ORIGINAL ARTICLE

Evaluation of Conventional Treatment Planning Techniques for Radiotherapy of Gastroesophageal Junction Cancer: A Dosimetric Comparison between Male and Female Patients

Mohamad Pursamimi [1], Mahdi Ghorbani [1*], Mehdi Khosravi [2], Ghazal Mehri-Kakavand [3], Wrya Parwaie [4], Seyed Mohammad Hosseini [5], Ali Mohammad Sharifi [6], Meysam Tavakoli [7*]

[1] *Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2] *Vali-e-Asr Radiotherapy and Oncology Center, Vali-e-Asr Hospital, Qom, Iran*

[3] *Department of Anatomy and Medical Imaging, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand*

[4] *Department of Medical Physics, Faculty of Paramedical Sciences, Ilam University of Medical Sciences, Ilam, Iran*

[5] *Department of Medical Physics and Medical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[6] *Clinical Research Development Center, Shahid Modarres Educational Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[7] *Department of Radiation Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA*

*Corresponding Authors: Mahdi Ghorbani, Meysam Tavakoli
Email: mhdghorbani@gmail.com, meysam.tavakoli@emory.edu

Received: 10 May 2023 / Accepted: 14 December 2023

Abstract

Purpose: Gastro-Esophageal (GE) junction cancer has been increasingly prevalent worldwide. This study aims to compare dosimetric and radiobiological parameters for target areas and Organs At Risk (OARs) in men and women patients diagnosed with GE junction cancer.

Materials and Methods: Here, thirty patients who underwent radiotherapy using a 6-MV photon beam from a linear accelerator (Shinva Medical, Shandong, China) were selected. Dosimetric and radiobiological parameters within the Planning Target Volume (PTV) and OARs were compared among all patients using a paired-sample t-test. Additionally, a comparative analysis of Field-In-Field (FIF), three-Field (3F), and four-Field Box (4FB) planning techniques was conducted for both men and women patients.

Results: In terms of dose distribution in the PTV, a significant difference exists between male and female patients regarding TCP and Monitor Unit (MU). Furthermore, in terms of dose distribution in OARs, there is also a significant difference between males and females in terms of NTCP for the right lung and V20 Gy for the right lung.

Conclusion: In general, most dosimetric parameters exhibited similarities between male and female patients. However, notable differences surfaced in TCP, MU, and specific parameters, including NTCP and V20Gy for the right lung. Hence, it is prudent to emphasize meticulous attention in treatment planning for GE junction cancer, considering the anatomical variations between males and females.

Keywords: Radiotherapy; Gastroesophageal Junction Cancer; Dosimetric Parameters; Treatment Planning.

DOI: https://doi.org/10.18502/fbt.v12i2.18273

1. Introduction

The eighth most common cancer worldwide is Gastro-Esophageal (GE) junction cancer, with a significant proportion of cases being diagnosed at advanced stages [1, 2]. In recent years, the incidence of adenocarcinoma in the GE junction has been on the rise. It is worth noting that tumors located in the GE junction generally have a worse prognosis compared to those confined solely to the stomach [3]. The conventional treatment for locally advanced GE junction cancer has traditionally involved neoadjuvant or definitive chemoradiotherapy. However, patient outcomes have proven unsatisfactory, with recurrence rates reaching as high as 30–50% [4]. In cancer treatment, radiotherapy techniques play a significant role, particularly for patients with GE junction cancer [5, 6]. The goal is to expose abnormal cancer cells to the highest radiation dose possible while minimizing radiation exposure to normal cells that are either in or near the radiation path [7]. Consequently, several methods have been developed, including helical tomotherapy, fixed-field Intensity-Modulated Radiotherapy (IMRT), Volumetric Modulated Arc Radiotherapy (VMAT), and three-Dimensional Conformal Radiotherapy (3D-CRT) [8-11].

According to the study conducted by Allaveisi *et al.* [12], the field-in-field technique yielded a dose distribution that was more homogeneous and exhibited similar conformity compared to the four-field box method in this particular case. Fu *et al.* [13] assessed various fixed-field IMRT plans. Their findings indicated that, among the different IMRT plans offering comparable coverage, the maximum dose, mean dose, and conformity index should be consistent. Lin *et al.* [14] evaluated middle-thoracic esophageal carcinoma and also compared the fixed-field IMRT and VMAT plans in terms of target coverage, lung dose, and delivery time. In another comparative study, Fawaz *et al.* [15] evaluated these treatment techniques from a dosimetric perspective and concluded that both 3D-CRT and VMAT are suitable approaches for delivering the required doses to the target.

However, all of these dosimetric evaluations were conducted using all the techniques, and there hasn't been a specific comparison made for the same esophageal cases between male and female patients. Several studies have explored the comparison of radiotherapy outcomes between male and female patients for different organs. Incrocci and Jensen [16] conducted a review study on sexual dysfunction in individuals of both genders after undergoing pelvic radiotherapy. Courcy *et al.* [17] conducted a literature review on the effectiveness and outcomes of radiotherapy for both male and femle patients. Meunier and Marignol [18] conducted a review of various studies, assessing the role of sex as a biological variable in radiotherapy research. Macdonald *et al.* [19] assessed the significance of gender as a prognostic factor and its impact on outcomes in both male and female patients who underwent breast mastectomy. In their study, Page *et al.* [20] investigated the effects of radiotherapy in male and female patients diagnosed with head and neck cancer. Laaksomaa *et al.* [21] examined the disparities in setup accuracy between male and female patients undergoing radiotherapy for pelvic tumors. To the best of our knowledge, no study has been conducted to compare dosimetric parameters between males and females undergoing radiotherapy for GE junction cancer using conventional Field-In-Field (FIF), three-Field (3F), and four-Field Box (4FB) planning techniques. This study aims to compare radiotherapy dosimetric and radiobiological parameters in the target area and Organs At Risk (OARs) for male and female patients with GE junction cancer.

