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Research Article

Evaluation of helical tomotherapy as an alternative for left-sided breast cancer patients not compliant with deep inspiration breath hold

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ABSTRACT

Purpose: The aim of this study is to investigate, from a dosimetric perspective, whether helical Tomotherapy (HT) during free breathing (FB) can serve as an alternative technique for treating left-sided breast cancer patients who are unable to comply with the deep inspiration breath hold (DIBH) technique.

Material and Methods: For this purpose, the CT images of 20 left breast-only cancer patients acquired in both FB and DIBH phases were utilized. The left breast was contoured as the target volume, while the heart, LAD, ipsilateral and contralateral lungs, and contralateral breast were contoured as organs at risk on the CT images obtained in both DIBH and FB. Planning with the volumetric modulated arc therapy (VMAT) technique was performed on the CT scans obtained in the DIBH (VMAT-DIBH), while planning with the HT technique was carried out on the CT scans obtained in the FB (HT-FB). Subsequently, dosimetric comparison of the plans were done in terms of target coverage and preservation of normal tissues.

Results: Both techniques achieved the desired target coverage; however, in terms of D2, Vpres values, Conformity Number (CN), and Homogeneity Index (HI), the HT-FB technique was found to be superior. While the mean doses to the heart were similar for both techniques, doses to the LAD and left lung were found to be superior in plans generated with the HT-FB technique. When compared in terms of contralateral breast and right lung protection, VMAT-DIBH technique was found to be significantly superior.

Conclusion: The treatment of left breast-only patients with the HT-FB technique has been observed to provide similar heart protection and better LAD and ipsilateral lung protection compared to the VMAT-DIBH technique without compromising target coverage. However, when the HT-FB technique is used, doses to the contralateral lung and contralateral breast should be carefully evaluated.

Introduction

Breast cancer is the most common cancer among women. Despite the numerous systemic treatment options and refined surgical techniques available, RT remains a category 1 recommendation in the adjuvant setting following almost all breast-conserving surgeries and mastectomies for locally advanced disease [1,2]. Recent advancements in the

molecular characterization of breast cancer have led to the design of numerous trials aimed at omitting RT [3,4]. These efforts are driven by historical concerns associated with older technologies, which led to increased cardiotoxicity and a higher risk of contralateral breast cancer [5–9]. Additionally, the prolonged survival of breast cancer patients emphasizes the importance of considering the long-term side effects of RT. However, the introduction of new RT techniques and motion

Abbreviations: CTV, Clinical Target Volume; DIBH, Deep Inspiration Breath Hold; FB, Free Breathing; HT, Helical Tomotherapy; VMAT, Volumetric Modulated Arc Therapy; OAR, Organ at Risk; CT, Computerized Tomography; RT, Radiotherapy; LAD, Left Anterior Descending artery; IL, Ipsilateral Lung; CL, Contralateral Lung; CB, Contralateral Breast; PTV, Planning Target Volume; CN, Conformity Number; HI, Homogeneity Index (Vx was defined as the percentage of a given tissue volume receiving at least x Gy Dx% was defined as the dose delivered to x% of the volume); Vpres, prescribed dose volume (%) inside of the PTV; Avg, Average; STD, Standard Deviation; Dmax, Maximum Dose; Dmean, Mean Dose; 3DCRT, Three-Dimensional Conformal Radiotherapy; IMRT, Intensity Modulated Radiotherapy; FinF, Field in Field; DVH, Dose Volume Histogram.

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tracking methods, such as helical therapies and Deep Inspiration Breath Hold (DIBH), has significantly improved the protection of normal tissues [10–12]. Consequently, modern breast RT is associated with minimal side effects, thereby preserving the quality of life for patients.

