Volume 21, No 2 | International Journal of Radiation Research, April 2023

# Intensity-modulated radiation therapy (IMRT) with couch rotation in right unilateral breast cancer

**S.Y. Rakici*** **and M. Eren**

*Department of Radiation Oncology, Recep Tayyip Erdogan University Faculty of Medicine, Rize, Turkey*

► ***Original article***

***Corresponding author:***
*Sema Yilmaz Rakici, M.D.,*
***E-mail:***
*sema.rakici@erdogan.edu.tr*

**Received:** June 2022
**Final revised:** November 2022
**Accepted:** November 2022

***Int. J. Radiat. Res., April 2023; 21(2): 203-210***

**DOI:** 10.52547/ijrr.21.2.4

***Keywords:*** *Right unilateral breast cancer, postmastectomy radiotherapy, IMRT with couch rotation, OAR, cardiac toxicity.*

## ABSTRACT

***Background***: In this study, intensity-modulated radiation therapy plans were made with and without couch rotation in patients with right unilateral breast cancer, and a dosimetry analysis was carried out to compare the radiation doses received by target and normal tissues. ***Materials and Methods***: The radiotherapy planning tomography sets of 10 patients who underwent right unilateral mastectomies were retrospectively selected. Target volumes and normal at-risk organs were recontoured, two radiotherapy plans were created for each patient, and these plans were compared by dosimetry analyses. ***Results***: Doses in the target volume (D2%, D98, D50, HI, VRI, and T -PTV-V95) were similar between the plans. In terms of organs at-risk doses, the maximum doses in the contralateral breast were similar between the plans, while the differences in all other organs at-risk dose parameters between the plans were statistically significant. All dosimetry parameters of the heart were significantly lower in the plans with couch rotation. Ipsilateral lung doses were higher in the plans with couch rotation. Contralateral lung and mean breast doses were significantly lower in the plans with couch rotation. ***Conclusion***: In this study, organs at-risk doses were reduced, especially for the heart and the contralateral breast, in patients who were subjected to postmastectomy radiotherapy with right thoracic wall and regional nodal irradiation without compromising radiotherapy dose coverage for the target volumes by rotating the treatment couch by 270°.

## INTRODUCTION

Despite the increasing number of breast cancer cases, the number of survivors is also increasing with the help of early diagnosis and developments in treatment methods [1]. Current data indicate that breast cancer has a long-term survival time of 15-20 years. This means that surviving patients will live to experience the aftereffects of cancer treatments. It has been reported that breast radiotherapy reduces the risk of cancer-related mortality by 4% in 15-year follow-ups [2], while it is associated with 1-2% of non-cancer mortalities, and most of these mortalities are attributed to cardiac diseases [3]. Thus, it becomes even more important to make efforts to produce solutions to the chronic sequelae of breast cancer radiotherapy. Adverse aftereffects to emerge in relation to radiotherapy can originate from mainly the heart, as well as the lungs and the contralateral breast (Cont-Breast).

Studies on reducing potential radiotherapy-related adverse effects in breast cancer patients are going on. Advanced technological radiotherapy devices involve the use of techniques such as intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), holding one's breath during deep inspiration=deep inspiration breath-hold (DIBH) technique during 3-dimensional conformal radiotherapy (3D-CRT)[4], positioning the patient (prone position-supine position)[5], proton therapy, or combined treatment methods. The methods that are implemented need to be repeatable, as well as tolerable and adaptable by the patient.

In radiotherapy, which is frequently used in the treatment of breast cancer, it is needed to develop new techniques that will reduce the radiation exposure of normal tissues. We think the IMRT technique with couch rotation we present here will be beneficial, especially because it can reduce contralateral lung (Cont-Lung), Cont-Breast doses to prevent cardiac toxic effects.

## MATERIALS AND METHODS

### *Patient selection and data collection*

Our study included 10 female patients who underwent radiotherapy due to breast cancer at our clinic. This study was approved by the Ethics Committee of the Faculty of Medicine at our university for collecting, evaluating, analyzing, and interpreting the data (number: 40465587-50, decision no: 2017/50 and date: 31.03.2017). All procedures including informed consent process were carried out in compliance with the ethical standards



[ DOI: 10.52547/ijrr.21.2.4 ]

of committees (institutional and national) responsible for human experiments, the 1975 Declaration of Helsinki, and its version revised in 2000. Archives were searched retrospectively, and the computed tomography (CT) images of patients taken with the Aquilion LB brand CT radiotherapy simulator scanner (Toshiba Medical Systems, Tokyo, Japan) were examined. CT images that were taken from above the larynx laid onto the breast board (MAX3 ™ PLUS Breast Board, USA) containing both lungs and had a slice thickness of 3 mm were identified. Images with the patient in the supine position, her ipsilateral arm above the head and rotated towards the outside, her head slightly rotated towards the left, her neck in an open position, and the board's inclination in the thoracic wall and supraclavicular regions from 5° to 15° were preferred.

The sample of the study included patients who underwent modified radical mastectomy with the diagnosis of right unilateral breast cancer. The tumor characteristics of the patients met their postmastectomy radiotherapy (PMRT) indications. Patient characteristics are summarized in table 1.

