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INCIDENTAL IRRADIATION DOSE OF LIVER INCREASES IN RIGHT-SIDED BREAST RADIOTHERAPY WITH IMRT

Oncology

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ABSTRACT

The aim of this study was to evaluate the incidental dose of the liver received in breast cancer radiotherapy and to investigate the effects of intensity modulated radiation therapy (IMRT) on liver doses. The breast treatment plans of 225 women with right-sided breast cancer who underwent postoperative radiotherapy were retrospectively examined. Liver V20 (cc) and liver V10 (cc) with IMRT were significantly higher in both with boost and no boost groups. Liver Dmean, V20 (%) and V10 (%) with IMRT were statistically higher in both with boost and no boost groups in which the whole liver was displayed. Liver may be affected at different rates due to anatomic variations in breast cancer radiotherapy. In right-side breast cancer, the use of IMRT increases the doses that the liver is exposed to incidentally.

KEYWORDS

Breast Cancer, Intensity Modulated Radiation Therapy, Liver

INTRODUCTION

The benefit of radiotherapy (RT) was demonstrated in patients treated with mastectomy, and breast conserving therapy (1). In breast cancer RT, the heart, and lungs are organs at risk (OARs) and their dose constraints are evaluated in the treatment plan. In the right-sided breast cancer RT, the liver is close to the treatment field, but it is not defined as an OAR.

The liver is an important organ with numerous functions such as bile production, metabolism of ingested nutrients, elimination of waste products, glycogen storage, and protein synthesis. The liver is frequently incidentally irradiated during RT for tumors of upper abdomen, right lower lung, distal esophagus, or RT of whole abdomen. Serious adverse events following RT are rare. In liver function tests, acute post-RT changes are more frequent, were seen during or after RT, presumably related to self-limited liver inflammation (2).

Liver parenchyma consists of numerous functional subunits. This parallel architecture provides liver tolerance to focal damage. Even if only 20-25% of the liver is left in non-cirrhotic patients, surgical resection is well tolerated (3). Emami reported that the total dose of 5/5 for whole-liver radiation was estimated to be 30Gy/15fr (4).

Studies from Michigan (5-6) (primary liver cancer and hepatic metastasis) and S. Korea (Kim) (7) related with partial liver irradiation have shown that the mean dose and V30 (volume receiving $\geq$ 30 Gy) are associated with increased risk of liver toxicity. Due to lack of long follow-ups for 5 or more years, delayed liver injury or intrahepatic biliary ductal damage is less understood. Guidelines reported the irradiation dose limits of liver for 5% of less risk of radiation induced liver disease (RILD), as follows. Palliative whole liver doses in liver metastases and in primary liver cancer were $\leq$ 30 Gy, in 2 Gy per fraction, and $\leq$ 28 Gy, in 2 Gy per fraction, respectively. Partial liver RT for primary liver cancer mean normal liver irradiation dose was < 28 Gy in 2 Gy fractions.

RILD is rarely seen below in conventional fractionation when the liver mean dose is below 30 Gy. It is not usually possible to exceed this dose in the right breast cancer radiotherapy. However, considering the principle of minimal exposure to normal tissue, which is the basic principle of radiation therapy, the aim of our study was to investigate the effects of intensity modulated radiotherapy (IMRT) on liver doses through the assessment of randomly received doses of the liver in the right breast radiotherapy and through the increased use of IMRT.