Many modern techniques have been examined to improve dose distribution in breast cancer radiotherapy. The most used modern techniques are field in field (FinF), intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and Helical Tomotherapy (HT). Recently, the VMAT technique has been shown to provide improvements in delivering homogeneous doses to the target and in protecting critical organs compared to traditional planning techniques [13,14]. Previous studies have shown that the doses to which patients are exposed during left breast radiotherapy can lead to coronary heart diseases. Heart-related side effects are particularly associated with the doses received by the heart and the left anterior descending coronary artery (LAD) [5–7]. With the DIBH technique, the heart and LAD move away from the target structures, assuming a more favorable position during radiation therapy to minimize the doses they will be exposed to [15,16]. However, when the DIBH technique is applied, it is essential to monitor the patient's breath-hold level both inter and intrafractionally using a respiratory control system. When the DIBH technique is combined with the VMAT (VMAT-DIBH) treatment technique, the patient's compliance can be monitored using the Real-time Position Management (RPM) system (Varian, Palo Alto).

When some patients with left breast cancer cannot comply with the DIBH technique, they need to receive radiotherapy in free breathing (FB). However, when planning for free breathing, keeping doses to the heart and LAD below clinical limits can be challenging. In this case, plans are made for different treatment techniques to determine the most suitable technique that will provide dosimetric advantages to the patient.

Another modern technique that provides an advantage in dose distribution in breast radiotherapy is HT [10,17]. However, since there is currently no integrated respiratory control system in Tomotherapy treatment machine, the DIBH technique cannot be applied with this machine. Hence, all breast cancer patients, regardless of the affected breast side, receive radiotherapy with FB treatment using this device.

A recent dosimetric study has shown that HT-FB technique may be an alternative to 3D conformal RT during the DIBH in terms of heart and LAD sparing for left breast cancer radiotherapy [18]. However, as far as we know, there is no study evaluating the HT-FB technique against the modern technique of similar complexity such as VMAT-DIBH. This study will be the first to address this issue.

This study investigates whether HT technique for left breast-only cancer patients who cannot comply with the DIBH technique can serve as an alternative to radiotherapy plans created in the DIBH-VMAT technique.

Material and methods

Patient characteristics

Patients diagnosed with early stage left-sided breast cancer who were referred for adjuvant radiotherapy following breast-conserving surgery were included in this research. We collected DIBH and FB CT images of 20 patients who had previously undergone left breast-only radiotherapy using the DIBH-VMAT technique and prospectively performed new plans for both techniques. The median age for patients included in the study was 58 years (range: 37–73). The mean PTV-DIBH volume was 1064 cc (range: 599–1834), and the mean PTV-FB volume was 1088 cc (range: 647–1905). This study was deemed ethically appropriate by the Acibadem Mehmet Ali Aydınlar University Ethics Committee, with the reference number 2019–17/39, on NOV 07, 2019.

Immobilization, patient setup and CT acquisition

The patients were positioned supine on the breast board. The breast board was used in a flat position without elevation. Their left arms were placed above their heads, while their right arms were positioned alongside their bodies. Additionally, to expose the supraclavicular region, the patients' heads were positioned to face towards the right. The CT images were acquired with a 3 mm slice thickness to encompass all relevant target structures and critical organs (Siemens go Up, Erlangen Germany). During CT simulation, patients who can hold their breath for at least 20 s during the deep inspiration phase and can repeat this three times at the same gating window level are selected as suitable for treatment using the DIBH technique (Varian RGSC). Patients are guided with audio-visual coaching to ensure that they maintain the same gating window level. In our clinical routine, even if left breast patients are found suitable for DIBH during CT simulation, an additional CT scan is still acquired during FB. The reason for this is to enable the individual evaluation of the DIBH technique for each patient. Previous studies have shown that due to anatomical variations, using the DIBH technique does not achieve a dosimetric benefit for the heart and LAD doses in every patient [19,20]. Therefore, before contouring begins, an in-clinic evaluation is conducted to determine whether the heart and LAD significantly deviate from the target structure in the CT images acquired during deep inspiration compared to those obtained during FB. During this in-clinic evaluation, the axial CT slices are reviewed to find the section where the LAD and PTV are closest to each other. When comparing the FB and DIBH CT scans, if there is an increase of at least 5 mm in the distance between the LAD and PTV, it is considered that using the DIBH technique will provide a dosimetric benefit for the patient. Thus, if the DIBH technique does not sufficiently move the heart away from the target structure to achieve a significant dosimetric advantage, the patient is not unnecessarily subjected to this technique for treatment.