2. Materials and Methods

In this retrospective study, a cohort of thirty patients with GE junction cancer was analyzed, who had been treated with external 6 MV photon beam radiotherapy using a medical Shinva linear accelerator (Shinva Medical, Shandong, China) equipped with Multileaf Collimators (MLCs). The patient group consisted of 15 males and 15 females, ranging in age from 35 to 60 years (mean age: 46). Relevant patient information, such as age at diagnosis, gender, smoking status, histology, tumor location, tumor size, nodal status, treatment settings, and treatment dates, was collected. Table 1 provides an overview of the patient characteristics, including the number of patients, their age, tumor stage, and the volumes for the Planning Target Volume (PTV) and OARs.

Table 1. Characteristics of the patients with GE junction cancer in the present study

Characteristics	Number
Number of men patients	15
Number of women patients	15
Age, mean (range) in years	40 (35-45)
Tumor stage	II-III
Prescribed dose (Gy)	50.4
PTV volume (cc)	810.80 ± 214.62
Heart volume (cc)	628.78 ± 141.36
Right kidney volume (cc)	130.98 ± 27.90
Left kidney volume (cc)	139.98 ± 32.85
Right lung volume (cc)	2017.58 ± 418.23
Left lung volume (cc)	1635.39 ± 437.92
Liver volume (cc)	1359.60 ± 408.45
Spinal cord volume (cc)	58.67 ± 15.13

As part of the treatment protocol, a Neusoft Computed Tomography (CT) scanner (NeuViz 16, Neusoft Medical Systems, PR, China) was utilized to obtain CT images, which were subsequently imported into a PCRT3D Treatment Planning System (TPS) developed by RF Tecnicas Radiofizicas, Zaragoza, Spain. The treatment plans were formulated as three-dimensional conformal radiation therapy (3D-CRT) plans. In contouring the Gross Tumor Volume (GTV), the guidelines outlined by the radiation therapy and oncology group (RTOG) were adhered to for both male and female patients [22]. The Clinical Target Volume (CTV) was established by incorporating the GTV with a 15 mm margin. Furthermore, a 10 mm isotropic margin was applied to determine the CTV, which subsequently defined the PTV. For each patient, treatment plans using three-Field (3F), four-Field Box (4FB), and field-in-field (FIF) techniques were developed and compared. The CT images of the patients were used to contour the heart, right kidney, left kidney, right lung, left lung, liver, and spinal cord as OARs.

The treatment protocol remained consistent across the three treatment planning techniques (3F, 4FB, and FIF), with a prescribed dose of 50.4 Gy for the PTV, delivered at a rate of 1.8 Gy per fraction, five fractions per week. The dosimetric and radiobiological parameters in the PTV and OARs were compared between male and female patients. For the PTV, parameters such as mean dose (D_{mean}), maximum dose (D_{max}), homogeneity index (HI), conformity index (CI), and tumor control probability (TCP) were calculated. Additionally, the monitor unit (MU) was compared among the three techniques. Regarding the OARs, parameters including D_{mean}, D_{max}, V_{20} Gy, and Normal Tissue Complication Probability (NTCP) were calculated. Statistical analysis between the groups was conducted using the t-test, and p-values were calculated.

2.1. Treatment Planning

Each patient underwent treatment planning with 3F, 4FB, and FIF techniques utilizing a 6 MV photon beam. To ensure a minimum of 95% of the prescribed dose of 50.4 Gy was delivered to the PTV, adjustments were made to variables such as wedge angles, orientations, and beam weights. The 3F treatment plan involved anterior, posterior, and left lateral fields, all equipped with wedges. The 4FB treatment plan consisted of anterior, posterior, and two lateral fields, with the angles between the fields customized based on individual patient anatomy and treatment volume by the radiation oncologist. If necessary, a wedge was employed in one or more fields. The FIF plans were designed either as a 4FB plan with a 5 mm PTV margin and no wedges or by utilizing four fields to shield high-dose regions (above 107%), with the selection of appropriate points guided by the International Commission on Radiation Units and Measurements (ICRU) report 50 (23) Since all the 3D-CRT planning methods yield dose distributions that fall within the range of -5% to +7%, adjustments were made to the beam weights to achieve a desired dose distribution with sufficient homogeneity in the PTV [12, 24, 25]. Figure 1 presents sample treatment planning images, showcasing coronal views for male and female patients with GE junction cancer. The images correspond to the 3F, 4FB, and FIF treatment planning techniques. Part (a) depicts a male patient treated with the 3F planning technique, part (b) shows a male patient treated with the 4FB technique, and part (c) illustrates a male patient treated with the FIF technique. Similarly, part (d) represents a female patient treated with the 3F technique, part (e) showcases a female patient treated with the 4FB technique, and part (f) pertains to a female patient treated with the FIF technique. It is important to note that among all the FIF plans, approximately 95% of the prescribed dose was achieved using the first plan, while the remaining 5% was delivered using the second plan. These techniques were exclusively designed for planning purposes and were not actually administered to the patients during their regular