MATERIALS AND METHODS:

Radiotherapy plans of 225 female patients with right breast cancer diagnosed at Istanbul University, Institute of Oncology were examined retrospectively. After the selection of the patients, previous basic scannings of the patients were re-called back into the radiotherapy planning station. There was actually no patient joined to the simulation process in fact. Neither names nor any identifying information related to the study population were used. Due to the retrospective and simulative nature of our study, no informed consent, and no ethical approval were obtained. Whereas, the study was performed in compliance with the declaration of Helsinki. Radiotherapy treatment fields, treatment doses, and radiotherapy planning techniques were determined. When the simulation computerized tomography (simCT) is performed in patients with breast cancer in our clinic, imaging boundaries are between at least 5 cm above the upper-level cricoid cartilage and at the level of the lower bilateral lungs. In patients with right breast cancer, simCT is taken while free-breathing. We determined whether or not the whole liver was included in simCT of patients. Whole liver was not imaged in simCT in app. half of the patients. All patients received radiotherapy, with the treatment field including right breast or right chest wall. In 52 patients, the chest wall was irradiated, and in 73 patients the tumor bed boost plan does not exist in the same simCT scan. So, in 125 out of 225 patients the treatment plans were developed to treat the breast to 50Gy/25fr. Because the incidentally liver irradiation doses differ with or without tumor bed boost irradiation, 225 patients were divided into two groups as "with boost" and "no boost". In 110 (48.9%) patients, the whole liver was fully visualized in simCT. Because of this we determined in all of 225 patients the maximum dose of liver (liver Dmax), at least 30 Gy or more dose received liver volume (V30) in cc, at least 20 Gy or more dose received liver volume (V20) in cc, at least 10 Gy or more dose received liver volume (V10) in cc. In 110 patients with whole liver visualization the V30 (%) value, V20 (%) value, V10 (%) value, and the liver mean dose (liver Dmean) were collected. The effects of IMRT on liver doses were analyzed by Mann-Whitney U test. Statistical analyzes were performed with the SPSS software system (SPSS for Windows, version 22; SPSS Inc., Chicago, IL). $P < 0.05$ was considered statistically significant.

RESULTS:

All patients were treated with right-sided whole breast radiotherapy or right-sided postmastectomy radiotherapy. Twentyfive patients (55.6%) were treated with 50Gy/25fr, 27 patients (12%) with 50Gy/25fr followed by 12Gy/6fr with boost, 59 patients (26.2%) with 59.92Gy/28fr with simultaneous integrated boost technique, 4 patients (1.8%) with 50Gy/25fr followed by 14Gy/7fr with boost, 10 patients (4.4%) with 50Gy/25fr followed by 10Gy/5fr with boost, through external radiotherapy. Radiotherapy treatment plan was in 85 patients (37.8%) three dimensional conformal radiotherapy (3D-CRT), in 30 patients (13.3%) the field in field technique, and in 110 patients (48.9%) IMRT. Since the angles of the treatment field in "field in field RT" are similar to 3D-CRT, these two are combined to form "no IMRT" group. In 110 patients (48.9%), whole liver existed on simulation CT, while did not exist in 115 (51.1%).

The whole patient group was examined, the liver maximum dose median was 44 Gy (2.7-52.5), liver V30, V20, V10 median was 6.3 cc (0-226.5), 17.2 cc (0-592), 53.3 cc (0-1138), respectively. Radiotherapy treatment techniques, treatment fields, and doses are presented in table 1.

Table 1. Radiotherapy characteristics and liver maximum dose data

N = 225	
	Value
Characteristics	N (%)
Treatment field	
Right-sided breast	86 (38.2)
Right-sided breast + axilla + supraclavicular fossa	38 (16.9)
Right-sided breast + axilla + supraclavicular fossa + MI	49 (21.8)
Right-sided chest wall + axilla + supraclavicular fossa	10 (4.4)
Right-sided chest wall + axilla + supraclavicular fossa + MI	38 (16.9)
Right-sided chest wall	4 (1.8)
Treatment dose	
50Gy/25fr (only chest wall or breast)	125 (55.6)
50Gy/25fr + 12Gy/6fr (tumor bed boost)	27 (12)
60Gy / 28fr (simultaneous integrated boost)	59 (26.2)
50Gy/25fr + 14Gy/7fr (tumor bed boost)	4 (1.8)
50Gy/25fr + 10Gy/5fr (tumor bed boost)	10 (4.4)
With or no tumor bed boost	
With boost	100 (44.4)
No boost	125 (55.6)
Treatment technique	
3D-CRT	85 (37.8)
IMRT	110 (48.9)
FinF	30 (13.3)
Whole or partial liver in the simCT	
Whole liver	110 (48.9)
Partial whole	115 (51.1)
	Median (min.-max.)
Liver Dmax (Gy)	44 (2.7 - 52.5)
Liver V30 (cc)	6.3 (0 - 226.5)
Liver V20 (cc)	17.2 (0 - 592)
Liver V10 (cc)	53.3 (0 - 1138)