Target volume definition and organs at risk definition

For DIBH-VMAT plans, all structures were contoured on CT images acquired during the deep inspiration phase, while for HT-FB plans, they were contoured on CT images acquired during free breathing. The radiologically visible breast tissue was defined as the Clinical Target Volume (CTV) based on the Radiation Therapy Oncology Group (RTOG) breast atlas [21]. The axilla and supraclavicular lymph nodes were not included in the target volume. To prevent variability among target structures, all CTV volumes were contoured by the same experienced radiation oncologist. A Planning Target Volume (PTV) volume was created by adding a 5 mm margin in all directions to the CTV. To ensure accuracy in dose distribution calculation, the PTV volume was uniformly shifted 3 mm beneath the skin surface for all patients. Dose prescription in the planning was based on the PTV volume. Additionally, a virtual bolus was created in DIBH-VMAT plans to prevent a decrease in skin dose, but it was not used in HT-FB plans. However, in HT-FB plans as well, to determine the arc start-stop positions, a dummy contour in the shape of a teardrop, as shown in [Supplementary Fig. 1](#), was created [22]. The Left Anterior Descending Artery (LAD), heart, ipsilateral lung (IL), contralateral lung (CL) and contralateral breast (CB), were contoured as organs at risk (OAR). During OAR contouring, the RTOG atlas was also used as a reference, similar to target contouring [21]. All contouring processes were performed using the Eclipse treatment planning system [version 13.6, Varian Palo Alto], and the data was transferred to the Volo treatment planning system (Version 2.1.4, Accuray Sunnyvale, CA) for HT-FB planning without any loss of resolution.

Plan objectives

In all plans, efforts were made to ensure that the maximum dose within the PTV did not exceed 110 % of the prescribed dose, and that at

least 95 % of the PTV volume received 95 % of the prescribed dose (95 % of 50.4 Gy, which is 47.88 Gy). The desired clinical tolerance doses for critical organs are provided in Table 1. To mitigate differences in experience and perspective among the medical physicists conducting the planning, the original plans that patients underwent treatment with were not utilized. Consequently, for all patients included in the study, both VMAT-DIBH and HT-FB plans were reconstructed by the same experienced medical physicist.

Planning technique for DIBH-VMAT

DIBH-VMAT plans were created on CT images acquired during the deep inspiration phase in the Eclipse (Version 13.6, Varian Palo Alto) treatment planning system using the VitalBeam (Varian Palo Alto) treatment machine. In the planning, four partial arcs were used with a gantry starting angle of 300–330 degrees and an ending angle of 130–160 degrees (Fig. 1). Different collimator angles were assigned to each arc (0, 350, and 80, 90 degrees) to mitigate the tongue and groove effect. Field sizes were adjusted to encompass the entire PTV, and a 6FFF energy was selected. The Photon Optimizer optimization algorithm and the AcurosXB dose calculation algorithm were used. The NTO (Normal Tissue Objective) option was used to control the dose falloff from the PTV.

Planning technique for HT-FB

The CT images acquired during free breathing and the contoured structures were imported into the Accuray Volo (Version 2.1.4, Accuray Sunnyvale, CA) treatment planning system for HT-FB planning purposes. The treatment plans were created with the Tomotherapy HDA treatment machine selected. In the planning, a field width of 5 cm, a pitch factor of 0.287, and a modulation factor in the range of 2–3 were used. The dynamic jaw feature was selected to reduce the doses to normal tissues in the superior-inferior directions of the target. To create partial arcs in HT planning, the “Complete Blocking” option for the teardrop structure was activated. This prevented the beam entry and exit from occurring through this structure. Additionally, three shell structures, each 10 mm thick, were created around the PTV, and a 3 mm gap was ensured between the innermost shell and the PTV. These shell structures were used during optimization to control the dose gradient starting from the PTV.

