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Original Article

Clinical practicality and patient performance for surface-guided automated VMAT gating for DIBH breast cancer radiotherapy

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ABSTRACT

Background and purpose: To evaluate the performance of automated surface-guided gating for left-sided breast cancer with DIBH and VMAT.
Materials and methods: Patients treated in the first year after introduction of DIBH with VMAT were retrospectively considered for analysis. With automated surface-guided gating the beam automatically switches on/off, if the surface region of interest moved in/out the gating tolerance (±3 mm, ±3°). Patients were coached to hold their breath as long as comfortably possible. Depending on the patient's preference, patients received audio instructions during treatment delivery. Real-time positional variations of the breast/chest wall surface with respect to the reference surface were collected, for all three orthogonal directions. The durations and number of DIBHs needed to complete dose delivery, and DIBH position variations were determined. To evaluate an optimal gating window threshold, smaller tolerances of ±2.5 mm, ±2.0 mm, and ±1.5 mm were simulated.
Results: 525 fractions from 33 patients showed that median DIBH duration was 51 s (range: 30–121 s), and median 4 DIBHs per fraction were needed to complete VMAT dose delivery. Median intra-DIBH stability and intrafractional DIBH reproducibility approximated 1.0 mm in each direction. No large differences were found between patients who preferred to perform the DIBH procedure with ($n = 21$) and without audio-coaching ($n = 12$). Simulations demonstrated that gating window tolerances could be reduced from ±3.0 mm to ±2.0 mm, without affecting beam-on status.
Conclusion: Independent of the use of audio-coaching, this study demonstrates that automated surface-guided gating with DIBH and VMAT proved highly efficient. Patients' DIBH performance far exceeded our expectations compared to earlier experiences and literature. Furthermore, gating window tolerances could be reduced.

Radiotherapy (RT) is applied after breast-conserving surgery to enhance local control and overall survival in breast cancer patients [1]. As a consequence and particularly among patients with left-sided breast cancer, radiation dose is incidental partially delivered to the heart and lungs, which is known to increase the risk of cardiovascular and lung disease [2,3]. Advanced radiation techniques like volumetric modulated arc therapy (VMAT) have been developed to deliver more precise and conformal doses to better spare the heart and lungs [4–6]. In breast cancer patients, VMAT is best applied with deep inspiration breath-hold (DIBH) to further decrease the potential risk of radiation toxicity to the heart and lungs [7,8], at the cost of increased patient volume receiving low dose. Various methods exist for performing DIBH [9], including surface guidance techniques. With surface-guided radiotherapy (SGRT), the patients' external surface is monitored and tracked while the patient is on the treatment table [10–13]. During surface-guided DIBH treatments, the cameras monitor the breast/chest wall surface moving in a predefined DIBH tolerance window, ensuring a secure alignment for dose delivery.

In our clinic, standard treatment for left-sided breast cancer involves a hybrid intensity-modulated radiotherapy (IMRT) technique, where radiotherapy technologists (RTTs) manually initiate the delivery of 4–8 beams, and patients are instructed to hold their breath for the duration of each beam segment, which typically ranges from 10 to 30 s [11]. By employing an automatic beam-interruption device that connects the

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SGRT system and the linear accelerator (linac), the monitored DIBH signal can serve as a trigger to automatically switch the radiation beam on and off when the DIBH falls within or outside the predefined tolerance window [14–16]. Recently, for a selected group of breast cancer patients, we have introduced this automated surface-guided DIBH treatment using the VMAT technique. After initiating the VMAT arc (requiring only one manual action by an RTT), the dose delivery is automatically switched on/off, until the entire VMAT arc is delivered. Furthermore, these patients are now instructed to hold their breath as long as comfortably possible, which will minimize beam-interrupts, and potentially shorten the overall time per fraction. Automated respiratory gating has been applied for multiple other sites [17–19]. However, limited studies are available on the use of automated surface-guided DIBH in breast cancer radiotherapy [12,20,21], where data was only presented for vertical direction [12,20], and studies did not focus on patients' compliance and DIBH durations.

This study aims to evaluate the performance of this automated surface-guided DIBH gating treatment for patients with left-sided breast cancer during the first year of implementation in our clinic, with a specific focus on patients' compliance, and the number and duration of DIBHs required to complete VMAT dose delivery. The second aim of this study is to quantify intra-DIBH and intrafractional variations in breast/chest wall surface position during DIBH in order to explore the potential for using smaller tolerance gating windows.

