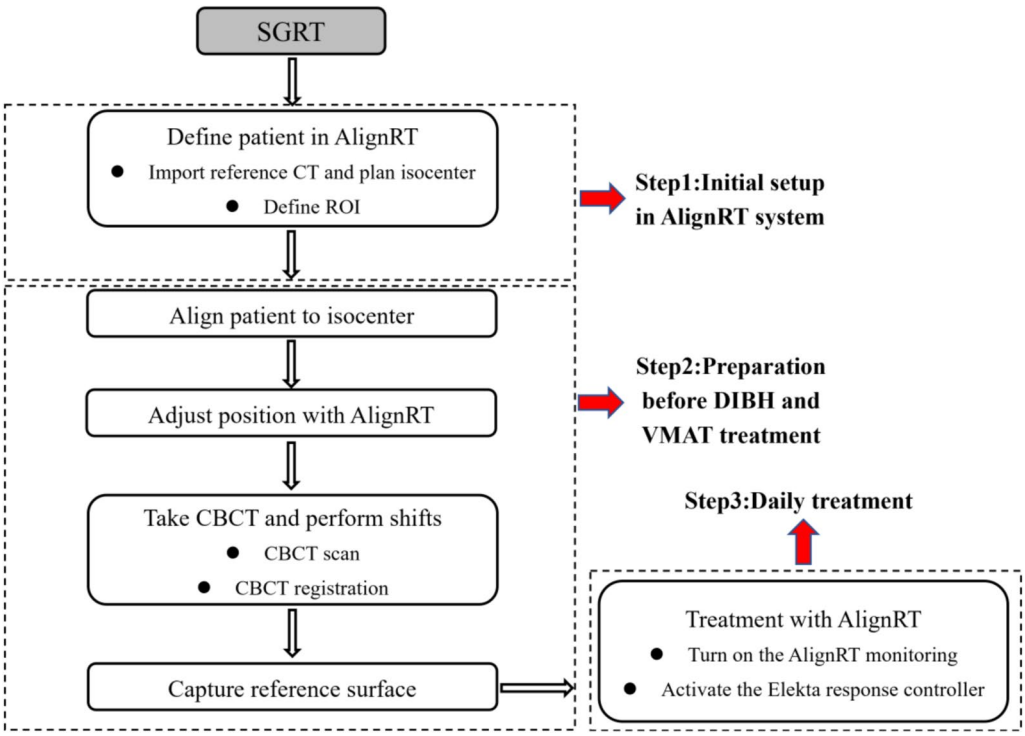

Fig. 2 The workflow of DIBH and FB with SGRT

dosimetric parameters were evaluated for the lung, heart, spinal cord, breast, liver, thyroid, esophagus, and trachea. The dose administered to the ipsilateral lung was evaluated using V_5, V_{10}, V_{20}, and the D_{mean}, and for the contralateral lung using V_5, V_{10}, and the D_{mean}; the D_{max} of the spinal cord was also recorded. For the heart, the V_5, V_{10}, V_{20}, and the D_{mean} were scored; D_{max} and D_{mean} for the esophagus; D_{mean} for the thyroid; D_{mean} for the trachea; and V_5 and D_{mean} for the liver. D_x represented the dose (in Gy) received by x% of the volume, V_y the volume (in percentage) receiving y Gy, D_{max} the maximum dose, and D_{mean} the mean dose.

Datasets were statistically analyzed using SPSS 19.0 software (IBM, New York, USA). The dosimetric parameters of the PTV and OARs were compared using the Wilcoxon Cox test. A p-value < 0.05 indicates statistically significant differences.

Results

Surface imaging system validation

In summary, we analyzed 255 treatment fractions and 510 breath-hold sessions during beam-on time, which included 12,750 points with a one-second interval for DIBH treatment, and 300 treatment fractions and 600 breath-free sessions during beam-on time, which included 69,000 points with a one-second interval for FB treatment. The mean treatment session times were 50 s and 230 s for DIBH and FB treatment, respectively. The setup errors (lateral, longitudinal, and vertical) across all patients and sessions during the CBCT session from the AlignRT system and XVI system for DIBH and FB treatments are shown in Table 4. For both treatments, the setup errors were below 0.30 cm. There were significant differences found in the vertical direction for FB and DIBH treatments ($p < 0.05$), and no significant differences were found in other directions for FB and DIBH treatments ($p > 0.05$). The setup deviations between AlignRT and XVI for DIBH treatment were 0.04 cm, 0.08 cm, and 0.02 cm in lat, lng, and vrt directions, respectively, and 0.16 cm, 0.30 cm, and 0.11 cm in lat, lng, and vrt directions for FB treatment, respectively.

Table 5 shows the result of intra-fraction respiratory motion at beam-on time in terms of mean, standard deviation and ± 95%-confidence interval (CI) for DIBH and FB treatments, respectively. Overall, the mean changes for the maximum magnitude of the respiratory motion on the vertical axis were 0.12 ± 0.12 (± 95%-confidence interval: [−0.12–0.36] cm) and 0.14 ± 0.20 (± 95%-confidence interval: [−0.25–0.53] cm) cm for DIBH and FB treatment, respectively. Along the lateral and longitudinal axes, changes were quite similar: −0.06 ± 0.07, 0.12 ± 0.15, −0.02 ± 0.06, and 0.08 ± 0.08 mm for DIBH and FB treatments, respectively. Figure 4 shows histograms representing the differences between conventional patient