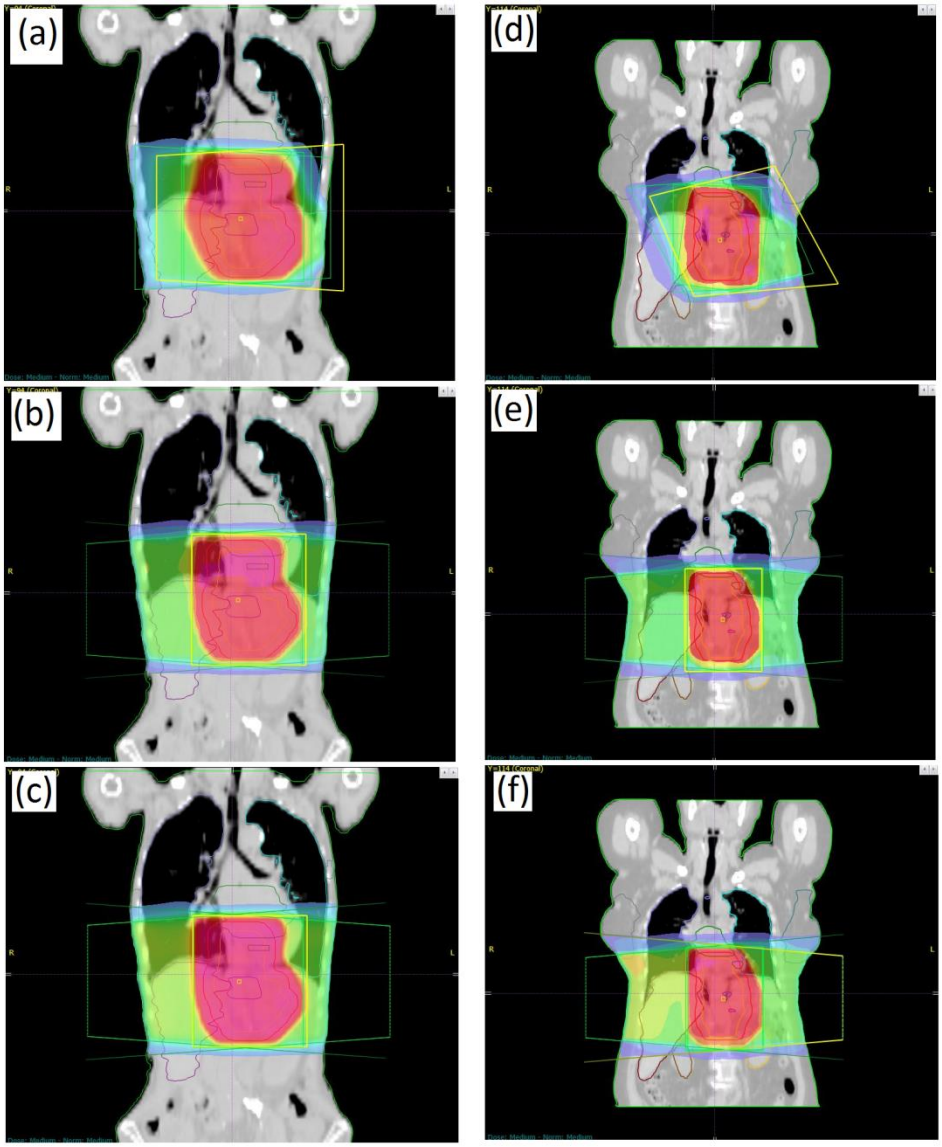

Figure 1. Sample treatment planning images for a male and a female patient with GE junction cancer. (a) male with 3F; (b) male with 4FB; (c) male with FIF; (d) female with 3F; (e) female with 4BF; (f) female with FIF treatment planning techniques. The images in this figure are coronal views

treatment. Wedges were exclusively utilized for the 3F and 4FB techniques, if necessary, but not for the FIF technique.

The Dose Volume Histograms (DVHs) were obtained for the PTV and OARs such as the heart, right kidney, left kidney, right lung, left lung, liver, and spinal cord, corresponding to the three treatment techniques. Various dosimetric parameters were used to compare the three planning techniques for the PTV, including D_{mean} (mean dose), D_{max} (maximum dose), Homogeneity Index (HI), Conformity Index (CI), and TCP. Additionally, the MUs were compared for the three techniques. For the OARs, the parameters considered were D_{mean}, D_{max}, V20 Gy (volume receiving greater than or equal to 20 Gy), and NTCP. Specifically, V20 Gy (%) represents the percentage volume of the lung receiving the specified dose. The reported values for each parameter were accompanied by the corresponding Standard Deviation (SD) to indicate the uncertainty associated with that value.

2.2. Dosimetric and Radiobiologic Parameters

The conformity index was determined using the provided equation, wherein the volume of tissue encompassed by the reference isodose (e.g., the 95% isodose) [26] is utilized (Equation 1).

$$\mathrm{CI} = V_{\mathrm{PTV}} \times \frac{V_{\mathrm{TV}}}{\mathrm{TV_{PV}}^2} \quad (1)$$

In the given Equation, VTV represents the treatment volume covered by the prescribed isodose, VPTV denotes the volume of the PTV, and TVPV represents the fraction of VPTV that lies within VTV. Typically, the CI ranges from 0 to 1, with higher values indicating greater dose conformity within the PTV [27, 28]. The HI was computed using the following formula (Equation 2):

$$\mathrm{HI} = 100 \times \frac{(D_{2\%} - D_{98\%})}{D_{\mathrm{prescribed}}} \quad (2)$$

Where D2% and D98% are the minimum dose and maximum dose in the target volume, and Dprescribed is the prescribed dose. Smaller HI values are equal to a more homogeneous dose distribution in the target volume [29-31].