Materials and methods

All patients treated for left-sided breast cancer with surface-guided DIBH VMAT technique in the first year after introduction (February 2022–2023) with informed consent (MEC-2022-0817) were retrospectively considered for analysis. Radiotherapy dose prescription after breast-conserving surgery or mastectomy was 15 × 2.67 Gray (Gy) without or with a simultaneously integrated boost (20 × 2.67 Gy). Treatment plans for sequential boost dose (5 × 2.67 Gy) were excluded from analysis, as well as patients with double-sided breast cancer, or an indication for the use of a bolus on the chest wall.

Patients received a DIBH training three or four days prior to their planning computed tomography (CT) scan to comfortably hold their breath while lying in radiation treatment position, with a special emphasize on relaxing the shoulders and without arching of the back. At CT simulation in our institution, one scan is made in free breathing (FB) and one in DIBH. Patients $\leq$70 years of age were eligible for DIBH, if they were capable of holding their breath comfortably for at least 35–40 s during CT acquisition. Additionally, for VMAT in DIBH, a difference between focus skin distance of the CT in FB and DIBH larger than 1 cm was indicated. This difference is required to distinguish between FB and DIBH, to assure that dose is only delivered when the DIBH is within tolerances. A VMAT plan was generated on the DIBH planning CT-scan with a maximum of 2 arcs (dual arc) of approximately 200 degrees each, while ensuring a total estimated delivery time <200 s (Monaco 6.0.0.1, Elekta AB, Stockholm, Sweden). Plans were optimized with the flash margin option in Monaco, and – after optimization – checked for robustness by recalculating the plan with an isocenter shift of 5 mm in medial and posterior direction ensuring PTV coverage of $V95 > 95$ %, $V110 < 1$ %, and $V115 \leq 0.1$ cc. Patients who did not fulfil these requirements were treated with VMAT in FB (without gating) and were consequently not included in this study.

SGRT is used in our clinical workflow for both initial patient positioning and DIBH monitoring, described in detail by Penninkhof et al [11]. Automated gating was performed with surface scanning imaging (AlignRT, VisionRT Ltd., London, UK) in combination with an automatic beam-interruption device (Response Module, Elekta AB, Stockholm, Sweden) and linac (Versa HD/Synergy, Elekta AB, Stockholm, Sweden). If the left breast/chest wall surface (ROI, region of interest) moved in or out the gating window, the beam was automatically switched on or off, respectively. The ROI of the breast/chest wall is large enough to provide sufficient ROI surface for detection, even if one of the three surface guidance cameras is blocked during VMAT. Clinically, the automatically enforced gating window was ±3 mm and ±3° for all orthogonal directions and rotational axes, which lies within the range of thresholds reported in the literature [7,9,12,20–23]. Depending on the patient's preference, patients received audio instructions during treatment delivery. Visual feedback was provided to all patients using the Real Time Coach device (VisionRT Ltd., London, UK).

During each fraction, the surface guidance system collected real-time FB and DIBH positional translations and rotations with respect to the reference surface of the day, in combination with the status of the beam (on/off). Fig. 1 shows an example of a time plot of the DIBH position variation in vertical (VRT) direction for four consecutive DIBHs within one fraction. For each patient, per fraction, the total number of DIBHs and DIBH durations to complete dose delivery were collected. We initiated the counting of DIBHs when the ROI maintained within gating window tolerances and the beam status remained 'on' for at least 10 s, defining such periods as number of DIBHs. Shorter durations were identified as deep inhales during FB. For each fraction, intra-DIBH stability was calculated as the median over the 5–95 % span of motion or rotation from each single DIBH [24]. For fractions with a minimum of 2 DIBHs, intrafractional reproducibility of DIBHs (indicated with a red arrow in Fig. 1) was quantified as the maximum difference between mean DIBH positions for both translations and rotations [12,22]. DIBH parameters were analysed per patient (median of fraction values) and over the complete group (median over all patients). For translations only, differences in DIBH parameters between patients with/without audio-coaching were also analysed. To evaluate an optimal gating window threshold, smaller tolerances of ±2.5 mm, ±2.0 mm, and ±1.5 mm for each orthogonal direction and in VRT direction only were simulated.

Results

Thirty-three patients with informed consent were included (Table 1). Data of 530 fractions (range 15–20 fractions per patient) were included for data analysis. Five fractions were excluded due to errors in the log data, totalling 525 fractions. Twelve patients performed the DIBH procedure without audio-coaching.

