Received: 26 Oct 2021 | **Accepted:** 23 Feb 2022
DOI: 10.54005/geneltip.1014659

ORIGINAL ARTICLE

In Left-Sided Breast Cancer Radiotherapy Simulation; Prone or Supine position?

Sol Meme Kanseri Radyoterapisi Simülasyonunda Pron pozisyon mu Supin pozisyon mu ?

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How to cite ?

Güzle Adaş Y, Kekilli E. Left Sided Breast Cancer Irradiation ; Prone or Supine Simulation ?. Genel Tıp Derg. 2022; 32(2): 138-143

ABSTRACT

Aim: The aim of this study was to compare radiation doses of target volumes and critical organs among prone and supine positions for left-sided breast cancer patients who were treated with breast-conserving surgery and adjuvant radiotherapy.
Materials and Methods: The doses of critical organs and target volumes were evaluated by using dose-volume histograms on the new radiotherapy plans of twenty patients.
Results: The median heart mean dose was lower in the prone position (mean heart doses 662cGy and 871cGy respectively p = .007). Median lung mean doses for prone and supine positions were 416 cGy and 1042 cGy (p =.006); lung V5 13.8% and 33.4% (p =.008); lung V10 8.9% and 25.4% (p =.009); lung V20 6.1% and 18% (p =.007).
Conclusion: Considering that lower doses of normal structures may reduce side effects, prone position may be preferred in patients with left breast cancer.

Key words: breast cancer, radiotherapy, prone position, supine position

ÖZ

Amaç : Bu çalışmanın amacı meme koruyucu cerrahi sonrası adjuvant radyoterapi uygulanmış sol meme kanseri tanısı olan hastalarda pron ve supin radyoterapi pozisyonlarının hedef hacim ve kritik organ dozları açısından karşılaştırılmasıdır.
Gereç ve Yöntem: Hedef hacim ve kritik organ dozları doz-hacim histogramları kullanılarak değerlendirildi.
Bulgular: Ortanca kalp dozu pron pozisyonda düşük bulundu (pron ve supin pozisyon için sırasıyla 662 cGy ve 871 cGy (p=.007). Pron ve supin pozisyonlar için ortanca akciğer dozları sırasıyla 416 cGy ve 1042 cGy (p=.006); akciğer V5 %13.8 ve %33.4 (p=.008); akciğer V10 %8.9 ve %25.4 (p=.007); akciğer V20 %6.1 ve %18 (p=.009) olarak tespit edildi.
Sonuç: Kritik organlardaki düşük dozlar değerlendirildiğinde sol meme kanseri radyoterapisinde prone pozisyonun tercih edilebileceği söylenebilir.

Anahtar Kelimeler : Meme kanseri, radyoterapi, pron pozisyon , supin pozisyon

Introduction

Breast cancer is the most common type of cancer in women. Survival rate is high when it is properly treated. According to the 2019 American cancer statistics data, 5-year survival rates in Stage I, II, III, and IV breast cancers were reported as 98%, 92%, 75%, and 27%, respectively (1). High survival rates, especially in the early-stage, make treatment-related side effects more important.

Today, early-stage (Stage I-II) breast cancer cases are generally treated with breast-conserving surgery. Post-surgery radiotherapy is recommended as a standard in patients who undergo a breast-conserving surgery. The rate of local recurrence decreased by 26% in 5 years with radiotherapy after breast-conserving surgery. Moreover, an increase of 5% in overall survival was observed in 15 years with regard to a decrease in local recurrence (2-5). Despite the advantages it provides, radiotherapy may also cause toxicity. In studies conducted with old radiotherapy techniques, it was reported that there was an increase in the risk of heart diseases and lung cancer after radiotherapy applied due to the left breast cancer (6,7).

However, these studies are the ones evaluating patients treated with the old radiotherapy techniques. While adequate dose the distribution in target volume is provided with modern radiotherapy techniques, doses for normal tissues can be kept at a very low level.