MI: Mammary interna lymph nodes; Gy: Gray; fr: Fraction; 3D-CRT: Three dimensional conformal radiation therapy; IMRT: Intensity modulated radiation therapy; FinF: Field in field; VMAT: Volumetric arc therapy; cc: cubic centimeter; simCT: simulation computed tomography; Liver Dmax: Maximum received liver dose; Liver V30: Volume of liver received at least 30 Gy; Liver V20: Volume of liver received at least 20 Gy; Liver V10: Volume of liver received at least 10 Gy

Whole patient group

The liver Dmax non-boost group was examined, the median was 44.7 Gy (2.7-51.4) in the IMRT group while was 43.2 Gy (3.3-48.6) in the no IMRT group and there was no statistical difference (p = 0.185). Liver Dmax was ≥ 50 Gy in 5 patients in the IMRT group. Approximately 60% of patients in both the IMRT and no IMRT groups had liver Dmax being < 50 - ≥ 40 Gy. When the boosted group was examined, the median liver Dmax was 42 Gy (2.8-52.5) in the IMRT group while was 44.3 Gy (3.3-51.9) in the no IMRT group and there was no statistical difference (p = 0.325). Liver Dmax was ≥ 50 Gy in 6 patients of IMRT group, ≥ 50 Gy in 1 of no IMRT group. 28 (45.2%) patients in the IMRT group and 15 (65.8%) patients in the no IMRT group had liver Dmax being < 50 - ≥ 40 Gy (Table 2).

TABLE 2. Liver irradiation doses in whole group treated with IMRT or not

N=225				
	Group	**IMRT (n=110)**	**No IMRT (n=115)**	**Mann-Whitney U test P value**
Liver Dmax (Gy)				
No boost		48	77	
	≥ 50	5 (10.4%)	0 (0%)	
	<50 - ≥ 40	33 (68.8%)	47 (61%)	
	<40 - ≥ 30	5 (10.4%)	10 (13%)	
	< 30 - ≥ 20	1 (2.1%)	8 (9.2%)	
	< 20 - ≥ 10	2 (4.2%)	4 (5.2%)	
	< 10	2 (4.2%)	8 (10.4%)	
	Median (min-max)	44.7 (2.7-51.4)	43.2 (3.3-48.6)	U=1587 p=0.185
With boost		62	38	
	≥ 50	6 (9.7%)	1 (2.6%)	
	<50 - ≥ 40	28 (45.2%)	25 (65.8%)	
	<40 - ≥ 30	11 (17.7%)	2 (5.3%)	
	< 30 - ≥ 20	8 (12.9%)	3 (7.9%)	
	< 20 - ≥ 10	6 (9.7%)	2 (5.3%)	
	< 10	3 (4.8%)	5 (13.2%)	
	Median (min-max)	42 (2.8-52.5)	44.3 (3.3-51.9)	U=1039.5 p=0.325
Liver V30 (cc)		48	77	
No boost	≥ 200	2 (4.2%)	0 (0%)	
	<200 - ≥ 100	9 (18.8%)	0 (0%)	
	<100 - ≥ 50	7 (14.6%)	2 (2.6%)	
	< 50	25 (52.1%)	51 (66.2%)	
	0	5 (10.4%)	24 (31.2%)	
	Median (min-max)	19.7 (0-226.5)	3.1 (0-57.3)	U=992 P < 0.001
With boost		62	38	
	≥ 200	0 (0%)	0 (0%)	
	<200 - ≥ 100	3 (4.8%)	1 (2.6%)	
	<100 - ≥ 50	8 (12.9%)	2 (5.3%)	
	< 50	32 (56.1%)	25 (43.9%)	
			10 (26.3%)	
	Median (min-max)	5.3 (0-155)	4.3 (0-140)	U=1135 p=0.757
Liver V20 (cc)		48	77	
No boost	≥ 500	3 (6.2%)	0 (0%)	
	< 500 - ≥ 400	0 (0%)	0 (0%)	
	< 400 - ≥ 300	2 (4.2%)	0 (0%)	
	< 300 - ≥ 200	7 (14.6%)	0 (0%)	
	< 200 - ≥ 100	5 (10.4%)	1 (1.3%)	
	< 100 - ≥ 50	13 (27.1%)	4 (5.2%)	
	< 50	14 (29.2%)	59 (76.6%)	
	0	4 (8.3%)	13 (16.9%)	
	Median (min-max)	65 (0-591.6)	8.8 (0-112.9)	U=679 P < 0.001
With boost		62	38	
	≥ 500	0 (0%)	0 (0%)	
	< 500 - ≥ 400	0 (0%)	0 (0%)	