Data analysis

Paired-samples *t*-test (IBM, SPSS version 23) was used for pairwise comparisons in the study. $p < 0.05$ value indicates a statistically significant difference in comparisons between HT-FB and DIBH-VMAT treatment techniques. The conformity number (CN) formula, as defined by Van’t Riet and colleagues, was used to measure the conformity of target coverage [23]. Additionally, homogeneity index values were calculated using the formula specified in the ICRU 83 report to determine the homogeneity of dose distribution within the target [24].

Results

The dosimetric parameters for dose coverage, homogeneity, and conformity, obtained from the dose-volume histograms (DVH) of DIBH-

VMAT and HT-FB plans, along with the statistical comparison results, are presented in Table 2. Additionally, Fig. 2 shows a comparative display of the 46 Gy and 25 Gy dose distributions for the two techniques used in the study.

Statistically significant difference was not found among the PTV_{V105} values. Although there is a statistically significant difference among the PTV_{D2} values, this difference is not clinically relevant. It is observed that the most dramatic difference in the table is between the PTV_{Vpres} values. The abbreviation $Vpres$ represents the percentage volume of the target structure receiving the prescribed dose (50.4 Gy). This difference has been found to be both statistically significant and clinically relevant. In the HT-FB technique, the volume of the PTV receiving the prescribed dose is 85.86 %, whereas this value decreases to 64.04 % in the DIBH-VMAT technique. Additionally, when comparing the PTV_{D95} , CN, and HI values, a significant difference in favor of the HT-FB technique has been found.

Although the doses to the heart were kept within threshold values with both techniques, the maximum dose to the heart was found to be significantly higher in the HT-FB technique ($p = 0.003$) (Table 3). When comparing the D_{mean} doses for the heart, although a significant difference was found ($p < 0.001$), both techniques met the dose constraints. When evaluating the V5 and V20 doses of the ipsilateral lung, the HT technique was found to be significantly superior ($p < 0.001$ and $p < 0.001$, respectively), while there was no significant difference between the two techniques in V30 doses ($p = 0.062$). Although planning was performed on CT scans acquired during FB, it was observed that the LAD could be significantly better protected with the HT-FB technique. However, for the protection of the contralateral lung and contralateral breast, the DIBH-VMAT technique was found to be significantly superior. In the HT-FB technique, the dose tolerances for D_{max} and D_{mean} in the contralateral breast could not be met and were exceeded at a minor level.

Discussion

Minimizing radiation doses to the heart and LAD is crucial, especially in left-sided breast cancer patients, to reduce potential morbidity related to coronary artery disease. [19,25–27]. It has been shown that rates of major coronary events increase linearly by mean dose to the heart, with no apparent threshold [7]. In routine clinical practice, treatment in DIBH is preferred to increase the distance between the heart and the target structure [20,27–29]; however, not every patient may comply with treatment using this technique. Or the lack of equipment capable of enabling respiratory-controlled radiotherapy may render the application of the DIBH technique unfeasible in the clinic. Given these conditions, if the patient is to undergo treatment with free breathing, it remains essential to ensure that the dose threshold limits for critical structures are met. Therefore, alternative treatment techniques must be explored for left-sided breast cancer patients who require treatment in FB, aiming to find the best treatment technique that provides optimal protection of the heart and LAD without compromising target coverage. For this purpose, the study investigated whether plans created using the HT technique in FB could serve as an alternative to plans generated using the VMAT technique with DIBH. It has been observed that the HT-FB technique can protect the heart and LAD as effectively as the VMAT-DIBH technique with better target coverage. However, it results in an increased dose to contralateral organs.

Target coverage

Due to the motion effect observed in the CT images acquired during FB, the PTV-FB volumes were found to be larger than the PTV-DIBH volumes. Both techniques ensured that at least 95 % of the PTV volume received 95 % of the prescribed dose. However, the HT-FB technique has been found to significantly enhance both the $D95$ and $Vpres$ metrics, which are important indicators of target coverage for the PTV.

