

# Development of deep-inspiration breath-hold system that monitors the position of the chest wall using infrared rangefinder

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## ABSTRACT

We conducted a prospective study to quantitatively evaluate the movement of the chest wall to establish the simple and reproducible deep-inspiration breath-hold (DIBH) method. The left nipple position was monitored to confirm the inspiratory state. Planning computed tomography (CT) was performed under DIBH and free-breath. We conducted radiation plans with DIBH and free-breath CT and evaluated organ at risk (OAR) and target doses according to two different plans. The relationship between positioning errors of the chest wall and patient factors was evaluated using univariate analysis and fixed-effects models. Twenty-three patients aged  $\leq 60$  years were enrolled during January–August 2021; 358 daily radiation treatments were evaluated. The median time of treatment room occupancy was 16 minutes (interquartile range, 14–20). The area of the planning target volume (PTV) surrounded by the 95% isodose line was more extensive in DIBH than in free breathing (71.6% vs 69.5%,  $P < 0.01$ ), whereas the cardiac and left anterior descending (LAD) artery doses were lower (both  $P < 0.01$ ). In the fixed-effects model analysis, the occupation time of the treatment room was correlated with positioning error. The difference between the planned and irradiated dose was the largest in the LAD branch of the coronary artery ( $-2.5$  Gy), although the OAR dose decreased owing to positional error. The current DIBH method, wherein a single point on the chest wall is monitored to confirm that the patient is in an inspiratory state, allows radiation to be performed in a short time with a small dose error.

**Keywords:** radiotherapy; breast cancer; deep-inspiration breath holding; reproducibility; cardiac toxicity

## INTRODUCTION

Partial mastectomy followed by postoperative whole breast radiation is the current standard of care for early-stage breast cancer [1]. This treatment can be safely performed with extremely rare serious acute toxicities, but reduced occurrence of late adverse events, such as pneumonitis, cardiovascular events and secondary cancers, has been emphasized [2, 3]. Darby *et al.* reported that, for every 1-Gy increase in mean cardiac dose (MCD), there is a 7% increase in the relative risk of cardiovascular events [4]. Veerle *et al.* also reported that the volume of the left ventricle irradiated with 5 Gy correlated better with cardiovascular risk [5]. Radiation to the heart causes pericarditis, valvular disease and rhythm disorders, with risk of cardiovascular events

[6–9]. Various radiotherapy techniques of MCD reduction, such as accelerated partial breast irradiation (APBI), intraoperative radiation and intensity-modulated radiation therapy (IMRT) technique have been used [10, 11]. Recent studies have reported that APBI has problems with cosmetic results and that intraoperative radiation shows relatively high local recurrence rates [11, 12]. IMRT increases low-dose radiation of the contralateral breast and surround tissues and the complexity of preparation and workload. Therefore, the deep-inspiration breath-hold (DIBH) method has become widely used for dose reduction in the radiation field. Deep inspiration causes the left lung to expand, increasing the distance between the breast and heart and causing

the heart to shift to the midline, which reduces the dose to the heart while providing sufficient dose to the breast. Currently, various DIBH methods are available. However, there are few studies that evaluated the relationship between changes in chest wall and heart position and cardiac dose due to DIBH [13, 14]. As the movement of organs in the body differs depending on the form of respiration, it is important to understand the variation in the organs in the body by accurately measuring the position of the thorax [15]. Although several studies have reported on the benefits of DIBH, most of these studies have presented criteria for determining deep inspiration, performed CT imaging based on those criteria, planned treatment and examined the organ at risk (OAR) dose [16, 17]. A previous study has reported on the acceptance criteria and irradiation results of DIBH performed at facilities with Catalyst (Elekta, Stockholm, Sweden) or AlignRT (VisionRT, London, UK) [18–20]. However, these devices are expensive to install. Moreover, it is unrealistic to introduce these devices in the absence of a new linear accelerator. In addition, few studies have reported on actual DIBH irradiation using systems other than those mentioned above.

We reported that monitoring the nipple position using an infrared rangefinder allows us to confirm that the patient was in a deep inspiratory state [21]. By continuously monitoring the nipple position, the chest wall and heart positions can be accurately reproduced. In this study, we prospectively examined the applicability of the simple and reproducible DIBH method by quantitatively evaluating the movement of the reference point. The actual radiation doses to the target and OAR were also examined in patients with the largest position error.

## MATERIALS AND METHODS

### Patient criteria

Patients aged  $\leq 60$  years who were scheduled to undergo postoperative whole breast radiation after partial resection of early-stage left breast cancer were eligible. Other eligibility criteria included good performance status (Eastern Cooperative Oncology Group Performance Status [ECOG-PS] of 0 or 1), ability to hold an inspiratory for at least 30 seconds, and no history of respiratory disease or normal respiratory function test if there was a history of respiratory disease. The exclusion criteria were pregnancy or possible pregnancy, active collagen disease, previous history of radiation therapy to the chest and schedule for receiving radiation to supraclavicular region.