The aim of this study was to make a dosimetric comparison in target volumes and normal tissues for radiotherapy applied in supine and prone positions in patients with early-stage breast cancer who underwent breast-conserving surgery due to left breast cancer.

Material and Methods

This retrospective study included a total of 20 patients over the age of 18 who were diagnosed with left breast cancer in the radiation oncology clinic of an oncology training and research hospital, and who received radiotherapy after breast-conserving surgery between August 2016 and October 2019. Patients with pathological stages of T1-T2 and N0 were included in the study. Margins of resection were negative, and no distant metastases were detected in the patients. The images of the planning computed tomography (CT), obtained for the radiotherapy, were used to perform this study. The target volumes and the critical organs were re-countered and re-planned for this study on the CT images which were obtained for the treatment.

Planning CT scan was obtained in the prone position for whole breast radiotherapy and in the supine position for the boost plan, without using a intravenous contrast agent. CT scans were obtained with free breathing method. CT scans were performed using a Philips Brilliance CT Big Bore Oncology tomography device at 3-mm slice intervals. The patients were immobilized with the arms on the head using a Q2 fix Access™ Supine Breast board for the supine position. Q2 Fix Access™ Prone G2 Breast prone breast board was used for the prone position. The upper and lower borders of the breast, the midline of the sternum and the ipsilateral midaxillary line were marked by the radiation oncologist and the tomography borders were determined. Figure 1 and figure 2 shows the prone and supine simulation positions of a patient.

Then, the CT images were transferred to the Eclipse™ treatment planning system. The same radiation oncologist performed contouring of the target volumes and the critical organs for all patients in prone and supine positions. The glandular breast tissue observed on CT scan was contoured as clinical target volume (CTV). The CTV of the tumor bed was contoured for the boost dose by evaluating preoperative mammography and breast MR images, if any, and leaving a 5-mm margin to the post lumpectomy seroma observed in planning CT. The heart, the left anterior descending coronary artery (LAD), lung (total lung, right and left lung separately) and contralateral breast were contoured as critical organs. The contours of the heart were determined cranially from the infundibulum of the right ventricle to the last section where the pericardium was observed. The LAD contouring was done with the help of a radiologist. The lungs were contoured using the automatic program in the Eclipse planning system. International breast contouring guidelines were used for contouring (8). Planned target volume (PTV) was obtained by adding a margin of 1 cm from the inferior and 5 mm from other directions to the CTV. The PTV volume beyond the skin was pulled 5 mm back into the skin border with automatic crop function. A 3-dimensional conformal planning was made from inner-outer tangential areas for both positions using the Eclipse version 11 planning system. 6MV photon beams were used for both supine and prone positions in the planning of the whole breast PTV. The dose was defined as 50 Gy in 25 fractions to whole breast and 10-16 Gy in five to eight fractions boost to the tumor bed with a daily fraction dose of 2 Gy. Considering the depth, 6-9 MeV electrons were used for the boost plan. However, the boost dose was not taken into consideration not to disturb the homogeneity of the study group, as the location, size and dose of the tumor bed differ in each patient. Figure 3 shows the whole breast planning of a patient in prone position and figure 4 shows the whole breast planning of the same patient in supine position.

