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## Dosimetric Comparison of 3D-CRT, IMRT, IMAT and Helical Tomotherapy for Thoracic Esophageal Carcinoma

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Abstract: In this study, we compared the dose-volume parameters for treatment of thoracic esophageal cancer with treatment plans for 3D-CRT, IMRT, IMAT and HT. 15 thoracic esophagus patients who were treated in our clinic between 2017-2018 years were selected. PTV volumes were between 205 and 445.4 cc with an average of 355.2 cc. 3D-CRT, IMRT, IMAT and HT radiotherapy plans were created for each patient using the same contours and the same dose planning prescription. Total dose of 50.4 Gy for all patients was planed with 180 cGy dose per a fraction in total 28 fractions. For PTV; when the four treatment techniques were compared, HI values were 3D-CRT 0.84  $\pm$  0.0, IMRT 0.57  $\pm$  0.05, IMAT 0.06  $\pm$  0.013, HT  $0.08 \pm 0.03$  (p <0.05). CI values were found for 3D-CRT as  $1.84 \pm 0.2$ , for IMRT as  $1.25 \pm$ 0.05, for IMAT as  $1.19 \pm 0.04$ , for HT as  $1.2 \pm 0.06$  (p <0.05). IMRT and IMAT techniques provided better OAR protection compared to other techniques in all lung and heart comparisons. The lowest doses for  $D_{max}$  and  $D_{1\%}$  of Spinal Cord were provided by HT technique. We found that IMRT, IMAT and HT techniques have lower critical organ doses than 3D-CRT technique for treating torasic esophageal cancer. Considering the current evidence of the relationship between radiation-induced cardiac toxicity in the literature and the dose-volume parameters after treatment for esophageal cancer in our study, we can say that dose plans are better for IMRT and IMAT plans than 3D-CRT and HT in terms of lung and heart doses.

Key words: Esophageal carcinoma, 3D-CRT, IMRT, IMAT, HT

## Torasik Özofagus Karsinomunda 3D-CRT, IMRT, IMAT ve Helical Tomoterapinin Dozimetrik Karşılaştırması

**Özet:** Bu çalışmada, torasik özofagus kanserinin tedavisi için 3D-CRT, IMRT, IMAT ve HT tedavi planlarının doz-hacim parametrelerini karşılaştırdık. Çalışma için kliniğimizde 2017-2018 yılları arasında tedavi edilen 15 torasik özofagus hastası seçildi. PTV hacimleri 205 cc ile 445.4 cc arasındaydı ve ortalama değer 355,2 cc idi. Her hasta için aynı konturları ve aynı doz

planlama reçetesini kullanarak 3D-CRT, IMRT, IMAT ve HT radyoterapi planları oluşturuldu. Her bir plan için, toplam 28 fraksiyon ile fraksiyon başına 180 cGy doz ile toplamda 50,4 Gy'lik bir doz uygulanmıştır. PTV için; dört tedavi tekniği karşılaştırıldığında HI değerleri 3D-CRT için 0,84  $\pm$  0,0, IMRT için 0,57  $\pm$  0,05, IMAT için 0,06  $\pm$  0,013 ve HT için 0,08  $\pm$  0,03 (p <0.05) bulundu. CI değerleri için ise 3D-CRT için 1,84  $\pm$  0,2, IMRT için 1,25  $\pm$  0,05, IMAT için 1,19  $\pm$  0,04 ve HT için 1,2  $\pm$  0.06 (p <0,05) vardı. IMRT ve IMAT teknikleri, tüm akciğer ve kalp dozu karşılaştırmalarında, diğer tekniklere kıyasla daha iyi OAR koruması sağlamıştır. Omurilik D<sub>max</sub> ve D<sub>1%</sub> dozları için en düşük dozlar HT tekniği ile sağlanmıştır. IMRT, IMAT ve HT tekniklerinin torasik özofagus kanserini tedavi etmek için 3D-CRT tekniğinden daha düşük kritik organ dozlarına sahip olduğunu bulduk. Çalışmamızda özofagus kanseri tedavisinden sonra radyasyona bağlı kardiyak toksisite ile doz-hacim parametreleri arasındaki ilişkinin literatürdeli mevcut kanıtları da göz önüne alındığında, IMRT ve IMAT planları için doz planlarının 3D-CRT ve HT'den akciğer ve kalp dozları açısından daha iyi olduğunu söyleyebiliriz.