**Table 1.** Patient and tumor characteristics.

| Patient no | Age | Tumor diameter (cm) | Axillary metastatic lymph node (IM) | Pathological type | Hormone receptor ER/PR positivity% | c-erb B2 | Other |
|---|---|---|---|---|---|---|---|
| 1 | 45 | 2,1 | 5 | IDC | 80/50 | 0 | Multifocal |
| 2 | 53 | 2.8 | 3 | IDC | 90/50 | 2 | |
| 3 | 61 | 3 | 3 | IDC | 0/30 | 3 | |
| 4 | 50 | 3.5 | 4 | IDC | 80/60 | 0 | |
| 5 | 48 | 3 | 2 (ECI+) | IDC | 90/90 | 2 | |
| 6 | 50 | 4.6 | 2 (ECI+) | SRC + %10-15 IDC | 70/40 | 2 | NAC |
| 7 | 43 | 5 | 7 | ILC | 90/90 | 0 | NAC |
| 8 | 65 | 1.7 | IM+ | IDC | 5/5 | 3 | NAC |
| 9 | 58 | 1.5 | 2 | IDC | 90/15 | 0 | Multifocal |
| 10 | 60 | 2.5 | 8 | IDC | 70/70 | 2 | |

ECI: Extracapsular invasion, IM: Internal mammary, IDC: Invasive ductal carsinom, ILC: Invasive lobular carcinoma, SRC: Signet ring cell carcinoma, NAC: Neoadjuvant chemotherapy.

### *Contouring of target and normal structures*

For the planning targets, the clinical target volume (CTV), planned target volume (PTV), and organs at-risk (OAR) were recontoured on the CT datasets of all patients. Regional lymph nodes were contoured in all patients. All volumes were outlined according to the RTOG Breast Cancer Contouring Atlas [6]. Target volume contouring was carried out to include the thoracic wall and the regional nodal irradiation (RNI) area (level-1-2-3 axilla, supra, infra, and scalene). The internal mammary was included in the area in one patient. PTV-1 constituted the RNI area, and PTV-2 constituted the thoracic wall area. These two targets were combined to create a single PTV-T. This way, it became possible to observe the total PTV dose consisting of the PTV-1 and PTV-2 doses in the dose-volume histogram (DVH). As the patients fit into a single PTV-T area, there was no need for the dual-isocenter technique or two separate PTV areas. Additionally, for RNI, there was no need for difficult procedures such as a half beam block or collimator rotation for the gantry angle or the position above the area. PTV was modified to exclude the 3-mm build-up region close to the skin surface [7]. The isodose volumes covering the target volume (volume of reference isodose: VRI) were calculated on the treatment planning system (TPS).

The volumes outside the irradiated target volume were defined as OAR: ipsilateral lung (Ip-Lung), Cont-Lung, Cont-Breast, liver, heart, and esophagus (Eso). For the dosimetric comparisons of the target and OAR doses, Dv (dose "d" received by the volume "v" (%/ml) of the selected organ), Vd (volume "v" for the selected organ (V5, V20, V25; %/ml), and dose "d" (%/Gy) were calculated separately for each plan. Minimum (min) and maximum (max) dose definitions were also recorded.

### *Dose constraints*

While applying the dose to the planned target, it was aimed to cover at least 95% of the nominal dose and create a homogeneous dose in 95% to 107% of the defined target. The dose-volume constraints that were used in this study for the target and critical structures were created based on our clinical experiences, the guidelines of the Radiation Therapy and Oncology Group (RTOG), and the recommendation reports 50-62 of the International Commission on Radiation Units and Measurements (ICRU), and these constraints were kept fixed throughout the implementation of the plans.

The dose for the thoracic wall and regional lymphatics (axilla, supra, and infraclavicular region, mammaria interna=MI) that were defined as targets was decided as 2 Gy/fraction per day →50 Gy. It was aimed to achieve the conditions of 95% of the target volume and 95% of the dose, V105<10%, and Dmax 108%.

For OAR, the dose constraints for the heart were in accordance with the RTOG recommendations as follows: Heart V40<5%, V25<10%, Ip-Lung V20≤15%, Cont-Lung: V5<10%, Cont-Breast: max 3 Gy, total lung V20<35%, V40<20%.

### *Radiation therapy planning*

All plans were designed using 6 MV photon rays



[ DOI: 10.52547/ijrr.21.2.4 ]

with the Varian Trilogy Clinac iX (Varian Medical System, Palo Alto, CA, United States) Eclipse™ Treatment Planning System Version 13.6. The treatment device, the Millennium 60 Paired Multileaf Collimator, offers 40 paired 0.5-cm leaf resolutions at the isocenter and 1.0 cm leaf resolutions in the remaining areas. Its maximum leaf speed is 2.5 cm/s, and its leaf transmission rate is 1.6%. A constant dose rate of 400 MU/min was selected in the IMRT plans. For the plans, the analytical anisotropic algorithm (AAA) version 13.6.23 was implemented in the Eclipse photon dose calculation algorithm that was used.

For each patient, the same tangential standard 5-zone IMRT gantry angles were used as ±15° (gantry 45°, 60°, 205°, 220°, 320°). In the IMRT with couch rotation plan, the couch rotation angle was 270° in one zone, and by applying two different IMRT plans, twenty different plans were created. The plans were optimized to reach the targets and achieve the nominal dose. In one of the patients as an example, for both IMRT plans, the 3-dimensional isodose distribution, DVH, the numbers of areas for both plans, and the gantry, collimator, and couch rotation data are presented comparatively (figure 1).

In the plans with couch rotation, the couch was positioned at an angle of 270°, and the gantry was positioned at 345±15° so that the lung and heart doses would be reduced. Figure 2 shows the 3D reconstruction and beam's eye view (BEV) images of the plan with couch rotation.