Figure 1: CT simulation in prone position

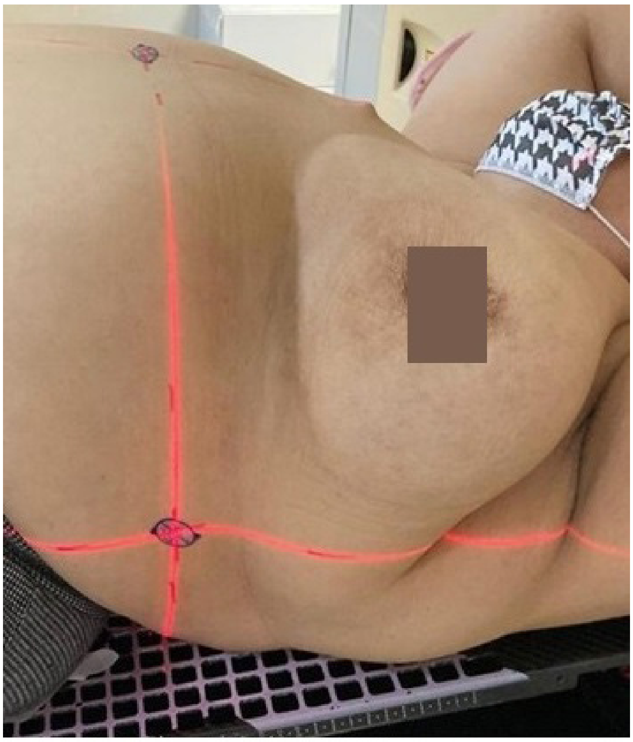

Figure 2: CT simulation in supine position

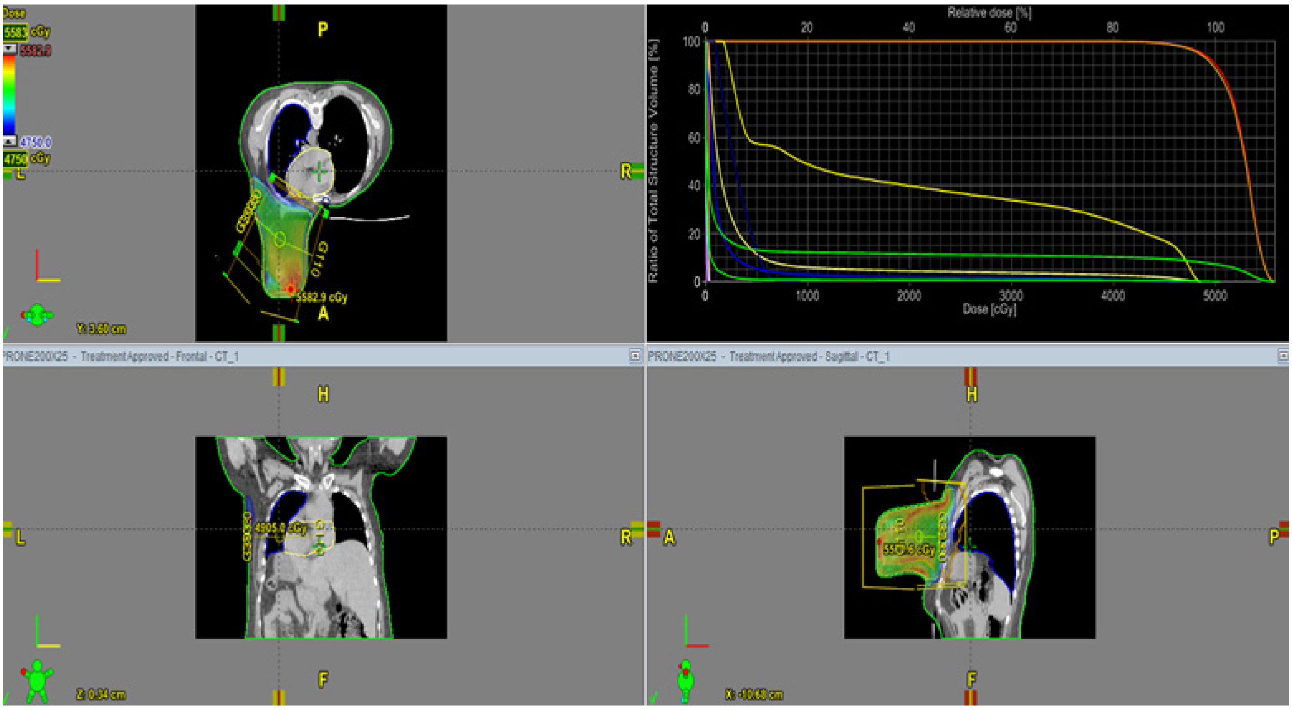

Figure 3: Whole breast planning of a patient in prone position

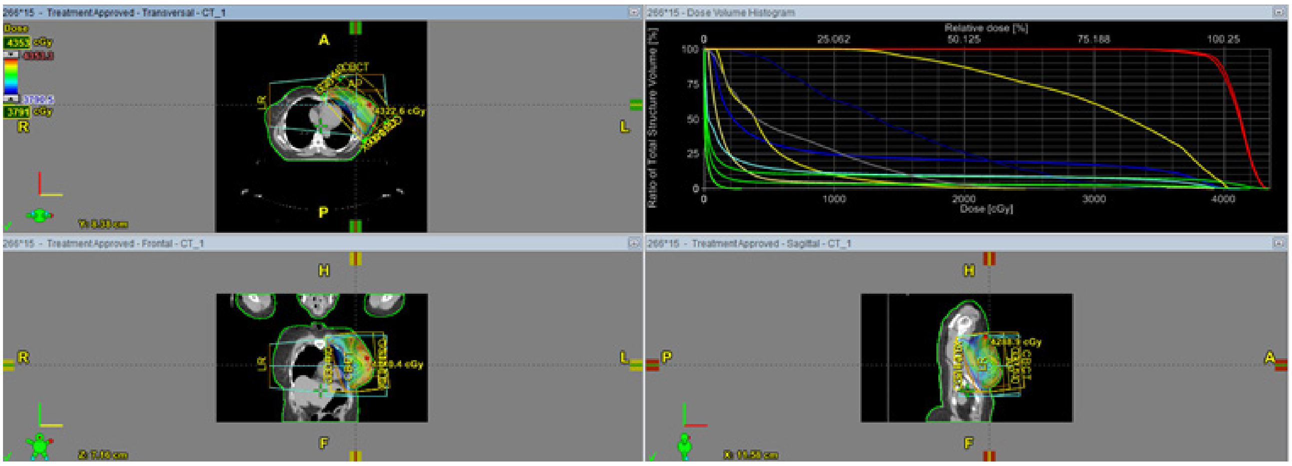

Figure 4: Whole breast planning of a patient in supine position

Dose-volume histograms (DVH) were used for dosimetric evaluation International Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) and other international guidelines were taken into account while evaluating normal tissue doses (9-12). Mean dose of heart; maximum dose for the LAD; V5, V10, V20, and mean doses for the ipsilateral lung and the maximum contralateral breast doses were compared. The PTV D 98%, D 2% (defining the minimum and maximum doses in the ICRU 83 report) and mean doses for the PTV were compared (13).

The study protocol was approved by ethical board of Ankara Oncology Training and Research Hospital on 12 December 2019 with a decision number of 2019-12/479.

Statistical Analysis

The data obtained from the DVH were evaluated using the SPSS (The Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) version 22.0 software for both planning positions. Since the sample size was less than 50, the Shapiro Wilk-W Test was used to analyze whether the variables showed normal distribution or not and it was concluded that the variables did not follow a normal distribution. Therefore, The Wilcoxon signed-rank test, which is a non-parametric test, was used for the analysis of the variables and the data was presented as median with interquartile range (iqr). Data were considered statistically significant at p< .05.

Results

Twenty early-stage breast cancer patients underwent breast-conserving surgery and received adjuvant radiotherapy were included in this study. Median age was 55 (range 35-76). All patients had left sided breast cancer. Tumors were located in the upper outer quadrant in 6, upper inner quadrant in 7, lower outer quadrant in 5 patients and lower inner quadrant in 2 patients. eighteen patients had invasive ductal carcinoma and 2 had invasive lobuler carcinoma. Seven of the tumors were pathologically on T1N0 stage and 13 were T2N0; none of the patients had distant metastasis. The characteristics of patients were summarized in table 1.