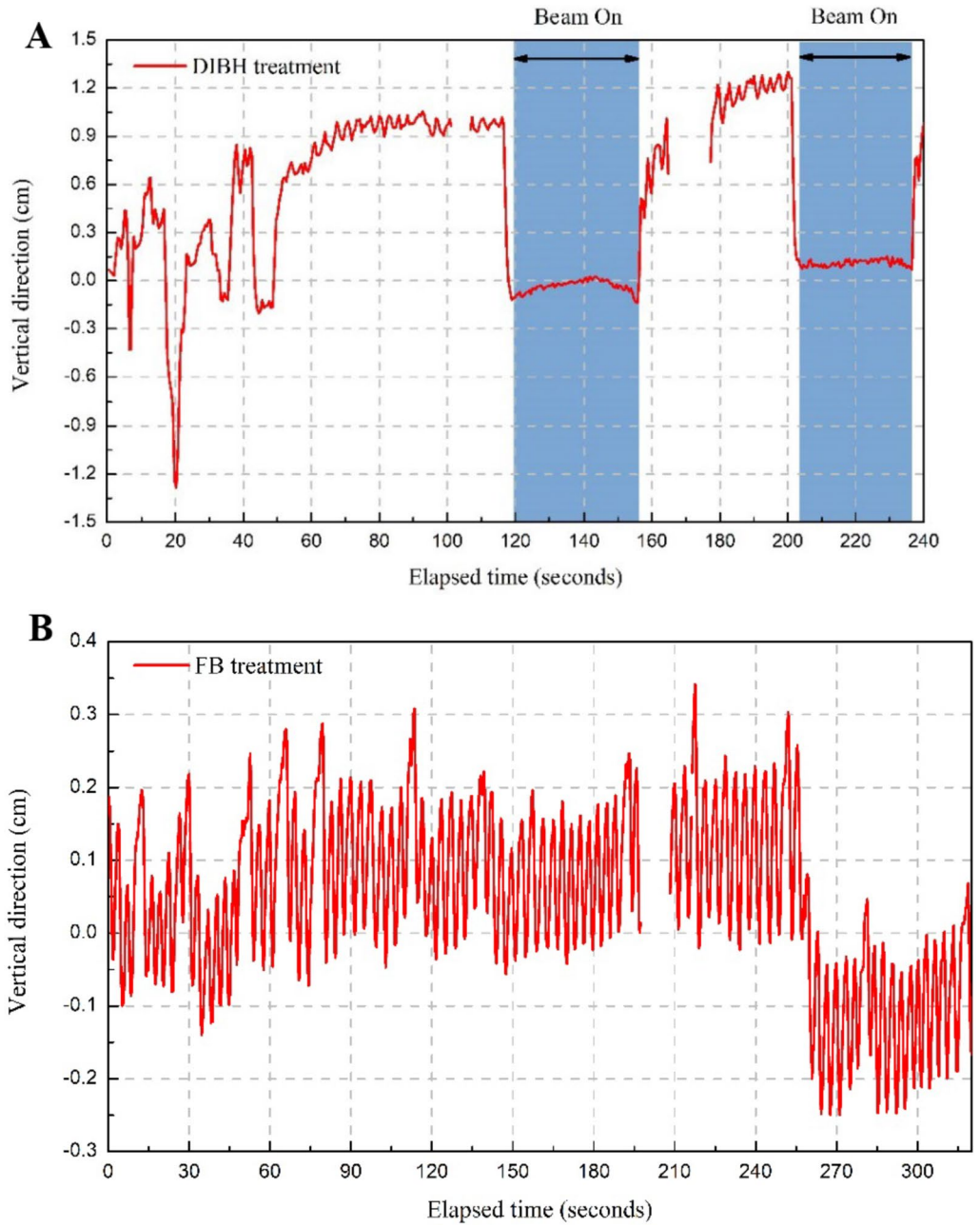

Fig. 3 The result of typical session as tracked in the AlignRT system in vertical direction: **A** DIBH treatment; **B** FB treatment

positioning and the surface-based alignments for DIBH and FB treatment. More than 61.67% and 78.14% of the deviations were smaller than 2 mm in the lateral direction for DIBH and FB, respectively; more than 58.48% and 68.72% of the deviations were smaller than 2 mm in the longitudinal direction for DIBH and FB, respectively; and more than 63.76% and 75.35% of the deviations were smaller than 2 mm in the vertical direction for DIBH and FB, respectively.

Target doses

The CTV dosimetric parameters (mean and standard) obtained for the DIBH and FB treatments are shown in Table 6 and Fig. 5. The target coverage of the original plans was clinically acceptable for both techniques, with D_{95} values of 40.1 ± 1.36 Gy and 40.52 ± 0.19 Gy for DIBH and VMAT treatments, respectively. For DIBH treatment, there was no significant difference in the D_{99} of the CTV between $DIBH_{org}$ and $DIBH_{max}$ plans

Table 2 The detail of new eight plans

Plans	Isocenter (cm)		
	lateral	longitudinal	vertical
plan1	x + (a + a1*1.96)	y + (b + b1*1.96)	z + (c + c1*1.96)
plan2	x + (a + a1*1.96)	y + (b + b1*1.96)	z−(c−c1*1.96)
plan3	x + (a + a1*1.96)	y−(b−b1*1.96)	z + (c + c1*1.96)
plan4	x + (a + a1*1.96)	y−(b−b1*1.96)	z−(c−c1*1.96)
plan5	x−(a−a1*1.96)	y + (b + b1*1.96)	z + (c + c1*1.96)
plan6	x−(a−a1*1.96)	y + (b + b1*1.96)	z−(c−c1*1.96)
plan7	x−(a−a1*1.96)	y−(b−b1*1.96)	z + (c + c1*1.96)
plan8	x−(a−a1*1.96)	y−(b−b1*1.96)	z−(c−c1*1.96)

Table 3 Dose-volume constraints for OARs

OARs	Dose volume parameters
Spinal cord	$D_{max} < 40$ Gy
Ipsilateral lung	$D_{mean} < 15$ Gy, $V_{20} < 30\%$, $V_5 < 50\%$
Contralateral lung	$V_5 < 20\%$
Heart (left-side breast cancer)	$D_{mean} < 15$ Gy, $V_5 < 50\%$
Heart (right-side breast cancer)	$D_{mean} < 15$ Gy, $V_5 < 50\%$
Liver	$V_5 < 20\%$
Thyroid	$D_{mean} < 30$ Gy