### Confirmation of inspiration

The laser rangefinder was fixed at 180 cm from the head end of the computed tomography (CT) and linear accelerator top, and 50 cm height from the CT and linear accelerator table (Figs. 1 and 2). The laser rangefinder used was GLM40 (Robert Bosch GmbH, Gerlingen, Land Baden-Württemberg, Deutschland), which can measure distances from 0.15 m to 40 m with an error of less than 2 mm. The distance from the left nipple to rangefinder (nipple-rangefinder distance [NRD]) was continuously measured while breathing. The longest distance measured during free breath was defined as the exhalation NRD, and the inspiratory distance change (IDC) was defined as exhalation NRD minus inspiration NRD. The NRD during inspiration was defined as NRD\_RT. We have reported in a previous study that the target and OAR dose errors are  $< 5\%$  when the IDC at DIBH is between

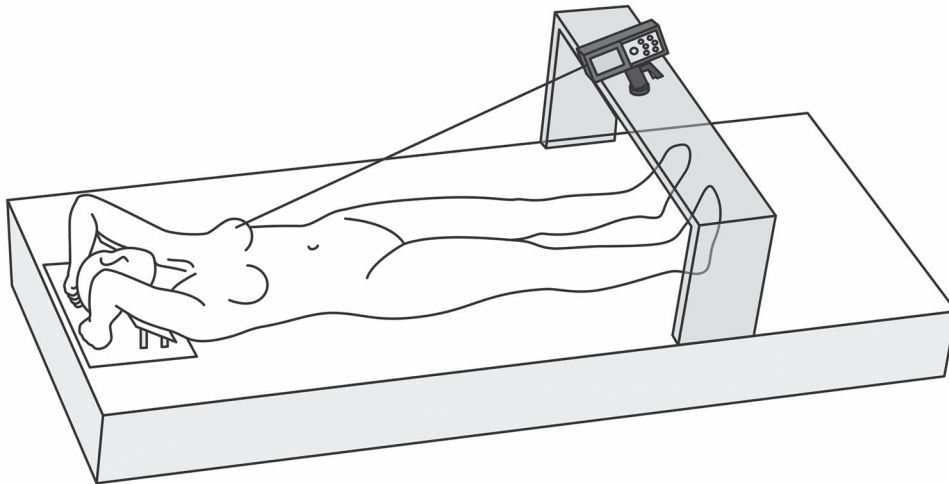
70% and 130% of the IDC at planned CT [21]. In the study, CT scans were taken of five patients on inspiration and expiration. From the CT images, we used a deformable image registration technology to generate CT images from 0% inspiratory (expiratory) to 150% inspiratory (hyper-expiratory) states. We created a plan to radiate the whole left breast in the 100% inspiratory state. The median clinical target volume (CTV) dose, median planning target volume (PTV) dose, median left lung V20 Gy and median left anterior descending (LAD) dose were evaluated when radiation was performed to patients in each inspiratory state according to the created plan. We reported that the error margin of the evaluated doses was less than 5% for the 70–130% inspiratory conditions. The distance obtained by subtracting  $IDC \times 0.7$  from NRD\_RT was defined as the minimum inspiratory target distance (INTD), and the distance obtained by subtracting  $IDC \times 1.3$  from NRD was defined as the maximum INTD (MNTD). If the NRD was between INTD and MNTD when inspiration was performed, it was judged that appropriate inspiration was being performed, and radiation was performed (Fig. 3).

### Planning CT imaging

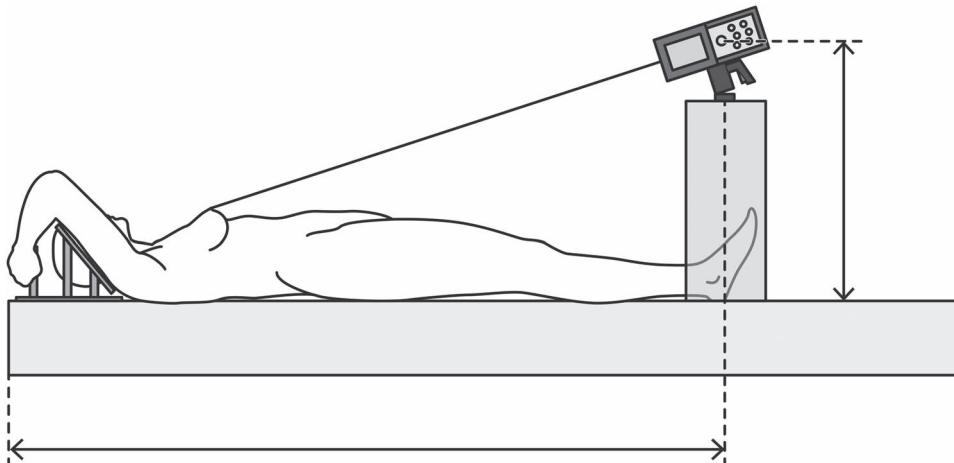
All CT images were obtained in the supine position with both upper arms elevated, and the tube voltage was set at 120 kV. Free-breath CT images were obtained, and DIBH CT images were obtained three times, and the median value was obtained from each NRD. CT with the median NRD was adopted as the planned CT. Reconstruction conditions were gapless with a slice thickness of 3 mm. Free-breath CT was performed to irradiate the whole breast at the time of withdrawal from the study and compare the dose volume histogram (DVH) of free-breath CT with those of DIBH CT. DIBH CT was performed three times to confirm the reproducibility of inspiratory breath hold. Images with poor reproducibility of inspiration or images in which inspiration holding could not be maintained were discarded, and the images were obtained again. Treatment planning CT uses Aquilion LB (CANON MEDICAL SYSTEMS CORPORATION, Otawara, Tochigi, Japan), which comprises 16 rows of multidetector and supports helical imaging. For all CT scans, imaging was performed using low-dose CT with optimized conditions for this radiation.