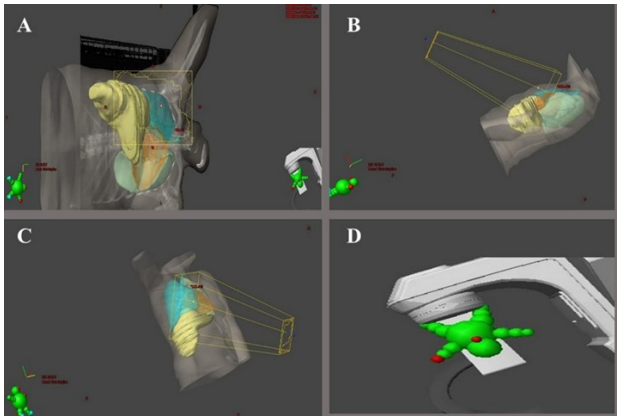


**Figure 1.** Dosimetric comparison of two plans is shown in a patient as an example. **A:** (Painted in dark blue as a frame) Plan without couch rotation: 3-dimensional isodose distributions in axial (1), sagittal (2), and coronal (3). Number of areas, gantry, collimator, and couch rotation information (4). **B:** (Painted in green as a frame). Plan with couch rotation 3-dimensional isodose distributions in axial (1), coronal (2), and sagittal (3). Number of areas, gantry, collimator, and couch rotation information (4). **C:** (Painted in yellow as a frame). Dose volume histogram (DVH) comparing both plans. Target volumes; red, ipsilateral lung; dark green, contralateral lung; light blue, heart; light brown, esophagus; yellow, liver; brown, left anterior descending (LAD); pink, contralateral breast; light green, spinal cord; dark blue.

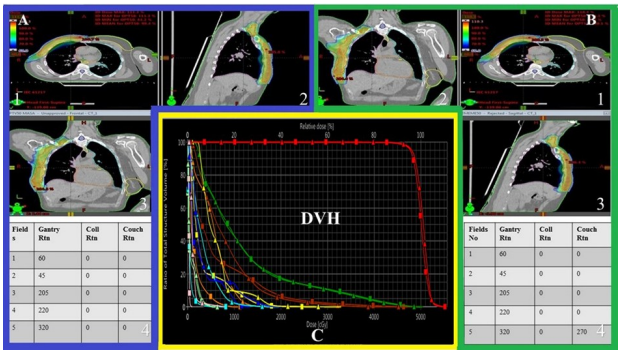


**Figure 2.** Images of the IMRT field positioned on the patient in a couch and gantry rotation plan (couch: 270° gantry: 345°). **A, B, C:** 3D reconstruction images and beam's eye view (BEV) at different angles in the couch-rotated plan. D: Schematized view of the patient during treatment gantry-couch-patient position.

The DVH that was calculated automatically by the planning system was used to calculate the doses received by PTV and OAR. For PTV, homogeneity index (HI) and conformity index (CI) values were calculated using predefined formulae (HI: D2% –D98%/D50%, CI: VRI/TV) [8]. Monitor unit (MU) values that were calculated based on the treatment output were used for the comparisons between the techniques.

### *Statistical analyses*

Differences in the dosimetric parameters between the two treatment techniques were tested in terms of statistical significance using pairwise comparison tests. This test design was implemented to eliminate inter-patient variability. The Shapiro-Wilk test was used to test the normality of the distributions of the data. The normally distributed data are expressed as mean ± standard deviation values, and paired-samples t-tests were used in their statistical comparisons. The non-normally distributed data are expressed as median (min-max) values, and the Wilcoxon test was used in their comparisons. In all analyses, the level of statistical significance was accepted as $p<0.05$. All analyses were conducted using the SPSS 22.0 (IBM Corporation, Armonk, NY, USA) package program.

## RESULTS

### *Patient characteristics*

Table 1 presents the demographic and tumor-related characteristics of the patients. The patients were 43-65 years old (mean: 53.3), and their tumor size range was between 1.5 and 5 cm (mean: 2.9). Metastatic lymph nodes included at least two positive extracapsular invasions (ECI+) and a positive internal mammary in one patient. Regarding hormone receptor status, ER was negative in one patient, and c



[ DOI: 10.52547/ijrr.21.2.4 ]

-ErbB2 was negative in three patients. One patient had invasive lobular carcinoma, one had signet-ring cell carcinoma including little invasive ductal carcinoma (IDC), and the others had IDC. Three patients were operated on following neoadjuvant chemotherapy, and the others were patients who were scheduled for treatment after surgery.

***Target Volume and OAR Doses***

Dosimetric parameters for the target volume, D2%, D98%, D50%, HI, CI, VRI, T-PTV, and MU, are comparatively displayed in table 2 for the plans with and without couch rotation.

As an indicator that both plans were implemented without compromising the dose coverage of the target volume, the D2%, D98%, D50%, HI, CI, VRI, and P-PTV-V95 values of both plans were similar. MU values, on the other hand, were significantly higher in the plans with couch rotation in comparison to the plans without couch rotation (p=0.017). The comparison of the doses received by PTV in both plans and the HI and CI values of the plans did not reveal a statistically significant difference.

In terms of the OAR doses, for the Heart-max, Heart-mean, Heart-V10, Heart-V5, Liver-mean, Liver-max, Ip-Lung-V25, and Cont-Lung-max values, there were significantly lower radiation exposure values in the plans with couch rotation than in the plans without couch rotation. The exposure doses for the Heart, Cont-Breast, and Eso in both plans are shown in table 3.

Heart-max, Heart-mean, heart-V10, and Heart-V5 dosimetric values were significantly lower in the plans with couch rotation than in the plans without couch rotation (respectively, p=0.032, p=0.000, p=0.005, and p=0.000) (table 3). The difference was more substantial, particularly in terms of the Heart-mean and Heart-V5 doses (Heart-mean: 351.55cGy vs 735.75cGy and Heart-V5: 20.05 cGy vs 63.55 cGy).

