Prediction of Ipsilateral Lung Doses in Breast Radiotherapy by Anatomical Measurements Before Treatment Planning

💿 Zümrüt Arda KAYMAK, 💿 Alper ÖZSEVEN

Department of Radiation Oncology, Süleyman Demirel University Faculty of Medicine, Isparta-Turkey

OBJECTIVE

To evaluate the predictive value of the patient's anatomical measurements on ipsilateral lung doses before the whole breast radiotherapy (WBRT) planning.

In planning WBRT, the ipsilateral lung is a major organ at risk. Prediction of lung doses can be helpful to choose the RT technique.

METHODS

Thoracic diameters, length and volume of the breast and ipsilateral lung, the height of the contralateral breast, and distance between two breasts were measured as anatomical parameters on the RT simulation computerized tomography (CT) images. Also, the ratios and differences of thoracic diameters were calculated. The correlation between the ipsilateral lung doses and anatomical parameters were evaluated in order to specify cut-off values that can predict high lung doses.

RESULTS

102 patients who undergone breast-conserving surgery+WBRT were enrolled in this study. The anterior-posterior diameter of the thorax at the level of sternal notch (AP- D_{notch}) and xiphisternal junction (AP- D_{xiphi}); the ratios of anterior-posterior and left-right diameters of the thorax (R_{notch} and R_{xiphi}); the difference between AP- D_{xiphi} and AP- D_{notch} (APDdiff) and the difference between the left-right diameters of the thorax at the level of sternal notch and xiphisternal junction (LRD_{diff}) were the statistically significant correlated parameters with lung doses. It can be predicted that the ipsilateral lung doses will be above average if the patients' measurements are as AP- D_{notch} <17.5cm, AP- D_{xiphi} <23.5cm, R_{notch} <0.91cm, R_{xiphi} <0.86cm, APD_{diff}>1.95cm and LRD_{diff}<6.96cm.

CONCLUSION

This is the first study that is evaluating the correlation between patient's anatomical features and ipsilateral lung doses in WBRT. Measuring and calculating $AP-D_{notch}$, $AP-D_{xiphi}$, R_{notch} , R_{xiphi} , $AP-D_{diff}$ and $LR-D_{diff}$ on RT simulation CT images can be predictive.

Keywords: Ipsilateral lung doses; whole breast radiotherapy; 3DCRT. Copyright © 2021, Turkish Society for Radiation Oncology

Introduction

In early-stage breast cancer, mastectomy and breastconserving surgery (BCS) plus whole breast radiation therapy (WBRT) have similar local control and surviv-

Received: October 14, 2020 Accepted: November 02, 2020 Online: November 27, 2020

Accessible online at: www.onkder.org



al rates.[1-4] In addition, it has been shown that local control is enhanced with WBRT after BCS.[5, 6] Therefore, BCS + WBRT is the preferred treatment method for patients who prefer organ preservation and have no contraindications for RT.

Dr. Zümrüt Arda KAYMAK Süleyman Demirel Üniversitesi Tıp Fakültesi, Radyasyon Onkolojisi Anabilim Dalı, Isparta-Turkey E-mail: ardakaymak84@yahoo.com

In the treatment planning of WBRT without lymphatic irradiation, the target volume and critical organ doses were quantitatively documented by 3D conformal RT (3DCRT) unlike in conventional RT [7] thus, the RT side effects became more predictable. With technical improvements, intensity-modulated RT (IMRT) started to be performed, and more homogeneous dose distributions could be obtained in target volumes (reduction of hot spots), also there would be a possibility to keep the heart and ipsilateral lung doses at lower limits.[8] Afterward, tomotherapy and volumetric modulated arc therapy (VMAT) provided more homogeneous dosimetry. 3DCRT, inverse planned IMRT, forward planned IMRT, tomotherapy and VMAT were compared dosimetrically in many studies. [9-11] As a conclusion of all these studies, the percentage volumes of the ipsilateral lung exposed to 20Gy or 30Gy and above (V20, V30) by 3DCRT are higher than inverse-IMRT, tomotherapy and VMAT; however, by these three treatment planning techniques, low radiation doses such as normal tissue V5 and V10 have been demonstrated to be higher than 3DCRT. In forward-IMRT, both target volume homogeneity and coverage are better than 3DCRT, additionally normal tissue V5, V10 values do not increase.