($p > 0.05$), and the differences in other parameters were statistically significant ($p < 0.05$). The mean absolute differences ($DIBH_{max}$-$DIBH_{min}$) ΔD_{95}, ΔD_{98}, ΔD_{99}, ΔD_{mean}, ΔD_2, ΔD_{max}, ΔD_{50}, and ΔCI were 0.39 Gy, 0.58 Gy, 1.0 Gy, 0.56 Gy, 1.33 Gy, 1.67 Gy, 0.77 Gy, and 0.12 Gy, respectively. For VMAT treatment, there was no significant difference in the D_{98} and D_{99} of the CTV between FB_{org} and FB_{max} plans ($p > 0.05$), and the differences in other parameters were statistically significant ($p < 0.05$). The mean absolute differences (FB_{max}-FB_{min}) ΔD_{95}, ΔD_{98}, ΔD_{99}, ΔD_{mean}, ΔD_2, ΔD_{max}, ΔD_{50}, and ΔCI were 2.3 Gy, 3.96 Gy, 4.41 Gy, 1.27 Gy, 2.12 Gy, 3.21 Gy, 1.11 Gy, and 0.07 Gy, respectively. The mean absolute differences in CTV between $DIBH_{min}$ and $DIBH_{max}$ and FB_{min} and FB_{max} are shown in Fig. 6a. In Fig. 6a, for the CTV, the absolute differences in the dosimetric parameters of DIBH treatment were lower than the FB treatment.

OARs doses

OARs' DVH dosimetric parameters (mean and range values), obtained for the original ($DIBH_{org}$ and FB_{org}) and perturbed ($DIBH_{min}$, $DIBH_{max}$, FB_{min} and FB_{max}) DIBH and FB treatments, are shown in Table 7 and Fig. 6. The mean absolute differences ($DIBH_{max}$-$DIBH_{min}$) ΔV_5, ΔV_{10}, ΔV_{20} and ΔD_{mean} of the heart; ΔD_{max} of the spinal cord; ΔV_5, ΔV_{10}, ΔV_{20} and ΔD_{mean} of the ipsilateral lung; ΔV_5, ΔV_{10} and ΔD_{mean} of the contralateral lung; ΔD_{mean} of the breast; ΔD_{mean} of the thyroid; ΔD_{mean} of the trachea; and ΔD_{max} and ΔD_{mean} of the esophagus were 11.15%, 8.64%, 6.63%, 2.99 Gy, 0.1 Gy, 11.98%, 11.64%, 11.08%, 4.23 Gy, 0.3%, 0.13%, 0.16 Gy, 2.02 Gy, 0.19 Gy, 0.23 Gy, 0.34 Gy, 0.18 Gy, 0.12% and 0.13 Gy, respectively. The mean absolute differences (FB_{max}-FB_{min}) ΔV_5, ΔV_{10}, ΔV_{20} and ΔD_{mean} of the heart; ΔD_{max} of the spinal cord; ΔV_5, ΔV_{10}, ΔV_{20} and ΔD_{mean} of the ipsilateral lung; ΔV_5, ΔV_{10} and ΔD_{mean} of the contralateral lung; ΔD_{mean} of the breast; ΔD_{mean} of the thyroid; ΔD_{mean} of the trachea; and ΔD_{max} and ΔD_{mean} of the esophagus were

Table 4 The difference of setup errors (mean ± standard) between the AlignRT system and XVI system for the DIBH and FB treatment during a CBCT session

Parameters	DIBH (cm)			FB (cm)		
	AlignRT	XVI	p	AlignRT	XVI	p
Lateral	−0.05 ± 0.07	−0.01 ± 0.02	> 0.05	−0.05 ± 0.16	0.11 ± 0.17	> 0.05
Longitudinal	0.11 ± 0.07	0.03 ± 0.02	> 0.05	0.11 ± 0.18	−0.19 ± 0.12	> 0.05
Vertical	0.22 ± 0.10	0.20 ± 0.14	< 0.05	0.10 ± 0.17	0.21 ± 0.13	< 0.05

Table 5 The intra-fraction respiratory motion data acquiring by SGRT for FB and DIBH treatment during a beam on time

Treatment	Beam on time								
	Lateral (cm)			Longitudinal (cm)			Vertical (cm)		
	Mean ± SD	CI−95%	CI + 95%	Mean ± SD	CI−95%	CI + 95%	Mean ± SD	CI−95%	CI + 95%
DIBH	−0.06 ± 0.07	−0.20	0.07	0.12 ± 0.15	−0.17	0.41	0.12 ± 0.12	−0.12	0.36
FB	−0.02 ± 0.12	−0.26	0.22	0.08 ± 0.18	−0.27	0.43	0.14 ± 0.20	−0.25	0.53