Anahtar kelimeler: Özofagus kanseri, 3D-CRT, IMRT, IMAT, HT

# 1. Introduction

Radiotherapy (RT) for esophageal cancer is an important method of treatment because more than 60% of patients are in advanced stages and therefore surgical intervention cannot be performed [1]. With the addition of chemotherapy to radiotherapy, more patients survive in the treatment of esophageal cancer. On the other hand, more patients are at risk of treatment-related toxicity, which is a major concern.

Planning Target Volume (PTV) and some Organs at Risk (OARs) are surrounded by lungs, heart, liver, kidneys and spinal cord [2]. The anatomical proximity of the esophagus to the heart, the lungs and other parts of the esophagus may cause chronic toxicities that could risk the life quality of esophageal cancer survivors in these organs. After the treatment, late effects of RTmay occur such as congestive heart failure, ischemia, coronary artery disease, vascular disease or myocardial infarction [3].

It has been reported in the literature that the use of torasic lymphatic irradiation in the long life span of Hodghin lymphoma is a 2.5- fold increase in coronary heart disease [4,5]. In the left breast irradiation, the radiation dose has been shown to have an increased cardiac risk of average 7.4% per Gy [6]. However, in esophageal cancer, heart doses are generally significantly higher because the heart dose is close to the target dose.

There are many studies investigating radiotherapy techniques for the treatment of esophageal cancer in the literature. Application techniques such as 3D Conformal Radiation Therapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT), TomoTherapy (HT), Intensity Modulated Arc Therapy (IMAT) have also been investigated with changing results [7,8]. Cardiac toxicity is an important issue in the treatment of esophageal cancer. Currently, there is no clear guidelines for the relationship between radiation dose and organs at risk, lungs and heart in radiotherapy treatment planning of esophageal cancer [9]. As far as we know, there is no any study compared the dose volume parameter among the 3D-CRT, IMRT, IMAT and HT treatment techniques. We investigated the current evidence of the relationship between radiation-induced cardiac toxicity in literature and dose-volume parameters for treatment of esophageal cancer with treatment plans for 3D-CRT, IMRT, IMAT and HT.

## 2. Material and Method

In this study, 15 (4 women, 11 men) thoracic esophagus patients wo who were treated in our clinic between 2017-2018 were selected. The study was approved by the Ethics committee before the started (Date: 24.11.2017, Registration number: 2017/1356). 3D-CRT, IMRT, IMAT and HT radiotherapy plans were created for each patient using the same contours and the same dose planning prescription. Thus, a total of 60 plans were created. Philips Big Bord 4DCT (Philips Healthcare, Cleveland, OH) Computed Tomography (CT) device was used for treatment planning simulation. Immobilization devices were used to supply the patients comfortable and stable during the treatment period. CT images were performed for two patients on prone position and for thirteen patients on supine position with their arms above the head. Gross Target Volume (GTV), OAR contours (lungs, heart, spinal cord, right and left coronary arteries) were defined on CT sections. Contouring was performed according to ICRU 83 [10] protocol. In addition, PTV was created by giving 0.5 cm margin from all sides to GTV. PTV volumes were between 205 and 445.4 cc with an average of 355.2 cc. For each plan a dose of 50.4 Gy was administered with a total of 28 fractions of 180 cGy per fraction.

## 2.1. Treatment plans

All treatment plans were performed with 6 MV photon beam. GTV, PTV and OAR volumes were the same for all planning.

3D-CRT plans; Patients was planned in four fields by using Varian Eclipse 15.1 (Varian Medical Systems, Palo Alto, CA) The Treatment Planning System (TPS). Treatment fields; for the heart, medulla and lung, the field and gantry angles were determined so as to the lowest OAR dose can achive for each patient. OAR protection was provided in the most appropriate way using the Multi Leaf Colimator (MLC) shape in each area.

IMRT plans; Varian Eclipse15.1 (Varian Medical Systems, Palo Alto, CA) at TPS were used for IMRT plans of patients. The dose rate was 400 MU / min and the gantry angles (0 °, 52 °, 104 °, 156 °, 208 °, 260 ° and 312 °).