The median DIBH duration with beam-on time was 51 s (patient range: 30–121 s, Fig. 2A), and a median of 4 DIBHs per fraction (range: 1–5) was required to complete VMAT dose delivery. An overall large range of DIBH durations was found (Fig. 2B), as sometimes at the end of a fraction, shorter DIBHs were needed to complete total dose delivery.

Cumulative plots in Fig. 3 illustrate the distribution of the intra-DIBH stability (5–95 % span of motion) and intrafractional reproducibility (differences in min–max mean DIBH positions). Median intra-DIBH stability per fraction over all patients was 1.0 mm, 1.1 mm, and 0.9 mm for vertical, longitudinal and lateral directions, respectively (Fig. 3B). The span of motion range was largest in longitudinal direction. Median intrafractional reproducibility of DIBHs was 1.0 mm, 1.2 mm and 1.0 mm in each direction (Fig. 3D). No large differences were seen between patients who performed the DIBH procedure with ($n = 21$) or without ($n = 12$) audio-coaching regarding the total number of DIBHs, DIBH durations and intra-DIBH stability. A small difference was seen between the groups in intrafractional reproducibility (Fig. 3D), where patients without audio-coaching and only visual feedback performed slightly better (no statistical comparisons were performed due to small patient numbers).

Median rotations during DIBH exhibited minimal deviations from zero in all directions and intra-DIBH stability and interfractional reproducibility remained consistently below 1 degree for the majority of treatment fractions (Supplementary Fig. 1).

Fig. 4 illustrates that, by plotting the intra-DIBH stability and the intrafractional reproducibility, the majority of fractions remained within a gating window tolerance of ±2.0 mm (dashed-dotted line). This

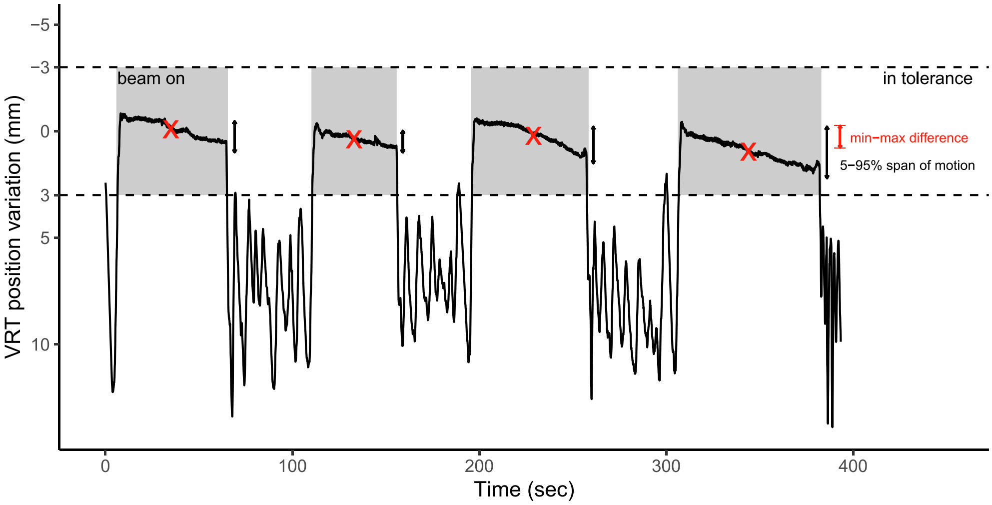

Fig. 1. A time plot showing the position variation in vertical (VRT) direction of the breast/chestwall surface for four consecutive DIBHs within one fraction. The grey boxes indicate the period where the breast/chestwall surface is in the predefined DIBH tolerance window (dashed lines at ±3.0 mm), indicating a safe position for dose delivery. Per DIBH, intra-DIBH stability is quantified as the 5–95 % span of motion (indicated by the black arrows). Intrafractional position variation is calculated as the min–max difference between mean DIBH positions within one fraction (red arrow indicates largest difference between the red crosses). DIBH: deep inspiration breathhold. (For interpretation of the references to colour in the figure legends, the reader is referred to the web version of this article.)

Table 1
Descriptive patient characteristics and radiotherapy parameters.