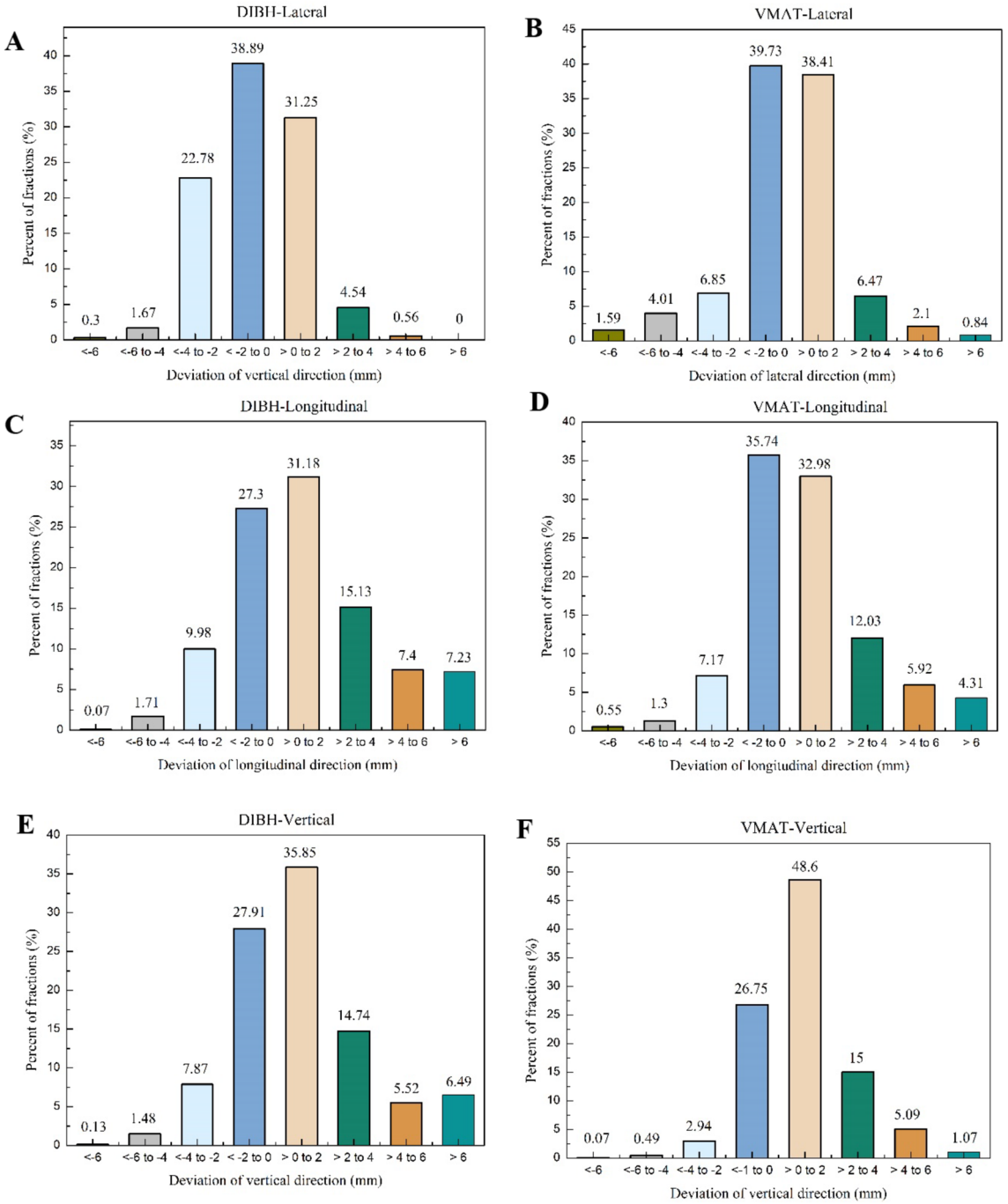

Fig. 4 The percent of fractions binned by deviation of three directions for all patients and all fractions: **A** lateral direction for DIBH; **B** lateral direction for FB; **C** longitudinal direction for DIB; **D** longitudinal direction for FB; **E** vertical direction for DIBH; **F** vertical direction for FB

11.65%, 5.39%, 1.52%, 1.48 Gy, 0.72 Gy, 10.69%, 11.96%, 10.14%, 3.45 Gy, 4.76% 1.39%, 0.4 Gy, 0.52 Gy, 0.52 Gy, 0.91 Gy, 1.71 Gy, 0.42 Gy, 5.38% and 0.94 Gy, respectively. The mean absolute differences in OARs between $DIBH_{min}$ and $DIBH_{max}$ and FB_{min} and FB_{max} are shown in Fig. 7b. In Fig. 6b, compared with DIBH treatment, the FB treatment provided a lower mean absolute difference V_{10}, V_{20}, and D_{mean} to the heart; V_5, V_{20}, and D_{mean} to the ipsilateral lung; and D_{mean} to the breast.

Table 6 Mean value and range of CTV dosimetric parameters absolute between the original and perturbed DIBH and FB treatments

Volume	Parameters	DIBH					FB				
		$DIBH_{org}$	$DIBH_{min}$	$DIBH_{max}$	*p* value		FB_{org}	FB_{min}	FB_{max}	*p* value	
					p1	p2				p1	p2
CTV	D_{95} (Gy)	40.10 ± 1.36	39.78 ± 0.86	40.17 ± 0.79	< 0.05	< 0.05	40.52 ± 0.19	38.46 ± 1.76	40.76 ± 0.31	< 0.05	< 0.05
	D_{98} (Gy)	39.10 ± 1.06	38.59 ± 1.36	39.17 ± 1.09	< 0.05	< 0.05	40.09 ± 0.22	36.54 ± 2.79	40.05 ± 0.48	< 0.05	0.795
	D_{99} (Gy)	38.37 ± 1.26	37.50 ± 2.03	38.50 ± 1.28	< 0.05	0.097	39.79 ± 0.30	35.13 ± 3.28	39.54 ± 0.59	< 0.05	0.173
	D_{mean} (Gy)	42.42 ± 0.14	42.26 ± 0.19	42.82 ± 0.31	< 0.05	< 0.05	43.44 ± 1.0	42.75 ± 1.01	44.02 ± 1.23	< 0.05	< 0.05
	D_2 (Gy)	43.69 ± 0.15	43.98 ± 0.40	45.31 ± 0.72	< 0.05	< 0.05	49.27 ± 2.68	48.67 ± 2.52	50.79 ± 3.17	< 0.05	< 0.05
	D_{max} (Gy)	44.11 ± 0.18	44.52 ± 0.55	46.19 ± 0.57	< 0.05	< 0.05	50.54 ± 2.77	49.90 ± 2.66	53.11 ± 3.67	< 0.05	< 0.05
	D_{50} (Gy)	42.75 ± 0.14	42.32 ± 0.14	43.09 ± 0.30	< 0.05	< 0.05	42.43 ± 0.86	41.95 ± 0.95	43.06 ± 1.07	< 0.05	< 0.05
	CI	0.67 ± 0.07	0.49 ± 0.09	0.61 ± 0.06	< 0.05	< 0.05	0.67 ± 0.12	0.65 ± 0.08	0.72 ± 0.09	< 0.05	< 0.05