	< 400 - ≥ 300	1 (1.6%)	0 (0%)	
	< 300 - ≥ 200	3 (4.8%)	0 (0%)	
	< 200 - ≥ 100	10 (16.1%)	1 (2.6%)	
	< 100 - ≥ 50	8 (12.9%)	2 (5.3%)	
	< 50	30 (48.4%)	27 (71.1%)	
	0	10 (16.1%)	8 (21.1%)	
	Median (min-max)	20.5 (0-330)	10 (0-155)	U=882.5 P =0.035
Liver V10 (cc)		48	77	
No boost	≥ 500	12 (25%)	0 (0%)	
	< 500 - ≥ 400	2 (4.2%)	0 (0%)	
	< 400 - ≥ 300	4 (8.3%)	0 (0%)	
	< 300 - ≥ 200	13 (27.1%)	1 (1.3%)	
	< 200 - ≥ 100	10 (20.8%)	4 (5.2%)	
	< 100 - ≥ 50	2 (4.2%)	13 (10.4%)	
	< 50	3 (6.2%)	51 (66.2%)	
	0	2 (4.2%)	8 (10.4%)	
	Median (min-max)	246.2 (0-1138)	17.2 (0-293.2)	U=336 P < 0.001
With boost		62	38	
	≥ 500	5 (8.1%)	0 (0%)	
	< 500 - ≥ 400	5 (8.1%)	0 (0%)	
	< 400 - ≥ 300	6 (9.7%)	0 (0%)	
	< 300 - ≥ 200	9 (14.5%)	0 (0%)	
	< 200 - ≥ 100	13 (21%)	4 (10.5%)	
	< 100 - ≥ 50	9 (14.5%)	4 (10.5%)	
	< 50	12 (19.4%)	25 (65.8%)	
	0	3 (4.8%)	5 (13.2%)	
	Median (min-max)	130 (0-643.7)	19.1 (0-180)	U=432.5 P < 0.001

IMRT: Intensity modulated radiation therapy; Liver Dmax: Maximum received liver dose; Gy: Gray; Liver V30: Volume of liver received at least 30 Gy; Liver V20: Volume of liver received at least 20 Gy; Liver V10: Volume of liver received at least 10 Gy; cc: cubic centimeter

The group of liver V30 (cc) no boost was examined, the median was 19.7 cc (0-226.5) in the IMRT group whereas was 3.1 cc (0-57.3) in the no IMRT group. The V30 (cc) in the IMRT group was significantly higher (p < 0.001). The liver V30 (cc) were ≥ 200 cc for 2 patients (4.2%) in IMRT group, < 200 - ≥ 100 cc for 9 patients (18.8%), whereas < 50 cc in 51(66.2%) patients and 0 cc in 24 (31.2%) patients in no IMRT group. For the boost group, the liver V30 cc median was 5.3 cc (0-155) in the IMRT group while was 4.3 cc (0-140) in the no IMRT group and there was no statistical difference (p = 0.757) (Table 2).