	N	(%)
Patients who completed DIBH treatment	33	(100%)
Fractionation schedule		
15 × 2.67 Gy	24°	(73%)
20 × 2.67 Gy (simultaneous integrated boost)	9*	(27%)
Radiotherapy		
Breast (total)	**22**	**(67%)**
Breast	8^{a}	(36%)
Breast + Axilla level 1-4	12^{a}	(55%)
Breast + Axilla level 1-2	1	(4.5%)
Breast + Axilla level 3-4	1	(4.5%)
Chest wall (total)	**11ˆ**	**(33%)**
Chest wall	3	(27%)
Chest wall + Axilla level 1-4	7^{a,b}	(64%)
Chest wall + Axilla level 1-2	1	(9%)
Chest wall + Axilla level 3-4	0	(0%)
Age at start radiotherapy (years)		
Mean	53	
Median	54	
Range	29–70	

° 3 patients received a sequential boost, which was not included in data analysis.
* 9 breast patients were indicated with SIB at tumor bed.
ˆ3 patients were treated with breast prosthesis in situ.
^{a,b} the internal mammary chain (n = 3) or sternum (n = 1) was part of the target volume.

was confirmed by our simulation of smaller gating windows, demonstrating that for the majority of simulations, beam-on status (DIBH within gating window) for reduced tolerances of ±2.5 mm and ±2.0 mm would not be affected much compared to the clinically used ±3.0 mm (Fig. 5A). When only VRT direction tolerances were reduced, and lateral and longitudinal tolerances were kept at ±3.0 mm, simulations showed that beam-on status during the treatment session (without set-up and imaging time) remained > 75 % for majority of patients, even for ±1.5 mm (Fig. 5B).

Discussion

Clinical implementation of automated DIBH gating combined with VMAT dose delivery for left sided breast cancer patients was assessed in this study. We have evaluated the clinical practicality of this automated approach and patients' individual compliance and performance. The main finding of our study was the fact that the patients' ability to comfortably sustain long DIBH durations exceeded our expectations (median 51 s, range 30–121 s), regarding to our previous clinical experiences [11], and far surpassed the reported range of voluntary DIBH lengths (11–27 s, without oxygenation) in previous literature [12,20,24,25]. Closer investigation of two outliers from two patients, who both exhibited DIBH durations approximating 125 s in their first fraction, possibly forced to hold their DIBH too long and had not comprehended the DIBH instruction to exhale when DIBH was no longer comfortable. Subsequent fractions showed improvement, and were completed in two or three stable and reproducible DIBHs.

Intra-DIBH stability, quantified as the span of motion, was largest in longitudinal direction. This may result from contraction of the shoulders during DIBH. In general, patients displaying signs of breathholding discomfort or visibly contracting their shoulders, received immediate and personalized audio-coaching throughout the procedure.

Compared to other DIBH techniques, such as active breathing control (ABC, Elekta AB, Stockholm, Sweden) and real-time position management (RPM, Varian Medical Systems, Palo Alto, USA), using SGRT for DIBH procedure shows advantages in terms of practicality and patient comfort [24,26]. All our patients performed voluntary DIBH without pre-oxygenation or hyperventilation. Visual feedback enhanced their interaction with the treatment process [27]. A significant proportion of our patients expressed a preference for undergoing the procedure without the assistance of audio-coaching. These preferences were based on patient-specific circumstances and even varied across different treatment fractions. To answer this variability, a pragmatic approach was adopted, allowing RTTs to adjust procedures in alignment with individual patient preferences. Aligning with the recent ESTRO guidelines [28], we underscore the crucial role of patient compliance to establish a successful and reproducible DIBH workflow. Therefore, in order to prevent that a conclusion could be drawn from the outcome of a statistical test in which either with or without audio-coaching is considered better, no formal statistical comparisons were drawn between these two groups.

All patients with a minimum difference of 1.0 cm between the focus skin distance on the FB and DIBH CT scan were eligible for DIBH with VMAT. This difference is usually achieved by chest respiration in combination with abdominal breathing. However, some patients spontaneously changed during their course of treatment into abdominal