Table 1
The targeted dose limits for organs at risk (OARs).

Heart	V25 < %25	V5 < %20	Dmean < 5 Gy
Ipsilateral Lung	V20 < %20	V10 < %63	Dmean < 18 Gy
Contralateral Lung	Dmax < 25 Gy	Dmean < 5 Gy	
Contralateral Breast	Dmax < 20 Gy	Dmean < 5 Gy	
LAD	Dmax < 35 Gy	Dmean < 16 Gy	

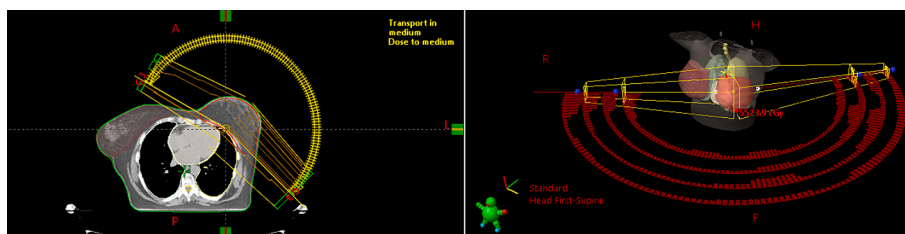


Fig. 1. The arc arrangement used in DIBH-VMAT plans.

Table 2
DVH Parameters and p-values regarding target coverage.

Metric	HT-FB Avg ± SD	DIBH-VMAT Avg ± SD	p Values
PTV V ₁₀₅ [%]	2.95 ± 2.544	2.81 ± 2.031	0.086
PTV D ₂ [Gy]	52.91 ± 0.75	52.94 ± 0.32	0.000
PTV V _{pres} [%]	85.86 ± 13.46	64.04 ± 5.22	0.000
PTV D ₉₅ [Gy]	49.61 ± 0.57	48.18 ± 0.52	0.000
CN	0.856 ± 0.138	0.630 ± 0.075	0.000
HI	0.08	0.20	0.001

Therefore, it has been observed that in the VMAT-DIBH technique, a lower dose could be administered to the PTV-DIBH volume to meet critical organ tolerance doses [30]. In the HT-FB technique, the increase in dose observed in contralateral organs may be attributed to the improvement in D95 and Vpres parameters. In radiotherapy, it is equally imperative to strive to enhance the probability of tumor control and to minimize the likelihood of complications in normal tissue. Therefore, increasing the percentage of the prescribed dose received by the PTV may hold significant value in augmenting local control, a crucial aspect in managing the patient's primary disease. Additionally, upon comparing CN and HI, it has been discovered that the HT-FB technique offers significantly superior dose conformity and homogeneity, even with a larger PTV volume. This result is consistent with the literature [31,32]. In a study conducted by Hacıislamoglu and colleagues, they compared the treatment plans generated during FB for patients with left-

sided breast cancer and calculated the CN value as 0.8 for HT and 0.74 for VMAT [p < 0.01] and HI value as 0.06 for HT and 0.18 for VMAT [p < 0.01] [10]. The calculated values of HI and CN in our study are consistent to the results of their study.

Heart and LAD

According to clinical trials, the recommended mean heart dose constraint should be around 3–5 Gy, and these values have been achieved for both VMAT-DIBH and HT-FB techniques [33]. But, many studies have shown that when planning with the VMAT technique under free breathing, the Dmean value for the heart cannot be kept below these values [<5 Gy] [10,28].

When comparing the D_{max} values for the heart, HT-FB was found to be significantly higher. This may be due to the higher Vpres value in the HT-FB plans. Moreover, based on numerous studies demonstrating the cardioprotective effect of DIBH, we know that this is an expected outcome [34,35].