For the group of liver V20 (cc) no boost, the median was 65 cc (0-591.6) in the IMRT group while was 8.8 cc (0-112.9) in the no IMRT group. The V20 (cc) was significantly higher in the IMRT group (p < 0.001). Liver V20 (cc) was ≥ 500 cc for 3 patients (6.2%) in IMRT group, ≤ 400 - ≥ 300 cc in 2 patients (4.2%), < 300 - ≥ 200 cc in 7 patients (14.6%) while all patients in the no IMRT group were in the < 200 cc group (76% were in the <50 group). For the with boost group, the median was 20.5 cc (0-330) in the IMRT group whereas 10 cc (0-155) in the no IMRT group. The V20 (cc) was significantly higher in the IMRT group (p = 0.035). The liver V20 (cc) were ≥ 300 cc for 1 (1.6%) patient in IMRT group, <300 - ≥ 200 cc for 3 (4.8%) patients, and <200 - ≥ 100 cc for 10 (16.1%) patients. In the no IMRT group, all patients were in the < 200 cc group (whereas 71.1% of the patients were in the <50 group) (Table 2).

For the group of liver V10 (cc) no boost, the median was 246.2 cc (0-1138) in the IMRT group whereas was 17.2 cc (0-293.2) in the no IMRT group. The V10 (cc) in the IMRT group was significantly higher (p <0.001). Liver V10 (cc) was ≥ 500 cc for 12 patients (25%) in IMRT group, ≤ 500 - ≥ 400 cc in 2 patients (4.2%), < 400 - ≥ 300 cc in 4 patients (8.3%) while all patients in the no IMRT group were in the < 300 cc group (66.2% were in the < 50 group). For the boost group, the median was 130 cc (0-643.7) in the IMRT group whereas was 19.1 cc (0-180) in the no IMRT group. The V10 (cc) in the IMRT group was significantly higher (p <0.001). The liver V20 (cc) were ≥ 500 cc for 5 (8.1%) patients in IMRT group, <500 - ≥ 400 cc for 5 (8.1%) patients and <400 - ≥ 300 cc for 6 (9.7%) patients. In the no IMRT group, all patients were in the < 200 cc group (65.8% of the patients were in the < 50 group) (Table 2).

Whole liver group

For the liver Dmean in no boost group, the median was 5.7 Gy (0.4-18.8) in the IMRT group and 2 Gy (0.5-3.5) in the no IMRT group, liver Dmean was significantly higher in the IMRT group (p <0.001). Liver Dmean was ≥15 Gy for 4 patients (11.1%) in IMRT group, < 15 - ≥ 10 Gy in 7 patients (19.4%), < 10 - ≥ 5 Gy in 14 patients (38.9%) while all patients in the no IMRT group had liver D mean < 5 Gy. For the with boost group, the liver Dmean median was 4.6 Gy (0.4-12.1) in the IMRT group, was 1.4 Gy (0.3-4.2) in the no IMRT group. For the IMRT group, liver Dmean was significantly higher (p < 0.001). Liver Dmean was 10 Gy in 8 (12.9%) patients of IMRT group, < 10 - ≥ 5 Gy in 6 (9.7%) patients, < 5 Gy in 19 (52.8%) patients (Table 3).