### Treatment planning

The radiation plans for both free-breath CT and DIBH CT were prepared in the same way. The CTV was created based on the European Organization for Research and Treatment of Cancer contouring guidelines [22], and the PTV was created with a setup margin of 5 mm from the CTV. Contouring was also performed on the heart, LAD and left lung for evaluation [23]. The medial radiation field was selected with an angle optimized for CTV and PTV between  $290^\circ$  and  $310^\circ$ . The right-side body beyond the midline was shielded using a multileaf collimator. To confirm the tumor bed, five radiopaque clips were placed on the cephalic and caudal sides, medial and lateral sides and bottom of the tumor bed at the time of surgery. For the lateral radiation field, an opposite radiation field of the original field was created, and the angle was optimized to become tangential to the body side. The prescription method was point prescription, and the prescription dose was 43.2 Gy in 16 fractions in 3 weeks and 1 day. The dose reference point was set so that the body side of the PTV was included in the 95% isodose line and



**Fig. 1.** Overall equipment view. View of the positional relationship of the patient, support platform and infrared rangefinder during CT imaging and radiation. The patient is in the supine position, with their upper arms raised on the bed. The rangefinder is fixed on a support form placed at the patient's feet and continuously measures the distance to the left nipple.



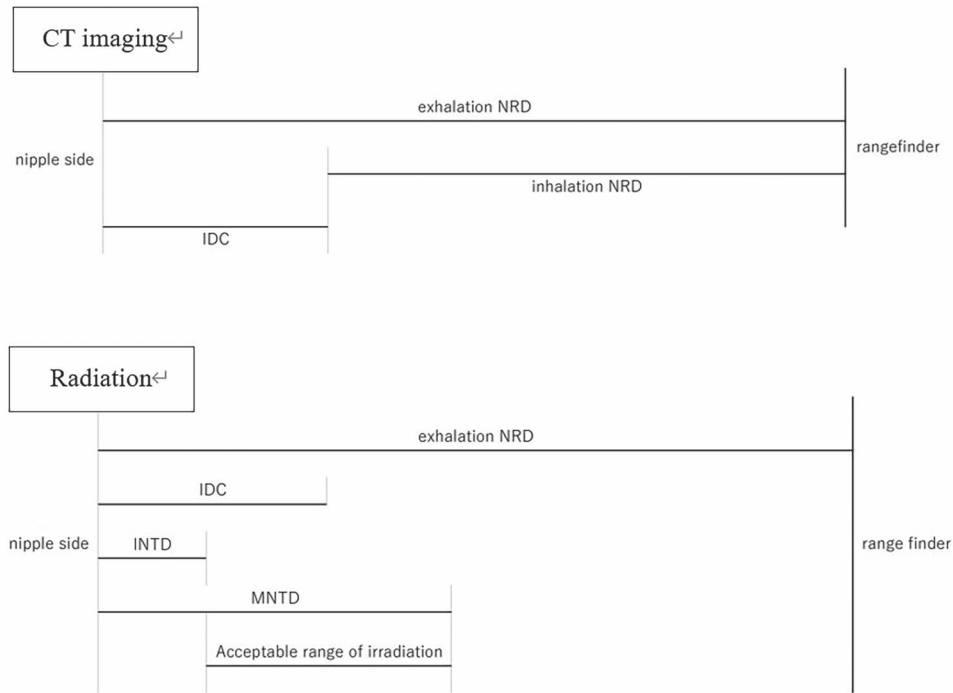
**Fig. 2.** Location of the equipment. Location of the CT or linac couch and platforms, the infrared rangefinder. The infrared rangefinder is fixed at 1800 mm from the head at a height of 500 mm.

shielding of the high-dose area was performed using the field-within-field technique to prevent a dose of  $\geq 105\%$ . All treatment plans were created using Eclipse version 13.0 (Varian Medical Systems Inc., Palo Alto, CA, USA). The Anisotropic Analytical Algorithm was used to calculate the dose. The mean dose of CTV, mean dose of PTV, left lung  $V_{20\text{Gy}}$  (irradiated lung volume  $\geq 20$  Gy), MCD and mean LAD dose were calculated for all prepared plans in free-breath and DIBH. It was confirmed before radiation that DIBH radiation was not inferior to free-breath radiation in terms of dose coverage to the target and dose reduction to the OAR.