Although D_{mean} doses were found to be similar for both techniques, it was observed that the HT-FB technique provided better heart protection when comparing V5 volumes. It has been demonstrated that the heart V5 value is also an important predictor for cardiac events [37]. In their study, where Xie and colleagues compared VMAT plans created with three different arc designs during FB. The three arc designs were: standard VMAT, noncoplanar VMAT, and multiple arc VMAT. They found

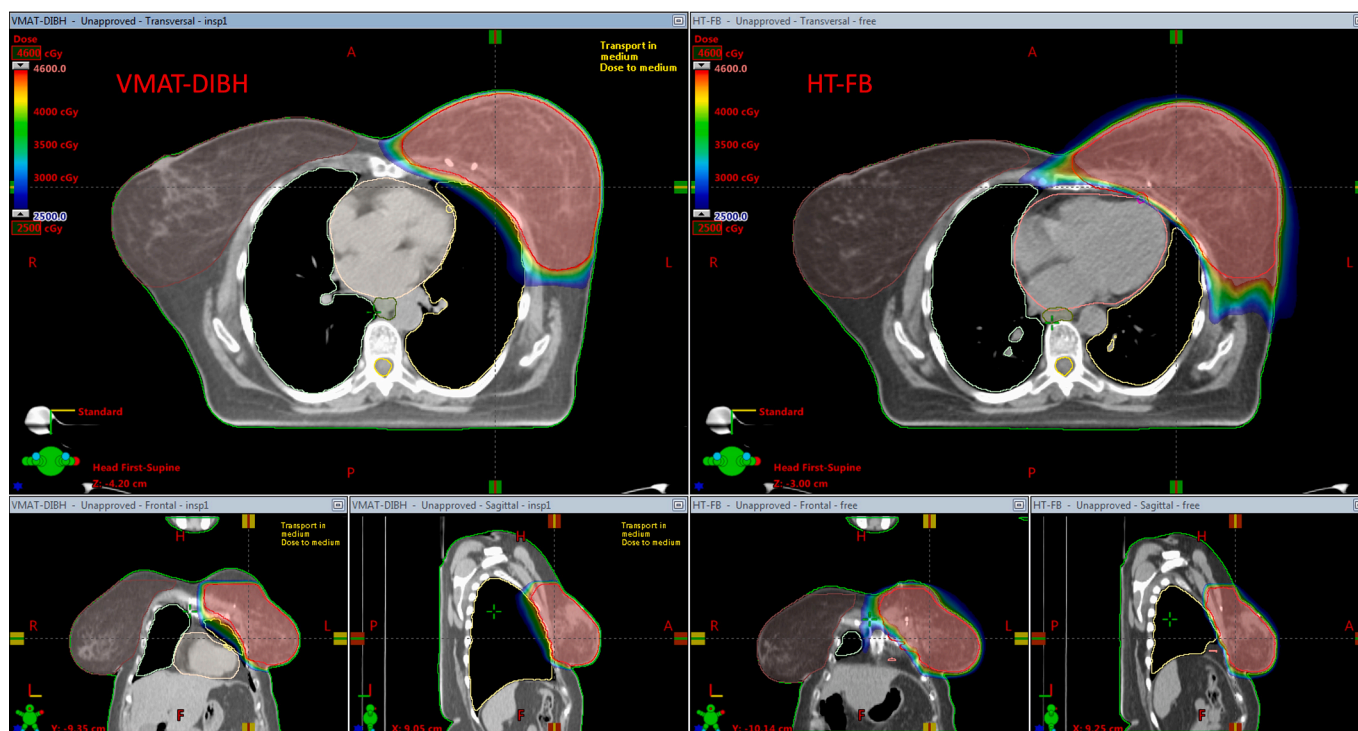


Fig. 2. Comparison of 25 Gy and 46 Gy doses in DIBH-VMAT and HT-FB plans.

Table 3
DVH parameters and p-values for critical organs.