IMAT plans; Varian Eclipse 15.1 (Varian Medical Systems, Palo Alto, CA) at TPS were also used for IMAT plans of patients. But, dose of 600 MU/min was selected with 2 full Arc. For the first arc the gantry was rotated counter clockwise at 179.9°-180.1°. The collimator angle was also given 30°. Second arc gantry was rotated 180.1°-179.9° clockwise and 330° angle was given for collimator.

HT plans; HDA (Accuracy Inc., Sunnyvale, CA) in the treatment planning system were used for HT plans of patients as field width 5.048, pitch factor 0.430 and modulation factor 2.000.

Each treatment plan were performed by using below criterias;

• 95% of PTV received 50.4 Gy and  $D_{max}$  does not exceed 110 % of PTV dose.

 $\bullet$  Volume of Lung-PTV (Lung minus PTV) received 20 Gy less than 20  $\%\,$  of total dose.

- The average dose of heart is below 26 Gy
- For spinal cord, maximum dose (D<sub>max</sub>) is below 45Gy.

 $\bullet$  For the lungs,  $V_{20Gy}$  (volume of lung received more than 20 Gy) less than 20 % of lung volume

•  $V_{30Gy}$  (volume of lung received more than 30 Gy) less than 18% of lung.

Table 1 shows the detail of the dose limits that we accept for OAR for each treatment techniques (3D-CRT, IMRT, IMAT and HT).

<b>Table 1.</b> Dose limits for OARs.								
OAR	<b>Dose Limitation</b>	Criteria						
	Avarage	<26 Gy						
HEART	$V_{30Gy}$	<50%						
	$V_{45Gy}$	<25%						
	$V_{10Gy}$	<40%						
LUNG	$V_{20Gy}$	<20%						
	V <sub>30Gy</sub>	<18%						
	Avarage	<15 Gy						
LUNG – PTV	V <sub>20Gy</sub>	<20%						
(LUNG minus PTV)	V <sub>5Gy</sub>	<60%						
SPINAL CORD	$D_{max}$	<45Gy						
SFINAL CORD	$D_{1\%}$	<45Gy						

Plan examples and its Dose Volume Histograms (DVH) for 3D-CRT, IMRT, IMAT and HT was given for patient one in Figure 1.





Figure 1. Treatment planning dose distribution and its dose volume histogram for patient one. a) 3D-CRT b) IMRT c) IMAT d) HT

## 2.2. Evaluation of patient plans

For the PTV dose evaluations, the values of  $D_{95\%}$ ,  $D_{98\%}$ ,  $D_{2\%}$  (dose received by 95%, 98% and 2% of the PTV) respectively and  $V_{95\%}$  (volume receiving 95 % of the prescribed dose) were analyzed.

The Conformity Index (CI) from (1) equations was calculated as follows [11,12];

$$CI = (VT95\%/VT) \times (VT95\%/V95\%)$$
(1)

VT is the PTV volume and VT95% is the PTV volume receiving atleast 95% of the prescribed dose. The value of the CI is necessarily between zero and one. A CI of one represents the idealsituation where the target volume coincides exactly with thetreatment volume. A value of 1 for the CI represented a beter PTV conformity. Target dose homogeneity was evaluated through the Homogeneity Index (HI) from (2) equations, defined as the difference between the maximum and minimum dose to the PTV ( $D_{2\%}$  and  $D_{98\%}$ ), divided by the prescription dose:

$$HI = (D_{2\%} - D_{98\%}) / D prescription.$$
(2)

A lower HI value indicates that a plan provides a morehomogeneous dose distribution.

#### 2.3. Statistical Analysis

In this study, "SPSS 21st version" was used and four different groups were compared. The One-Way Anova test was used to compare the normal distribution and the-Bonferonni veril test was used to make a double comparison. If any of the p values is less than p < 0.05 as a result of the normalization test in SPSS data analysis, it means that it does not fit the normal distribution. Kruskal-Wallis test was done. Mann-Whitney Test was applied to make binary comparisons. (p <0.05), there is a significant difference.

#### 3. Results

## 3.1. PTV Dose Evaluations

In this study, the first direct comparison between 3D-CRT, IMRT, IMAT and HT treatment techniques was performed in thoracic esophageal radiotherapy. Table 2 shows the,  $D_{min}$ ,  $D_{mean}$ ,  $D_{1\%}$ , D5%, D99%, V95%, V107%, CI and HI values for PTV.