In planning WBRT, the ipsilateral lung is a major organ at risk, because of the risk of radiation pneumonitis (RP) and radiation fibrosis. RP is an early inflammatory reaction that occurs four to twelve weeks after completion of thoracic irradiation, while radiation fibrosis is observed after six months of completion of the RT.[12] The mean dose of the lung $(D_{mean}) > 10$ Gy and V20 of the lung is the predictive dose-volume parameters for RP due to thoracic RT.[13, 14] RP is relatively much rarer after breast cancer RT because of the lower lung doses and single lung exposure. Because the incidence of RP after breast cancer RT is 1.2-13%[15-17], the institutes should take into consideration the ipsilateral lung dose limits according to institutional consensus despite the bilateral lung dose limits in lung cancer treatments are suggested as D_{mean}<20Gy and V20<35-40%.[13, 18]

In our radiation oncology department, early-stage breast cancer RT treatment planning is performed as forward-IMRT (field-in-field) and ipsilateral lung doses are considered to be limited as $D_{mean} \leq 15$ Gy, V20 $\leq 25\%$ and V30 $\leq 20\%$. Patients, whose ipsilateral lung doses could not be limited as detailed above, are informed about the other treatment techniques like inverse-IMRT or VMAT. The lung dose parameters are documented after hours of procedures such as simulation, target tissue

and critical organ delineation by the radiation oncologist and treatment planning by the medical physicist. The aim of our study is to investigate whether there is a correlation between simple anatomic measurements that can be performed on the computerized tomography (CT) slices of the patient and ipsilateral lung doses; before all the RT planning procedures. If such a correlation is detected, there will be a chance to inform patients about ipsilateral lung radiation exposure before target volume delineation and treatment planning.

Materials and Methods

Study Population and Treatment Planning

This is a single-center study and histopathologically diagnosed early-stage breast cancer patients who underwent BCS and adjuvant WBRT consecutively between the years of 2014 and 2019 were enrolled in this study. BCS was performed as consisting of lumpectomy or quadrantectomy and also sentinel lymph node biopsy (SLNB). The patients, who were pathologically staged T1-3N0 after BCS and undergone whole breast RT without any lymphatic irradiation, were the target population of this study.

All patients were scanned in a supine position with breast board immobilization equipment. CT images were obtained with a 2.5-mm slice thickness for the thorax region, from the upper abdomen to the bottom of the chin, a using CT scanner (General Electric Medical Systems). Treatment plans were created using the Eclipse treatment planning system (TPS) on Varian DHX linear accelerator. Anisotropic Analytical Algorithm (AAA) dose calculation algorithm was used in the planning process. A total of 50Gy was planned in 25 fractions with a daily dose of 2Gy/fraction as the prescribed dose. Tumor bed boost was prescribed as 10Gy in 5 fractions or 8 fractions if there is a positive surgical margin. For WBRT, the field-in-field (FIF) planning technique was performed with two open tangential fields by using 6 MV x-rays. All the treatment plans were performed by the same two medical physicists.

Ipsilateral lung dose data were collected from the dose-volume histograms after treatment planning. D_{mean} , V20, V25 and V30 values of the ipsilateral lung of each patient were noted. The patients were divided into two subgroups according to the mean values of lung doses as high lung dose and low lung dose groups.

Anatomical Parameters

RT simulation CT images were used to make the linear measurements. Lung and breast volumes were calcu-

lated by TPS after delineation. All the parameters are defined below.

Cranio-caudal length of the treated breast (L_{Breast})

Cranio-caudal length of the ipsilateral lung (L_{lung})

The intersection length of treated breast and ipsilateral lung ($IL_{breast-lung}$)

The absolute volume of the treated breast (V_{Breast}) and the absolute volume of the ipsilateral lung (V_{Lune})

The maximum height of the contralateral breast $(H_{ContrBreast})$: measured from the chest wall to the skin surface (Fig. 1a)

The thickness of the soft tissue over the sternum $(T_{sternum})$: measured at the level of manubriosternal joint (Fig. 1b)

The distance between two breasts $(D_{breasts})$: measured at the level of manubriosternal joint (Fig. 1b)

The anterior-posterior diameter of the thorax at the level of the sternal notch (AP- D_{notch}) (Fig. 1c)

The left-right diameter of the thorax at the level of

the sternal notch (LR-D_{notch}) (Fig. 1c)

The anterior-posterior diameter of the thorax at the level of xiphisternal joint $(AP-D_{xiphi})$ (Fig. 1d)

The left-right diameter of the thorax at the level of xiphisternal joint (LR- D_{xiphi}) (Fig. 1d)

Additionally, the ratio of $AP-D_{notch}$ and LR-Dnotch (R_{notch}); the ratio of $AP-D_{xiphi}$ and LR-Dxiphi (R_{xiphi}); the difference between $AP-D_{xiphi}$ and $AP-D_{notch}$ (APD-diff); the difference between LR-Dxiphi and LR-D_{notch} (LRD_{diff}); the ratio of $T_{sternum}$ and $D_{breasts}$ (Ts/Db) were calculated.