The TCP and NTCP were calculated as radiobiological parameters using the models presented by Niemierko [32]. To calculate TCP and NTCP, the first step involved the calculation of the equivalent uniform dose (EUD) using the following Equation. The EUD represents the biological effective dose when the dose distribution within the tumor mass is homogeneous [33].

$$\mathrm{EUD} = \left(\sum_{i=1} (V_i \mathrm{EQD}_i^{\alpha})\right)^{\frac{1}{\alpha}} \quad (3)$$

Where α represents the model parameter for the normal structure of the tumor [24]; Vi denotes the fraction of the volume receiving the Di dose (Gy). Finally, the Equivalent Dose (EQD) is calculated as the biologically equivalent dose for a 2 Gy dose per fraction, based on the following Equation:

$$\mathrm{EQD} = D \times \left(\frac{\frac{\alpha}{\beta} + \frac{D}{n_f}}{\frac{\alpha}{\beta} + 2}\right) \quad (4)$$

In the provided equation, n_f represents the number of fractions, and df = $\frac{D}{n_f}$ represents the dose per fraction during the treatment course. Additionally, α/β represents the linear-quadratic parameter for the organ, which is specific to the tissue [12, 34].

The model presented by Niemierko [32] is founded on the concept of EUD, which is used to determine the delayed response of normal tissue to radiation (Equation 5):

$$\mathrm{NTCP} = \frac{1}{1 + \left(\frac{\mathrm{TD}_{50}}{\mathrm{EUD}}\right)^{4\times\gamma_{50}}} \quad (5)$$

In this formula, TD50 represents the Tolerance Dose (TD) for a 50% complication rate at a specific time interval when the designated organ receives homogeneous irradiation. γ_50 is the model parameter that is unique to the normal tissue or tumor and is contingent upon the slope of the dose-response curve [12, 25].

To calculate the TCP for the tumor, the following equation was used:

$$\mathrm{TCP} = \frac{1}{1 + \left(\frac{\mathrm{TCD}_{50}}{\mathrm{EUD}}\right)^{4\times\gamma_{50}}} \quad (6)$$

In this equation, TCD represents the tumor control dose, and TCD50 corresponds to the dose at which a 50% control rate is achieved for a tumor that has been uniformly exposed. As previously mentioned, γ_(50)is the model parameter dependent on the slope of the dose-response curve [24, 35, 36]. The number of MUs required for tumor irradiation was documented and compared among the treatment planning techniques for both male and female patients.

2.3. Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, version 28, SPSS Inc., Chicago, USA) software was utilized for the analysis and comparison of the data. For this purpose, the Kolmogorov-Smirnov test was employed to ascertain whether the data's distribution is normal. The paired t-test was used for the comparison of the data with normal distribution. Comparisons with a p-value of less than 0.05 were taken to indicate a real difference between the two groups. In order to analyze these data with non-normal distribution, the Chi-square test was used. Dosimetric parameters in PTV and OARs between different planning techniques and between male and female patients were compared.

3. Results

Figure 2 displays sample DVHs for male and female patients with GE junction cancer using different planning techniques (3F, 4FB, and FIF). In this figure, part (a) shows a male patient with the 3F

planning technique, part (b) shows a male patient with 4FB, part (c) shows a male patient with FIF, part (d) shows a female patient with 3F, part (e) shows a female patient with 4FB, and part (f) shows a female patient with the FIF treatment planning technique.

Dosimetric parameters (D_{mean}, D_{max}, HI, CI, TCP) for PTV and MUs for male and female patients with GE cancer are presented in Tables 2 and 3, respectively. These tables provide a comparison of the 3F, 4FB, and FIF planning techniques. In Table 4, a comparison of these dosimetric parameters is made between male and female patients.

Dosimetric parameters (D_{mean}, D_{max}, V20 Gy, and NTCP) for OARs in male and female patients with GE cancer are presented in Tables 5 and 6, respectively. These tables provide a comparison of the 3F, 4FB, and FIF planning techniques. In Table 7, a comparison of these dosimetric parameters is made between male and female patients.