Table 2. D <sub>max</sub> ,	D <sub>min</sub> ,	Dmean, D1%	6, D5%, D99%	, V <sub>95%</sub> ,	V107%,	CI and HI values of PT	ſV
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					3D-CRT	3D-CR	IMRT	IMRT	IMAT	
					VS	VS	VS	VS	VS	VS
					IMRT	IMAT	HT	IMAT	HT	HT
	<b>3D-CRT</b>	IMRT	IMAT	HT	P*	<b>P</b> *	P*	P*	P*	P*
D <sub>max</sub> (Gy)	54.88	53.423	54.528	55.571	$<\!\!0.05$	1.000	0.06	$<\!0.05$	$<\!\!0.05$	< 0.05
D <sub>mean</sub> (Gy)	52.5	51.26	51.7	51.84	< 0.05	< 0.05	< 0.05	$<\!0.05$	< 0.05	0.071
$D_{min}(Gy)$	46.842	32.08	43.122	42.744	$<\!\!0.05$	$<\!\!0.05$	$<\!0.05$	1.000	1.000	1.000
D <sub>1%</sub> (Gy)	54.34	52.04	52.74	53.8	< 0.05	< 0.05	< 0.05	$<\!0.05$	< 0.05	< 0.05
D5% (Gy)	53.97	51.8	52.37	53.17	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05
D <sub>99%</sub> (Gy)	59.53	49.64	49.11	48.81	0.455	< 0.05	< 0.05	$<\!0.05$	< 0.05	0.533
V <sub>95%</sub> (cc)	99.97	99.97	99.8	99.58	0.686	0.28	< 0.05	0.138	< 0.05	0.383
V107% (cc)	6.14	0.00	0.00	1.00	< 0.05	< 0.05	< 0.05	$<\!0.05$	< 0.05	< 0.05
CI	1.838	1.247	1.186	1.197	< 0.05	< 0.05	< 0.05	0.807	1.000	1.000
HI	0.083	0.43	0.056	0.08	$<\!\!0.05$	< 0.05	0.120	< 0.05	< 0.05	< 0.05
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p \*: Significance was found when variables are compared to 3D-CRT versus IMRT, 3DCRT versus IMAT, 3DCRT versus IMAT, IMRT versus HT, IMAT versus HT, p-value < 0.05 determines significance.

#### 3.2. OARs Dose Evoluation

#### 3.2.1. Dose Evoluation of Heart

The statistical results of Heart doses ( $D_{mean}$ ,  $D_{5\%}$ ,  $D_{10\%}$ ,  $D_{15\%}$ ,  $D_{20\%}$ ,  $D_{25\%}$ ,  $D_{30\%}$ ,  $D_{35\%}$ ,  $D_{40\%}$  and  $D_{45\%}$ ) are shown in Table 3.

<b>Table 3.</b> $D_{mean}$ , $D_{5\%}$ , $D_{10\%}$ , $D_{15\%}$ , $D_{20\%}$ , $D_{25\%}$ , $D_{30\%}$ , $D_{35\%}$ , $D_{40\%}$ and $D_{45\%}$ values for heart												
					3D-CRT	3D-CRT	3D-CRT	IMRT	IMRT	IMAT		
					VS	VS	VS	VS	vs	VS		
					IMRT	IMAT	HT	IMAT	HT	HT		
	<b>3D-CRT</b>	IMRT	IMAT	HT	P*	P*	P*	P*	P*	P*		
$D_{mean}(Gy)$	26.8	18.3	16.52	19.59		p	>0.05 (Kru	ıskal-Wall	is)			
$V_{5\%}(\%)$	79.08	95.15	97.7	100		p	>0.05 (Kru	ıskal-Wall	is)			
D <sub>10%</sub> (Gy)	73.47	73.0	67.87	91.33	p>0.05 (Kruskal-Wallis)							
D15% (Gy)	68.3	44.66	42.05	58.31		p	>0.05 (Kru	ıskal-Wall	is)			
D <sub>20%</sub> (Gy)	65.07	29.50	31.55	31.34	< 0.05	< 0.05	0.440	0.917	0.576	0.548		
D <sub>25%</sub> (Gy)	62.9	20.13	22.76	19.9	< 0.05	$<\!0.05$	< 0.05	0.917	0.901	0.852		
D <sub>30%</sub> (Gy)	59.0	13.39	16.14	13.57	< 0.05	$<\!0.05$	< 0.05	0.950	0.950	0.950		
D <sub>35%</sub> (Gy)	34.903	10.523	11.624	11.632	< 0.05	$<\!0.05$	< 0.05	1.000	1.000	1.000		
D <sub>40%</sub> (Gy)	15.063	7.837	8.933	8.919	0.069	0.156	0.183	1.000	1.000	1.000		
D <sub>45%</sub> (Gy)	10.37	5.22	5.64	6.03		p	>0.05 (Kru	ıskal-Wall	is)			