Metric Avg \pm SD	HT-FB Avg \pm SD	DIBH-VMAT Avg \pm SD	p Values
Heart D _{max} (Gy)	25.42 \pm 5.43	20.94 \pm 3.97	0.003
Heart D _{mean} (Gy)	3.56 \pm 0.97	3.54 \pm 0.37	0.000
Heart V ₅ (%)	16.53 \pm 6.55	22.18 \pm 12.63	0.073
LAD D _{max} (Gy)	15.26 \pm 7.49	16.85 \pm 4.42	0.000
LAD D _{mean} (Gy)	5.80 \pm 2.35	7.97 \pm 1.56	0.002
L Lung V ₅ (%)	30.22 \pm 7.84	67.33 \pm 5.08	0.000
L Lung V ₂₀ (%)	9.67 \pm 3.08	14.55 \pm 2.05	0.000
L Lung V ₃₀ (%)	4.53 \pm 1.87	5.51 \pm 1.65	0.062
L Lung V ₄₀ (%)	1.31 \pm 0.83	1.19 \pm 0.62	0.000
R Lung D _{max} (Gy)	22.05 \pm 3.16	18.03 \pm 2.69	0.000
R Lung D _{mean} (Gy)	4.69 \pm 1.06	2.96 \pm 0.63	0.000
R Lung V ₅ (%)	35.18 \pm 10.32	17.03 \pm 10.26	0.000
Contralateral Breast D _{max} (Gy)	21.37 \pm 2.36	16.49 \pm 4.26	0.000
Contralateral Breast D _{mean} (Gy)	5.82 \pm 1.80	4.15 \pm 1.18	0.000

that the D_{mean} [5.5, 5.8, and 7.8 Gy] and D_{max} [44.5, 41, and 45 Gy] doses for the heart, as well as the V₅ volume [53.2 %, 30.5 %, and 22.1 %], were higher than the values obtained from VMAT-DIBH plans in our study, as expected [13]. However, it is also observed that these values obtained for the heart are higher than the values obtained with HT-FB plans in our study. Additionally, in a study comparing the two techniques based on plans made from CT scans taken during FB, both heart and LAD doses were found to be significantly lower in the HT technique compared to the VMAT technique [10].

The development of late-onset coronary artery disease secondary to radiotherapy, due to the radiation dose received by Heart and LAD, is a significant cause of morbidity and mortality [7]. But contemporary studies have revealed that LAD doses have a greater impact on cardiac side effects compared to mean heart doses [15,16].

Contrary to expectations, despite being planned in FB, the HT-FB technique provided better LAD protection in terms of both mean and maximum doses. While this result is similar to Abdullahi's study, it is more expected because in that study, the technique used with DIBH was 3DCRT (Three-Dimensional Conformal Radiotherapy) [18]. This is because achieving a similar concave dose distribution to those obtained with intensity-modulated techniques is not feasible with conventional techniques [17,36–38].

Osman et al. have also stated that under DIBH, VMAT technique provides better heart protection compared to the 3DCRT technique [39]. Nevertheless, when comparing 3DCRT-DIBH to VMAT-FB techniques, they have stated that while the VMAT-FB technique provides similar target coverage with better conformity, it does not offer comparable heart protection.

Ipsilateral and contralateral lung

When the DIBH technique is used alongside 3DCRT, despite the increased lung volume compared to the FB technique, no significant decrease has been demonstrated in either total lung or IL doses [34,35]. The reason for this could be the increased lung volume entering the tangential radiation field with the DIBH technique. However, when a similar comparison is made with the VMAT technique, which has a higher dose shaping [modulating] capacity, significant dose reduction has been demonstrated [28]. Additionally, the success of VMAT plans in reducing ipsilateral and total lung doses compared to 3DCRT has also been demonstrated in the DIBH technique [39]. In our study, however, despite using similar dose modulation capacities in both planning techniques, it is observed that the HT-FB technique provides better dose reduction in the IL compared to the DIBH-VMAT technique. Actually, when we compare the DVH values for the VMAT-DIBH technique with the DVH parameters for the HT-FB technique from different studies, we

