Original Article

Analysis of Planning Risk Volume for Heart during Radiotherapy Delivery with Breath-Hold Technique for Carcinoma of Left Breast

Radhika Jain[1,2], Rose Kamal[3], Manoj K. Semwal[4], Deepak Thaper[3], Shefali Kanwar[1], Tripti Saxena[2]

[1]Department of Physics, Amity Institute of Applied Sciences, Amity University, Noida, Uttar Pradesh, [2]Department of Radiation Oncology, Max Super Speciality Hospital, [4]Department of Radiation Oncology, Research and Referral, Army Hospital, New Delhi, [3]Department of Radiation Oncology, Amrita Hospital, Faridabad, Haryana, India

Abstract

Purpose: The purpose of the study was to analyze and estimate planning risk volume (PRV) margin for heart in deep inspiration breath hold (DIBH)-based left breast radiotherapy. **Materials and Methods:** Fifty left-sided cancer breast cases treated with volumetric modulated arc radiotherapy were included in this retrospective study. Treatment plans were created using the Eclipse treatment planning system from Varian Medical System. The treatment was delivered on TrueBeam linear accelerator (Varian). Onboard cone-beam computed tomography (CBCT) images were generated and image registration between the planning computed tomography images and the CBCT images was performed before treatment delivery. The registration provided the shifts (errors) values in 6° of freedom, namely three translational and three rotational. From the shift values, the systematic and random errors were estimated which were used to estimate PRV margin for the heart after incorporating the rotational errors with the translational errors. **Results:** The systematic error values after incorporating rotational errors with translational errors were 0.13 cm (lateral) and 0.11 cm (cranio caudal [CC] and anterioposterior each), and the random error values were 0.16 cm (lateral) and 0.13 cm (CC and anterioposterior each). Based on these values, the PRV margins for the heart in all three directions were 0.24 cm (lateral), 0.20 cm (CC), and 0.19 cm (anterioposterior). **Conclusion:** As per our institutional practice, the 2 mm value for PRV margin for the heart in all the three directions would suffice for appropriate sparing of the heart during DIBH-based radiation therapy.

Keywords: Deep inspiration breath hold, left breast radiotherapy, planning risk volume

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Introduction

Breast cancer is the most prevalent ailment globally which needs a multidisciplinary approach to improve clinical outcomes. Radiation therapy plays a crucial role in the management of breast cancer in reducing the risk of local recurrence and enhancing overall survival rates. However, the proximity of the breast to vital organs, such as the heart and lungs, presents a challenge in delivering optimal radiation doses to the target while sparing healthy tissues from unnecessary exposure.[1]

To achieve as low a dose as possible to the heart, sources of uncertainty in dose delivery in the various steps of treatment planning and delivery should be minimized. The sources of uncertainty that might change the planned dose during the treatment are positional shift, shift from respiratory pattern, and planning uncertainty. Numerous studies have demonstrated that even low doses of radiation to the heart can lead to increased risks of cardiac morbidity such as coronary artery disease, myocardial infarction, and valvular dysfunction.[2] The risk of heart toxicity increases by 5%–7% for every 1Gy incremental of mean heart dose.[3] The sources of uncertainty include absolute calibration of the treatment machine, modeling of radiation transport within the patient, and day-to-day positioning of the patient. Therefore, reducing radiation exposure to this vital organ is imperative to ensure optimal long-term outcomes for breast cancer patients.

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Address for correspondence: Ms. Radhika Jain,
Department of Physics, Amity University, Noida, Uttar Pradesh, India.
E-mail: radhikajain331@gmail.com

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The studies that remain the primary basis for cardiac toxicity from radiation are from the pre-three-dimensional (3D) conformal radiation therapy era. Advances in radiotherapy technology since then have decreased the cardiac toxicities in radiotherapy.[2,4-6] Some techniques like treating the patients in a prone position to keep the breast away from the heart, intensity-modulated radiation therapy (IMRT), and volumetric-modulated arc therapy (VMAT) are effective in reducing the heart dose. However, in IMRT and VMAT though the higher dose to heart is reduced significantly, the lower dose spill is higher.[7]

In recent years, the deep inspiration breathhold (DIBH) technique has been emerging to mitigate the potential adverse effects of heart in left breast treatment. DIBH technique involves training the patient to take a deep breath and hold it for >15 s at least at a specific point of the breathing cycle. DIBH will inflate the tidal volume to a sufficient capacity which facilitates pushing the heart away from treatment fields. This displacement provides a wider safety margin for the heart during radiation therapy. The immobilization resulting from DIBH improves the precision and accuracy of dose delivery, thus allowing for tighter margins around the target volume. This results in a reduction in radiation dose to normal surrounding tissues and minimizing side effects such as pulmonary toxicities, apart from the cardiac complications.

