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EFFECT OF COMPLETE BLOCK OF IRRADIATED LUNG VOLUME IN BREAST CANCER WITH TOMOTHERAPY

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Abstract: *The purpose of this study was to evaluate the dosimetric value of the Tomo Helical (TH) plans with the complete block where located posterior of the sided lung compared to TH plans with no block in patients with intact breast cancer. TH plans with intact breast cancer were retrospectively created for 17 patients with blocked or no TH techniques in our clinic. The beam angles were arranged to cover PTV intact breast and to minimize doses to Organ at Risks (OARs), sided lung and contralateral breast in TH plans. There was no difference between the values of Conformity Index (CI) and Homogeneity Index (HI) of both plans (p>0.05). The values of Dmean, V5, and V20 of the sided lung in Tomo Helical with the block (HTb) were significantly lower than that Tomo Helical with no block (TH) for all 17 patients (p=0.01, p=0, p=0.002). The values of Dmean and V5 of heart in HTb were significantly lower than that in TH (p=0.004, p=0). Both of HTb and TH plans produce acceptable target dose coverage in intact breast Radio Therapy (RT). Especially we produce lower dose V5 values in sided lung volume when using complete block posteriorly. Aimed to decrease scattering low dose regions in irradiated volume and around the breast, so we may prevent the probability of secondary malignancy in the breast region.*

Key Word: Breast Cancer, Tomotherapy, Complete Block, Irradiation.

1. Introduction

The number of patients diagnosed with breast cancer increases with more widely used screening mammography programs around the world [1]. Breast-conserving therapy (BCT) has become the method of choice for the treatment of early-stage breast cancer. Conservative surgery plus axillary radiotherapy is superior to axillary node dissection in stage I breast cancer patients [2]. Whole breast radiotherapy has been shown to cause low rates of axillary recurrence after breast-conserving surgery (BCS) [3]. In patients with breast cancer, compliance with adjuvant radiotherapy is good, the rate of toxicity is often acceptable, and the patients often have significantly better survival [4].

Conventional radiotherapy (RT) after conservative breast surgery is performed with 2D and 3D conformal RT with tangential beams and mixed photons/electron beams [5]. Additionally, in recent decades, various techniques such as intensity-modulated radiotherapy (IMRT) and hybrid IMRT have been developed to improve dose distribution in the breast and to reduce the dose delivered to organs at risk (OAR) [6]. Also, 3D Conformal RT (3DCRT) and rotational IMRT with fixed gantry angles have also been shown to reduce the dose delivered to critical structures and healthy tissues in patients with breast cancer [7].

Radiotherapy to the breast is a complex task which includes numerous different techniques that can be employed to ensure adequate dose target coverage while minimizing doses to OAR [8]. In this study, we aimed to compare the role of two helical techniques, TH with blocking (THb) and TH without blocking (TH), in the reduction of doses delivered to critical organs, by creating an optimal planning target volume (PTV) in breast cancer patients. Block was created by using binary multi-leaf collimator (MLC) in the lower region of the sided lung with the optimization system.

2. Materials and Methods

2.1. Patients

The study included 17 patients with an intact primary breast tumor that underwent helical tomotherapy (TH) for BCT between January 2016 and January 2017 at Dicle University Medical School Department of Radiation Oncology. TH plans were created for each patient after informed consent was obtained from each patient. The eligibility criterion was histopathologically proven early stage I-II breast cancer according to the American Joint Committee on Cancer (AJCC) cancer staging system, We compared two modes of tomotherapy for BCT: (I) TH with blocking (THb) and (II) TH without blocking (TH).

2.2.Simulation, Contouring, Planning, Plan Assessment, and Complete Block

Patients were simulated using computed tomography (CT) simulator and were positioned on a breast board (CIVCO) with their head turned to the contralateral side and their contralateral arm raised above their head. CT images with 3.0 mm thickness were obtained for TH planning. The CT images and the contours of the planning target volume (PTV) and OAR were transferred to the tomotherapy planning system (Accuray Inc., Sunny vale) to create treatment plans.

Helical tomotherapy (TH) plans were generated using IMRT with rotational dose delivery systems to create an optimal PTV and to minimize the doses delivered to OAR, contralateral lung, and contralateral breast. The intact breast was also included in the target volume. The TH plans were created with a pitch, field width, and modulator factor of 0.287, 5.048, 3.0 (range, 0.5-4.0) cm, respectively.