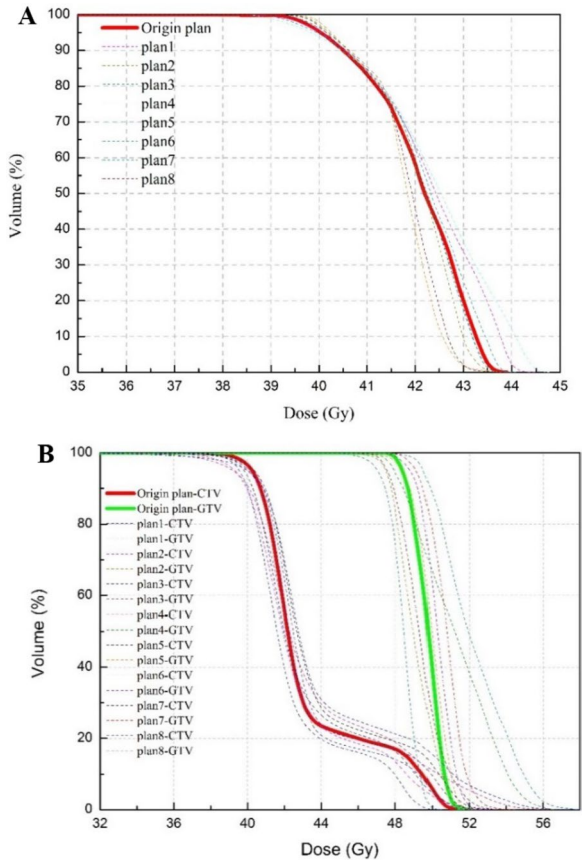

Fig. 5 The original and eight perturbed plans dose volume histograms of CTV and GTV from the two treatments: **A** CTV of DIBH treatment; **B** CTV and GTV of FB treatment

Discussion

In recent years, radiotherapy techniques such as FB and DIBH have been used widely in the radiotherapy of breast cancer. The present study addresses the topic of FB and DIBH stability and reproducibility during surface-guided breast radiotherapy. Surface imaging can be used to monitor the chest wall position during DIBH and the FB. We report on inter-fraction reproducibility and intra-breath-hold and intra-free-breath stability during DIBH and FB radiotherapy in a breast cancer patient study (17 patients with 12,750 points for DIBH and 20 patients with 69,000 points for VMAT) and using an Align RT system.

DIBH and FB techniques have different dosimetry advantages in the radiotherapy of breast cancer, respectively. However, in addition to dosimetry considerations, patient positioning and respiratory movement are major concerns for dose delivery in FB and DIBH radiotherapy for breast cancer. This requires patient positioning monitoring be maintained as accurately as possible during treatment to ensure that the dose is delivered as intended. Shah et al. analyzed 50 patients undergoing radiation therapy for whole breast; these patients were aligned daily using optical surface imaging, and shifts from skin marks were recorded, in comparison with MV port films [22]. Reitz et al. evaluated intra-breath-hold stability and inter-fraction breath-hold reproducibility in clinical practice [23].

Compared with general images from CBCT, SGRT (non-invasive and non-radiative) uses optical surface imaging to verify the position. Several studies have evaluated the setup accuracy of SGRT systems compared to CBCT [24–26]. In our study, CBCT was used to verify AlignRT system corrections, showing the stability gained when using SGRT for intra-fraction patient setup, where the setup error is similar to CBCT. Average setup differences between both AlignRT and CBCT were below 0.08 cm for DIBH treatment and below 0.30 cm for FB treatment, in three directions. This result is in agreement with previous studies [26, 27]. Alderliesten et al. [26] also compared the AlignRT system to CBCT imaging setup errors for DIBH radiotherapy, and showed similar results. Batin et al. [27] demonstrated that positioning with