There are published studies on setup accuracy in patients undergoing left-sided breast radiotherapy with gated techniques such as DIBH (Lutz CM *et al*. (2015), Rajko Topolnjak).[1,8] Most of these studies are on smaller sets of patients. Very few studies are found on larger sets of patients, especially when rotational shifts have been converted to translational shifts to estimate the planning risk volume (PRV) of the heart. Lutz CM *et al*. (2015) estimated setup errors and motion using continuous portal imaging for 58 patients who were treated for left-sided breast cancer with the DIBH technique. Topolnjak *et al.* carried out a four-dimensional motion-based estimation of PRV (heart) for breast radiotherapy.[8] We could not find any comprehensive study that included rotational corrections along with the linear shifts for PRV heart estimation while treating the left breast with the DIBH immobilization technique. Further, we believe that setup errors and other uncertainties associated with a complex technique like DIBH are strongly influenced by the locally available institutional expertise and practice. Therefore, studying a technique systematically for a sufficiently large set of patient data at a center provides valuable information regarding the robustness of the technique and the protocols.

This is a retrospective single institutional study, in which we systematically analyzed the setup errors of 50 patients who underwent left-sided VMAT for breast cancer. DIBH-based gating was used for motion management in all these cases. The assessment of the errors provided us with the data for estimating the PRV margins after quantifying the movement of the heart during treatment. Rotational shifts were taken into account by converting them into linear shifts for PRV estimation.

Materials and Methods

The 50 left-sided breast carcinoma patients of both the chest wall and BCS were picked up randomly which were treated in the year 2019–2021, and total dose of 40Gy was planned, they were treated by VMAT technique using DIBH which involves optical gating called real-time position management (RPM) system version 7.5 (Varian Medical Systems, Palo Alto, CA, USA). The linear accelerator model used was TRUEBEAM STX version 6 (Varian Medical Systems). The RPM camera monitored the external block with infrared rays (IR) markers which were placed on the patient's surface near the xiphoid process. The treatment delivery was allowed only when this block was located in a predefined gating position. Before undergoing planning computed tomography (CT), the patient was called for 3–4 days for training of 30-min sessions on each day. The gating level was determined according to the individual patient's comfort limit to hold the breath during the inhalation for at least 15–20 s.

Patient positioning and setup

A thermoplastic mask with a slop board was used to position the patient in such a way that the IR marker was placed the inferior end of thermoplastic mask at the Xiphoidal process. Before the day of CT scan, patient was video coached for 3–4 days. During the CT scan, patient was audio and video coached to hold the breath during the scan, and gating window was amplitude base, and baseline was captured for treatment planning and delivery. The day of the treatment, the patient was positioned in the same way as the day of CT scan and with the help of audio coaching and gated kilovoltage cone-beam, CT the positional uncertainty was estimated and corrected then only with the help of consultant and medical physicist. The point of benefit of gated treatment is that during the baseline shift of the patient respiratory motion, it automatically holds the treatment, and the patient was asked to relax and recoached for the treatment to complete the fraction.

Image acquisition and contouring

The planning of noncontrast CT (Bright Speed, GE Healthcare) for all the patients was performed with both arms above the heads and with a thermoplastic mask to immobilize the patient for the treatment. A gated CT scan with a slice thickness of 2.5 mm was acquired with DIBH technique. The gating level and window for each patient were recorded subsequently during the CT scan and were reproduced during the treatments too. Soma vision (Varian Medical Systems (Palo Alto,California). Ver-15.6) was used to delineate the target and organ at risk (OAR). Gross tumor volume and clinical target volume (CTV) were drawn using positron emission tomography CT (Discovery IQ Gen 2, GE Healthcare) images registered with the planning CT. A 5 mm margin was added all around the CTV to generate planning target volume (PTV).