The Cont-Breast-mean dose in the plans with couch rotation was significantly lower than that in the plans without couch rotation (p=0.005). There was no statistically significant difference between the plans with and without couch rotation in terms of their Cont-Breast-max doses (p=0.878).

Eso-mean and Eso-max dose values were significantly lower in the plans with couch rotation compared to the plans without couch rotation (respectively, p=0.022 and p=0.002).

The Ip-Lung-V25 and V20, Cont-Lung, Liver-mean, and Liver-max doses of the patients are summarized in table 4. Ip-Lung doses (V25 and V20) were significantly higher in the plans with couch rotation (respectively, p=0.001 and 0.014).

The Cont-Lung (V5 and max) doses in the plans with couch rotation were significantly lower than those in the plans without couch rotation (respectively, p=0.005 and p=0.009).

The Liver-mean doses in the plans with couch rotation were significantly lower than those in the plans without couch rotation (p=0.000). The Liver-max doses in the plans with couch rotation were slightly higher (p=0.047).

**Table 2.** Dosimetric data on the doses for both plans.

| | | %D2 cGy | %D98 cGy | %D50 cGy | HI | CI | RIV | T-PTV-V95 % | MU |
|---|---|---|---|---|---|---|---|---|---|
| **Mean ±Sd** | CR | 5248,09±62,72 | 4674,33±76,744 | 4997,11±28,94 | 0,11±0,02 | 1,34±0,14 | 914,62±210,02 | 95,68±0,86 | 1222,10±73,45 |
| | NCR | 5255,71±67,49 | 4712,16±68,462 | 5004,77±39,69 | 0,11±0,01 | 1,31±0,09 | 899,10±217,85 | 95,73±0,85 | 1125,40±110,62 |
| **Median (min-max)** | CR | 5267,05 (5114,90-5302,50) | 4651,64 (4583,84-4840,54) | 4998,87 (4938,10-5039,31) | 0,12 (0,06-0,13) | 1,33 (1,11-1,59) | 844,47 (696,73-1257,20) | 95,30 (95,00-97,70) | 1205,50 (1113,00-1377,00) |
| | NCR | 5273,25 (5102,20-5327,40) | 4704,29 (4631,11-4826,84) | 5009,18 (4937,25-5055,22) | 0,11 (0,07-0,13) | 1,31 (1,14-1,44) | 847,90 (671,95-1208,71) | 95,80 (94,20-97,30) | 1120,00 (931,00-1311,00) |
| | p | 0,799* | 0,176** | 0,599** | 0,247** | 0,267** | 0,289** | 0,441* | **0,017**** |

*Wilcoxon signed-ranks test ** Paired T test. * p<0.005. CR: Couch rotasyon, NCR: No Couch rotasyon, HI: Homogeneity index, CI:conformality index, RIV: Reference Isodose Volume, T-PTV-V95: PTV receiving 95% of the defined dose, MU: Monitör unit.

**Table 3.** Statistics on the doses received by OAR in both plans.

| | | Heart Max cGy | Heart Mean cGy | Heart V10 cGy | Heart V5* cGy | Cont-Breast Max* cGy | Cont-Breast Mean cGy | Eso Mean cGy | Eso Max cGy |
|---|---|---|---|---|---|---|---|---|---|
| **Mean ±Sd** | CR | 2369,20±694,22 | 345,56±105,75 | 10,23±5,637 | 20,90±8,94 | 1753,13±1368,81 | 170,63±135,29 | 710,12± 327,63 | 3560,16± 796,04 |
| | NCR | 2602,65±707,43 | 724,52±159,78 | 26,73±14,15 | 64,24±13,018 | 1655,65±1223,35 | 201,29±155,084 | 876,10± 255,77 | 3975,69± 601,33 |
| **Median (Min-max)** | CR | 2270,50 (1158,10-3466,10) | 351,55 (145,30-533,90) | 10,25 (0,0-20,10) | 20,05 (6,10-40,70) | 1013,20 (527,10-3860,90) | 103,35 (37,10-403,00) | 679,45 (309,50-1391,60) | 3464,40 (2738,40-4977,70) |
| | NCR | 2429,85 (1770,30-4193,70) | 735,75 (441,30-973,50) | 28,80 (6,80-50,70) | 63,55 (38,80-81,70) | 1163,90 (652,90-4176,10) | 116,85 (55,90-502,00) | 783,45 (601,10-1495,10) | 3751,70 (3295,00-5084,70) |
| | p | **0,032*** | **<0,001*** | **0,005*** | **<0,001*** | 0,878** | **0,005**** | **0,022**** | **0,002*** |

*Paired T test, ** Wilcoxon signed-ranks test. CR: Couch rotasyon, NCR: No Couch rotasyon, SD: Standard Deviation, max: maximum dose, min: minimum dose, Cont-Breast: Contralateral breast, Eso: Esophagus, V5 Gy the volume receiving >5 Gy of the prescription dose, V10 Gy the volume receiving >10 Gy of the prescription dose.