p \*: Significance was found when variables are compared to 3D-CRT versus IMRT, 3DCRT versus IMAT, 3DCRT versus IMAT, IMRT versus HT, IMAT versus HT. p-value < 0.05 determines significance.

#### 3.2.2. Dose Evoluation of Lung

The statistical results of lung dose values ( $D_{mean}$ ,  $D_{5\%}$ ,  $D_{10\%}$ ,  $D_{15\%}$ ,  $D_{20\%}$ ,  $D_{25\%}$ ,  $D_{30\%}$ ,  $D_{35\%}$ ,  $D_{40\%}$  and  $D_{45\%}$ ) are shown in Table 4.

	<b>Table 4.</b> $D_{\text{mean}}$ , $D_{5\%}$ , $D_{10\%}$ , $D_{15\%}$ , $D_{20\%}$ , $D_{25\%}$ , $D_{30\%}$ , $D_{35\%}$ , $D_{40\%}$ and $D_{45\%}$ values for lung										
					<b>3D-CRT</b>	<b>3D-CRT</b>	<b>3D-CRT</b>	IMRT	IMRT	IMAT	
					VS	VS	VS	VS	VS	VS	
					IMRT	IMAT	HT	IMAT	HT	HT	
	3D-CRT	IMRT	IMAT	HT	P*	P*	P*	P*	P*	P*	
D <sub>mean</sub> (Gy)	12.26	11.27	11.68	13.03		p>	0.05 (Krus	kal-Wallis	s)		
D <sub>5%</sub> (Gy)	60.748	70.37	72.793	76.012	p>0.05 (Kruskal-Wallis)						
D10% (Gy)	44.54	46.981	55.381	67.692	1.000	0.134	$<\!0.05$	0.446	$<\!0.05$	0.060	
D <sub>15%</sub> (Gy)	36.439	29.259	32.613	38.169	0.097	1.000	1.000	1.000	0.019	0.361	
D <sub>20%</sub> (Gy)	21.89	19.25	17.87	29.95	0.233	0.079	0.700	1.000	1.000	1.000	
D <sub>25%</sub> (Gy)	13.569	10.892	10.329	10.476	< 0.05	$<\!0.05$	< 0.05	1.000	1.000	1.000	
D <sub>30%</sub> (Gy)	11.292	6.682	6.355	6.381	< 0.05	$<\!0.05$	$<\!0.05$	1.000	1.000	1.000	
D35% (Gy)	8.433	4.335	4.252	4.38	< 0.05	$<\!0.05$	< 0.05	1.000	1.000	1.000	
D <sub>40%</sub> (Gy)	5.968	3.148	3.055	3.251	< 0.05	$<\!0.05$	$<\!0.05$	1.000	1.000	1.000	
D45% (Gy)	4.321	2.45	2.266	2.439		p>	0.05 (Krus	kal-Wallis	s)		

p \*: Significance was found when variables are compared to 3D-CRT versus IMRT, 3DCRT versus IMAT, 3DCRT versus HT, IMRT versus IMAT, IMRT versus HT, IMAT versus HT, p-value < 0.05 determines significance.

# 3.2.3. Dose Evoluation of Lung-PTV (Lung minus PTV), Spinal Cord, Right and Left Coronary Artery

The statistical results of lung- PTV, Spinal Cord, Right and Left Coronary Artery dose values are shown in Table 5.