Statistical Analyses

Statistical analyses were performed by the Statistical Package for the Social Sciences software program version 21.0 (SPSS Inc., Chicago, IL, USA). All the anatomical and dose parameters were evaluated about normal distribution. Pearson's correlation coefficient was performed to analyse the correlations between anatomi-

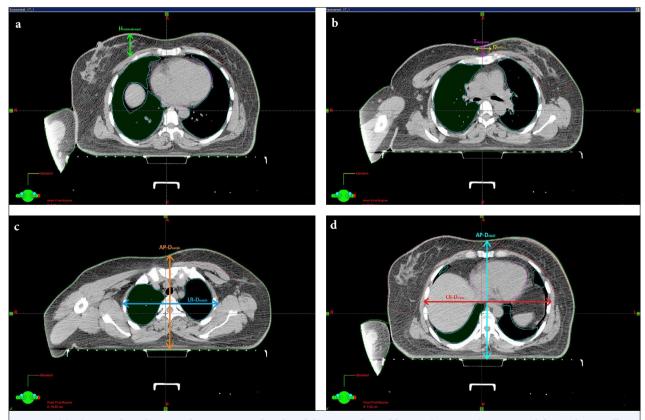


Fig. 1. (a) The CT slice showing the maximum height of the contralateral breast ($H_{ContrBreast}$): measured from chest wall to the skin surface, (b) the CT slice at the level of manubriosternal joint showing the thickness of the soft tissue over sternum ($T_{sternum}$) and the distance between two breasts ($D_{breasts}$), (c) the CT slice at the level of sternal notch showing the anterior-posterior (AP-D_{notch}) and left-right diameter of thorax at the level of sternal notch (LR-D_{notch}), (d) the CT slice at the level of xiphisternal joint showing the anterior-posterior (AP-D_{notch}) and left-right diameter of thorax at the level of sternal notch (LR-D_{notch}), (d) the CT slice at the level of xiphisternal joint showing the anterior-posterior (AP-D_{xiphi}) and left-right (LR-D_{xiphi}) diameter of thorax.

cal and dose parameters which are normally disturbed and Spearman's correlation test was performed for non-parametric data. Additionally, a receiver operating characteristics curve (ROC curve) was performed for the anatomical parameters which were detected as significantly correlated with lung doses to determine the best cut-off value.

Results

Data of 102 consecutive patients who underwent whole breast RT between September 2014 and August 2019 in our radiation oncology department were reviewed. 53 (51.96%) left and 49 (48.03%) right-sided breast cancer patients were enrolled in the study. The mean or median values of all dose parameters and anatomic parameters are detailed in Table 1. The anatomical parameters were compared in low and high lung dose groups and as a result Llung and APDdiff were statistically significant higher(p=0.046 and p=0,002 respectively); HContrBreast, Tsternum, AP-D_{notch}, ,AP-D_{xiphi}, R_{notch}, R_{xiphi}, LRD_{diff} and Ts/Db were statistically significant lower (p=0.009, 0.031, 0.008, 0.003, 0.002, 0.015, 0.009 and 0.049 respectively) in high lung dose group.

Afterward, a Spearman correlation test was conducted for the nonparametric anatomical parameters and a Pearson correlation test was conducted for normally disturbed anatomic parameters to evaluate the correlations between anatomical measurements and the ipsilateral lung dose parameters (Table 2). Llung, Lbreast, ILlung-breast, VBreast, VLung, HContrBreast, Tsternum, Dbreasts, LR-Dnotch, LR-Dxiphi and Ts/Db were weakly correlated with the ipsilateral lung doses and the p values were not significant. AP- $\rm D_{notch}, AP\text{-}D_{xiphi}, \rm R_{notch}, \rm R_{xiphi}, and \rm LRD_{diff}$ were negatively statistically significantly correlated with ipsilateral lung doses. In contrast, APDdiff, was the only parameter that statistically significantly positively correlated with the ipsilateral dose parameters. The best correlated anatomic parameters were R_{notch} and APDdiff, (p values are between <0.001-0.001 for both of them).