Treatment planning

The OARs such as left and right lungs, heart, esophagus, and spinal cord were delineated on the planning CT. A total dose of 40Gy in 15 fractions was prescribed to the PTV. A single isocenter technique was used for all patients with 6 MV beam energy. The VMAT treatment plans were generated with partial arcs (300°–175°, different combinations of collimators) using Eclipse treatment planning system version 15.6 (Varian Medical Systems, Palo, Alto, CA, USA) with the photon optimizer (PO, ver. 15.6) for fluence optimization. An analytical anisotropic algorithm was used for dose calculation with a grid size of 2.5 mm. The dose constraints as recommended in the radiation therapy oncology group 1005 protocol were achieved for all the OARs.[9] For reference the [Figures 1-4] was acquired during the Planning for DIBH patient and was acquired On-Site.

Image matching

For image matching, daily gated CBCT was performed for verification. On Board Image (OBI®, Varian Medical Systems, Palo, Alto, CA, USA) integrated with the Varian True beam linear accelerator was used for acquiring CBCT images. A total of 700 pretreatment 3D CBCT scans were acquired using on-board imager.

A total of 696 datasets of errors were extracted from the whole set of 50 patients of daily image registration. The rigid registration between the CBCT scan and planning CT scan (both in DIBH) was then performed. For this, bone-to-bone matching was performed at sternum level, and the heart matching was also observed simultaneously. Setup errors were noted in 6 degrees of freedom (6DoF): Three in translational left–right (LR), cranio caudal (CC), and anterior posterior (AP); and three in rotational axes namely rotation/roll, yaw, and pitch.

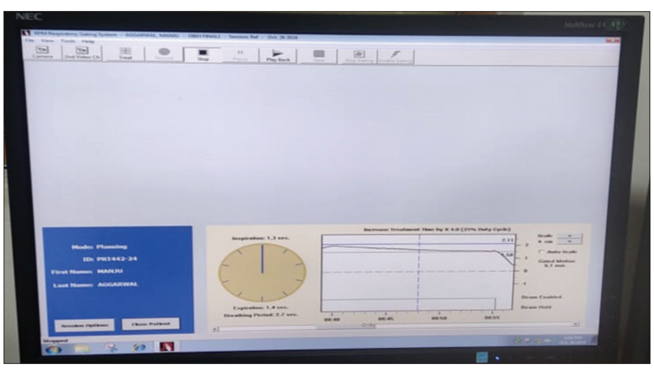

Figure 1: The RPM system can support both breath-hold techniques (where the patient holds their breath to keep the target in place) and respiratory gating, where the radiation beam is activated only at specific phases of the breathing cycle. Respiratory waveform: On the right, there is a graph showing the respiratory trace, representing the patient's breathing pattern in real time. The waveform helps clinicians assess and adjust the timing of radiation delivery based on the patient's respiratory cycle. Gating thresholds: The chart may show gating thresholds, marked as upper and lower limits on the respiratory waveform. These thresholds indicate the phase of the breathing cycle where the radiation beam should be active

The 3D-CBCT images were registered (bone to bone matching) with the planning CT and the 6D shifts were applied online automatically using 6D motion enabled Perfect Pitch couch with IGRT couch Top (True Beam, Varian Medical Systems). This matching was done during the treatment of patients. Further, offline matching was performed where the two sets of images were registered considering the heart as the primary structure. The corresponding 6D shifts were calculated to calculate the corresponding PRV margins.

Data analysis

The standard Van Herk Formula for PRV was used to calculate the PRV heart which employs 3D shifts. PRV margin = 1.3 × ∑ + 0.5 × σ, σ is the mean of the population standard deviation (SD) and accounts for random errors, and ∑ is the SD of the mean population shifts and accounts for systematic errors.[10,11] The measured 6D shifts were then converted into 3D shifts. The conversion was needed to combine the contribution of rotational shifts with translational shifts. Sarkar *et al*. studied the basis for the conversion of rotational shifts into their translational equivalent values,[12] but the suggested formula was modified and it is as follows:

$$x3d \quad y3d \quad z3d = \begin{matrix} cos\theta cos\varnothing & -cos\theta sin\varnothing & -sin\theta \\ -sin\theta sin\varphi cos\varnothing + cos\varphi sin\varnothing & sin\theta sin\varphi sin\varnothing + cos\varphi cos\varnothing & -sin\varphi cos\theta * x6d \quad y6d \quad z6d \\ -sin\theta cos\varphi cos\varnothing - sin\varphi sin\varnothing & sin\theta sin\varnothing cos\varphi - sin\varphi cos\varnothing & cos\theta cos\varphi \end{matrix}$$

The formula by Sarkar *et al*.[12] was modified as there was an observation that during the calculation for one translational axis, we were achieving the value zero for all the patients which was not acceptable so after applying the formula for Euler angles we were able to calculate the translational values including rotational shifts.