Table 1: Patient Characteristics

	Values
Age, years	
Median	55
Range	35-76
Breast side	
Left	20
Tumour localization	
Upper outer quadrant	6
Upper inner quadrant	7
Lower outer quadrant	5
Lower inner quadrant	2
Tumour Characteristics	
Invasive ductal carcinoma	18
Invasive lobuler carcinoma	2
TNM stage	
T1	7
T2	13
N0	20
M0	20

The results of this retrospective study showed that there was no statistically significant difference between the median PTVmean doses and PTV D2, (the median PTVmean doses 5208 cantigray (cGy) (iqr=37) vs 5211 cGy (iqr=11); p=.138; PTV D2% 5475 cGy(iqr=32) and 5482 cGy(iqr=40); p=.138) for the prone and supine positions, respectively) PTV D98 was significantly lower with high effect size (r=-0.108) in prone position (4583 cGy (iqr=88) and 4726 cGy (iqr=114) ;p=.008 for the prone and supine positions, respectively).

The median heart mean dose was significantly lower with a moderate effect size (r=-0.679) in the prone position (the median heart mean doses 662cGy (iqr=11.98) and 871cGy (iqr=834); p= .007 for the prone and supine positions, respectively). Although the median LADmaximum doses were lower in the prone position, there was no statistically significant difference (4435cGy (iqr=142) and 4716cGy (iqr=230) in the prone and supine positions, respectively; p=.878)

When both plans were evaluated in terms of ipsilateral lung doses; the median lung mean doses, lung V5 and V10, were lower in the prone position. The median lung mean doses for the prone and supine positions were 416 cGy (iqr=366) and 1042 cGy (iqr=151), respectively (p=.006); lung V5 was 13.8% (iqr=12.3) and 33.4% (iqr=9.7) (p= .008), lung V10 was 8.9% (iqr =8.6) and 25.4% (iqr=11.15) (p=.009), and lung V20 was 6.1% (iqr =8.1) and 18% (iqr=3.48) (p =.007), respectively.

The median contralateral breast dose maximum was 859 cGy (iqr=698) in the prone position and 326 cGy (iqr=329) in the supine position, there was no statistically difference (p=.06).

All dosimetric results were summarized in table 2.

Table 2: Dosimetric Results

	Prone position	Supine position	p
PTV Doses			
D98 (cGy)	4583	4726	=.008
D2 (cGy)	5475	5482	=.03
Median D_{mean} (cGy)	5208	5211	=.138
Heart Doses Median D_{mean} (cGy)	662	871	= .007
LAD Doses Median D_{max} (cGy)	4435	4716	=.878
Ipsilateral Lung Doses			
Median D_{mean} (cGy)	416	1042	=.006
Median V5 (%)	13.8	33.4	= .008
Median V10 (%)	8.9	25.4	=.009
Median V20 (%)	6.1	18	=.007
Contralateral Breast Dose Median D_{max} (cGy)	859	354	=.06

Abbreviation's;
D : dose; PTV: Planning Target Volume; LAD: left ascending artery; cGy:cantigray

Discussion

Radiotherapy is essential in the treatment of breast cancer. However, there have been discussions whether it causes side effects such as secondary cardiovascular disease. Long survival, especially in early-stage breast cancer or not, makes the side effects of the treatment and the doses administered to normal tissues more important during the treatment.

There are ongoing discussions about whether RT increases the risk of cardiac death in patients who undergo RT for breast cancer. In some studies, it was concluded that RT increased the risk of cardiac death, and some studies showed that it had no effect on cardiac death (14,15).

In a study by Merzenich et al., patients who received RT due to breast cancer between 1998 and 2008 were evaluated. There was no difference in cardiac death rates between the patients who underwent RT for the right breast cancer and the left breast cancer. In multivariate analysis, it was shown that only the cardiac disease history was associated with cardiac death.

A study by Mousavi et al. stated that radiotherapy applied to the thoracic region might increase the risk of diastolic dysfunction; therefore, these patients should be closely followed (15).

Darby et al. evaluated 2168 patients who underwent radiotherapy for breast cancer between 1958 and 2001 and reported that each 1 Gy increase in cardiac dose increased the risk of coronary events by 7.4%. They stated that the coronary event risk started to increase in the fifth year following radiotherapy and was sustained until the third decade after radiotherapy (16). The present study identified a difference of approximately 3 Gy in the mean cardiac dose between the prone and supine positions. Considering that every 1 Gy increase in the cardiac dose increases the risk of cardiac events by 7.4%, the prone position seems to be much more advantageous than the supine position in terms of the cardiac dose.