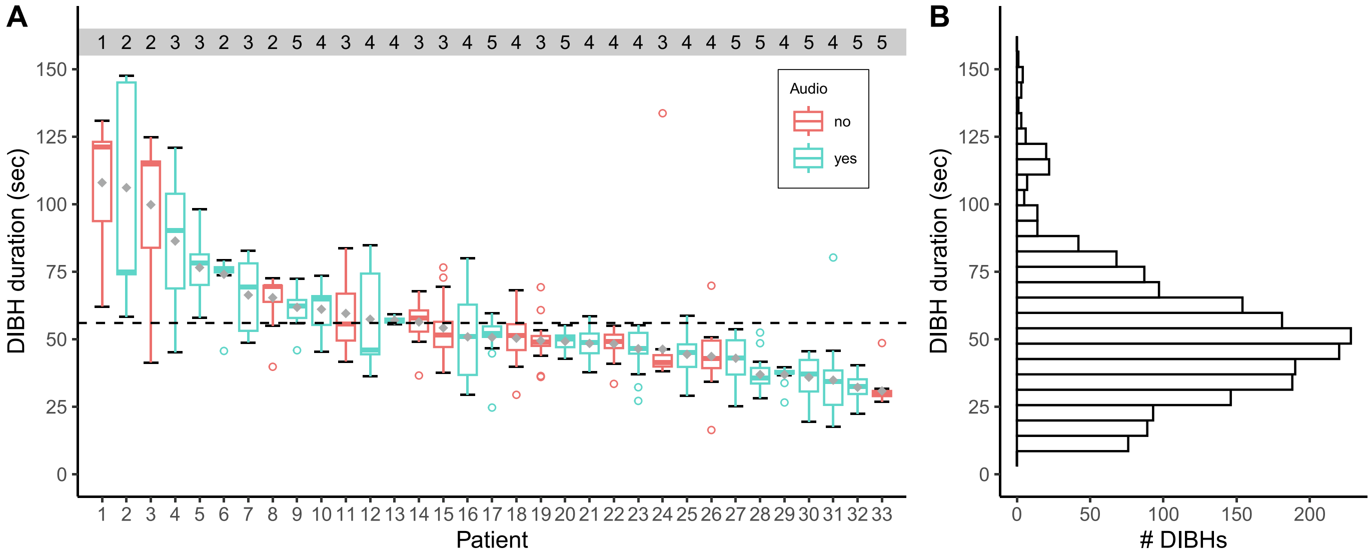

Fig. 2. A) Boxplots showing median DIBH durations per fraction for patients with (blue) and without (red) audio-coaching. Median number of DIBH per fraction to complete the VMAT delivery is shown in the upper grey row. Patients are ordered in decreasing average DIBH duration (indicated with grey diamonds). DIBH durations over all fractions and patients are shown in a histogram in (B), indicating that also shorter DIBHs occurred, often required to complete final MU delivery. Boxplots show median values (horizontal lines), and upper and lower quartiles, whiskers: 5–95%, circles: outliers. DIBH: deep-inspiration breathhold.

breathing while attempting DIBH, resulting in challenges associated with the precise surface tracking of the breast/chest wall ROI required for automatic gating. This issue could be effectively resolved through enhanced audio-coaching toward chest respiration and/or an expansion of the ROI to encompass a small abdominal area. Given the unexpected long DIBH durations found in our study, this inclusion requirement could possibly be used as a selection criteria for patients who are able to do well in DIBH performance.

At present, our protocol requires a minimum breath-holding duration of 35–40 s during CT simulation, aligning with the time required for a CBCT on C-arm linac systems due to a limitation in the gantry rotation speed. To expand DIBH availability for more patients, CBCTs could be acquired in two separate DIBHs [28]. Furthermore, newer O-ring gantry systems allow a faster image generation [29,30]. While Varian linacs feature shorter beam interrupt time-delays compared to Elekta [31], the current set-up of their O-ring linac (Ethos, Varian Medical Systems, Palo Alto, USA) with the Identify SGRT system, lacks automatic gating functionality. Consequently, RTTs are still required to manually initiate beam-interrupts. Another potential solution could involve employing a split VMAT technique [32], allowing patients to breathhold for the duration of each split arc. However, this approach also necessitates manual initiation of each split arc.

Interestingly, most prior studies did not report DIBH duration, but mainly focused on intra-DIBH stability and intrafraction reproducibility and showed an uncertainty of circa 2.0 mm or less is achievable [11,12,22,23,33]. Notably, those values were linked to the chosen gating window threshold, whereby lower thresholds enhanced stability and reduced the maximum offset in mean DIBH position [12,22], and larger or no window resulted in higher values [23,33]. Only one study also reported both translational motion and rotations [21], and found similar results of 1.0 mm and 1.0 degree for intra-DIBH stability and intrafraction reproducibility across all directions and rotations, respectively. These and our results and simulation outcomes indicated the possibility for reduction in gating window tolerances. This potentially leads to more DIBHs required to deliver the full fraction, and may consequently lead to longer treatment times because patients may need to take a few breaths between each DIBH. We have therefore been hesitant to permanently implement smaller gating windows in the clinical workflow, but individual adjustments per patient are now accepted.