Figure 2: The IR camera captures and monitors infrared light, which is often reflected off markers placed on the patient's body. These markers help the system to track even subtle movements, which is essential for maintaining precision throughout the treatment

where x3d, y3d, and z3d are new translational shift values after rotational shift values were incorporated with the initial translational shifts. x6d, y6d, and z6d are the translational shifts for 6D CBCT shifts acquired. Angle θ (rotational), angle ϕ (pitch), and angle ψ (roll) are rotational shifts. After the multiplication of the matrix from right-hand side, we derived the new x, y, and z values which was the representation of 6DoF in 3DoF.

Computed tomography simulator system

Bright Speed GE CT system.

Treatment delivery system

Varian TrueBeam STX.

Results

The CBCT image registration was performed in 6DoF. For every patient, the mean absolute correction, and SD was calculated.

The two types of shifts are estimated one is online and the second is offline. During online correction, patient was matched bone to bone on treatment couch and the shift was noted down. For offline correction, the heart-to-heart match was done to calculate the residual shift, and PRV margins were calculated using residual shifts to know the exact movement of heart during the treatment. The translational shifts for the right left (RL), CC, and AP orientations resulted in mean absolute interfractional errors 0.12 cm ± 0.15 mm, 0.10 cm ± 0.12 mm, and 0.10 cm ± 0.12 mm in RL, CC, and AP orientations, respectively.

The systematic error and random error calculated for 3DoF after the conversion from 6DoF for offline matching protocols are shown in Table 1. The summation of errors in 6DoF for offline matching protocols is presented in Table 2.

PRV heart was calculated individually for each direction, i.e., RL, AP, and CC directions. This PRV calculation was expected to be more accurate as it includes the effect of rotational shifts. In the other methods, the rotational shits were not taken into account. Whereas during off-line correction the heart motion was considered the main parameter during matching and results were estimated, and in such cases, the PRV heart in all three directions was 0.24 cm (LR), 0.20 cm (CC), and 0.20 cm (AP) and it is represented in [Figure 6].

Table 1: Systematic error, random error, planning risk volume heart margin for offline corrections in all three directions where the rotational effect was considered in all the translational directions

	RL (cm)	CC (cm)	AP (cm)
Systematic error (∑)	0.126	0.105	0.105
Random error (σ)	0.159	0.127	0.127
PRV margin	0.243	0.200	0.200

RL: Right to left, CC: Cranio caudal, AP: Anterior posterior

The error distribution resulted (or shows) in a reduction in the range/spread of setup errors for heart matching (offline) in Figure 5. It provides a visual summary of the central tendency, dispersion, and skewness (asymmetry) of the data. The below is the representation of data.

- Box: The box in the plot represents the interquartile range, which is the middle 50% of the data. The bottom and top edges of the box mark the first quartile (Q1) and third quartile (Q3), respectively. The length of the box indicates the spread of the middle 50% of the data
- Median (Q2): A line inside the box marks the median of the dataset, also known as the second quartile (Q2). The median represents the middle value of the dataset when it is ordered from smallest to largest
- Whiskers: The whiskers extend from the edges of the box to the minimum and maximum values of the dataset within a certain range.

The difference in the number of events corresponding to setup errors of <3 mm, 3–5 mm, and >5 mm are shown in Figure 7, in all three directions, i.e., x, y, and z. It is the cumulative representation of errors in three different directions.

Discussion

PRV margins are an important aspect for ensuring the sparing of normal tissues effectively. These entail the uncertainties in the

Figure 3: Real-time monitoring: During treatment, the system compares the patient's current position with the planned treatment position. If the patient moves out of the set threshold, the system alerts the clinicians or even pauses the radiation beam, preventing mistargeting

Table 2: Six-dimensional error values for offline correction

	Δx (cm)	Δy (cm)	Δz (cm)	Δpitch (°)	Δroll (°)	Δrotation (°)
Mean±SD	0.020±0.204	0.026±0.317	−0.018±0.172	−0.157±1.099	−0.154±1.036	−0.139±1.007