Table 5. For Lung-PTV (Lung minus PTV); D <sub>mean</sub> , D <sub>5%</sub> and D <sub>20%</sub> ; For Spinal Cord; D <sub>max</sub> and D <sub>1%</sub> ; Right
and Left Coronary Artery; $D_{mean}$ and $D_{5\%}$ values

	•				<b>3D-CRT</b>	<b>3D-CRT</b>	<b>3D-CRT</b>	IMRT	IMRT	IMAT
					VS	VS	VS	VS	VS	VS
	<b>3D-CRT</b>	IMRT	IMAT	HT	IMRT	IMAT	HT	IMAT	HT	HT
					P*	P*	P*	P*	P*	P*
Lung-PTV D <sub>mean</sub> (Gy)	12.8	10.82	11.86	12.97		p>(	0.05 (Krus	kal-Walli	s)	
Lung-PTV D5% (Gy)	59.974	69.902	70.199	75.602	2 p>0.05 (Kruskal-Wallis)					
Lung-PTV D <sub>20%</sub> (Gy)	20.1	17.8	16.67	18.35		p>(	).05 (Krus	kal-Walli	s)	
Spinal Cord D <sub>max</sub> (Gy)	39.74	40.34	39.16	28.53	0.663	0.395	< 0.05	0.158	< 0.05	$<\!0.05$
Spinal Cord D <sub>1%</sub> (Gy)	38.06	36.90	36.56	26.3	0.917	0.419	$<\!0.05$	0.419	< 0.05	$<\!0.05$
RCoronary Artery D <sub>mean</sub> (Gy)	26.28	16.14	14.35	14.45	0.915	0.122	$<\!0.05$	1.000	1.000	1.000
RCoronary Artery D <sub>5%</sub> (Gy)	35.34	19.06	14.19	16.5	0.290	0.360	$<\!0.05$	0.567	0.724	0.548
LCoronary Artery D <sub>mean</sub> (Gy)	26.78	19.5	19.275	19.78	0.115	0.950	0.144	1.000	1.000	1.000
L Coronary Artery D <sub>5%</sub> (Gy)	39.241	29.504	27.447	28.976	0.210	< 0.05	0.130	1.000	1.000	1.000

p \*: Significance was found when variables are compared to 3D-CRT versus IMRT, 3DCRT versus IMAT, 3DCRT versus HT, IMRT versus HT, IMRT versus HT. p-value < 0.05 determines significance.

#### 4. Conclusion and Comment

Because of the location of the thoracic esophagus and the presence of critical organs around it, radiotherapy treatment plans is very difficult. Today, in line with the current developments in RT, Clasic therapies have been replaced by IMRT, IMAT and HT planning. Although these RT techniques show similar results in terms of PTV compliance, each technique has different advantages in terms of normal tissue protection.

As shown in Table 2 in our study, PTV coverage was achieved as the best in IMAT plan with CI (1.186) and HI (0.056) values. Karaoguz et al. in their IMRT and IMAT plans, they found the best values of CI and HI in the IMAT plan as in our study [13]. In

addition, in our study  $D_{max}$ ,  $D_{min}$ ,  $D_{mean}$ ,  $D_{1\%}$ ,  $D_{5\%}$  doses for PTV were found as lowest value in IMRT.

Konski et al. [14] evaluated 74 oesophageal cancer patients using FDG-PET. After RT, changes in 18F-FDG PET for myocardium were associated with cardiac toxicity. They noted a significant difference in the dosimetric parameters of  $V_{20}$ ,  $V_{30}$  and  $V_{40}$  among patients with and without symptomatic heart toxicity. They reported that there was no symptomatic heart toxicity if the  $V_{20}$ ,  $V_{30}$  and  $V_{40}$  doses were below 70%, 65% or 60% of the total dose, respectively [14]. An average heart dose of 26.1 Gy, a maximum heart dose of 47.0 Gy, and  $V_{30}$ > 46 Gy on Esophageal cancer have been shown to be decisive for pericarditis [15,16].

Patients who received 74 Gy dose in the conformal RT of non-small cell lung cancer were generally reported to have poor heart doses, and the heart  $V_{5Gy}$  and  $V_{30Gy}$  dose volume parameters were important determinants of the patient's survival [17]. In addition, Wei et al. [16] reported that various DVH parameters (eg V<sub>3</sub> and V<sub>50</sub> and mean dose) were predicted for pericardial effusions.