[ DOI: 10.52547/ijrr.21.2.4 ]

**Table 4.** Statistics on the doses received by OAR (both lungs and the liver) in both plans.

| | | Ip-Lung V25 % | Ip-Lung V20 % | Cont-Lung V5 % | Cont-Lung Max cGy | Liver Mean cGy | Liver Max cGy |
|---|---|---|---|---|---|---|---|
| Mean ±Sd | CR | 17,44±1,92 | 25,82±3,61 | 1,010±1,47 | 1014,72±553,21 | 530,99±227,63 | 4568,73±912,78 |
| | NCR | 16,40±1,50 | 24,35±2,69 | 34,48±12,43 | 1568,86±412,19 | 763,65±274,76 | 4427,17±1032,95 |
| Median Min-max | CR | 17,80 (13,40-19,90) | 26,20 (16,90-29,10 ) | 0,20 (0,00-4,20) | 747,00 (385,50-116,80) | 558,55 (233,60-833,90) | 5007,65 (2652,10-5190,20) |
| | NCR | 16,35 (13,40-18,20) | 24,65 (17,60-26, 90 ) | 35,30 (16,20-50,80) | 1695,45 (770,90-1961,90) | 759,80 (392,80-237,30) | 4894,75 (2452,30-5043,10) |
| | p | **0,001*** | **0,014**** | **0,005**** | **0,009*** | **0,000*** | **0,047**** |

* Paired T test, ** Wilcoxon signed-ranks test. CR: Couch rotasyon, NCR: No Couch rotasyon, Ip-Lung: Ipsilateral lung, cont-Lung: Contralateral lung, max: maximum dose, V25 Gy the volume receiving >25 Gy, V20 Gy the volume receiving >20 Gy, V5 Gy the volume receiving >5 Gy.

## DISCUSSION

Randomized studies and meta-analyses have shown that radiotherapy has a significant role in the treatment of locally advanced breast cancer. All guidelines recommend radiotherapy as a standard treatment modality in the management of locally advanced malignant diseases [9-12]. PMRT covers the following areas: the thoracic wall, axilla, supraclavicular, and ±ipsilateral IMLNs. The definite indications for PMRT are as follows: a tumor larger than 5 cm (T3), a positive margin, a 1-mm surgical margin, 4+ LNs, or 3+ LNs [13], >20% LNs involved, and tumor >3.5 cm (MDACC) [14]. Although some have lost their validity, its relative indications are as follows: <10 LNs resected, >20% LN involvement, and tumor <3.5 cm, or <20% LNs involved and tumor > 5 cm, gross multicentric, muscle involvement, G3, and HER2+. After the recently increased rates of neoadjuvant chemotherapy followed by mastectomy, the contraindications of RT for these patients were listed as follows: cT1-2 N0-1 tumors, achieving pCR, ypN0; or ypN1 and ER+, age >40, no LVI, and no ECE. Most patients undergo PMRT after NAC. All efforts aiming to identify groups that will not undergo RT are as valuable as methods that are developed for reducing radiation toxicity. The most significantly at-risk organs in terms of deterministic aftereffects following irradiation in breast cancer patients are the heart, the coronary arteries, and the Ip-Lung. Moreover, it is known that these effects are, in fact, dose-independent effects. The IMRT with couch rotation plans that we implemented in our study served this purpose by reducing radiation doses for OAR substantially.

Some strategies have been developed to achieve optimal irradiation in right unilateral breast cancer patients who have undergone mastectomy. These strategies require the usage of radiotherapy techniques that have been developed for the optimum local control, the lowest acute and late toxicity levels, and the lowest probability of secondary cancer induction. Many modern irradiation techniques, including the deep inspiration breath hold (DIBH) technique, IMRT, tangential IMRT, VMAT, VMAT-hold breath, tangential IMRT-VMAT, and proton therapy, are used for this purpose [15]. The superiority of 3D-DIBH where the breath-hold technique that mainly aims to protect the heart in terms of the improvement of OAR doses to conventional 3D-CRT has been shown [15-17]. Similarly, it has been reported that VMAT and IMRT are more homogeneous and conformal in terms of dose distribution compared to the 3D-DIBH RT technique [18, 19]. For the optimum OAR protection strategy, it is needed to propose novel methods that can be integrated into IMRT and VMAT or proton therapy plans that provide better technological opportunities. In comparison to the VMAT breath-hold technique, proton therapy can reduce the mean heart dose by 3.4 Gy [20]. The DIBH technique is one of the techniques developed to reduce cardiac doses. It requires patient compliance and proper training. Therefore, this technique can be unnecessarily expensive, cumbersome to use, and time-consuming in terms of healthcare costs. Furthermore, not all patients may benefit from the use of this technique [21]. Although it was reported that the tangential IMRT technique reduces heart and Ip-Lung doses, there are some concerns. It is stated that it may not always be a reasonable choice due to differences in maximum and average PTV volumes [22]. Although the VMAT-DIBH technique provides OAR protection, it is a concern that it increases the risk of radiation-induced secondary cancer due to the increased volume of normal tissues exposed to low doses [23]. Tangential IMRT-VMAT hybrid techniques resulted in better OAR dosimetry overall compared to many techniques, but the results were in early-stage breast cancer patients. Therefore, it was stated that the results may not be valid for patients requiring treatment to both breast and regional nodes [24].The difference of proton therapy from existing treatments is based on the interaction of protons and photons in tissues. Due to the high dose gradient, it is possible to irradiate the tumor volume while avoiding excessive radiation of the surrounding tissues, and thus, a lower probability of complications in normal tissues is expected [25]. However, proton therapy is not currently considered a standard treatment for patients with breast cancer [26]. One possible reason for this may be the lack of information in clinical evidence, as there is little research confirming the advantage of protons over photons. The fact that proton therapy is not prevalent everywhere limits its usage. Compared to all these techniques, the technique we offer seems to have an advantage as it can be easily applied in clinics with



[ DOI: 10.52547/ijrr.21.2.4 ]

IMRT facilities. With this technique, without needing difficult steps such as establishing two different setups for two different areas in the dual-isocenter technique, a shorter setup time can be achieved. Although the treatment durations in the plans with couch rotation appeared a bit longer, considering the prolonged setup times due to the difficulties mentioned above and the error rates in techniques that require much higher care and precision like the double-isocenter technique, we can argue that the IMRT technique with couch rotation that we are proposing here is more practical to implement. Proton therapies are not widely available, and there are axillary dose ambiguities in the conformal DIBH or VMAT breath-hold technique.