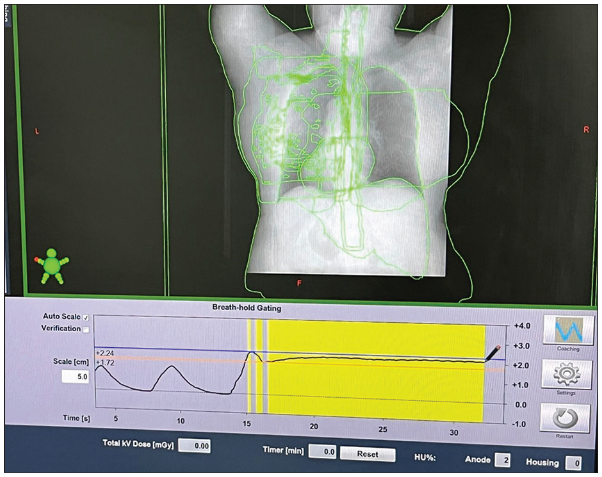

Figure 4: This image shows the delivery of treatment during breath hold where yellow signifies the time during which radiation beam is on. Once the patient is in the correct position with a deep breath-hold, the radiation is delivered. Each radiation beam session is usually very brief (a few seconds) to allow the patient to breathe between each breath-hold. The cycle of deep breath, hold, and radiation delivery is repeated until the entire planned dose is administered for that session. Depending on the radiation plan, several breath-hold cycles may be required per session

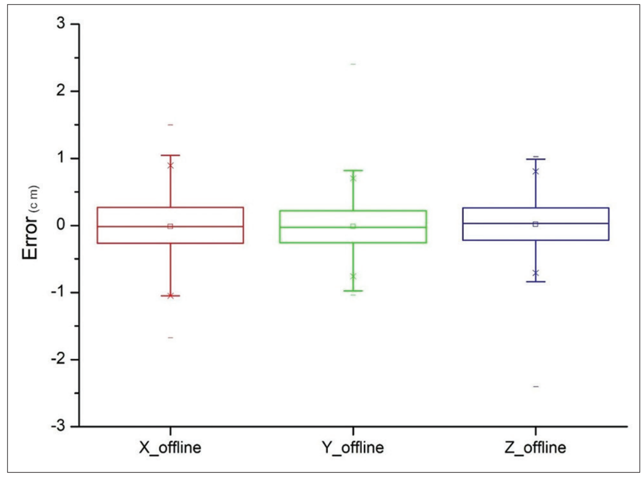

Figure 5: Error distribution (cm) in each dimension for heart-to-heart image matching after 6D to 3D conversion of errors

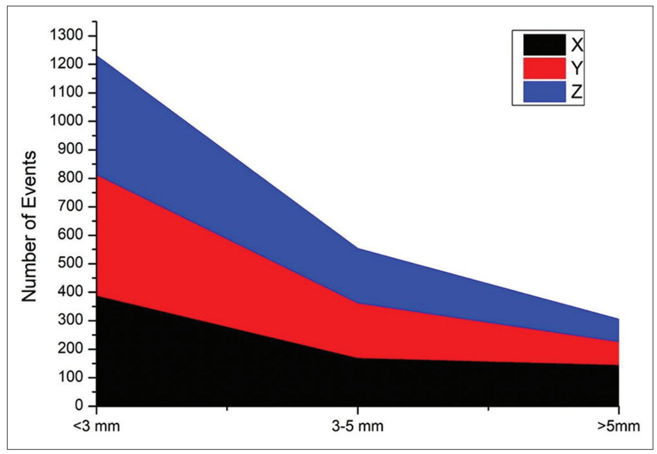

Figure 7: Error distribution for offline matching along (a) x direction (b) y direction (c) z direction

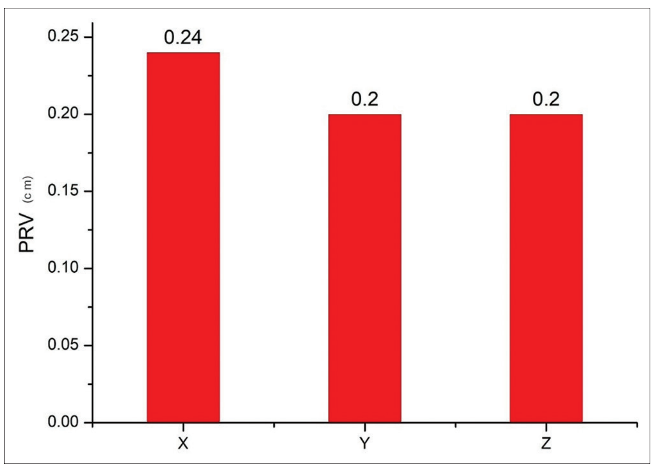

Figure 6: Planning risk volume margins (cm) in each translational direction (x, y, and z)