A total of 50 Gy was prescribed in 25 fractions (2 Gy per fraction). In the dose limits for PTV, (I) the minimum dose delivered to 95% of the PTV was defined as D95 and D95%≥95% was achieved and (II) the percentage of the PTV receiving a minimum of 95% of the dose was defined as V95% (V47.5 Gy) and V95%≥95% was achieved. For PTV, the percentage of the PTV receiving a minimum of 107% of the prescribed dose was defined as V107 (V53.5 Gy) and was used for comparing the HT plans.

The conformity Index (CI) was used for the evaluation of the target dose conformity. The CI was calculated according to the following formula defined by ICRU (International Commission on Radiation Units and Measurements) [9]:

CI=the Volume of PTV surrounded by the reference dose /PTV Volume.

CI=1.00 is the optimal case.

The uniformity of dose distribution in the target volume was analyzed based on the Homogeneity Index (HI). HI was calculated using the HI = (D2 - D98) / D50 formula, where D2 and D98 represent the doses delivered to 2% and 98% of the PTV, respectively, and D50 represents the mean target dose (50%) [10]. A lower HI value indicates greater homogeneity, whereas a higher CI value indicates better conformity. The effects of HT on the target and OAR doses and the duration of treatment were assessed for each plan by one radiation oncologist.

The complete block is created with MLC. MLC is made of tungsten and MLC thickness is 6.25 mm. Block has placed the lower part of the lung with the optimization system (Volo planning program). Block is used for decreasing the low dose region in the sided lung.

2.3.Statistical Analysis

All data were analyzed using SPSS 16.0 (SPSS, Chicago, IL, USA). All the variables were expressed as median and mean. Wilcoxon signed-rank test for related samples was used for comparing the dosimetric end-points between the HT plans. A *p* value of <0.05 was considered significant.

3. Results

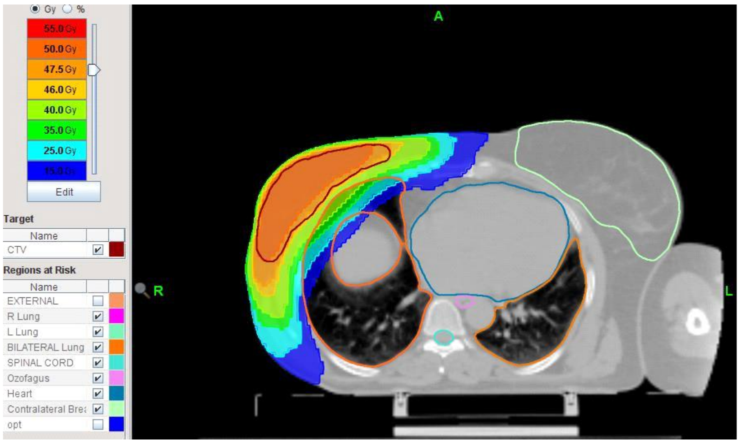
The study included 17 patients with breast cancer, of whom 8 (47.1%) patients had right and 9 (52.9%) patients had left breast cancer. The median age was 48 (range, 24-80) years. Median PTV volume in intact breasts was 607.9 cc (range, 338.0-1850.68). The CI values were 0.93 and 0.96 in THb and TH, respectively ($p>0.05$). The CI values were 0.21 and 0.23 in THb and TH, respectively, and no significant difference was found ($p>0.05$). Both techniques demonstrated clinically acceptable target dose coverage for the intact breasts. However, a significant difference was found in the Dmax values between the two techniques. Besides, a significant difference was found between the mean values of V107 (the volume receiving 53.5 Gy) between THb and TH (2.5% *vs.* 0.68%) ($p=0.01$). Table 1 summarizes the PTV dose parameters in the TH plans. A total of 50 Gy doses were given patient, while the dose distribution of PTV and critic organs were shown in Figure 1.

Table 1. Comparison of dosimetric parameters for the PTV between THb and TH plans.