TABLE 3. Liver irradiation doses in whole liver group treated with IMRT or not

	N=110			
	Group	**IMRT (n=72)**	**No IMRT (n=38)**	**Mann-Whitney U test and P value**
Liver Dmean (Gy)				
No boost		36	22	
	≥ 15	4 (11.1%)	0 (0%)	
	< 15 - ≥ 10	7 (19.4%)	0 (0%)	
	< 10 - ≥ 5	14 (38.9%)	0 (0%)	
	< 5	11 (30.6%)	22 (100%)	
	Median (min-max)	5.7 (0.4-18.8)	2 (0.5-3.5)	U = 47 P < 0.001
With boost		36	16	
	≥ 10	8 (12.9%)	3 (7.9%)	
	< 10 - ≥ 5	6 (9.7%)	2 (5.3%)	
	< 5	19 (52.8%)	16 (100%)	
	Medyan (min-max)	4.6 (0.4-12.1)	1.4 (0.3-4.2)	U = 73.5 P < 0.001
Liver V30 (%)				
No boost		36	22	
	≥ 10	5 (13.9%)	0 (0%)	
	<10 - ≥ 3	11 (30.6%)	0 (0%)	
	< 3	17 (47.2%)	18 (81.8%)	
	0	3 (8.3%)	4 (18.2%)	
	Median (min-max)	2.2 (0-16.6)	1.1 (0-2.9)	U = 243 P = 0.014
With boost		36	16	
	<10 - ≥ 3	11 (30.6%)	3 (18.8%)	
	< 3	19 (52.8%)	10 (62.5%)	
	0	6 (16.7%)	3 (18.8%)	
	Median (min-max)	1.3 (0-9.9)	0.8 (0-5.8)	U = 253 P = 0.493
Liver V20 (%)				
No boost		36	22	
	≥ 30	3 (8.3%)	0 (0%)	

	< 30 - ≥ 20	4 (11.1%)	0 (0%)	
	< 20 - ≥ 10	8 (22.2%)	0 (0%)	
	< 10	19 (52.8%)	20 (90.9%)	
	0	2 (5.6%)	2 (9.1%)	
	Median (min-max)	5.5 (0-40.8)	1.8 (0-3.6)	U = 154 P < 0.001
With boost		36	16	
	≥ 20	1 (2.8%)	0 (0%)	
	< 20 - ≥ 10	7 (19.4%)	0 (0%)	
	< 10	27 (75%)	14 (87.5%)	
	0	1 (2.8%)	2 (12.5%)	
	Median (min-max)	4 (0-21)	1.2 (0-7)	U = 169.5 P = 0.019
Liver V10 (%)				
No boost		36	22	
	≥ 50	6 (16.7%)	0 (0%)	
	< 50 - ≥ 40	4 (11.1%)	0 (0%)	
	< 40 - ≥ 30	3 (8.3%)	0 (0%)	
	< 30 - ≥ 20	5 (13.9%)	0 (0%)	
	< 20 - ≥ 10	13 (36.1%)	0 (0%)	
	< 10	5 (13.9%)	22 (81.5%)	
	Median (min-max)	20 (0-85)	3.3 (0-9.6)	U=49.5 P < 0.001
With boost		36	16	
	≥ 40	5 (14%)	0 (0%)	
	< 40 - ≥ 30	3 (8%)	0 (0%)	
	< 30 - ≥ 20	6 (17%)	0 (0%)	
	< 20 - ≥ 10	11 (30.5%)	0 (0%)	
	< 10	11 (30.5%)	16 (0%)	
	Median (min-max)	15.2 (0-47.1)	1.7 (0-8.7)	U = 49 P < 0.001

IMRT: Intensity modulated radiation therapy; Liver Dmean: Mean received liver dose Gy: Gray; Liver V30: Volume of liver received at least 30 Gy; Liver V20: Volume of liver received at least 20 Gy; Liver V10: Volume of liver received at least 10 Gy; cc: cubic centimeter

For the liver V30 (%) in no boost group, the median was 2.2 % (0-16.6) in the IMRT group and 1.1 % (0-2.9) in the no IMRT group. In the IMRT group, V30 (%) was significantly higher (p < 0.014). Liver V30 (%) was ≥ 10% in 5 patients of the IMRT group, < 10% - ≥ 3% in 11 (30.6%) patients, and < 3% in all patients of the IMRT group. For the with boost group, the median was 1.3% (0-9.9) in the IMRT group while was 0.8 % (0-5.8) in the no IMRT group and there was no statistical difference (p = 0.493) (Table 3).