In addition to the advantages with SGRT for set-up positioning and real-time monitoring, the main advantage in the present study is the automated gating mechanism. This mechanism assures instantaneous beam interrupt, which is an improved safety aspect, as RTTs no longer have to manually pause the beam when a patient has difficulties holding her breath within tolerances. Several studies with different measuring methods for various combinations of SGRT systems, gating devices and linacs have demonstrated that time delays significantly differ, ranging from 209 to 1664 ms for beam-on time delays and 25–529 ms beam-off time delays [14,15,31,34]. Therefore, as suggested by [14,31] and also recommended by ESTRO guidelines on SGRT implementation and quality assurance [35], careful characterization of the beam-on and beam-off delays were tested before implementing our surface-guided gating system using the automatic beam-interruption device. Also, delivering complex VMAT plans with high dosimetric accuracy, despite frequent beam interruptions due to DIBH gating, was validated for our linacs (1.0 %/0.1 mm, Gamma $>$ 99 %).

One limitation of this study is that the dosimetric implications of DIBH variability within and across fractions are not discussed. Others, who reported similar values of DIBH variabilities (circa 1.0 mm and 1 degree), applied isocenter shifts to the original treatment plan which resulted in similarly small dosimetric consequences [21,24]. However, for outliers (up to 5.0 mm), large dosimetric deviations for target and organs at risks were reported [22]. Therefore, as mentioned before, smaller gating windows can assure DIBHs with good stability and low intra- and interfraction variability, consequently leading to smaller deviations in dosimetric delivery and thus more conformal dose delivery. This will be especially important in ultra-hypofractionated treatments with higher fraction doses [36], since compensating for deviations in fewer fractions is less achievable.

Another potential solution could involve delivering a plan with varying complexity in a single prolonged DIBH (up to minutes), which has been investigated in breast cancer patients by combining deep inspiration, hyperventilation and pre-oxygenation using a mechanical ventilator [37–40]. In prolonged DIBHs from healthy volunteers (median 6–7 min), diaphragm drifts (quantified with MR imaging) in cranial direction were still 3.0 and 4.4 mm/minute during inhalation and exhalation DIBHs, respectively [40]. As longer preparation for these techniques are time-consuming and require experienced staffing, it seems difficult to implement in the daily routine of radiotherapy