#### Location and dosimetry evaluation

The position accuracy of radiation fields was quantified by chest wall and nipple positions in the mega-voltage portal imaging and comparison with the digitally reconstructed radiograph (DRR). Horizontal

and vertical errors were obtained for all main radiation fields. From the errors in the vertical and horizontal directions, the overall error amount was calculated as the shift vector and acquired as the radiation error amount. Treatment was started from the medial radiation field (radiation field, approximately  $300^\circ$ ); then, radiation of the lateral radiation field (radiation field, approximately  $120^\circ$ ) was performed. As for the patient's positioning error, both the medial and lateral radiation fields were acquired. For the patient with the largest error, we created a virtual radiation field that considers the daily positioning error and examined the degree to which the DVH parameter changes. Treatment planning and DVH acquisition, DRR creation and positioning error acquisition by mega-voltage portal imaging were performed using Eclipse 13.0. A large position error among the medial and lateral radiation fields on the same radiation day was defined as the position error of the day (PEoD).



**Fig. 3. Position of the range finder and the nipple during planning CT imaging and radiation. Position of the nipple from the infrared range finder during CT imaging. The distance from the range finder to the nipple during free-breathing exhalation was defined as the exhalation NRD, the distance from the range finder to the nipple during deep inhalation was defined as the inhalation NRD, and the exhalation NRD minus the inhalation NRD was defined as IDC. Location of the infrared range finder relative to the nipple during radiotherapy. The distance obtained by multiplying the IDC acquired during CT imaging by 0.7 was defined as INTD, and the distance obtained by multiplying the IDC by 1.3 was defined as MNTD. The distance from exhalation NRD minus MNTD to exhalation NRD minus INTD was defined as the acceptable irradiation range. Radiation was allowed when the nipple was located within the acceptable range by deep inhalation.**

The time of treatment room occupancy was measured from the time they entered the treatment room to the time they left. We measured the time required for DIBH and examined whether it correlated with patient information and PEOd.

**Statistical analysis**

We collected the data including the age, ECOG-PS, height, weight, body mass index (BMI), breast size (determine by the size of the underwear), location of the disease (determination using ICD-O-3 classification), and occupation time of treatment room and examined whether there was a correlation with the position PEOd [24]. Statistical analyses were conducted using t-tests to compare DVH between the two groups. Furthermore,  $\chi^2$  test was performed to examine patient information and PEOd. In the current study, radiation position errors were not only influenced by patient-specific factors but also by patient familiarity with radiation and staff familiarity with radiation techniques as the number of radiation sessions increased. The use of a mixed-effects model enables separate analysis of patient and staff familiarities with the radiation method from patient-specific factors [25]. Therefore, the mixed-effects model was used in this study. The increase in accuracy due to patient familiarity and the relationship

with PEOd were separately examined using the radiation frequency (first, 1–100; second, 101–200; third,  $\geq 201$ ) and the number of radiation frequencies per patient. All analyses were performed using JMP Pro version 16.0.0 (SAS Institute Inc., Cary, NC, USA).

**Ethical matters**

All patients have been informed about this study, and written informed consent was obtained. This study was designed in accordance with the Declaration of Helsinki and the Ethical Guidelines for Life Science and Medical Research Involving Human Subjects, and the study was reviewed and approved by our institutional review board (approval no. H20-0224).

**RESULTS**

Twenty-three patients were enrolled in this study from January 2021 to September 2021. Twenty-three DVH data and 362 radiation field data sets were analyzed (four radiation field sets were excluded from the analysis due to missing mega-voltage portal imaging data) (Table 1). The median time of treatment room occupancy was 16 min (interquartile range [IQR], 14–20).

**Table 1. Patient characteristics**

Age	48 (45–56)*
ECOG-PS	0 (0–1)*
Height (cm)	157.3 (154.9–164.6)*
Body weight (kg)	54.0 (50.2–57.6)*
BMI**	21.0 (19.7–24.0)*
Location of the disease***	A:3 AC:2 B:1 BD:3 C:11 CD:2 D:1 B:2 C:8 D:5 E:3 F:1 G:1 Unknown:3
Breast size****	

\*median (95% confidence Interval) \*\*BMI, body mass index \*\*\*Location of the disease is determined based on the ICD-O-3 localization code. \*\*\*\*Breast size is expressed in terms of underwear size used in Japan. It is indicated by the difference in distance between the under bust and top bust. The difference in distance between top and under bust is represented by B, 11.5–13.5 cm; C, 14–16 cm; D, 16.5–18.5 cm; E, 19–21 cm; F, 21.5–23.5 cm; and G, 24–26 cm.