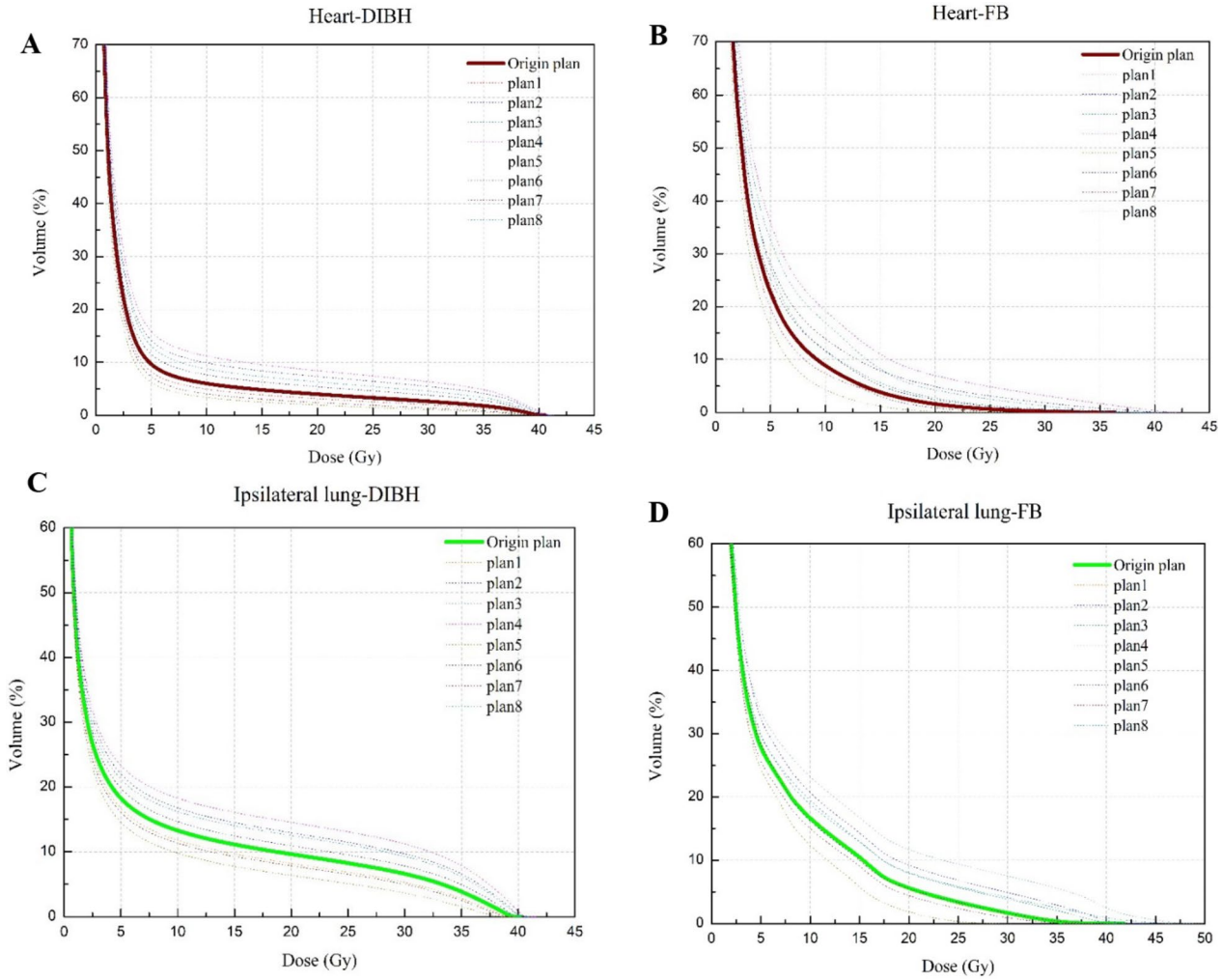

Fig. 6 The original and eight perturbed plans dose volume histograms of ipsilateral lung and heart from the two treatments: **A** heart of DIBH treatment; **B** heart of FB treatment; **C** ipsilateral lung of DIBH treatment; **D** ipsilateral lung of FB treatment

AlignRT after laser alignment is more accurate than when only the laser is used. In Table 3, it can be observed that the setup errors from AlignRT were slightly larger than with the CBCT. This is because for the CBCT, the setup error was based on the target volume, but the AlignRT was based on the patient's surface imaging. In addition, due to the different ROI position, AlignRT mainly looks at the ventral side of the breast, which can differ in shape during an optical imaging acquisition session. Thus, AlignRT has reliable patient positioning stability similar to CBCT and the potential to replace CBCT for positioning in breast cancer patients using FB and DIBH.

At present, analyses of dosimetry between DIBH and FB have been reported in many studies [28–30]. In addition to dosimetry comparisons, the impact of patient respiration on both techniques needs to be evaluated. Patient respiration can lead to an increase in dose delivery uncertainty, prompting the monitoring of treatment delivery to ensure that the target and OAR-delivered dose correspond to those planned. However, most prior studies did not report dosimetric deviation due to patient respiration during beam-on duration, but mainly focused on the three directions of motion of the patient [23, 24, 31]. Zhao et al. [15] compared the impact of setup errors in FB and tangential field-in-field (TFiF) plans for breast treatments, but the setup errors in the three directions were artificially set to 3, 5, and 10 mm, and not taken from the surface-guided system. In addition to the advantages provided with SGRT for setup positioning, the main advantage in the present study is the opportunity for real-time monitoring. In this study, firstly, patient respiratory data were acquired from AlignRT for DIBH and FB treatments; secondly, perturbations were introduced to the plans.

Table 7 Mean value and range of OARs dosimetric parameters absolute between the original and perturbed DIBH and FB treatments