position of normal tissues during irradiation. Not considering these uncertainties may prove harmful either as acute or late toxicities. PRV margin adds to confidence to maintain the efficacy of the radiation therapy and is important, especially in left breast cases where the heart is a critical organ. Long-term survival of breast patients is high, and hence it is imperative to minimize the long-term toxicities in these cases. Further, the breast and heart being moving organs may result in an underdose or overdose of these structures. However, in DIBH technique, the interplay effect; the relative movement of machine parameters such as multi leaf collimators (MLC) movement, gantry rotation with respect to moving tumors can be eliminated. In this study, we have analyzed the image registration based on heart structures to find out the PRV margins of the heart.

In the paper by Stefanovski *et al*.[13] found that the PRV margin around the lung and heart during left breast irradiation was unambiguous as it involved overlapping of the PRV with the other structures such as esophagus and PTV. The study showed that the PRV heart overlapping caused heart overdoses in 23% of patients and lung overdoses in 11% of patients.

Alderlieste[14] compared the different methods available for monitoring or controlling respiratory motion during DIBH for left-sided breast irradiation.[14] During different breath holds, average heart shifts concerning bony anatomy were 0.20 ± 0.30 cm caudal, 0.10 ± 0.20 cm right, and 0.10 ± 0.30 cm posterior. Their study indicated that there was a moderate correlation between the surface and heart displacement during the treatment.

Topolnjak *et al*.[8] showed that the PRV margins in online setup for cardiac uncertainties were $\sum$ (systematic error) = 2.2/3.2/2.1 mm, σ (random error) = 2.1/2.9/1.4 mm, and PRV heart = 1.6/2.3/1.3 mm for LR/CC/AP, respectively. For offline setup correction, they were $\sum$ (Systematic error)

= 2.4/3.7/2.2 mm, σ (random error) = 2.9/4.1/2.7 mm, and PRV heart = 1.6/2.1/1.4 mm. Cardiac motion induced by breathing had σ_{resp} = 1.4/2.9/1.4 mm for LR/CC/AP. The PRV underestimated the accumulated heart dose in 9.1% of patients using online and 13.6% of patients using offline bony anatomy setup correction.

The PRV heart margins in our study for left-sided breast cases were calculated for the uncertainty in heart position that was not corrected during online registration. The breathing window during DIBH and the involuntary motion of the heart cause uncertainty in the positioning of the heart. Further, the geometric uncertainties were calculated in 6DoF and the contribution of rotational shifts was added to calculate equivalent translational shifts. The 6DoF matching was preferred for accurately matching the heart isotropically, whereas in 3D matching, some parts of the heart may remain unmatched. In the previous studies, the calculation of PRV margins for the heart was performed after 3D matching. The PRV margin and PTV overlapping were minimal due to the DIBH technique which helped in achieving the total coverage of PTV, i.e., 95% as per the standard rules by ICRU.

The PRV margins for the heart were calculated corresponding to setup errors extracted from offline matching. The resulting PRV margins were 2.4, 2 mm, and 2 mm in RL, CC, and AP directions, respectively. The accurate determination of PRV margins is important for better control of irradiation of the surrounding normal structures.[10,11]

The heart being situated closer to the left breast is prone to late toxicities even if lower doses are delivered during the radiation therapy. Even a small increase in radiation dose to the heart can cause severe toxicities at a later age. As the overall survival for breast patients is very high in general, accurate determination as well as delivery is of utmost importance to offer a better quality of life to patients. In this study, we focused on quantifying the PRV margins of the heart without considering other uncertainties such as delineation errors.

Conclusion

A quantification of PRV margins helps to facilitate the confidence of the radiation oncology team in the accuracy and precision of treatment administration. In our study, equivalent contributions of the rotational errors were also taken into account with translational errors for the estimation of PRV margins in the DIBH technique. We found that a PRV margin of 2 mm in all directions would suffice for appropriate sparing of the heart during DIBH-based radiation therapy.

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Conflicts of interest

There are no conflicts of interest.

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