**Table 2. DVH parameters**

	Free breathing	DIBH	P values
CTV median dose (cGy)	4048.1 (3933.5–4083.5)*	4092.2 (4017.7–4142.3)*	0.02
PTV median dose (cGy)	4007.2 (3986.3–4083.5)*	4095.7 (4070.1–4125.6)*	0.03
PTV covered at 95% of Target dose (%)	69.5 (65.5–74.4)*	71.6 (68.9–76.2)*	< 0.01
Left lung V <sub>20Gy</sub> (%)	12.2 (9.1–15.8)*	12.0 (9.5–14.3)*	0.91
Heart mean dose (cGy)	130.4 (104.4–143.8)*	102.3 (82.5–122.4)*	< 0.01
LAD mean dose (cGy)	986.3 (568.2–1488.8)*	717.0 (397.6–874.2)*	< 0.01
LAD max dose (cGy)	3167.0 (2651.3–3769.0)*	3048.3 (1018.7–3311.1)*	< 0.01

\*median (95% confidence Interval).

### DVH parameters

The CTV and PTV median doses were 40.92 Gy (IQR, 40.18–41.42) and 40.96 Gy (IQR, 40.70–41.26) for DIBH radiation, which were higher than those for free-breathing radiation (CTV, 40.48 Gy [IQR, 39.34–40.84]; PTV, 40.07 Gy [IQR, 39.86–40.84]) ( $P = 0.02$  and  $P = 0.03$ , respectively). The area of the PTV surrounded by the 95% isodose line was more extensive in DIBH than in free breathing (71.6% [IQR, 68.9–76.2] vs 69.5% [IQR, 65.5–74.4],  $P < 0.01$ ). The MCD and mean LAD dose on DIBH radiation were 0.10 Gy (IQR, 0.83–1.22) and 7.17 Gy (IQR, 3.98–8.74), which were lower than those for free-breathing radiation (MCD, 0.13 Gy [IQR, 1.04–1.44], mean LAD dose, 9.86 Gy [IQR, 5.68–14.89]) ( $P < 0.01$ ,  $P < 0.01$ ). There was no difference in the left lung V<sub>20Gy</sub> between the two techniques ( $P = 0.91$ ) (Table 2).

### Positioning error and patient factors for each radiation

The median positioning error of the medial radiation field was 4.1 mm (IQR, 2.2–6.0), and the positioning error of the lateral radiation

field was 4.1 mm (IQR, 2.2–6.1). The median PEoD was 4.5 mm (IQR, 3.2–6.7) (Table 3). The error directions were caudal and dorsal (Table 3). In the univariate analysis, the factors correlated with PEoD were age, ECOG-PS, height, body weight, BMI, location of the disease, breast size, radiation time and the radiation frequency (Table 4). In the multivariate analysis, the factors correlated with PEoD were age, PS and the radiation frequency ( $P < 0.01$ ,  $P < 0.01$  and  $P = 0.03$ , respectively) (These data is not shown in the tables). In the analysis using a mixed-effects model that included factors that were significantly different than those in the univariate analysis, it was found that the treatment room occupancy time correlated with age, ECOG-PS, body weight and BMI (Table 5). Therefore, other factors were determined to be influenced by the total number of radiation treatments.

### Verification of the difference between planned and radiation doses

Daily position errors were used to calculate dose distribution in the planning system to examine the effect of position errors to the dose

**Table 3. Error of the inner/outer radiation fields**

	Amount of error	Cranial and caudal direction of error	Dorsal side direction of error
Error of the medial radiation field (mm)	4.1 (2.2–6.0)*	−0.6 (−3.5–2.3)*	−0.9 (−6.7–7.9)*
Error of the lateral radiation field (mm)	4.1 (2.2–6.1)*	−1.0 (−3.9–2.8)*	−0.8 (−7.2–6.9)*
Position error of the day (mm)	4.5 (3.2–6.7)*	−0.7 (−4.1–3.1)*	−0.9 (−7.6–8.0)*

\*median (95% confidence Interval).

**Table 4. Positional error and patient factors for each irradiation in the univariate analysis**

	Medial radiation field	Lateral radiation field	PEoD
Age	$P < 0.01$	$P = 0.14$	$P = 0.01$
ECOG-PS	$P = 0.01$	$P < 0.01$	$P < 0.01$
Height (cm)	$P = 0.64$	$P = 0.03$	$P = 0.04$
Body weight (kg)	$P = 0.03$	$P < 0.01$	$P < 0.01$
BMI	$P = 0.03$	$P < 0.01$	$P < 0.01$
Location of the disease	$P < 0.01$	$P < 0.01$	$P < 0.01$
Breast size	$P = 0.08$	$P = 0.02$	$P = 0.02$
Occupation time of the treatment room	$P = 0.01$	$P = 0.02$	$P = 0.01$
Number of radiation frequency	$P < 0.01$	$P < 0.01$	$P < 0.01$

BMI, body mass index.

PEoD, position error of the day.

**Table 5. Analysis of inter- and inpatient factors in the fixed-effects model**

	Estimated value	P value
Age	−0.003	0.01
ECOG-PS	0.362	<0.01
Height	−0.049	0.06
Body weight	0.081	0.03
BMI	−0.212	0.05
Breast size	0.009	0.58
Occupation time of the treatment room	8.680e-5	0.09

Notes: The estimates of the total number of radiation treatments were derived from the linear mixed-effects exponential model. The number of radiation frequencies and the number of radiation frequencies per patient were used as terms for the random effects.

distribution (Table 6). The dose error to the target owing to patient position error was only approximately 0.20 Gy, whereas the dose error to the OAR was approximately −2.50 Gy with the largest error in the LAD. The dose errors for the OARs were all shifted to the lower dose side.