Volume	Parameters	DIBH					FB				
		$DIBH_{org}$	$DIBH_{min}$	$DIBH_{max}$	*p* value		FB_{org}	FB_{min}	FB_{max}	*p* value	
					p1	p2				p1	p2
Heart	V_5 (%)	4.86 ± 2.92	1.83 ± 1.77	12.98 ± 7.14	< 0.05	< 0.05	11.07 ± 9.40	7.18 ± 8.85	18.83 ± 11.22	< 0.05	< 0.05
	V_{10} (%)	2.75 ± 1.94	0.71 ± 1.05	9.35 ± 5.93	< 0.05	< 0.05	2.59 ± 3.54	1.12 ± 1.69	6.51 ± 7.12	0.051	< 0.05
	V_{20} (%)	1.56 ± 1.29	0.30 ± 0.63	6.93 ± 4.95	< 0.05	< 0.05	0.31 ± 0.59	0.03 ± 0.07	1.55 ± 2.60	0.144	0.104
	D_{mean} (Gy)	1.83 ± 0.68	1.13 ± 0.41	4.12 ± 2.01	< 0.05	< 0.05	2.63 ± 0.91	2.17 ± 0.07	3.65 ± 1.55	< 0.05	< 0.05
Spinal cord	D_{max} (Gy)	0.24 ± 0.07	0.20 ± 0.06	0.30 ± 0.06	< 0.05	< 0.05	2.82 ± 1.84	2.57 ± 1.70	3.29 ± 2.03	< 0.05	< 0.05
Ipsilateral lung	V_5 (%)	23.50 ± 2.76	18.61 ± 2.55	30.59 ± 3.89	< 0.05	< 0.05	33.46 ± 5.66	28.72 ± 5.16	39.41 ± 6.37	< 0.05	< 0.05
	V_{10} (%)	17.47 ± 2.32	12.84 ± 2.12	24.48 ± 3.62	< 0.05	< 0.05	19.40 ± 5.77	14.14 ± 4.64	26.10 ± 7.02	< 0.05	< 0.05
	V_{20} (%)	12.84 ± 1.91	8.55 ± 1.82	19.63 ± 3.29	< 0.05	< 0.05	6.97 ± 4.28	3.0 ± 2.62	13.14 ± 6.68	< 0.05	< 0.05
	D_{mean} (Gy)	6.07 ± 0.71	4.48 ± 0.69	8.71 ± 1.26	< 0.05	< 0.05	6.08 ± 1.53	4.80 ± 1.08	8.25 ± 2.26	< 0.05	< 0.05
Contralateral lung	V_5 (%)	0.01 ± 0.02	0 ± 0	0.30 ± 0.69	0.347	0.229	12.37 ± 11.66	10.12 ± 10.71	14.88 ± 12.24	< 0.05	< 0.05
	V_{10} (%)	0 ± 0	0 ± 0	0.13 ± 0.31	0.145	0.260	1.82 ± 2.66	1.19 ± 1.90	2.58 ± 3.40	0.085	< 0.05
	D_{mean} (Gy)	0.22 ± 0.05	0.18 ± 0.03	0.34 ± 0.17	< 0.05	< 0.05	2.28 ± 0.96	2.11 ± 0.93	2.51 ± 1.01	< 0.05	< 0.05
Breast	D_{mean} (Gy)	1.19 ± 2.06	0.61 ± 0.64	2.63 ± 4.79	0.252	0.153	3.10 ± 1.22	2.91 ± 1.18	3.43 ± 1.33	< 0.05	< 0.05
Thyroid	D_{mean} (Gy)	0.29 ± 0.13	0.22 ± 0.11	0.41 ± 0.20	< 0.05	< 0.05	0.83 ± 0.31	0.63 ± 0.19	1.15 ± 0.54	< 0.05	< 0.05
Trachea	D_{mean} (Gy)	0.37 ± 0.06	0.29 ± 0.06	0.52 ± 0.10	< 0.05	< 0.05	2.22 ± 1.51	1.79 ± 1.26	2.70 ± 1.79	< 0.05	< 0.05
Esophagus	D_{max} (Gy)	0.54 ± 0.09	0.44 ± 0.05	0.78 ± 0.20	< 0.05	< 0.05	5.38 ± 2.84	4.68 ± 2.58	6.39 ± 3.17	< 0.05	< 0.05
	D_{mean} (Gy)	0.44 ± 0.09	0.26 ± 0.05	0.44 ± 0.09	< 0.05	< 0.05	1.63 ± 0.89	1.44 ± 0.77	1.86 ± 1.0	< 0.05	< 0.05
Liver	V_5 (%)	0 ± 0	0 ± 0	0.12 ± 0.23	0.231	0.160	7.30 ± 5.33	5.17 ± 3.95	10.55 ± 7.30	< 0.05	< 0.05
	D_{mean} (Gy)	0.17 ± 0.05	0.13 ± 0.04	0.26 ± 0.10	< 0.05	< 0.05	1.65 ± 0.90	1.30 ± 0.68	2.24 ± 1.29	< 0.05	< 0.05

Intra-DIBH and intra-FB stability were both smallest in the vertical direction during beam-on time, as shown in Table 4. This may be due to patient respiration factors during beam-on time. The deviation values in the vertical direction averaged over all patients were 0.12 ± 0.12 cm for DIBH and 0.14 ± 0.20 cm for FB, respectively. The average value and standard deviation showed that the respiratory motion amplitude of FB technology is greater than DIBH. The reason for this situation is that patients use FB technology in a state of free breathing, and inhalation and exhalation have a positive and negative relationship in the AlignRT system, which leads to a greater average value. Our surface-based alignments specifically showed that across all patients, skin-mark alignments were poorer in the three directions (especially the deviation within the range from −2 to 2 mm) for DIBH treatment in comparison with the FB treatment (Fig. 4). This result indicates that the stability of the FB treatment is better than the DIBH treatment of inter-fractional motion. This is because DIBH treatment has higher requirements for patients; patients must be able to hold their breath for at least 25 s and to replicate the breath retention setting five times in succession. One potential solution could involve increasing patient's breath-holding training.

When perturbations were introduced to DIBH and FB plans, however, DIBH techniques guaranteed an accurate target coverage with deviations in the target DVH dosimetric, whereas FB plans seemed more sensitive to setup errors, with mean deviations of 2.3 Gy and 3.96 Gy for D_{95} and D_{98}, respectively. In Table 5 and Fig. 6(A), it is possible to observe that respiratory movement has a dosimetric impact on CTV that is larger for FB plans than for DIBH plans. Zhao et al. [15] also found such dosimetric effects. For breast cancer radiotherapy, dose sparing of the ipsilateral lung, contralateral breast, and heart are particularly important. For the OARs, DIBH plans appeared to be more sensitive to the setup errors' mean absolute difference ($Plan_{max}$-$Plan_{min}$) for V_{10}, V_{20}, and D_{mean} to the heart, V_5, V_{20}, and D_{mean} to the ipsilateral lung, and D_{mean} to the contralateral breast. In addition, the well-known second cancer risk for contralateral breast and lung forces us to monitor treatment delivery to ensure that the OAR-delivered dose corresponds to the planned one [33]. One possible solution is to increase the threshold in the optical surface imaging system, with beam delivery interruption if patients' positions exceed their tolerance limits.