In the QUANTEC study evaluating cardiac deaths following the breast cancer RT, patients who received RT due to early-stage breast cancer between 2002 and 2006 were evaluated. The patients were divided into two groups: those who died due to cardiovascular disease and those who did not. The groups were balanced in terms of age, receiving a hormonotherapy, and whether or not they received adjuvant chemotherapy. The study concluded that the risk of cardiac death was very low in patients for whom the mean cardiac dose was 3.3 Gy and the maximum LAD dose below 45.4 Gy (17). In the present study, the mean cardiac doses were lower in the prone position. Although there was no statistically significant difference, the maximum LAD doses were also lower in the prone position. These results show that planning in the prone position may be more beneficial regarding future cardiac risks. But the mean cardiac dose obtained in both prone and supine positions were higher than 3.3 Gy, which was reported to have a very low risk of cardiac death in the QUANTEC study. This study used three conformal radiotherapy planning systems and free-breathing. It is possible to lower mean cardiac doses by using different radiotherapy techniques like real position management (RPM) or intensity-modulated planning systems.

Lung doses, like cardiac doses, are also important in terms of the risk of developing side effects. Kahan et al. clinically and radiologically evaluated 119 patients who received RT with the diagnosis of breast cancer in terms of lung damage. The risk of developing radiation pneumonia and radiological changes due to RT were identified to be associated with patient age, the mean lung dose, and lung V20. They stated that the risk of radiation pneumonia increased as the volume of the lung receiving RT and the dose increased (18). In a study by Mulliez and Sethi comparing the prone and supine positions in breast cancer radiotherapy, the ipsilateral lung dose in the prone position was lower than that of the supine position, as in the present study (19,20). This result can be evaluated as a factor that can lower the risk of radiation pneumonia in patients.

In a study by Stowall et al. evaluating the effect of the dose received by the contralateral breast on the contralateral breast cancer development in patients who underwent RT due to early-stage breast cancer, it was found that a contralateral breast dose level of >1 Gy in patients under the age of 40 might increase 2.5 times the risk of developing contralateral breast cancer. They concluded that this effect was not observed in patients over the age of 40 (21). In the present study the contralateral breast dose in the prone position was higher than the supine position. Although the contralateral breast dose was higher than 1 Gy in both positions, it was within the dose limitations recommended by the QUANTEC in supine position (9). It is necessary to reduce the contralateral breast dose as much as possible to decrease the risk of contralateral breast cancer.

Taylor et al compared different simulation techniques of 10 left sided. Breast cancer in the COVID-19 era. Dosimetric comparison was made for prone position, supine position with free breathing and supine position with deep inspiration hold. They reported that prone position provides dosimetric advantage over both supine positions in terms of organ at risk as reported in this study. They also pointed that prone position could reduce the COVID-19 infection transmission risk when compared with the supine positions (22).

Yu et al compared the dosimetric differences between prone and supine positions for external partial breast irradiation. After breast-conserving surgery. They reported that ipsilateral mean lung dose was lower in prone position (1.59 Gy vs. 1.72 Gy, p=.029) similar to our study (23).

There was no statistically significant difference in target volume doses between the mean PTV doses. In both positions, the PTV targeted doses were within the aimed limits. Achieving the targeted doses in both plans can be considered an indicator that both plans can be applied safely in the treatment.

Conclusion

This retrospective dosimetric study evaluating 20 patients, showed that normal tissue doses except the contralateral breast were lower in prone position when compared to supine position. When evaluated in terms of RT toxicity, the risk of toxicity decreases as the radiation dose of critical organ decreases; therefore, the prone position seems to be more advantageous than the supine position. However, this advantage observed dosimetrically needs to be supported by clinical studies with long-term follow-up, including a larger study population.

Acknowledgments

No financial supports

No conflict of interest

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