find that the results are consistent with our study. For example, in the study by Osman et al., the IL V₂₀ value for the VMAT-DIBH technique is reported as 26.5 %, while in the study by Abdollahi et al., it is reported as 18.6 % for HT-FB. In our study, the IL V₂₀ value for the HT-FB technique is even lower than the value presented in the study by Abdollahi et al. [18,39]. This discrepancy can be attributed to the higher mean doses we obtained for the CB (5.0 vs. 5.8 Gy) and CL (3.0 vs. 4.6 Gy) compared to the values reported in Abdollahi's study. In breast cancer patients, the risks of early and late radiation-induced lung sequelae are strongly associated with the irradiated lung volume and dose. The mean lung dose (MLD) and V₂₀ are particularly linked to the development of radiation pneumonitis and radiation-induced fibrosis [40]. When the same treatment technique is used in conjunction with the DIBH method, lung doses can be reduced due to an absolute increase in lung volume, which leads to a relative decrease in the irradiated volume. In fact, when the V₂₀ value is equal in both DIBH and FB methods, the amount of irradiated lung tissue is greater in the FB method compared to the DIBH method. Hence, when employing the FB technique, it may be crucial to maintain lower lung doses compared to the DIBH technique to attain a similar probability of side effects.

Consistently with the literature, higher doses to the contralateral organs have been found in HT-FB plans in exchange for the improvement achieved in ipsilateral organs [10,18]. Additionally, in our study, we also suggest that the reason for the higher doses to contralateral organs in HT-FB plans compared to DIBH-VMAT plans is due to the differences in arc arrangements used in the two techniques. In VMAT-DIBH plans, the semi-circular partial arc design (Fig. 1) results in beam exits through the ipsilateral lung. In contrast, the HT-FB technique employs a blocking method that creates bowtie-shaped tangentially angled arcs (Supplementary Fig. 1), resulting in beam exits primarily through the contralateral organs. Zhang et al. have demonstrated that due to higher doses received by the IL, the risk of radiation-induced secondary cancer is higher compared to the contralateral organs [41]. Therefore, it may be more important to minimize the dose to the IL as much as possible without compromising target coverage.

Contralateral breast

The dose to the contralateral breast, like the contralateral lung, was found to be high in the HT-FB technique. Despite meeting our clinical constraints for the contralateral breast D_{mean} value with the DIBH-VMAT technique, this value was found to be high compared to the literature [28,39]. However, we could not meet our dose constraints for the contralateral breast D_{mean} value with the HT-FB technique; nevertheless, this value was found to be highly consistent with the literature [18,32]. One reason for this could be the expansion of the thoracic cage during the DIBH technique, leading to an increase in the distance between the contralateral breast and the target breast. Several studies in the literature have showed that when the DIBH technique is used, the contralateral breast could be better protected compared to the FB technique [39,42]. The dose increase observed in the contralateral breast with the HT-FB technique should be particularly evaluated during the clinical decision-making of the treatment technique for patients under the age of 40, considering local tumor control, cardiac side effects, and secondary cancer risks.

One limitation of this study is that a covariance analysis model was not developed, which prevented the identification of other independent variables that could have influenced the differences between the groups.

Conclusion

The utilization of the HT-FB technique for treating left breast cancer patients, ineligible for DIBH treatment, has shown comparable heart protection and improved preservation of the LAD and ipsilateral lung compared to the DIBH-VMAT technique, while achieving more homogeneous and conformal target coverage. Nevertheless, meticulous

evaluation of doses to the contralateral lung and contralateral breast is crucial when employing the HT-FB technique.

Author contributions

E Goksel conceived and designed the study. All contributed to the design, analysis, and interpretation of the data. O Kuru and Goksel E prepared the first draft, and all contributed to subsequent drafts and the final paper. All authors read and approved the final manuscript.

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.

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Ethical Disclosure

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. This study was deemed ethically appropriate by the Acibadem Mehmet Ali Aydinlar University Ethics Committee, with the reference number 2019-17/39, on NOV 07, 2019.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tipsro.2024.100268>.

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