When the liver V20 (%) no boost group was examined, the median was 5.5% (0-40.8) in the IMRT group and 1.8% (0-3.6) in the no IMRT group. In the IMRT group, V20% was significantly higher (p <0.001). Liver V20 (%) was ≥ 30% in 3 patients of the IMRT group, < 30% - ≥ 20% in 4 (11.1%) patients, < 20% - ≥ 10% in 8 (22.2%) patients. V20(%) was <10% in all of the patients in no IMRT group. When the boosted group was examined, the liver V20(%) median was 4% (0-21) in the IMRT group, and 1.2% (0-7) in no IMRT group. V20 (%)in IMRT group was significantly higher (p = 0.019). Liver V20 (%) was ≥ 20% in 1 (2.8%) patient of IMRT group, < 20% - ≥ 10% in 7 patients (19.4%), < 10% in 27 (75%) while <10% in all patients of no IMRT group (Table 3).

For the liver V10 (%) non-boost group, the median was 20% (0-85) in the IMRT group, while was 3.3% (0-9.6) in the no IMRT group. In the IMRT group, V10 (%) was significantly higher (p <0.001). Liver V10 (%) was ≥ 50% in 6 patients (16.7%) of the IMRT group, < 50% - ≥ 40% in 4 patients (11.1%), < 40% - ≥ 30% in 3 (8.3%) patients, and 10% in whole patients of no IMRT group. For the with boost group, the median was 15.2% (0-47.1) in the IMRT group whereas was 1.7% (0-8.7) in the no IMRT group. In the IMRT group, V10 (%) was significantly higher (p <0.001). Liver V10 (%) was ≥ 40% in 5 (14%) patients of the IMRT group, < 40% - ≥ 30% in 3 (8%) patients, < 30% - ≥ 20% in 6 (17%) patients, <20% - ≥ 10% in 11 (30.5%) patients, <10% in all patients of no IMRT group (Table 3).

Discussion:

The liver is frequently irradiated incidentally during upper abdomen, right lower lung, distal esophagus, whole abdomen or whole body radiotherapy (2). It is also incidentally irradiated according to the anatomical variations in the right-sided breast cancer irradiation. There are only a few studies evaluating the received irradiation dose of liver during breast cancer radiotherapy.

Haciismailoglu et al compared 5 different techniques 3D-CRT, forward-planned IMRT, inverse-planned IMRT, helical tomotherapy and volumetric modulated arc therapy (VMAT) in the whole breast radiotherapy of right-sided breast cancer patients (8). Heart, left anterior descending (LAD) coronary artery, and contralateral breast, and lung doses are significantly lower in 3D-CRT and forward IMRT than inverse-planned IMRT, helical tomotherapy and VMAT. In addition, the exposed volume of the heart, LAD, ipsilateral lung and contralateral lung in inversed-planned IMRT were higher compared to the helical tomotherapy and VMAT. The liver dose had not been evaluated.

In the present study, liver V10 was < 10% in all patients of no IMRT group with right breast cancer in free-breathing. 15 (13.6%) patients in the IMRT group had liver V10 being ≥ 40%. In one of these patients, liver V10 was 85%. In the no IMRT group, all patients had liver V20 being < 10% while 8 (7.3%) patients of IMRT group had liver V20 being ≥ 20%. In one of these patients, liver V20 was 40.8%. In all patients of the no IMRT group, liver V30 was < 10% while was ≥ 10% in 5 (4.5%) patients of the IMRT group. In one of these patients, liver V30 was 16.6%. In the no IMRT group, liver Dmean was < 5 Gy in all patients of the IMRT group while ≥ 15 Gy in 4 (3.6%) patients of the IMRT group.