## DISCUSSION

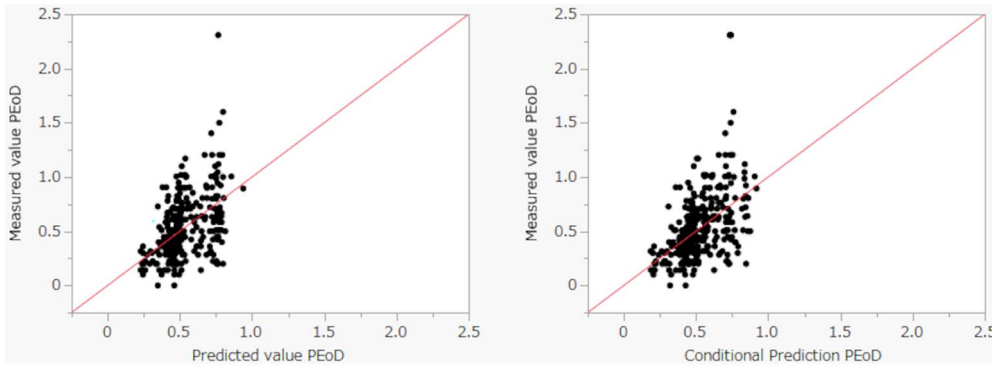
DIBH is often performed using instruments attached to linear accelerators, such as Real-time Positioning Management (RPM) (Varian, California, USA), AlignRT and Catalyst [18–20]. However, although RPM can monitor the inspiratory phase of the patient, it does not evaluate the quantitative nature of the inspiratory depth. Since RPM can determine the percentage of intake at daily maximum intake, Korreman *et al.* and Pedersen *et al.* used relative percentages to determine radiation permission criteria but did not determine the absolute intake [26, 27]. AlignRT and Catalyst can quantitatively evaluate the inspiratory state by monitoring the body position [18–20]. However, the installation of

AlignRT and Catalyst is costly, and these instruments must be simultaneously installed with a linear accelerator, making the installation of AlignRT and Catalyst difficult. In this study, our system can be easily implemented while obtaining the advantages of the body surface position evaluation system, which evaluates a specific point on the body surface in absolute coordinates. Moreover, quantitative position monitoring can be performed by introducing ExacTrac or SyncTraX to the linear accelerator, but there is an increase in radiation dose associated with position monitoring. In this study, treatment planning CT was performed three times to evaluate the quantitative performance when repeated inspiration was performed. In our institution, the preliminary dosimetry in the phantom revealed that the radiation dose per imaging was reduced from 7.6 mGy for normal imaging to 1.2 mGy for low-dose imaging. Therefore, even if the number of imaging sessions was increased to three, the total radiation dose was reduced compared with that of normal imaging. Recently, dose reduction methods, such as the successive approximation method, have become available for CT, and

**Table 6. Difference between planned dose and radiation dose**

	Difference
CTV mean dose [cGy]	10.9 (4.3–19.5)*
PTV mean dose [cGy]	0.7 (–8.1–18.5)*
Left lung V <sub>20Gy</sub> [%]	–0.7 (–1.3–0.1)*
Heart mean dose [cGy]	–7.7 (–16.5–0.8)*
LAD mean dose [cGy]	–82.6 (–254.0–4.65)*

\*median (95% confidence Interval).



**Fig. 4. Analysis of inter- and inpatient factors in the fixed-effects model. Plot of conditional predictions and measured values of the medial radiation field in the fixed-effects model. In the graph on the left, the position error predicted from the fixed-effects model is the horizontal axis, while the actual positional deviation is the vertical axis. In the right graph, the position error predicted from the mixed-effects model is the horizontal axis, while the actual position error is the vertical axis.**

the dose increase by this method (for two treatment planning CT) is approximately 4 mGy. Onimaru *et al.* reported that the PTV dose increases by 1.9% due to the radiation exposure caused by tracking during irradiation using SyncTraX [28]. When converted to whole breast irradiation, the radiation exposure was calculated as approximately 90 mGy. Therefore, we expect that the increase in radiation exposure in the present method is sufficiently low compared with the tracking radiation using X-rays.

Existing studies chose the sternum as the region of interest for determining inspiration [18–20]. These studies employed AlignRT or Catalyst, which used CT to establish the region of interest. The sternum is a very clear marker on CT, but locating it quickly on the body surface is difficult, especially in women with high subcutaneous fat. Therefore, in this study, the nipple was chosen as the region of interest because it can be instantly identified on the body. In addition, previous studies have shown that the closer the position to the radiation field, the stronger is the correlation between inspiration and position; hence, we decided to place the region of interest in the radiation field [19].