As opposed to the information that the heart is a radioresistant organ, recent studies have claimed that cardiovascular diseases can emerge at mean doses as low as 3 to 17 Gy [27]. In our study, while the mean heart dose in the plans with couch rotation was approximately 3 Gy, the mean heart dose in the plans without couch rotation was approximately 7 Gy.

It is known that there is an increase in especially coronary events and cardiac deaths associated with adverse effects caused by RT on OAR in patients irradiated for left unilateral breast cancer [28]. The fact that cardiac problems have a long latent period may lead adverse effects to remain undetected. Darby *et al*. [29] reported that a 1-Gy dose added to the mean heart dose could increase the prevalence of ischemic heart disease by 7.4% regardless of the threshold dose, and there was a linear correlation between the mean heart dose and coronary events. Furthermore, a relationship was reported between low radiation doses (~5 Gy) and cardiac mortality [30].

DIBH provides good planning and target volume coverage, and it may be considered a safe and repeatable technique for protecting the heart [16, 17]. However, at RT sites that include RNI, it is needed to consider dose ambiguities to be created by the anatomical changes of the mammary glands and significant movements of the axillary lymph node levels in the anterior and cranial directions in the DIBH technique [31]. It was reported that in comparison to spontaneous breathing, during DIBH, the RT dose at the axillary lymph node level 1 decreased [31]. Moreover, the effects of this dose variation in the accidental irradiation of the axillary level 1 lymph nodes in node-negative early-stage breast cancer patients are unknown [31]. Longitudinal follow-ups are needed to investigate the potential effects of all these uncertainties on oncological outcomes. Besides, the probability that the effects of this dose difference in node-positive patients could be even greater is also not completely known. Instead, the RT technique with couch rotation that is not dependent on the positioning of the patient seems more reasonable to prevent dose ambiguities to be caused by the position or breath-holding capacity of the patient in each treatment or efforts to stop and restart the irradiation procedure.

During PMRT, the lungs should also be carefully monitored in terms of adverse effects. Among patients who undergo irradiation to the thoracic wall or only the breast, 1% of cases develop pneumonia [32]. It is known that this rate increases in patients undergoing RNI, and the incidence of symptomatic radiation pneumonia is 2.3% [33]. Radiation pneumonia is associated with the mean lung dose (MLD, Lung-Mean) and V20 which indicate the irradiated lung volume and radiation dose [34]. For example, the incidence of radiation pneumonia that is accompanied by asymptomatic minimal pulmonary radiological changes or mild dry cough was found higher in patients with MLD ≥20.5 Gy or normal tissue complication probability (NTCP) ≥23% Gy [35]. Moreover, it was reported that V20Gy and V30Gy Ip-Lung doses were the main predictive parameters for symptomatic radiation pneumonia [36]. In the same study, it was stated that V20 and V30 values were independent predictors of symptomatic radiation pneumonia in patients undergoing RNI, while V20 values were independent predictors for only those undergoing single-breast irradiation. It was reported that the optimum threshold of V30 for symptomatic radiation pneumonia was 25.7%, and by using this threshold, symptomatic radiation pneumonia could be predicted with an accuracy of 79.9%, a sensitivity of 69.2%, and a specificity of 80.5% [36]. In patients who are subjected to RNI, Ip-Lung V20 values should be <39.8%, and V30 values should be <25.7%. One should pay attention to keeping Ip-Lung V20 values under 20.2% in the irradiation of only the breast or the thoracic wall[36]. Although the Ip-Lung doses we obtained in our study were high in the treatment plans with couch rotation, these doses were V25: 17.80% and V20: 26.20%. These values in our study were on acceptable levels in terms of radiation pneumonia risk reported for patients undergoing RNI (table 4).

A marginally higher risk of second primary cancer development was reported in patients under the age of 45 (RR=1.08, 95% CI 0.99-1.18, p=0.069) [37]. Additionally, it was stated that the risk of the development of a second primary cancer in the Cont-Breast in the long run increases by 2.5 times when the Cont-Breast is exposed to a radiation dose higher than 10 Gy in women under the age of 40 [38]. Due to the increased long-term risk of RT-related second primary cancers, it is needed to avoid unnecessary radiation exposure in the Cont-Breast in mastectomy patients. Gao *et al*. reported the absolute increase in the risk of RT-related second primary cancers regarding 10-, 15-, and 20-year actuarial rates as 0.5%, 1.3%, and 1.6%, respectively[37]. In our study, especially regarding the Cont-Breast, while there was no significant difference between the plans in terms of the maximum doses, the mean doses in the treatments with couch rotation were significantly lower.



[ DOI: 10.52547/ijrr.21.2.4 ]

HI and CI are parameters that are used to estimate the degree of suitability of a plan. According to RTOG publications, the most ideal CI value is equal to 1, and HI values closer to zero indicate higher homogeneity for the plan [8]. The HI and CI median (min-max) values for the plans with vs without couch rotation were found respectively as HI: 0.12 (0.06-0.13) vs 0.11 (0.07-0.13) and CI: 1.33 (1.11-1.59) vs 1.31 (1.14-1.44), and based on the proximity of the respective values to 0 and 1, we may state that the plans with couch rotation were more homogeneous. In our study, the MU values that prolonged the total treatment duration to some degree were found to be higher in the plans with couch rotation. On the other hand, it was shown that 3DCRT and tangential-FIF treatments with shorter MU plans shortened the treatment durations, but their dose coverage for the target volumes was lower based on HI and CI values [39].