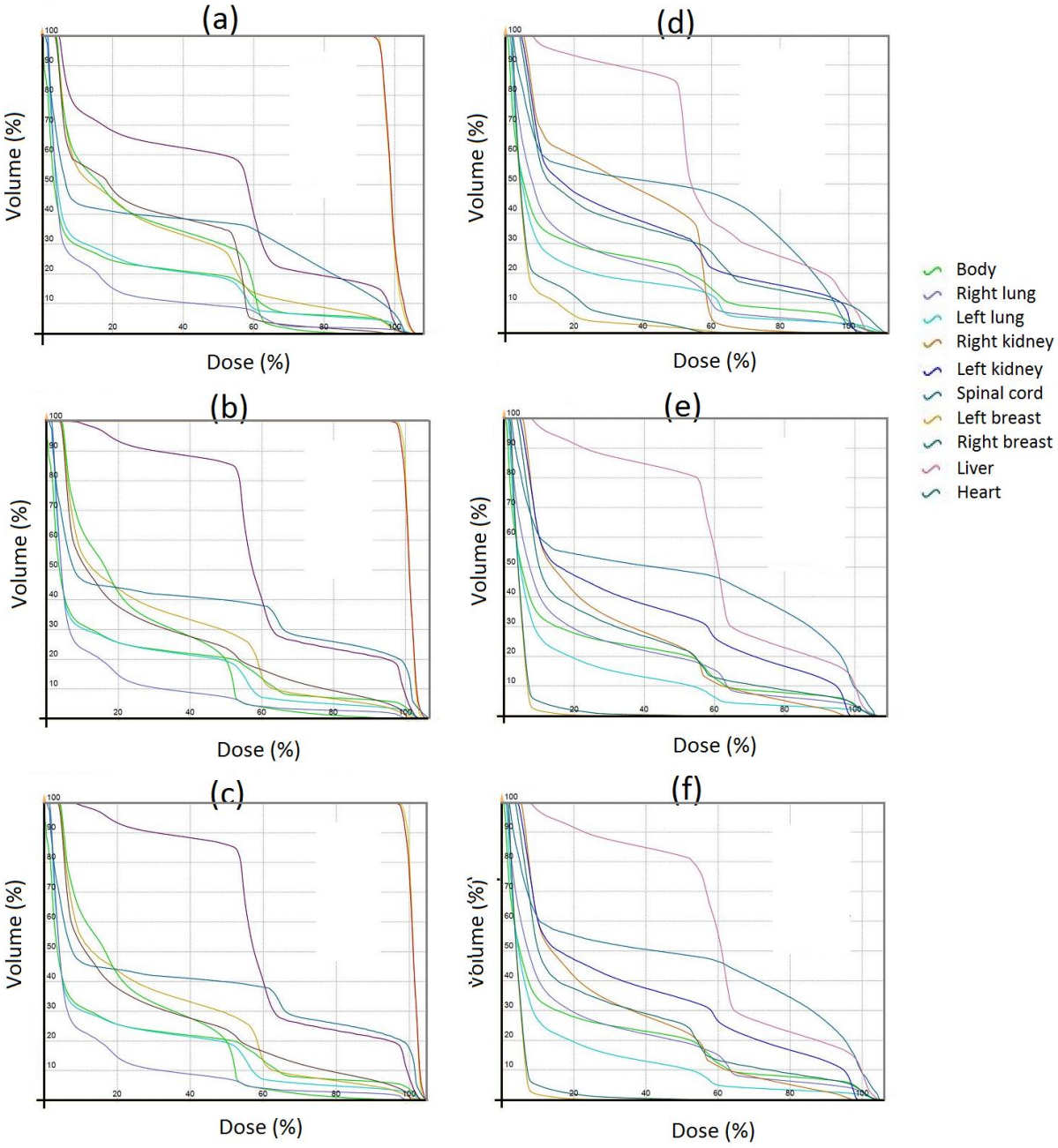

Figure 2. Sample DVHs for a male and a female patient with GE junction cancer. (a) male with 3F; (b) male with 4FB; (c) male with FIF; (d) female with 3F; (e) female with 4bF; (f) female with FIF treatment planning techniques

Table 2. Dosimetric parameters ± SD for PTV (D_{mean}, D_{max}, HI, CI, TCP) and MU for men with GE cancer: a comparison of 3F, 4FB, and FIF planning techniques

Parameter	3F	4FB	FIF	p-value
D_{mean}	51.07 ± 0.63	51.38 ± 0.48	50.61 ± 0.27	(3F vs 4FB) 0.20 (4FB vs FIF) 0.00* (FIF vs 3F) 0.03*
D_{max}	57.46 ± 2.45	55.59 ± 1.54	53.80 ± 0.96	(3F vs 4FB) 0.2 (4FB vs FIF) 0.01* (FIF vs 3F) 0.00*
HI	0.12 ±0.02	0.10 ± 0.02	0.07 ± 0.01	(3F vs 4FB) 0.06 (4FB vs FIF) 0.00* (FIF vs 3F) 0.00*
CI	1.92 ± 0.25	1.85 ± 0.20	1.78 ± 0.24	(3F vs 4FB) 0.38 (4FB vs FIF) 0.38 (FIF vs 3F) 0.38
TCP	53.80 ± 2.19	54.84 ± 1.52	52.32 ± 1.22	(3F vs 4FB) 0.44 (4FB vs FIF) 0.00* (FIF vs 3F) 0.00*
MU	310.33 ± 22.27	259.42 ± 24.99	242.06 ± 6.06	(3F vs 4FB) 0.00* (4FB vs FIF) 0.03* (FIF vs 3F) 0.00*

Table 3. Dosimetric parameters ± SD for PTV (D_{mean}, D_{max}, HI, CI, TCP) and MU for women with GE cancer: a comparison of 3F, 4FB, and FIF planning techniques