ROC curve analyses were performed for each statistically significant correlated anatomic parameter to define a cut-off value which canindicate that the ipsi-

Table 1 Localization of the treated breasts and the mean or median values of dose and anatomical parameters							
	High lung dose group (n=47)	Low lung dose grup (n=55)	Total (n=102)	р			
Treated Breast							
Left (n)	18 (38.3%)	35 (63.6%)	53 (51.96%)	0.011			
Right (n)	29 (61.7%)	20 (36.4%)	49 (48.03%)				
Dmean (mean±SD)	11.5Gy±2	7.41Gy±1.41	9.31 Gy±2.67	< 0.001			
V20 (mean±SD)	20.68%±4.08	12.1%±3.07	16.06 Gy±5.58	< 0.001			
V25 (mean±SD)	19.57%±4.01	11.17%±2.98	15.04%±5.45	< 0.001			
V30 (mean±SD)	18.56%±3.95	10.34%±2.88	14.13%±5.34	< 0.001			
L _{lung} (median; min-max)	17.80 cm (15.33-21.28)	17.10 cm (14.17-22.76)	17.33 cm (14.17-22.76)	0.046			
L _{breast} (mean±SD)	15.73 cm±1.71	15.59 cm±1.84	15.66 cm±1.78	0.689			
IL _{lung-breast} (mean±SD)	14.37 cm±1.59	14.15 cm±1.71	14.25 cm±1.65	0.503			
V _{Breast} (mean±SD)	824.23 cc±321.29	819.76 cc±249.70	821.82 cc±283.47	0.937			
V _{Lung} (mean±SD)	1223.28 cc±263	1143.3 cc±247.67	1180.16 cc±256.72	0.117			
H _{ContrBreast} (mean±SD)	3.55 cm±1.16	4.15 cm±1.11	3.88 cm±1.17	0.009			
T _{sternum} (mean±SD)	1.51 cm±0.55	1.74 cm±0.52	1.64 cm±0.55	0.031			
D _{breasts} (median; min-max)	3.84 cm (2.10-8.57)	3.84 cm (1.55-6.45)	3.84 cm (1.55-8.57)	0.690			
AP-D _{notch} (mean±SD)	17.09 cm±1.51	17.92 cm±1.55	17.54 cm±1.58	0.008			
LR-D _{notch} (mean±SD)	19.98 cm±1.72	19.41 cm±2.21	19.67 cm±2.01	0.158			
AP-D _{xiphi} (mean±SD)	22.34 cm±2.15	23.69 cm±2.24	23.07 cm±2.29	0.003			
LR-D _{xiphi} (median; min-max)	26.49 cm (22.25-29.67)	27.28 cm (22.38-29.79)	26.92 cm (22.25-29.79)	0.167			
R _{notch} (median; min-max)	0.83 cm (0.70-1.16)	0.92 cm (0.70-1.16)	0.88 cm (0.70-1.18)	0.002			
R _{xiphi} (median; min-max)	0.72 cm (0.68-1.07)	0.87 cm (0.69-1.18)	0.85 cm (0.68-1.18)	0.015			
APD _{diff} (median; min-max)			2.21 cm (-5.11-6.42)	0.002			
LRD _{diff} (median; min-max)	6.23 cm (2.83-11.39)	7.28 cm (2.91-12.64)	6.84 cm (2.83-12.64)	0.009			
Ts/Db (median; min-max)	0.36 cm (0.12-0.92)	0.46 cm (0.15-1.6)	0.40 cm (0.12-1.70)	0.049			

The abbreviations of all the parameters are defined in materials and methods section. The statistically significant p values are bold