## CONCLUSION

In this retrospective study, using the IMRT method with couch rotation, we aimed to reduce the doses applied to the heart, the Cont-Lung, and the Cont-Breast in right thoracic wall and regional lymphatic region radiotherapy without compromising dose homogeneity and the dose coverage of the target volumes. This treatment technique will contribute to a reduction in the incidence of long-term complications and radiation-related secondary malignancies in breast cancer patients with long survival durations. With the development of RT technologies, it is known that various studies have been carried out to reduce the radiation dose to which normal tissue will be exposed. As a result, as in our study, the optimum OAR protection strategy should involve the proposal of novel methods that can be integrated with RT plans that provide superior technological opportunities such as IMRT.

**ACKNOWLEDGMENTS**

*We would like to thank the patients who contributed to this study.*

***Ethical considerations*:** This study was approved by the Ethics Committee of the Faculty of Medicine at our university (number: 40465587-50, decision no: 2017/50 and date: 31.03.2017). All procedures including informed consent process were carried out in compliance with the ethical standards of committees (institutional and national) responsible for human experiments, the 1975 Declaration of Helsinki, and its version revised in 2000.

***Funding*:** None.

***Conflicts of interest*:** The authors report no conflicts of interest.

***Author contributions*:** Supervision, conceptualization, methodology, validation, writing—review, and editing: (R.SY). Formal analysis, visualization, preparation, writing —original draft: (R.SY) and (E.M). All authors have read and agreed to the submitted version of the manuscript. Yours sincerely.

## REFERENCES

1. Autier P, Boniol M, LaVecchia C, Vatten L, *et al.* (2010) Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. **341** (7784), 1201-7.
2. Group EBCTC (2011) 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. *The Lancet,* **378**: *1707-16*.
3. Group EBCTC (2005) Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *The Lancet,* ***366:*** *2087-106*.
4. Bartlett FR, Colgan RM, Donovan EM, McNair HA, *et al.* (2015) The UK HeartSpare Study (Stage IB): randomised comparison of a voluntary breath-hold technique and prone radiotherapy after breast conserving surgery. *Radiol Oncol,* ***114:*** *66-72*.
5. Ramella S, Trodella L, Ippolito E, Fiore M, *et al.* (2012) Whole-breast irradiation: a subgroup analysis of criteria to stratify for prone position treatment. *Medical Dosimetry,* ***37:*** *186-91*.
6. White J, Tai A, Arthur D, Buchholz T, MacDonald S, Marks L (2009) Radiation Therapy Oncology Group (RTOG): Breast cancer atlas for radiation therapy planning: consensus definitions. *Int J Radiat Oncol Biol Phys,* ***73(****3): 944-51*.
7. Rakici SY and Eren M (2020) Method to prevent the target volume from escaping out of the field in breast irradiation: Forming a "fall-off margin". *J Cancer Res Ther,* ***16:*** *1336-43*.
8. Rakici SY, Cinar Y, Mehmet E (2017) Total scalp irradiation: the comparison of five different plans using volumetric modulated arc therapy-simultaneous integrated boost (VMAT-SIB) technique. *Turk J Oncol,* ***32****:106–115*.
9. Harris JR, Halpin-Murphy P, McNeese M, Mendenhall NP, *et al.* (1999) Consensus statement on postmastectomy radiation therapy. *Int J Radiat Oncol Biol Phys,* ***44:*** *989-90*.
10. Taylor M, Haffty B, Shank B, Halberg F, Martinez A, *et al.* (2000) Postmastectomy radiotherapy. American College of Radiology. ACR Appropriateness Criteria. *Radiology,* ***215:*** *1153-70*.
11. Truong PT, Olivotto IA, Whelan TJ, Levine M (2004) Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. *Cmaj*, ***170:*** *1263-73*.
12. Katz A, Buchholz TA, Thames H, Smith CD, *et al.* (2001) Recursive partitioning analysis of locoregional recurrence patterns following mastectomy: implications for adjuvant irradiation. *Int J Radiat Oncol Biol Phys*, ***50:*** *397-403*.
13. McGale P, Correa C, Cutter D, Duane F, Ewertz M, *et al.* (2014) Effect of radiotherapy after mastectomy and axillary surgery on 10 -year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *The Lancet,* ***383:*** *2127-35*.
14. Brito RA, Valero V, Buzdar AU, Booser DJ, *et al.* (2001) Long-term results of combined-modality therapy for locally advanced breast cancer with ipsilateral supraclavicular metastases: The University of Texas MD Anderson Cancer Center experience. *J Clin Oncol,* ***19:*** *628-33*.
15. Karpf D, Sakka M, Metzger M, Grabenbauer GG (2019) Left breast irradiation with tangential intensity modulated radiotherapy (t-IMRT) versus tangential volumetric modulated arc therapy (t-VMAT): trade-offs between secondary cancer induction risk and optimal target coverage. *Radiol Oncol,* ***14:*** *1-11*.
16. Shah C, Badiyan S, Berry S, Khan AJ, *et al.* (2014) Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy. *Radiol Oncol,* ***112:*** *9-16*.
17. Chen MH, Cash EP, Danias PG, Kissinger KV, *et al.* (2002) Respiratory maneuvers decrease irradiated cardiac volume in patients with left-sided breast cancer. *J Cardiovasc Magn Reson*, ***4:*** *265-71*.