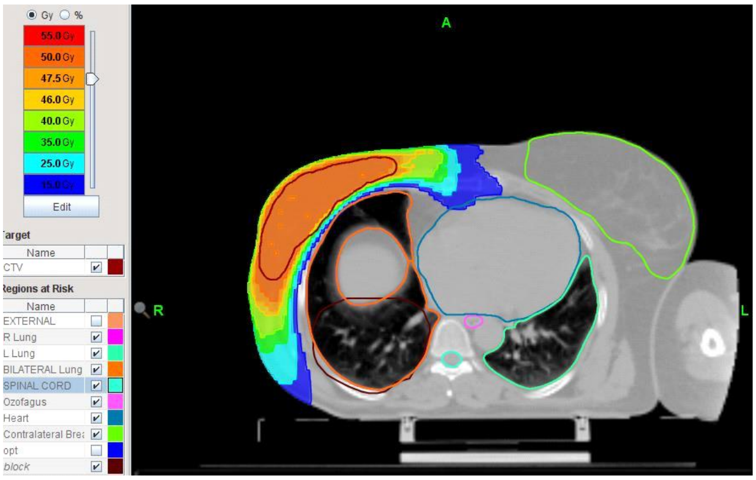
Parameter	TomoBlock		TomoHelical		P value
	Median	Range	Median	Range	
Dmean	50,68	49,12-51,20	50,72	49,93-50,94	0,453
Dmin	25,45	17,5-37,19	35,65	24,32-41,58	0,001
Dmax	57,27	54,61-61,24	55,47	53,66-58,14	0,002
V95	95,63	91,91-99,06	95,09	91,46-98,64	0,148
V107	2,55	0.01-14,65	0,68	0-1,78	0,001
D2	53,72	50,75-55,98	53,06	51,04-53,43	0,025

D50	50,88	49,32-51,4	50,76	50,01-51,08	0,326
D95	47,97	46,13-49,3	48,57	45,8-49,26	0,234
D98	45,4	44,8-48,41	46,37	43,45-47,5	0,255
CI	0,93	0,88-0,97	0,96	0,90-0,99	0,2
HI	0,21	0,09-0,35	0,23	0,08-0,29	0,16

Dmax , maximum dose; Dmean, mean dose; Dmin, minimal dose received by 99% of target target volume; Dx, the dose received x% of the target volume; Vx, the volume of (%)receiving x dose (Gy) or higher; CI, Conformity index; HI, Homogeneity index.



(a)



(b)

Figure 1(a). The dose distributions of Tomohelical plan without block. (b) The dose distributions of Tomohelical plan with block.

In the THb technique, the D2 and Dmin values for PTV, the V5 and V20 values for the ipsilateral lung, the Dmean and V5 values for the heart, and the V5 value were significantly lower compared to HT (p<0.005 for all). However, the Dmax value for PTV was significantly lower in TH compared to HTb (p<0.005).

Table 2 shows the dosimetric parameters for the ipsilateral lung, heart, contralateral breast, esophagus, and spinal cord. Table 3 shows the dosimetric comparisons of the THb and TH plans of right and left the intact breast. The greatest differences were found in the dosimetric parameters of the heart and the ipsilateral lung.

Table 2. Comparison of dosimetric parameters for the OARs THb and TH plans for 17 patients

Parameter	Tomoblock		TomoHelical		P value
	Median	Range	Median	Range	
Ipsilateral lung					
Dmean	4,9	1,79-8,09	10,95	4,39-26,65	0,01
v5	20,14	4,8-30,9	58,9	22,2-98,0	0
v20	3,23	0-11,53	18,7	0-35,0	0,002
Heart					
Dmean	5,67	2,84-12,58	7,25	4,32-10,99	0,004
V5	36,44	10,35-65,11	65,1	26,10-989,7	0
V25	0,2	0-5,3	2,25	0-7,7	0,064
V30	0	0-3,22	0,17	0-4,2	0,262
Spinal Cord					
Dmin	0,24	0,1-2,48	0,28	0,1-3,17	0,088
Dmax	7,95	1,68-30,01	9,7	2,37-26,57	0,959
D2	5,1	1,34-21,8	7,5	2,3-21,8	0,156
Contralateral Breast					
Dmean	4,39	1,76-7,84	5,29	1,65-7,54	0,136
V5	21,1	0,33-656,1	41,1	0-71,2	0,001
Osephagus					
Dmean	5,43	1,32-8,8	5,29	1,65-7,54	0,831
Vx, volume (%) receiving x dose (Gy) or higher; Dmax, maximum dose; Dmean, mean dose; D2, the					

Table 3. Comparison of dosimetric parameters of THb and TH plans of the right and left-sided intact breast