	Dmean	V20	V25	V30
ng*				
Correlation coefficient	0.131	0.140	0.139	0.14
р	0.181	0.159	0.164	0.15
ast**	0.400	0.405	0.106	
Correlation coefficient	0.190	0.185	0.186	0.18
р	0.056	0.063	0.061	0.05
ng-breast ** Correlation coefficient	0.159	0.150	0.147	0.14
p	0.111	0.130	0.139	0.14
Y ** east	0.111	0.132	0.155	0.11
Correlation coefficient	0.150	0.118	0.119	0.12
p	0.133	0.238	0.233	0.22
** ng				
^{ng} Correlation coefficient	0.159	0.163	0.161	0.16
p	0.111	0.101	0.106	0.10
** ontrBreast				
Correlation coefficient	-0.155	-0.149	-0.145	-0.14
p value	0.120	0.135	0.147	0.15
** rnum				
Correlation coefficient	-0.068	-0.088	-0.090	-0.09
р	0.497	0.378	0.371	0.36
* easts				
Correlation coefficient	-0.028	-0.032	-0.032	02
p	0.783	0.751	0.751	0.80
-D _{notch} **				
Correlation coefficient	-0.255	-0.266	-0265	-0.20
p **	0.010	0.007	0.007	0.00
D _{notch} ** Correlation coefficient	0.148	0.179	0.180	0.18
	0.138	0.071	0.070	0.07
p -D _{xiphi} **	0.150	0.071	0.070	0.07
Correlation coefficient	-0.246	-0.265	-0.264	-0.20
p	0.013	0.007	0.007	0.00
D _{xiphi} *				
Correlation coefficient	-0.076	-0.076	-0.076	-0.07
р	0.450	0.449	0.448	0.43
* tch				
Correlation coefficient	-0.331	-0.354	-0.351	-0.34
р	0.001	<0.001	<0.001	<0.0
* hi Correlation coofficient				
Correlation coefficient	-0.222	-0.248	-0.245	-0.24
p	0.025	0.012	0.013	0.01
D _{diff} *				
Correlation coefficient	0.330	0.353	0.350	0.34
р 	0.001	<0.001	<0.001	<0.0
D _{diff} *	0.210	0.220	0.220	0.00
Correlation coefficient	-0.210	-0.229	-0.229	-0.22
р Db *	0.034	0.021	0.021	0.02
Correlation coefficient	-0.074	-0.086	-0.085	-0.09
p	0.461	0.388	0.397	-0.09

Speraman's correlation test was performed for nonparametric data and denoted by (*); Pearson correlation test was performed for parametric data and denoted by (**). The abbreviations of the parameters are defined on materials and methods section

lateral lung doses will be high. The cut-off values for AP-D_{notch}, AP-D_{xiphi}, R_{notch}, R_{xiphi}, APDdiff, and LRD_{diff} were 17.5cm, 23.5cm, 0.91cm, 0.86cm, 1.95cm and 6.96cm respectively. The area under the curves (AUC), p values, 95% confidence intervals (CI), sensitivity and specificity values are detailed in Table 3.

Discussion

3DCRT, based on two tangential fields, is the conventional treatment planning technique for breast RT. Forward-IMRT is a treatment technique conducted by adding a few field-in-fields to the tangential fields to homogenize the dose distribution.[19-21] The novel RT techniques as inverse-IMRT, tomotherapy and VMAT provide lower V20, V30 and D_{mean} for the ipsilateral lung and heart. In inverse-IMRT, the monitor units (MU) and treatment time (TT) are prolonged while it is necessary to use additional immobilizing equipment such as breast thermoplastic mask or breathing adaptation; there is no need for extra immobilizing technique in VMAT since MU and TT are shorter than both 3DCRT and inverse-IMRT.11 Therefore forward-IMRT is considered to be cost-effective and convenient for WBRT.

In breast cancer RT, the lungs are exposed to less radiation than RT of lung cancer therefore there is no consensus on the ipsilateral lung dose limitations. The institutes are used to specify their own dose limit suggestions for organs at risk in breast RT. Exemplarily the Radiation Oncology Department of University of California San Francisco (UCSF), ipsilateral lung V20 is limited to $\leq 10\%$ with two-field tangents and $\leq 20\%$ with three-field (supraclavicular region) technique. [22] In our study patients treated with WBRT were enrolled in the study, not the ones with regional lymphatic irradiation, thus the effect of patients' anatomical features on the tangential fields could be evaluated.

Conventionally patients are simulated in a supine position on breast inclined board which provides to eliminate the inclination of the sternum and prevents the breast from sliding up. Thus, it is aimed to minimize the ipsilateral lung irradiation. Also, prone or lateral decubitus positions are known to be beneficial for lung and heart doses, especially for large and pendulous breasts. [23,24] In the current study patients were simulated with a breast board in a supine position which is most commonly used for WBRT therefore the results were considered to be useful for many radiotherapy centers.