The DIBH radiation method used in this study was designed to be as simple as possible while ensuring accuracy. The median time of treatment room occupancy per patient was 16 min at our hospital. There are few references on the time required for DIBH. Jensen *et al.* reported that the median time from entry into the room to the end of radiation was 7 min [29]. The treatment room occupancy time in this study was approximately 16 min, which is not significantly different from that in known studies, considering that Jensen *et al.* did not consider the

time needed for other activities, such as dressing. Our institution can perform right total breast radiation without DIBH on five patients per hour (12 min per patient). In addition, the treatment room occupancy time was related to the positioning error in the univariate analysis but was not a dominant factor in the multivariate analysis and mixed-effects model. Patients with longer occupancy times are considered to have some factor that worsens positional accuracy. This factor reduces treatment accuracy, thereby increasing the occupancy time. In addition, the mixed effect model examines the correlation between patient factors and accuracy, excluding staff proficiency. The model fit is good when staff proficiency is excluded, as shown in Fig. 4. This indicates that staff proficiency influences positional accuracy. Therefore, staff proficiency is an important factor in performing DIBH, and adequate staff training is necessary when performing DIBH.

The median positioning error was approximately 4.5 mm, which was close to the PTV margin of 5 mm. However, the dose error to the target was only approximately 0.20 Gy. Although the dose error to the OAR was larger than that to the target, approximately –2.50 Gy, the dose error to the OAR was a risk-reducing difference and would not increase the risk of late adverse events. Overall, the error was approximately 1 mm, but the error direction was in the insufficient aspiration direction during irradiation. This is thought to have reduced the OAR volume in the radiation field, resulting in a decreased OAR dose.

We have traditionally used a simple cardiac shielding method wherein the heart is shielded by the multi leaf collimator to exclude it from the radiation field, and the cardiac dose was originally extremely

low. However, cardiac shielding methods are discouraged when the shielding site overlaps the tumor bed in this method, the dose to the shielded area is reduced, adequate dose to the tumor bed may not be compatible with shielding the heart. The present technique showed a small but significant reduction in cardiac dose and improvement in PTV dose because the shielding area has been reduced. In this study, there were only a few patients with tumor occupation in the caudal side of the breast, where there was a large overlap between the tumor bed and shielded site, and thus there was little change in DVH. It is recommended that DIBH should be actively performed using the present technique in such cases.

In this study, a statistically significant difference in radiation position accuracy was obtained depending on the occupied position of the lesion. In addition, the number of cases was small, and the disease was in the upper lateral region in approximately half of them. A statistically significant difference might be incidentally obtained due to the above, but a larger study is needed to show whether the difference was incidentally obtained or not.

From this study, we found that patients with an ECOG-PS of 1, large body weight and large BMI and patients who took a long time to be radiated had a large position error. The dose error to the target is small, and the dose error to the OAR, although larger than the target, is in the direction of decreasing the dose and is not considered a problem. Schönecker *et al.* also noted that appropriate patient selection for unsuitable DIBH [18]. Our results suggest that DIBH can be performed successfully in patients with our criteria (age  $\leq$  60 years, ECOG-PS 0 or 1, good respiratory function). In this study, we excluded people aged  $>$  60 years as they are not expected to have stable breathing. Darby *et al.* reported that cardiovascular events increase from 5 years post-radiation, and it is expected that patients aged  $>$  60 years may benefit from DIBH [4]. Therefore, it is necessary to investigate whether the current method can be applied to elderly patients aged  $>$  60 years with good PS and pulmonary function who were not included in this study.

In this study, we showed that DIBH could be performed simply and reproducibly by monitoring a single point on the chest wall from a reference point. This DIBH technique enabled us to perform left whole breast radiation with low cardiac dose in a short time and with little radiation position error. This study showed good results for younger patients aged  $<$  60 years with good general health and respiratory function, but further studies are needed to include elderly patients.

#### ACKNOWLEDGMENTS

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#### CONFLICT OF INTEREST

The authors confirm they have no conflicts of interest to declare. Clinical trial registration number: UMIN000042888.

#### REFERENCES

1. Early Breast Cancer Trialists' Collaborative, Darby S, Mc Gale P et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis

- of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011;378:1707–16.
2. Nozaki M, Kagami Y, Machida R et al. Final analysis of a Multicenter Single-Arm Confirmatory Trial of hypofractionated whole breast irradiation after breast-conserving surgery in Japan: JCOG0906. *Jpn J Clin Oncol* 2021;51:865–72.
3. Meattini I, Poortmans PM, Aznar MC et al. Association of breast cancer irradiation with cardiac toxic effects: a narrative review. *JAMA Oncol* 2021;7:924–32.
4. Darby SC, Ewertz M, McGale P et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *N Engl J Med* 2013;368:987–98.
5. van den Bogaard VA, Ta BD, van der Schaaf A et al. Validation and modification of a prediction model for acute cardiac events in patients with breast cancer treated with radiotherapy based on three-dimensional dose distributions to cardiac substructures. *J Clin Oncol* 2017;35:1171–8.
6. Gagliardi G, Constine LS, Moiseenko V et al. Radiation dose-volume effects in the heart. *Int J Radiat Oncol Biol Phys* 2010;76:S77–85.
7. Ong DS, Aertker RA, Clark AN et al. Radiation-associated valvular heart disease. *J Heart Valve Dis* 2013;22:883–92.
8. Xu S, Donnellan E, Desai MY. Radiation-associated valvular disease. *Curr Cardiol Rep* 2020;22:167.
9. Larsen RL, Jakacki RI, Vetter VL et al. Electrocardiographic changes and arrhythmias after cancer therapy in children and young adults. *Am J Cardiol* 1992;70:73–7.
10. Landau D, Adams EJ, Webb S et al. Cardiac avoidance in breast radiotherapy: a comparison of simple shielding techniques with intensity-modulated radiotherapy. *Radiother Oncol* 2001;60:247–55.
11. Hickey BE, Lehman M, Francis DP et al. Partial breast irradiation for early breast cancer. *Cochrane Database Syst Rev* 2016;7:CD007077.
12. Whelan TJ, Julian JA, Berrang TS et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial. *Lancet* 2019;394:2165–72.
13. Laaksomaa M, Sarudis S, Rossi M et al. AlignRT((R)) and Catalyst in whole-breast radiotherapy with DIBH: Is IGRT still needed? *J Appl Clin Med Phys* 2019;20:97–104.
14. Fassi A, Ivaldi GB, de Fatis PT et al. Target position reproducibility in left-breast irradiation with deep inspiration breath-hold using multiple optical surface control points. *J Appl Clin Med Phys* 2018;19:35–43.
15. Plathow C, Zimmermann H, Fink C et al. Influence of different breathing maneuvers on internal and external organ motion: use of fiducial markers in dynamic MRI. *Int J Radiat Oncol Biol Phys* 2005;62:238–45.
16. Lai J, Hu S, Luo Y et al. Meta-analysis of deep inspiration breath hold (DIBH) versus free breathing (FB) in postoperative radiotherapy for left-side breast cancer. *Breast Cancer* 2020;27:299–307.
17. Misra S, Mishra A, Lal P et al. Cardiac dose reduction using deep inspiratory breath hold (DIBH) in radiation treatment of left sided



- breast cancer patients with breast conservation surgery and modified radical mastectomy. *J Med Imaging Radiat Sci* 2021;52:57–67.
18. Schonecker S, Walter F, Freisleder P et al. Treatment planning and evaluation of gated radiotherapy in left-sided breast cancer patients using the Catalyst(TM)/Sentinel(TM) system for deep inspiration breath-hold (DIBH). *Radiat Oncol* 2016;11:143.
  19. Kugele M, Edvardsson A, Berg L et al. Dosimetric effects of intrafractional isocenter variation during deep inspiration breath-hold for breast cancer patients using surface-guided radiotherapy. *J Appl Clin Med Phys* 2018;19:25–38.
  20. Li G, Lu W, O'Grady K et al. A uniform and versatile surface-guided radiotherapy procedure and workflow for high-quality breast deep-inspiration breath-hold treatment in a multi-center institution. *J Appl Clin Med Phys* 2022;23:e13511.
  21. Usui K. Analysis of correlation between breast surface position and internal organ deformation using deep-inspiration breath holding for left-sided breast irradiation. In: *2020 Annual meeting of American Society for Radiation Oncology (ASTRO)*. Chicago, Illinois, 2020.
  22. Offersen BV, Boersma LJ, Kirkove C et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. *Radiother Oncol* 2015;114:3–10.
  23. Duane F, Aznar MC, Bartlett F et al. A cardiac contouring atlas for radiotherapy. *Radiother Oncol* 2017;122:416–22.
  24. Organization WH. *ICD - O International Classification of Diseases for Oncology* 2013 [Available from: [https://apps.who.int/iris/bitstream/handle/10665/96612/9789241548496\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/96612/9789241548496_eng.pdf)].
  25. Breslow NE, Clayton DG. Approximate inference in generalized linear mixed models. *J Am Stat Assoc* 1993;88:9–25.
  26. Korreman SS, Pedersen AN, Nottrup TJ et al. Breathing adapted radiotherapy for breast cancer: comparison of free breathing gating with the breath-hold technique. *Radiother Oncol* 2005;76:311–8.
  27. Pedersen AN, Korreman S, Nystrom H et al. Breathing adapted radiotherapy of breast cancer: reduction of cardiac and pulmonary doses using voluntary inspiration breath-hold. *Radiother Oncol* 2004;72:53–60.
  28. Shiinoki T, Onizuka R, Kawahara D et al. Estimation of patient-specific imaging dose for real-time tumour monitoring in lung patients during respiratory-gated radiotherapy. *Phys Med Biol* 2018;63:065016.
  29. Jensen CA, Abramova T, Frengen J et al. Monitoring deep inspiration breath hold for left-sided localized breast cancer radiotherapy with an in-house developed laser distance meter system. *J Appl Clin Med Phys* 2017;18:117–23.