	Right-sided (n=8)					Left-sided (n=9)				
	THb		TH			TH		THb		
Parameter	Median	Range	Median	Range	P value	Median	Range	Median	Range	P value
PTV										
Dmean	50.66	49,12-51,2	50.68	49,93-50,9	1	50.76	50,65-50,94	50.68	50,42-50,8	0.192
Dmin	26.89	17,50-37,19	35.88	28,9-41,58	0.012	35.65	24,32-38,41	21.3	19,5-35,7	0.017
Dmax	57.43	54,81-59,82	55.26	53,66-58,1	0.012	55.55	54,98-56,75	57.2	54,61-61,2	0.05
V95	95.53	91,91-99,06	96.17	91,46-97,8	0.575	97.14	94,56-98,64	96.35	92,38-98,7	0.123
V107	3.02	0,64-12,85	0.28	0-1,36	0.017	0.93	0,25-1,78	2.55	0,01-14,65	0.036
D2	53.80	52,97-	52.81	51,56-	0.017	53.1	51,04-	53.72	50,75-55,9	0.374

		54,52		53,3			53,43			
D50	50.86	49,32-51,4	50.87	50,38-51,0	0.779	50.68	50,01-51,07	50.88	50,62-51,1	0.123
D95	47.83	46,15-49,3	48	45,8-48,98	0.779	48.58	46,2-49,4	48.43	45,66-48,7	0.76
D98	45.37	45,16-48,19	45.94	43,45-47,1	1	49.44	49,13-49,95	50.68	50,01-510	0.008
HI	0.14	0,10-0,31	0.12	0,09-0,18	0.56	0.16	0,08-0,23	0.18	0,11-0,33	0.215
CI	0.96	0,90-0,98	0.96	0,88-0,98	0.741	0.95	0,90-0,98	0.93	0,89-0,97	0.073
Sided lung										
Dmean	4.23	3,38-6,92	11.22	6,26-26,63	0.012	9.77	4,39-13,19	5.38	1,79-8,09	0.017
V5	17.21	14,13-34,3	61.95	37,8-98	0.012	56.22	22,2-74,5	28.9	4,8-38,9	0.012
V20	3.98	1,02-8,73	18.76	7,73-35	0.012	15.2	0-23,8	1.73	0-11,53	0.036
Heart										
Dmean	5.05	2,84-8,11	7.17	4,96-9,05	0.012	8.09	4,32-10,99	5.93	4,32-12,58	0.093
V5	33.17	10,35-65,11	65.9	32,8-71,12	0.012	59.65	26,1-98,7	42.3	19,8-63,1	0.012
V25	0.00	0,00-5,08	0.95	0-3,45	0.753	3.2	0-7,7	0.2	0-5,3	0.025
V30	0.00	0,00-3,22	0	0-1,25	0.715	1.3	0-4,2	0	0-3,1	0.058
Spinal Cord										
Dmin	0.20	0,10-2,48	0.26	0,1-2,39	0.204	0.34	0,13-3,17	0.55	0,12-1,13	0.233
Dmax	5.93	1,97-17,65	6.33	2,97-14,17	0.889	11.91	2,37-26,57	10.59	1,68-30,01	0.889
D2	4.17	1,7-12,89	5.22	2,45-11,34	0.327	8.97	2,3-21,8	6.79	1,34-21,8	0.237
Contralateral breast										
Dmean	3.54	1,76-4,39	4.85	1,65-7,54	0.05	5.55	4,46-6,49	5.45	3,08-7,84	0.953
V5	14.70	0,33-22,33	43.16	0-58,90	0.017	41.1	22,8-71,2	29.8	9,3-65,1	0.017
Esophagus										
Dmean	4.85	1,63-7,77	4.85	1,65-7,54	0.779	5.55	4,46-6,49	6.67	1.32-8,8	0.441

PTV, Planning target volume; Dmin, minimal dose; Dmean, mean dose; D2, the dose to 2% of the volume; D50, the dose to 50% of the target volume; Dmax, maximum dose; Vx, volume % receiving x dose (Gy) or higher.

4. Discussion

Helical tomotherapy (TH) and IMRT plans ensure superior target dose homogeneity and better normal tissue sparing in breast cancer RT. However, an increase in the doses delivered to low-dose regions is known to cause an increased rate of radiation-induced secondary malignancies [7,11,12]. Therefore, we aimed to compare these TH and THb in terms of achieving homogeneous dose distribution for the target volume for better local control and sparing healthy tissues to prevent life-threatening complications (heart disease and lung pneumonitis) as well as secondary malignancies.