AP-D $_{notch}$, AP-D $_{xiphi}$, R $_{notch}$, R $_{xiphi}$ and LR-D $_{diff}$ were negatively correlated with the ipsilateral lung doses and the only parameter that was positively correlated was APDdiff. The best-correlated parameters were R_{notch} and APDdiff (p≤0.001). Although the p values are ≤0.001 the correlation coefficients are between 0.330-0.356; which indicates the power of the study.[25]

Consequently, one would have a risk of high ipsilateral lung doses in WBRT if the anatomical parameters are as AP-D_{notch}<17.5cm, AP-D_{xiphi}<23.5cm, $R_{notch} < 0.91$ cm, $R_{xiphi} < 0.86$ cm, APD diff > 1.95 cm, and LRD_{diff}<6.96cm.

The volumes of ipsilateral lung or treated breast were not statistically significantly correlated with the ipsilateral lung doses (p=0.111-0.229). The volumetric parameters could be calculated by the treatment planning system (TPS) after delineation by a radiation oncologist. Our hypothesis of predicting ipsilateral lung doses before RT procedures was realized as the linear parameters measured on CT scans are predictive but the volume parameters measured after delineation are non-predictive.

The underlying logic of the geometrical relationship of the lung dose parameters, which are negatively correlated to R_{notch} and R_{xiphi} but positively correlated to APD-

lung	g doses			-		-
Parameter	AUC	р	95% CI	Cut-off value	Sensitivity (%)	Specificity(%)
AP-D _{notch}	0.650	0.009	0.543-0.757	17.5 cm	65.95	61.81
AP-D _{xiphi}	0.672	0.003	0.567-0.777	23.5 cm	76.59	60
R _{notch}	0.676	0.002	0.569-0.782	0.91 cm	76.59	60
R _{xiphi}	0.641	0.015	0.532-0.749	0.86 cm	65.95	61.81
APD	0.676	0.002	0.569-0.783	1.95 cm	76.59	62
	0.651	0.009	0.544-0.758	6.96 cm	68	60

Table 3 The ROC curve analysis results of anatomical parameters showing statistically significant correlation with high

ROC: receiver operating characteristics; AUC: Area under the curve; CI: confidence interval, the abbreviations of the parameters are defined on materials and methods section

diff, is shown in Figure 2 and Figure 3, respectively.

Since R_{notch} is the ratio of AP-D_{notch} (Fig.2a and Fig.2b green line) to LR-Dnotch (Fig.2a and Fig.2b yellow line), possible changes in the parameters that make up R_{notch} , also affect lung dose parameters. The possible differences of LR-Dnotch, which is defined for the lung at the sternal notch level, can change the volume of the lung irradiated by the radiation beam dramatically. The possible two scenarios were seen in Fig. 2a and Fig. 2b that when the treatment beam enters the body surface with the same θ gantry angle. In the first case, if the

length of the LR-Dnotch is short, a small portion of the lung will irradiate (Fig. 2a – the shaded area with cyan color). Oppositely, if LR-Dnotch length is longer, a larger portion of the lung will irradiate (Fig. 2b – the shaded area with cyan color). The obtained results with this approach are verified that changes in R_{notch} values were found statistically significant correlated with lung dose parameters. All these statements could be mentioned about R_{xinhi} .

On the other hand, since APDdiff is the difference between AP- D_{xinhi} (Fig. 3a light green line) and AP-

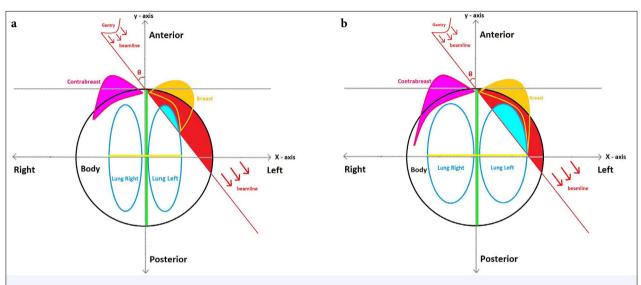


Fig. 2. The diagram demonstrating the correlation between the ratios of anterior-posterior and left-right diameters of thorax with lung irradiation in tangential field. Figure 2a shows a shorter left-right diameter and Figure 2b shows a longer left-right diameter with a same anterior-posterior diameter.

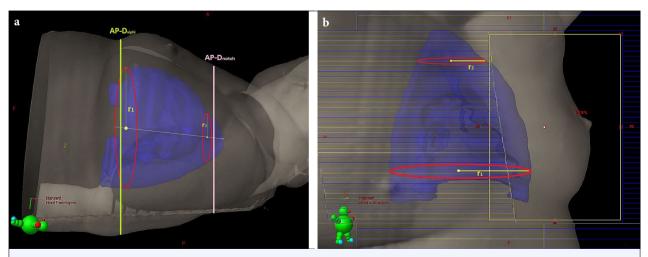


Fig. 3. The digitally reconstructed radiograms showing the effect of difference between anterior-posterior diameters of thorax (APD_{diff}) on the irradiated lung volume. Figure 3a shows the AP diameters at the level of sternal notch and xiphisternal joint; figure 3b is the beam eyes view of the tangential field.