[ DOI: 10.52547/ijrr.21.2.4 ]

18. Dumane VA, Bakst R, Green S (2018) Dose to organs in the supraclavicular region when covering the Internal Mammary Nodes (IMNs) in breast cancer patients: A comparison of Volumetric Modulated Arc Therapy (VMAT) versus 3D and VMAT. *PLoS One,* ***13:*** *e0205770*.
19. Yu P-C, Wu C-J, Nien H-H, Lui LT, Shaw S, Tsai Y-L (2018) Tangent-based volumetric modulated arc therapy for advanced left breast cancer. *Radiat Oncol,* ***13:*** *1-10*.
20. Settatree S, Dunlop A, Mohajer J, Brand D, *et al.* (2021) What Can Proton Beam Therapy Achieve for Patients with Pectus Excavatum Requiring Left Breast, Axilla and Internal Mammary Nodal Radiotherapy? *Clin Oncol (R Coll Radiol),* ***33:*** *e570-e7*.
21. Giordano SH, Kuo Y-F, Freeman JL, Buchholz TA, *et al.* (2005) Risk of cardiac death after adjuvant radiotherapy for breast cancer. *J Natl Cancer Inst,* ***97:*** *419-24*.
22. Ferini G, Molino L, Tripoli A, Valenti V, Illari SI, *et al.* (2021) Anatomical predictors of dosimetric advantages for deep-inspiration-breath-hold 3D-conformal radiotherapy among women with left breast cancer. *Anticancer Res,* ***41****: 1529-38*.
23. Jin G-H, Chen L-X, Deng X-W, Liu X-W, *et al.* (2013) A comparative dosimetric study for treating left-sided breast cancer for small breast size using five different radiotherapy techniques: conventional tangential field, filed-in-filed, tangential-IMRT, multi-beam IMRT and VMAT. *Radiat Oncol,* ***8****: 1-8*.
24. Racka I, Majewska K, Winiecki J (2022) Three-dimensional conformal radiotherapy (3D-CRT) vs. volumetric modulated arc therapy (VMAT) in deep inspiration breath-hold (DIBH) technique in left-sided breast cancer patients—comparative analysis of dose distribution and estimation of projected secondary cancer risk. *Strahlenther Onkol*, 1-12.
25. Chen SN, Ramachandran P, Deb P (2020) Dosimetric comparative study of 3DCRT, IMRT, VMAT, Ecomp, and Hybrid techniques for breast radiation therapy. *Radiat Oncol J*, ***38****: 270-281*.
26. Musielak M, Suchorska WM, Fundowicz M, Milecki P, Malicki J (2021) Future Perspectives of Proton Therapy in Minimizing the Toxicity of Breast Cancer Radiotherapy. *J Pers Med,* ***11****: 410*.
27. Chowdhary M, Lee A, Gao S, Wang D, Barry PN, Diaz R, *et al*. (2019) Is proton therapy a "Pro" for breast cancer? A comparison of proton vs. non-proton radiotherapy using the national cancer database. *Frontiers in oncology, 678*.
28. Pazos M, Fiorentino A, Gaasch A, Schönecker S, Reitz D, *et al*. (2019) Dose variability in different lymph node levels during locoregional breast cancer irradiation: the impact of deep-inspiration breath hold. *Strahlenther Onkol,* ***195:*** *13-20*.
29. Darby SC, McGale P, Taylor CW, Peto R (2005) Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300 000 women in US SEER cancer registries. *Lancet Oncol,* ***6:*** *557-65*.
30. Chung E, Corbett JR, Moran JM, Griffith KA, Marsh RB, *et al.* (2013) Is there a dose-response relationship for heart disease with low-dose radiation therapy? *Int J Radiat Oncol Biol Phys,* ***85:*** *959-64*.
31. Borm KJ, Oechsner M, Combs SE, Duma M-N (2018) Deep-inspiration breath-hold radiation therapy in breast cancer: a word of caution on the dose to the axillary lymph node levels. *Int J Radiat Oncol Biol Phys,* ***100:*** *263-9*.
32. Lingos TI, Recht A, Vicini F, Abner A, Silver B, Harris JR (1991) Radiation pneumonitis in breast cancer patients treated with conservative surgery and radiation therapy. *Int J Radiat Oncol Biol Phys,* ***21****: 355-60*.
33. Kim HJ, Jang WI, Kim TJ, Kim JH, Kim SW, (2009) Radiation-induced pulmonary toxicity and related risk factors in breast cancer. *Journal of Breast Cancer,* ***12****: 67-72*.
34. Mehta V (2005) Radiation pneumonitis and pulmonary fibrosis in non–small-cell lung cancer: Pulmonary function, prediction, and prevention. *Int J Radiat Oncol Biol Phys,* ***63****: 5-24*.
35. Chung Y, Yoon HI, Kim YB, Ahn SK, Keum KC, Suh C-O (2012) Radiation pneumonitis in breast cancer patients who received radiotherapy using the partially wide tangent technique after breast conserving surgery. *Journal of Breast Cancer,* ***15:*** *337-43*.
36. Wen G, Tan Y-T, Lan X-W, He Z-C, Huang J-H, *et al.* (2017) New clinical features and dosimetric predictor identification for symptomatic radiation pneumonitis after tangential irradiation in breast cancer patients. *Journal of Cancer*, ***8****: 3795*.
37. Gao X, Fisher SG, Emami B (2003) Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. *Int J Radiat Oncol Biol Phys,* ***56:*** *1038-45*.
38. Stovall M, Smith SA, Langholz BM, Boice Jr JD, Shore RE, *et al.* (2008) Dose to the contralateral breast from radiotherapy and risk of second primary breast cancer in the WECARE study. *Int J Radiat Oncol Biol Phys,* ***72:*** *1021-30*.
39. Kumawat N, Shrotriya AK, Heigrujam MS, Kumar S, *et al.* (2020) The Composite Planning Technique in Left Sided Breast Cancer Radiotherapy: A Dosimetric Study. *Eur J Breast Health,* ***16:*** *137-45*.



[ DOI: 10.52547/ijrr.21.2.4 ]