One limitation of this study is that the tolerance of linear translations and rotations are set to 3 mm and 3° in

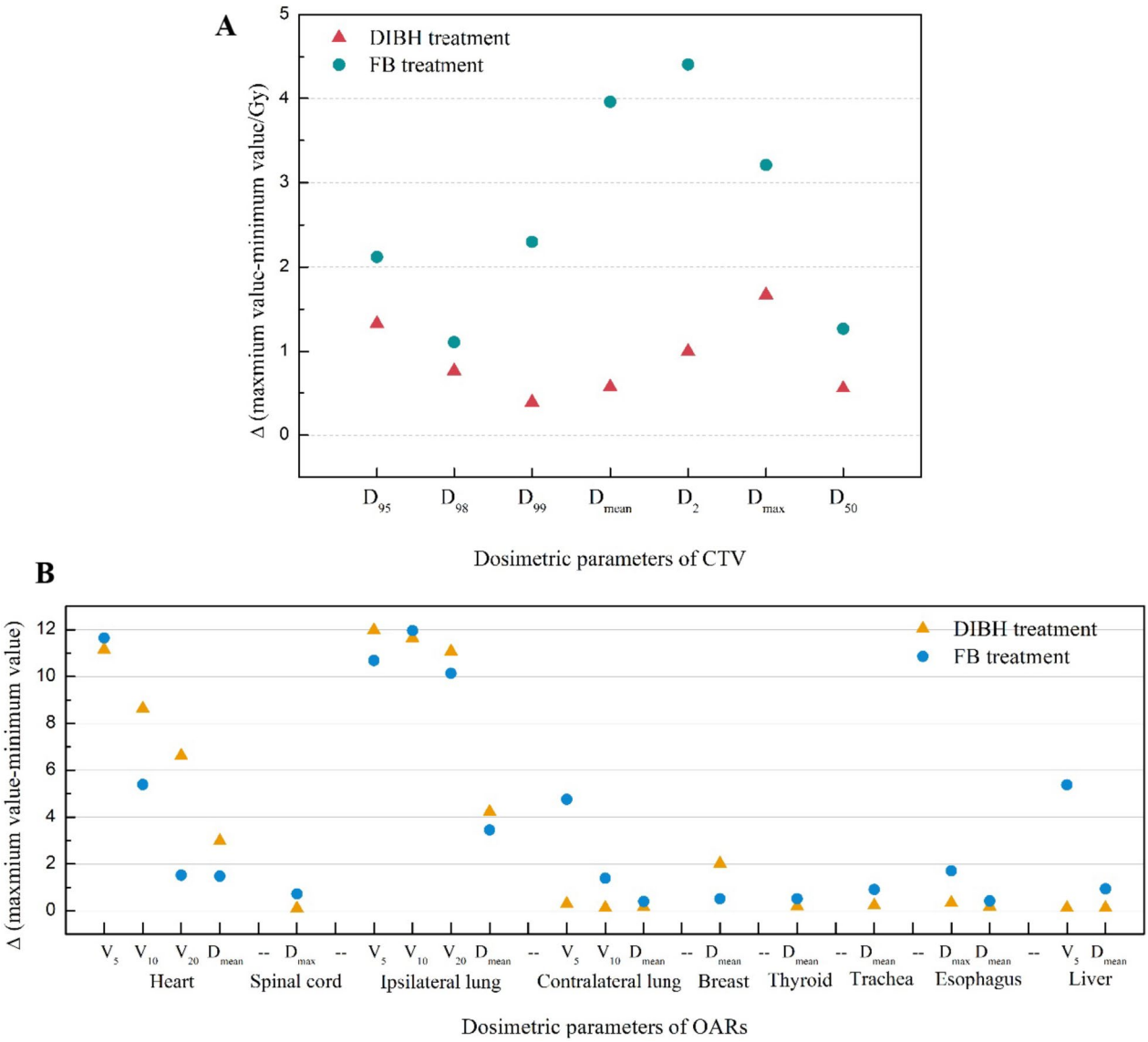

Fig. 7 Mean value and range of CTV and OARs dosimetric parameters absolute difference between the original and perturbed DIBH and FB treatments: **A** CTV; **B** OARs. The units of V_x is %, D_y is Gy

the AlignRT system. Xiao et al. [32] reported different values of variabilities (translation 1 mm and rotation 1˚), which resulted in small dosimetric consequences. Thus, a lower tolerance could assure DIBH and FB with good stability and low intra-fraction and inter-fraction variability, contributing to smaller deviations in dosimetric delivery. The three axis rotations from AlignRT were not discussed. Wiant et al. [33] showed that the mean rotations were all < 0.1˚ for thirty free-breathing breast patients. This indicates that rotation deviations might negligible in dosimetric delivery. Another limitation is that we simply think of the skin motion as the target motion. But, the further away the target is from the skin, the less SGRT correlates with the actual target. In the future, one could expand the investigation of the correlation between skin motion and target motion.

Conclusion

To conclude, due to the large amount of data analyzed, the optical real-time surface imaging system in the present study was demonstrated to be an important tool for inter-fraction patient positioning and intra-fraction patient respiratory motion management in DIBH and FB breast cancer radiotherapy. Regarding the reproducibility of DIBH and FB in the inter-fraction, the setup deviations between AlignRT and CBCT were both < 0.12 cm.

As a measure of DIBH and FB stability in the intra-fraction, the mean deviations were both < 0.2 cm. When the patient respiratory motion is large, the FB technology has greater possibility for the undercoverage of the target volume, while DIBH technology is more likely to result in increases in dose to OARs, especially the lung, heart, and breast. In addition, the tolerance of the optical surface imaging system could be reduced, and could then become a potential method for reducing the dose delivery uncertainty caused by patient respiratory motions.

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Author contributions
Design of the research: BT, JXW. Treatment plans: FW, FY. Statistical Analysis: OL, JL, KY, LPX. Manuscript preparation: FY, JXW. Manuscript writing: JXW. Manuscript final revision: BT, XLW. All authors contributed to the article and approved the submitted version.

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Availability of data and materials
The data are fully available without restriction in a public repository (Dryad). The reference treatment plans and corresponding perturbed plans were archived in the Informatic System of Sichuan Cancer Hospital.

Declarations

Ethics approval and consent to participate
This retrospective study was approved by the Ethics Committee of our hospital (Approval Number No. SCCHEC-02-2021-026).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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