Parameter	3F	4FB	FIF	p-value
D_{mean} (Gy)	51.26 ± 0.50	51.22 ± 0.57	50.57 ± 0.38	(3F vs 4FB) 0.97 (4FB vs FIF) 0.00* (FIF vs 3F) 0.03*
D_{max} (Gy)	57.16 ± 1.84	56.08 ± 1.58	54.12 ± 1.51	(3F vs 4FB) 0.09 (4FB vs FIF) 0.00* (FIF vs 3F) 0.00*
HI	0.11 ± 0.02	0.09 ± 0.2	0.07 ± 0.1	(3F vs 4FB) 0.02* (4FB vs FIF) 0.02* (FIF vs 3F) 0.00*
CI	1.97 ± 0.24	1.92 ± 0.22	1.86 ± 0.22	(3F vs 4FB) 0.80 (4FB vs FIF) 0.74 (FIF vs 3F) 0.36
TCP (%)	61.86 ± 6.02	61.14 ± 6.90	59.38 ± 6.83	(3F vs 4FB) 0.21 (4FB vs FIF) 0.21 (FIF vs 3F) 0.21
MU	305.20 ± 21.94	287.60 ± 23.83	257.90 ± 22.71	(3F vs 4FB) 0.12 (4FB vs FIF) 0.00* (FIF vs 3F) 0.00*

4. Discussion

In this study, dosimetric and radiobiological parameters in the target and OARs were compared between male and female patients who underwent 3D-CRT for GE junction cancer. According to the data presented in Table 2 for male patients, there is a significant difference between the FIF technique and the other techniques (3F and 4FB) in terms of D_{mean}, D_{max}, HI, TCP, and MU for PTV. These data indicate that the D_{mean} achieved with the FIF technique is closer to the prescribed dose of 50.4 Gy, which is considered an advantage of FIF over the other techniques. Additionally, the HI for the FIF technique is lower than that for the other techniques. A lower HI in the FIF technique signifies superior dose uniformity within the tumor compared to both 3F and 4FB techniques. Conversely, the FIF technique exhibits a lower TCP compared to the other methods, highlighting their advantage in this aspect. In terms of MUs, the FIF technique offers an advantage by requiring fewer MUs, reducing beam "on" time, and alleviating the workload on the linear accelerator while decreasing the production of neutrons and

Table 4. Dosimetric parameters ± SD for PTV (D_{mean}, D_{max}, HI, CI, TCP) and MU for patients with GE cancer: a comparison of men and women patients

Parameter	Gender	3F	p-value	4FB	p-value	FIF	p-value
D_{mean} (Gy)	Male	51.07 ± 0.63	0.90	51.38 ± 0.48	0.40	50.61± 0.27	0.83
	Female	51.26 ± 0.50		51.22 ± 0.57		50.57 ± 0.38	
D_{max} (Gy)	Male	57.46 ± 2.45	0.54	55.89 ± 1.54	0.88	53.80 ± 0.96	0.72
	Female	57.16 ± 1.84		56.08 ± 1.58		54.12 ± 1.51	
HI	Male	0.12 ± 0.22	0.56	0.10 ± 0.02	0.75	0.07 ± 0.01	0.54
	Female	0.11 ± 0.02		0.09 ± 0.02		0.07 ± 0.01	
CI	Male	1.92 ± 0.25	0.52	1.85 ± 0.20	0.49	1.78 ± 0.24	0.41
	Female	1.97 ± 0.24		1.92 ± 0.22		1.86 ± 0.22	
TCP (%)	Male	53.80 ± 2.19	0.00*	54.84 ± 1.52	0.08	52.32 ± 1.22	0.03*
	Female	61.86 ± 6.02		61.14 ± 6.90		59.38 ± 6.83	
MU	Male	310.33 ± 22.27	0.70	259.42 ± 24.99	0.00*	242.06 ± 6.06	0.00*
	Female	305.20 ± 21.94		287.60 ± 23.83		257.90 ± 22.71	

Table 5. Dosimetric parameters ± SD for OARs (D_{mean}, D_{max}, $V_{20\ Gy}$ and NTCP) for men with GE cancer: a comparison of 3F, 4FB, and FIF planning techniques

OAR	Parameter	3F	4FB	FIF	p-value
Heart	D_{mean} (Gy)	23.51 ± 9.38	21.45 ± 8.23	20.57 ± 8.54	(3F vs 4FB) 0.36 (4FB vs FIF) 0.36 (FIF vs 3F) 0.36
	NTCP (%)	0.05 ± 0.06	0.02 ± 0.02	0.01 ± 0.02	(3F vs 4FB) 0.18 (4FB vs FIF) 0.18 (FIF vs 3F) 0.18
Right Kidney	D_{mean} (Gy)	19.35 ± 5.63	14.48 ± 4.47	14.34 ± 4.25	(3F vs 4FB) 0.00* (4FB vs FIF) 0.84 (FIF vs 3F) 0.00*
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.02* (4FB vs FIF) 0.96 (FIF vs 3F) 0.02*
Left Kidney	D_{mean} (Gy)	24.29 ± 7.70	22.08 ± 6.84	21.83 ± 7.23	(3F vs 4FB) 0.53 (4FB vs FIF) 0.53 (FIF vs 3F) 0.53
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.58 (4FB vs FIF) 0.58 (FIF vs 3F) 0.58
Right lung	D_{mean} (Gy)	9.94 ± 3.41	9.50 ± 3.45	9.51 ± 3.44	(3F vs 4FB) 0.79 (4FB vs FIF) 0.79 (FIF vs 3F) 0.79
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.73 (4FB vs FIF) 0.73 (FIF vs 3F) 0.73
	$V_{20\ Gy}$ (%)	17.95 ± 2.99	14.76 ± 3.27	15.78 ± 3.03	(3F vs 4FB) 0.02* (4FB vs FIF) 0.64 (FIF vs 3F) 0.14
Left Lung	D_{mean} (Gy)	10.72 ± 1.55	9.89 ± 1.12	9.75 ± 1.14	(3F vs 4FB) 0.19 (4FB vs FIF) 0.95 (FIF vs 3F) 0.95
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.00* (4FB vs FIF) 0.09 (FIF vs 3F) 0.00*
	$V_{20\ Gy}$ (%)	24.12 ± 2.89	21.45 ± 2.53	21.24 ± 2.56	(3F vs 4FB) 0.02* (4FB vs FIF) 0.97 (FIF vs 3F) 0.01*