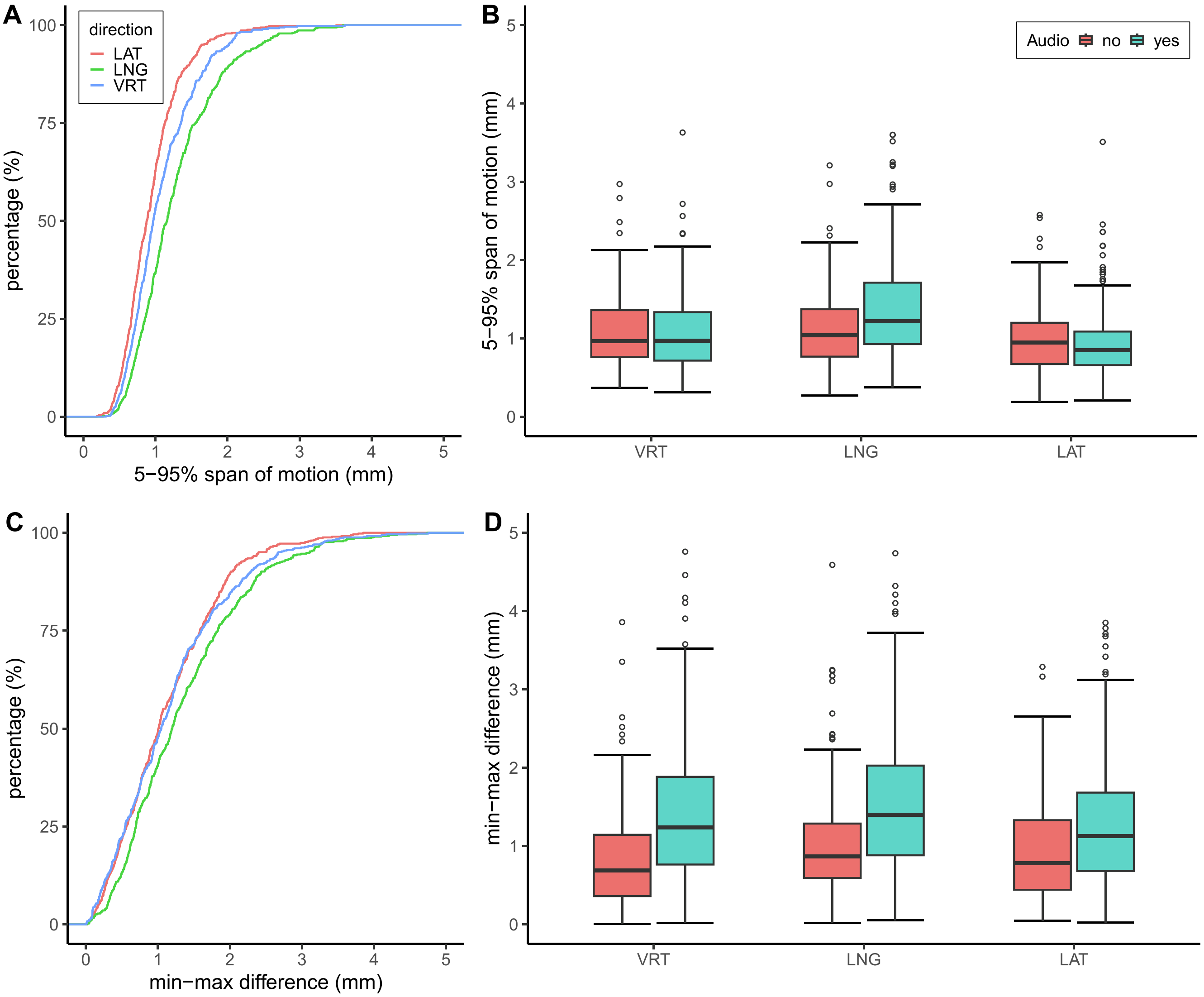

Fig. 3. Cumulative plots of the intra-DIBH stability (3A) and intrafractional reproducibility (3C) for each direction. Boxplots showing the intra-DIBH stability (3B) and intrafractional reproducibility (3D), for patients with (n = 21, blue) and without (n = 12, red) audio instructions. Boxplots show median values (horizontal lines), and upper and lower quartiles, whiskers: 5–95 %, circles: outliers. DIBH: deep-inspiration breathhold. VRT: vertical, LNG: longitudinal, LAT: lateral.

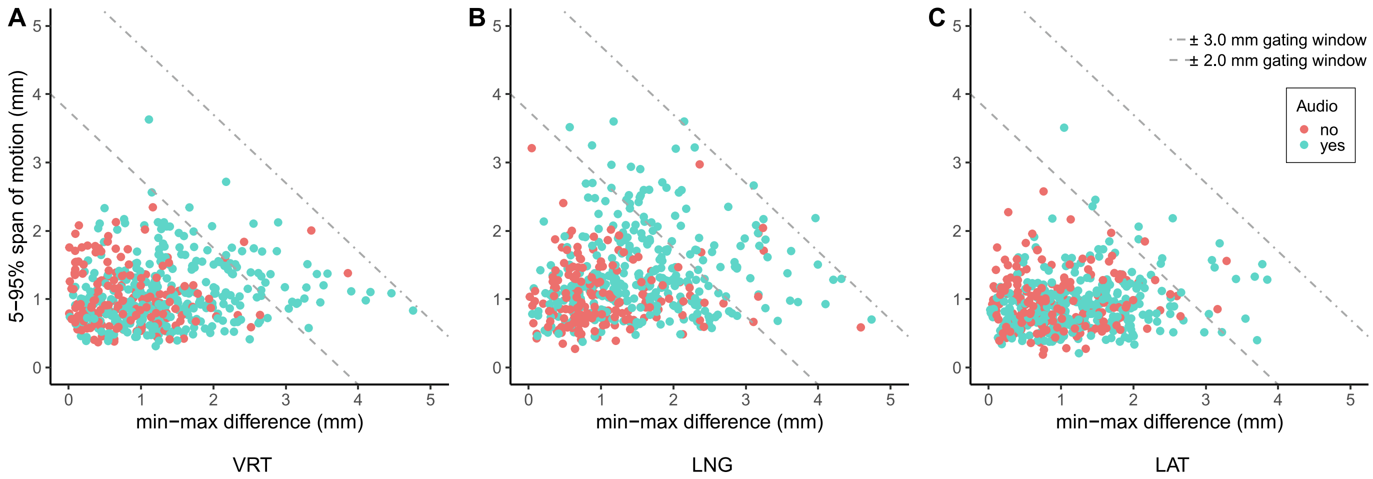

Fig. 4. Intra-DIBH stability (y-axis) plotted against intrafractional reproducibility (x-axis) for each fraction (one data point) for each direction separately. The dotted-dashed line implicates the ±3.0 mm gating window tolerance, while the dashed line shows the tolerance for a ±2.0 mm gating window. DIBH: deep-inspiration breathhold. VRT: vertical, LNG: longitudinal, LAT: lateral.