D_{notch} (Fig. 3a pink line), variations in the parameters that formulate APDdiff, also affect lung dose parameters. AP-D $_{\rm xiphi}$ and AP-D $_{\rm notch}$ values, which are used in the calculation of APDdiff value, are associated with the diaphragm and apex regions of the lung, respectively. Therefore, it would be logical to approach AP-D_{xinhi} and AP-D_{notch} by using the width or radii of the lungs at the diaphragm and apex, respectively (Fig.3a). It can be said that the shape of the human lung resembles the cones the most as a geometric shape.. Since the volume of the cone is directly proportional to the square of the radius of the base, small alterations in the radius of the base have a big effect on the volume changes. As seen from Fig. 3b (beam eye view of breast treatment planning) the effect of length changes in the radius r2 on the change in lung volume, will be much greater than the effect on the change in lung volume as a result of length changes in the radius r1. To be more precise, the rise in the subtraction of r2-r1 value will increase the lung dose parameters as it will increase the net lung volume covered by the radiation beam. In this study, calculations were made by using the $\operatorname{AP-D}_{\operatorname{xiphi}}$ and $\operatorname{AP-D}$ D_{potch} values that adjacent to the r1 and r2 radius values, respectively. As a result of these findings, changes in lung dose parameters were found statistically significant with the APDdiff value.

Conclusion

This is the first study that is evaluating the correlation between the patients' anatomical features and the ipsilateral lung doses in WBRT. AP-D_{notch}, AP-D_{xiphi}, R_{notch}, R_{xiphi} , AP-D_{diff}, LR-D_{diff} were identified as significantly correlated with the high ipsilateral lung doses and the cut-off values with best sensitivity and specificity were denoted. If the patient is evaluated with these parameters before RT planning and in case the ipsilateral lung dose is predicted to be over average; WBRT may be considered to be performed by arc therapy, not with tangential fields. Further studies are needed to specify more sensitive and specific cut-off values or some formulas in order to high lung dose risk assessment in tangential breast RT.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by the Süleyman Demirel University Faculty of Medicine Clinical Research Ethics Committee (no. 378, date: 23.12.2019).

Financial Support: Financial and material support was not received.

Authorship contributions: Concept – Z.A.K., A.O.; Design – Z.A.K.; Supervision – Z.A.K.; Materials – Z.A.K., A.O.; Data collection &/or processing – Z.A.K., A.O.; Analysis and/or interpretation – Z.A.K.; Literature search – Z.A.K.; Writing – Z.A.K., A.O.; Critical review – Z.A.K., A.O.

References

- Sarrazin D, Lê MG, Arriagada R, Contesso G, Fontaine F, Spielmann M, et al. Ten-year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. Radiother Oncol 1989;14(3):177–84.
- Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewehr DJ, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. Cancer 2003;98(4):697–702.
- van Dongen JA, Bartelink H, Fentiman IS, Lerut T, Mignolet F, Olthuis G, et al. Randomized clinical trial to assess the value of breast-conserving therapy in stage I and II breast cancer, EORTC 10801 trial. J Natl Cancer Inst Monogr 1992;(11):15–8.
- 4. Blichert-Toft M, Rose C, Andersen JA, Overgaard M, Axelsson CK, Andersen KW, et al. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. J Natl Cancer Inst Monogr 1992;(11):19–25.
- 5. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347(16):1233–41.
- Winzer KJ, Sauer R, Sauerbrei W, Schneller E, Jaeger W, Braun M, et al; German Breast Cancer Study Group. Radiation therapy after breast-conserving surgery; first results of a randomised clinical trial in patients with low risk of recurrence. Eur J Cancer 2004;40(7):998–1005.
- Purdy JA. 3-D conformal radiotherapy: a new era in the irradiation of cancer. Basel, Switzerland: Karger; 1996. p. 1–16.
- Rongsriyam K, Rojpornpradit P, Lertbutsayanukul C, Sanghangthum T, Oonsiri S. Dosimetric study of inverse-planed intensity modulated, forward-planned intensity modulated and conventional tangential techniques in breast conserving radiotherapy. J Med Assoc Thai 2008; 91(10):1571–82.