Liver	D_{mean} (Gy)	25.69 ± 1.19	29.00 ± 3.63	28.91 ± 3.55	(3F vs 4FB) 0.12 (4FB vs FIF) 0.99 (FIF vs 3F) 0.15
	NTCP (%)	0.56 ± 0.30	0.79 ± 0.40	0.77 ± 0.46	(3F vs 4FB) 0.25 (4FB vs FIF) 0.98 (FIF vs 3F) 0.33
Spinal Cord	D_{mean} (Gy)	22.53 ± 3.02	21.63 ± 3.62	21.26 ± 3.59	(3F vs 4FB) 0.75 (4FB vs FIF) 0.95 (FIF vs 3F) 0.57
	D_{max} (Gy)	55.46 ± 8.30	55.89 ± 1.54	53.80 ± 0.96	(3F vs 4FB) 0.97 (4FB vs FIF) 0.00* (FIF vs 3F) 0.00*
	NTCP (%)	0.04 ± 0.02	0.04 ± 0.02	0.03 ± 0.02	(3F vs 4FB) 0.71 (4FB vs FIF) 0.71 (FIF vs 3F) 0.71

Table 6. Dosimetric parameters ± SD for OARs (D_{mean}, D_{max}, $V_{20\ Gy}$ and NTCP) for women with GE cancer: a comparison of 3F, 4FB, and FIF planning techniques

OAR	Parameter	3F	4FB	FIF	p-value
Heart	D_{mean} (Gy)	20.21 ± 5.85	17.63 ± 5.47	16.51 ± 6.06	(3F vs 4FB) 0.45 (4FB vs FIF) 0.85 (FIF vs 3F) 0.20
	NTCP (%)	0.05 ±0.11	0.02 ± 0.05	0.02 ± 0.06	(3F vs 4FB) 0.08 (4FB vs FIF) 0.08 (FIF vs 3F) 0.08
Right kidney	D_{mean} (Gy)	19.13 ± 3.58	13.60 ± 3.09	13.50 ± 3.04	(3F vs 4FB) 0.00* (4FB vs FIF) 0.91 (FIF vs 3F) 0.00*
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.00* (4FB vs FIF) 0.78 (FIF vs 3F) 0.00*
Left kidney	D_{mean} (Gy)	23.59 ± 3.08	21.96 ± 3.19	22.71 ± 3.51	(3F vs 4FB) 0.29 (4FB vs FIF) 0.29 (FIF vs 3F) 0.29
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.61 (4FB vs FIF) 0.61 (FIF vs 3F) 0.61
Right lung	D_{mean} (Gy)	10.54 ± 1.98	10.48 ± 2.02	10.21 ± 1.97	(3F vs 4FB) 0.81 (4FB vs FIF) 0.81 (FIF vs 3F) 0.81
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.63 (4FB vs FIF) 0.63 (FIF vs 3F) 0.63
	$V_{20\ Gy}$ (%)	20.45 ± 3.29	18.98 ± 3.54	18.81 ± 3.58	(3F vs 4FB) 0.48 (4FB vs FIF) 0.99 (FIF vs 3F) 0.40
Left lung	D_{mean} (Gy)	10.08 ± 1.19	9.64 ± 1.51	9.37 ± 1.44	(3F vs 4FB) 0.67 (4FB vs FIF) 0.85 (FIF vs 3F) 0.35
	NTCP (%)	< 0.01	< 0.01	< 0.01	(3F vs 4FB) 0.03* (4FB vs FIF) 0.00 (FIF vs 3F) 0.39
	$V_{20\ Gy}$ (%)	21.77 ± 4.16	20.34 ± 2.97	20.46 ± 4.99	(3F vs 4FB) 0.61 (4FB vs FIF) 0.99 (FIF vs 3F) 0.66

Right breast	D_{mean} (Gy)	28.51 ± 0.91	27.99 ± 0.0.78	27.01 ± 0.76	(3F vs 4FB) 0.29 (4FB vs FIF) 0.01* (FIF vs 3F) 0.00*
Left breast	D_{mean} (Gy)	28.59 ± 0.91	28.04 ± 0.80	27.06 ± 0.75	(3F vs 4FB) 0.26 (4FB vs FIF) 0.01* (FIF vs 3F) 0.00*
Liver	D_{mean} (Gy)	26.90 ± 4.04	30.09 ± 2.73	29.71 ± 2.93	(3F vs 4FB) 0.03* (4FB vs FIF) 0.94 (FIF vs 3F) 0.06
	NTCP (%)	0.57 ± 0.40	0.85 ± 0.44	0.78 ± 0.39	(3F vs 4FB) 0.16 (4FB vs FIF) 0.89 (FIF vs 3F) 0.35
Spinal Cord	D_{mean} (Gy)	22.90 ± 4.92	21.94 ± 5.06	21.86 ± 5.06	(3F vs 4FB) 0.86 (4FB vs FIF) 0.99 (FIF vs 3F) 0.84
	D_{max} (Gy)	57.16 ± 1.84	56.08 ± 1.58	54.12 ± 1.51	(3F vs 4FB) 0.09 (4FB vs FIF) 0.00* (FIF vs 3F) 0.01*
	NTCP (%)	0.04 ± 0.03	0.05 ± 0.04	0.04 ± 0.04	(3F vs 4FB) 0.83 (4FB vs FIF) 0.83 (FIF vs 3F) 0.83

secondary particles, providing several advantages associated with lower MUs.