Both techniques provided adequate coverage of the PTV, which was consistent with previous studies [13]. Moreover, all the TH and IMRT plans achieved higher PTV coverage compared to conventional plans (Prescription of V47.5Gy of PTVs>95%). On the other hand, TH and conventional

IMRT led to greater target dose homogeneity compared to 11-field (11FBT) and 11FBT IMRT [14,15]. TomoDirect (TD), Elektra Volumetric Modulated Arc Therapy (E-VMAT), and Varian RapidArc (RA) plans were generated for whole breast irradiation and these plans achieved better target coverage (V95%) compared to Field-in-field (FinF) (97.7-98.3% *vs.* 96.6%) [16]. In our study, the mean V95 value was higher in THb than in TH (95.63% *vs.* 95.09%); however, no significant difference was established.

The conformity index (CI) and homogeneity index (HI) are two analysis tools of a treatment plan. The technique with segmental fields allowed us more homogeneity dose distribution compared to the standard two tangential fields [17]. They found that the mean HI values were 1.08 and 1.09 and mean CI values were 1.38 and 1.43, respectively [17]. We found that the mean HI value was 0.21 in THb and 0.23 in TH and the mean CI value was 0.93 in THb and 0.96 in TH. However, no significant difference was found between the CI and HI values in both THb and TH (p>0.05). Mean V107 value for PTV was 0.2% ± 0.1 in HT, and HT led to higher conformity and homogeneity compared to HTb [18]. Moreover, the V107 value was more favorable in TH compared to THb (0.68% vs. 2.55%). The volumetric-arc therapy (VMAT) plans were more inhomogeneous than the TH and TD plans [19].

The clinical benefit of radiotherapy in the treatment of breast cancer must be balanced against the documented risk of early and late toxicity [20]. Adverse effects after breast irradiation have been reported in heart disease, pneumonitis, and pulmonary fibrosis [21]. Increasing irradiated volume leads to pulmonary complications [22]. Moreover, the irradiated volume in an organ depends on the radiation technique used in the treatment [23]. A study showed the TD plans reduced the ipsilateral lung volume and the mean dose and also provided acceptable target dose homogeneity in the patients. However, TH is superior to TD when added nodal irradiation [24]. Moreover, the TH technique, compared to other techniques, decreases the doses delivered to the contralateral OAR while increasing the doses to low-dose regions [18]. In our study, the Dmean, V5 (volume of lung receiving at least 5 Gy), and V20 (volume of lung receiving at least 20 Gy) values for the ipsilateral lung in THb were significantly lower than those in TH in all the 17 patients (p=0.01, 0.00, 0.02, respectively). These findings can be attributed to the addition of complete block in the posterior aspect of the ipsilateral lung and the rotational delivery of TH.

Radiotherapy of breast cancer and other thoracic irradiations induce an ionizing radiation dose to the heart. Irradiation of the heart, associated with cardiovascular risk and the cancer treatment-induced cardiotoxicity, leads to increased risk of cardiovascular mortality. The high risk of cardiac events is related to the dose received by the heart and the irradiated cardiac volume. However, the limitation of cardiac irradiation is that it requires a priority in the planning of thoracic irradiations [25]. A previous study showed a low rate of ischemic cardiac disease for both radiation modalities in the women treated for breast cancer [26]. On the other hand, another study suggested that photon radiation therapy cannot achieve an MHD of <5Gy [27]. On the other hand, a previous study indicated that the relationship between the cardiac dose and late complications became prominent when 20% of the cardiac volume gained a dose of greater than 30 Gy [28]. In our study, the irradiated cardiac volume (V5) was significantly greater in TH compared to THb (65.10% vs. 36.44%; p=0.00). These rates suggest that these techniques do not pose a meaningful risk in terms of late cardiac complications.

Another important factor in the treatment of breast cancer is the contralateral breast. To avoid an increased risk of second cancer and the adverse effects such as fibrosis in the unaffected breast, the mean dose in this breast should be kept as low as possible. In our study, no significant difference was found between the two techniques with regards to the mean doses delivered to the contralateral breast. Moreover, the Dmean value was 4.39 Gy in THb as opposed to 5.29 Gy in TH (p>0.05).

5. Conclusion

When all the deterministic values are considered, the THb technique appears to be more useful than the TH technique, as the former causes the heart, lung and contralateral breast receive lower doses while adequately covering the PTV. In particular, the low-dose regions in the irradiated contralateral lung is decreased to a very low value in THb, in which complete block is administered in the lower portion of the contralateral lung. Moreover, these low-dose regions may cause secondary malignancy. In conclusion, the complete block may be standardized in helical irradiations of breast cancer.

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