- Schubert LK, Gondi V, Sengbusch E, Westerly DC, Soisson ET, Paliwal BR, et al. Dosimetric comparison of left-sided whole breast irradiation with 3DCRT, forward-planned IMRT, inverse-planned IMRT, helical tomotherapy, and topotherapy. Radiother Oncol 2011;100(2):241–6.
- 10. Popescu CC, Olivotto IA, Beckham WA, Ansbacher W, Zavgorodni S, Shaffer R, et al. Volumetric modulated arc therapy improves dosimetry and reduces treatment time compared to conventional intensity-modulated radiotherapy for locoregional radiotherapy of left-sided breast cancer and internal mammary nodes. Int J Radiat Oncol Biol Phys 2010;76(1):287–95.
- 11. Liu H, Chen X, He Z, Li J. Evaluation of 3D-CRT, IMRT and VMAT radiotherapy plans for left breast cancer based on clinical dosimetric study. Comput Med Imaging Graph 2016;54:1–5.
- 12. Tsoutsou PG, Koukourakis MI. Radiation pneumonitis and fibrosis: mechanisms underlying its pathogenesis and implications for future research. Int J Radiat Oncol Biol Phys 2006;66(5):1281–93.
- 13. Palma DA, Senan S, Tsujino K, Barriger RB, Rengan R, Moreno M, et al. Predicting radiation pneumonitis after chemoradiation therapy for lung cancer: an international individual patient data meta-analysis. Int J Radiat Oncol Biol Phys 2013;85(2):444–50.
- Vasiljevic D, Arnold C, Neuman D, Fink K, Popovscaia M, Kvitsaridze I, et al. Occurrence of pneumonitis following radiotherapy of breast cancer - A prospective study. Strahlenther Onkol 2018;194(6):520–32.
- 15. Oie Y, Saito Y, Kato M, Ito F, Hattori H, Toyama H, et al. Relationship between radiation pneumonitis and organizing pneumonia after radiotherapy for breast cancer. Radiat Oncol 2013;8:56.
- 16. Tsougos I, Mavroidis P, Rajala J, Theodorou K, Järvenpää R, Pitkänen MA, et al. Evaluation of dose-response models and parameters predicting radiation induced pneumonitis using clinical data from breast cancer radiotherapy. Phys Med Biol 2005;50(15):3535–54.

- 17. Werner ME, Eggert MC, Bohnet S, Rades D. Prevalence and Characteristics of Pneumonitis Following Irradiation of Breast Cancer, Anticancer Res 2019;39(11):6355–8.
- 18. Graham MV, Purdy JA, Emami B, Harms W, Bosch W, Lockett MA, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC), Int J Radiat Oncol Biol Phys 1999;45(2):323–9.
- 19. Herrick JS, Neill CJ, Rosser PF. A comprehensive clinical 3-dimensional dosimetric analysis of forward planned IMRT and conventional wedge planned techniques for intact breast radiotherapy. Med Dosim 2008;33(1):62–70.
- 20. Mihai A, Rakovitch E, Sixel K, Woo T, Cardoso M, Bell C, et al. Inverse vs. forward breast IMRT planning. Med Dosim 2005;30(3):149–54.
- 21. Cardinale RM, Steele J, Fein DA, Mao L, Chon BH. The minimal dosimetric benefit of breast IMRT as compared to using a small number of forward planned MLC segments does not justify the cost (abstract 2629). Int J Radiat Oncol Biol Phys 2007;69(3 Suppl):553–4.
- 22. Hansen EK, Roach M. Handbook of evidence-based radiation oncology. 3rd ed. New York: Springer; 2018. p. 388.
- 23. Formenti SC, DeWyngaert JK, Jozsef G, Goldberg JD. Prone vs supine positioning for breast cancer radiotherapy. JAMA 2012;308(9):861–3.
- 24. Campana F, Kirova YM, Rosenwald JC, Dendale R, Vilcoq JR, Dreyfus H, et al. Breast radiotherapy in the lateral decubitus position: A technique to prevent lung and heart irradiation. Int J Radiat Oncol Biol Phys 2005;61(5):1348–54.
- 25. Bishara AJ, Hittner JB. Testing the significance of a correlation with nonnormal data: Comparison of Pearson, Spearman, transformation, and resampling approaches. Psychological Methods 2012;17(3):399–417.