In our study, as seen in Table 3,  $D_{20\%}$ ,  $D_{30\%}$  and  $D_{40\%}$  doses were not statistically significant among the four treatment techniques, but these doses were at lowest in IMRT plan as 17.87 Gy, 13.39 Gy and 7.837 Gy, respectively.

For Dmean of heart in Table 3, although it was not statistically significant, the lowest dose was in IMAT plan as 16.52 Gy and then IMRT, HT and 3D-CRT plans respectively. V<sub>5%</sub> of the heart; although not statistically significant, the lowest dose was in the 3D-CRT plan as 79.08, then in the IMRT, IMAT and HT plans, respectively. The incidence of pericarditis is 7% for 6 Gy of V<sub>45</sub> of heart volume, incidence of pericarditis is 12 % for 6-15 Gy of V<sub>30</sub> of heart volume and the incidence of pericarditis for 15-30 Gy of V<sub>20</sub> of heart volume is 19%. The incidence of pericarditis was reported to be 50% with a total heart radiation dose of > 50 Gy [18]. Cardiac mortality due to the ischemic heart disease or myocardial infarction is closely related to the medial dose greater than 30 Gy and V<sub>35</sub> heart volume doses greater than 38 Gy. As a clinical endpoint, myocardial perfusion defects may occur when there are doses higher than  $V_{23Gy}$  or  $V_{33Gy}$  in the left ventricle. [19]. In our study, it was found that  $V_{45}$  heart volume received less than 6 Gy in IMRT, IMAT and HT techniques, V<sub>30</sub> heart volume received less than 15 Gy in IMRT and HT techniques,  $V_{20}$  heart volume received less than 30 Gy in IMRT. These results show that the lowest probability of pericarditis is in the IMRT technique with respect to dosimetry.

In the planning of esophageal cancer radiotherapy, dose distributions in the lungs, which are known to be one of the most radiation sensitive tissues in terms of toxicity, are also important. In the literature, there are studies reported that the mean lung dose and lung V<sub>5</sub>, V<sub>10</sub> and V<sub>20</sub> values are significantly associated with the risk of radiation pneumonia [20-24]. In our study, as shown in Table 4, for the mean lung dose; although it was not statistically significant among the 4 techniques, mean lung dose was obtained as the lowest in IMRT plan, then in IMAT, 3D-CRT and HT plans, respectively. For lung D<sub>5%</sub>, D<sub>10%</sub> doses; although not statistically significant, it was determined as the lowest in the 3D-CRT plan, then in the IMRT, IMAT and HT plans, respectively. For lung D<sub>20%</sub> dose; although it was not statistically significant, it was obtained as the lowest in IMRT plan and later in IMAT, HT and 3D-CRT plans.

As seen in Table 5, the doses of Spinal Cord  $D_{max}$  and  $D_{1\%}$  were found as the lowest in the HT technique with 28.3 Gy and 26.3 Gy, respectively.

In this study, we found that IMRT, IMAT and HT techniques have lower critical organ doses than 3D-CRT technique for treating torasic esophageal cancer. Considering that patients receive treatment with chemotherapy, it is important to take into consideration heart and lung toxicity. Considering the current evidence of the relationship between radiation-induced cardiac toxicity and the dose-volume parameters after treatment for esophageal cancer in our study, dose limits are better in IMRT and IMAT techniques in terms of lung and heart toxicity.

#### **Author Statement**

Murat OKUTAN: Investigation, Reviewand Editing, Original Draft Writing, Visualization, Supervision. Şeyda BAYRAM: Investigation, Instrument Supply, Resource Canan KÖKSAL: Data Curation, Observation. Evren Ozan GÖKSEL: Data Curation, Observation. Şule KARAMAN: Data Curation, Observation. Yunus Emre AKPINAR: Data Curation, Observation. Nergiz DAĞOĞLU: Instrument Supply, Observation. Bayram DEMİR: Reviewand Editing, Visualization, Advice.

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#### **Conflict of Interest**

As the authors of this study, we declare that we do not have any conflict of interest statement.

#### **Ethics Committee Approval and Informed Consent**

The study was approved by the Ethics committee before the started (Istanbul University, Istanbul Medical Faculty Clinical Research Ethics Committee; Date: 24.11.2017, Registration number: 2017/1356).

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