It is not possible to completely avoid the incidental lung and heart irradiation with conventional RT techniques in breast cancer radiotherapy (9). Today, breath-hold techniques are used in irradiation of left-sided breast cancer patients to reduce cardiac dose and thus cardiac risk (10-13). In a small number of studies, the use of breath-hold techniques in patients with right-sided breast cancer was investigated (14-18). With this technique, Essers et al detected a slight reduction in lung dose and a decrease in heart dose in some patients with right-sided breast radiation therapy (17). Conway et al applied the right-sided breast RT using deep inspiration breath-hold technique, a ≥??? 5% reduction in the ipsilateral lung V20Gy compared with free breathing, and reported a mean reduction of 42.3 cm3 (0-178.9 cm3, p <0.001) in the liver volume of 50% of the prescribed dose (18). Rice et al published a case report displaying deep inspiration breath-hold technique to minimize liver irradiation in the right-sided breast cancer patient. First of all, using “field in field” approach, they found that the normal liver volume in the free breathing right-sided breast radiotherapy planning scan high-dose target area was large (134 cc). After that, when they made the field in field plans with deep inspiration breath-hold technique, they found that all liver doses decreased, and V30 also decreased by 64% (19). Prabhakar et al evaluated the lung, heart, and liver doses (volume-V50, 50% of the prescription dose) in 13 patients with breast cancer (9 left-sided, 4 right-sided) in 3 breathing conditions (deep inspiration breath hold, normal breathing phase, deep expression breath hold). They reported that in patients with right breast cancer, they achieved excellent liver sparing with a 50.2% average reduction in V50 with deep inspiration breath hold technique (20).

Fixed-field IMRT shows significant reductions in normal tissue irradiation dose and significant improvement in dose distribution in the target region (21). However, IMRT increases low dose irradiated volumes of normal tissues and thus increases lung and opposite side breast irradiation doses (22,23).

The study, which includes fluoroscopy, four-dimensional CT, and cine-Magnetic Resonance Imaging, described the liver movement which was formed by respiration and the effect of radiation dose given due to this movement. Liver movement resulting from respiration can be controlled by methods such as abdominal compression, shallow respiration, breath holding (24-26). Breath-hold technique in the right-sided breast cancer RT can be used to minimize the exposure of the liver, as well as the doses exposed due to the minimization of its movement can be determined more accurately.

Clinical factors that increase the likelihood of RILD include chronic hepatitis B virus and hepatitis C virus infection, simultaneous systemic treatment, transarterial chemoembolization (TACE), and transarterial radioembolization (TARE), small hepatic reserve after previous partial hepatectomy,and portal vein thrombosis (27-30).

In the present study, we showed that the doses that the liver was exposed to were increased with IMRT use in the radiotherapy of right-sided breast cancer. This dose exposure will be affected by target volume size, liver size, and anatomical variations. In particular, we suggest that the patients with risk factors that increase the likelihood of RILD, or whose liver is anatomically close to the breast treatment field, should be evaluated for appropriate radiation therapy treatment technique. In patients who will be treated with IMRT, we think that the dose should be reduced as much as possible by participating liver in the treatment optimization. The use of the breast-hold technique in breast irradiation on the right-sided to reduce the liver dose will be appropriate to keep in mind.

During the present study, in the group with whole liver visualization, in 13.6% of the patients ≥ 40% of liver was determined to be exposed to 10 Gy dose and above, in 7.3% of the patients ≥ 20% of liver was determined to be exposed to 20 Gy dose and above, in 4.5% of the patients ≥ 10% of liver was determined to be exposed to 30 Gy dose and above. We showed that especially the volume of low doses of the liver, which can be affected by irradiation at different rates due to anatomical variations in breast cancer radiotherapy, increases with IMRT. For this reason, it is necessary to include the whole liver in the simCT, especially during the right-sided breast cancer radiotherapy, and to participate it in the treatment optimization as an OAR in the IMRT plan.

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