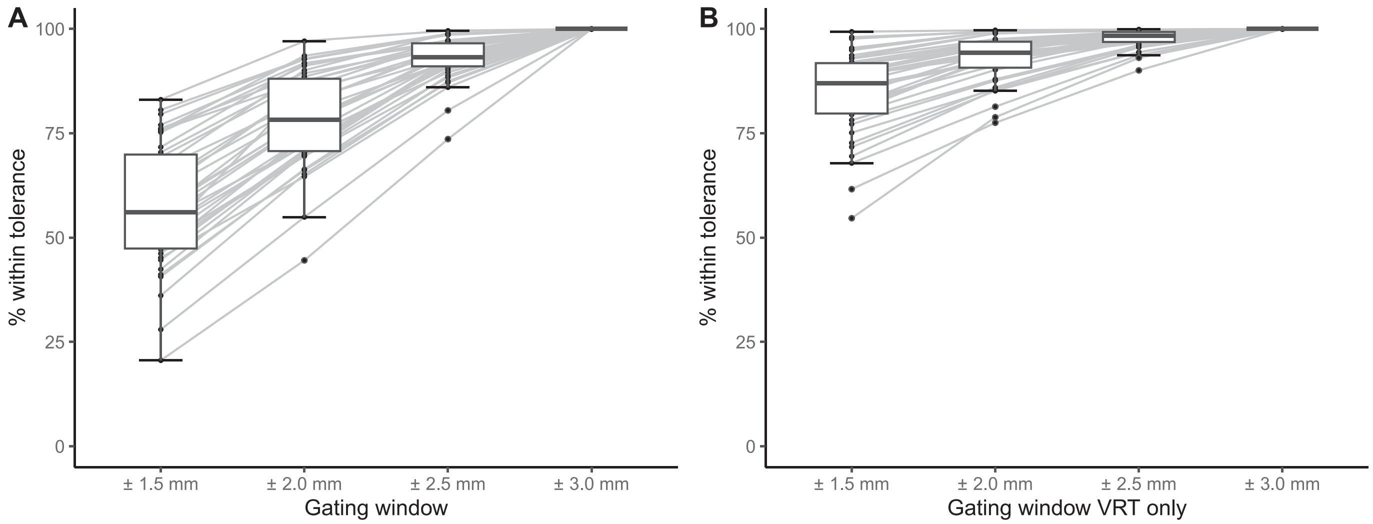

Fig. 5. Boxplots showing percentages of beam-on status (DIBH within gating window) for reduced tolerances of ±1.5 mm, ± 2.0 mm and ±2.5 mm compared to the clinically used ±3.0 mm, for all directions (A) and for reduced tolerances in vertical (VRT) direction only (B). Each dot with corresponding line represent median value for one patient. Boxplots show median values (horizontal lines), and upper and lower quartiles, whiskers: 5–95 %, circles: outliers.

departments facing personnel shortages.

To conclude, the present study shows a valuable insight into patient compliance and practicality of automated surface-guided VMAT gating for DIBH breast cancer radiotherapy. It far exceeded our understanding of patients' DIBH capabilities, but also highlighted the necessity of accommodating individual preferences to establish a robust and reproducible DIBH procedure. The applied technique proved highly efficient with unexpectedly long DIBHs, while staying far below clinically used gating window tolerances.

Credit authorship contribution statement

Sophie Huijskens: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Patrick Granton:** Writing – review & editing, Validation, Supervision, Software, Methodology, Investigation, Conceptualization. **Kimm Fremeijer:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Cynthia van Wanrooij:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kirsten Offereins-van Harten:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Suzanne Schouwenaars-van den Beemd:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mischa S. Hoogeman:** Writing – review & editing, Visualization. **Margriet G.A. Sattler:** Writing – review & editing, Visualization. **Joan Penninkhof:** Writing – review & editing, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2024.110229.

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