Based on the data presented in Table 3 for female patients with GE junction cancer, notable differences exist between the FIF technique and both 3F and 4FB regarding D_{mean}, D_{max}, HI, and MU for PTV. These patterns are consistent with the dose delivered to the target in female patients, including D_{mean}, D_{max}, HI, and MU, which aligns with the observations in male patients. Furthermore, there is a significant difference between male and female patients in terms of TCP and MU for PTV, as outlined in Table 4. Specifically, TCP for female patients using the 3F technique exceeds that of males, representing an advantage for female patients. This trend persists for female patients using the FIF technique. Conversely, the MUs for 4FB and FIF techniques are lower for male patients compared to female patients.

Examining the data in Table 5 for male patients with GE junction cancer, notable differences are evident between the FIF and 3F techniques concerning various dosimetric and radiobiological parameters for OARs, including D_{mean} in the right kidney, NTCP for the right kidney, NTCP for the left lung, V20Gy for the left lung, and D_{max} for the spinal cord. Specifically, D_{mean} for the right kidney is lower with the FIF technique compared to the 3F technique, and V20 Gy for the left lung is also reduced with the FIF technique compared to the others. Furthermore, the FIF technique exhibits a lower D_{max} for the spinal cord than the 3F and 4FB techniques, highlighting these as advantages of the FIF technique over its counterparts. Analyzing the data from Table 6 for female patients with GE junction cancer reveals significant differences between the FIF and 3F techniques in terms of D_{mean} in the right kidney, NTCP for the right kidney, Dmean for the left breast, D_{mean} for the right breast, and D_{max} for the spinal cord in OARs. Additionally, distinctions emerge between the FIF and 4FB techniques, particularly regarding D_{mean} in the left and right breast for female patients. Remarkably, the trends in D_{mean} for the right kidney and D_{max} for the spinal cord are consistent between male and female patients. In Table 7, a further difference is observed between male and female patients, specifically concerning NTCP for the right lung and V20 Gy for the right lung, with males demonstrating lower values, indicating an advantage for 3D-CRT treatment among male patients with GE junction cancer.

While there is no single optimal technique for treating GE junction cancer, and the choice of radiation therapy method should be made on a case-by-case basis, conventional techniques are known to reduce the dose to organs at risk, such as the lung and heart [5, 15]. Similarly, in terms of spinal cord protection, Erdem *et al.* [37] suggested that the 3D-

Table 7. Dosimetric parameters ± SD for OARs (D_{mean}, D_{max}, $V_{20\ Gy}$ and NTCP) for patients with GE cancer: a comparison of men and women patients

OAR	Parameter	Gender	3F	p-value	4FB	p-value	FIF	p-value
Heart	D_{mean} (Gy)	Male	23.51 ± 9.38	0.19	21.45 ± 8.23	0.09	20.57 ± 8.54	0.08
		Female	20.21 ± 5.86		17.63 ± 5.47		16.51 ± 6.06	
	NTCP (%)	Male	0.05 ± 0.06	0.39	0.02 ± 0.02	0.33	0.01 ± 0.02	0.30
		Female	0.05 ± 0.11		0.02 ± 0.05		0.02 ± 0.06	
Right kidney	D_{mean} (Gy)	Male	19.35 ± 5.63	0.82	14.48 ± 4.47	0.98	14.34 ± 4.25	0.95
		Female	19.13 ± 3.58		13.60 ± 3.09		13.50 ± 3.04	
	NTCP (%)	Male	< 0.01	0.39	< 0.01	0.98	< 0.01	0.82
		Female	< 0.01		< 0.01		< 0.01	
Left kidney	D_{mean} (Gy)	Male	24.29 ± 7.70	0.98	22.08 ± 6.84	0.72	21.83 ± 7.23	0.33
		Female	23.59 ± 3.80		21.96 ± 3.19		22.71 ± 3.51	
	NTCP (%)	Male	< 0.01	0.98	< 0.01	0.39	< 0.01	0.30
		Female	< 0.01		< 0.01		< 0.01	
Right lung	D_{mean} (Gy)	Male	9.95 ± 3.42	0.07	9.50 ± 3.46	0.03*	9.51 ± 3.45	0.08
		Female	10.54 ± 1.98		10.48 ± 2.03		10.21 ± 1.98	
	NTCP (%)	Male	< 0.01	0.05	< 0.01	0.00*	< 0.01	0.02*
		Female	< 0.01		< 0.01		< 0.01	
	$V_{20\ Gy}$ (%)	Male	17.95 ± 3.00	0.01*	14.76 ± 3.28	0.00*	15.79 ± 3.03	0.02*
		Female	20.46 ± 3.29		18.98 ± 3.55		18.82 ± 3.59	
Left lung	D_{mean} (Gy)	Male	10.72 ± 1.55	0.19	9.89 ± 1.12	0.46	9.75 ± 1.14	0.44
		Female	10.08 ± 1.19		9.64 ± 1.51		9.37 ± 1.44	
	NTCP (%)	Male	< 0.01	0.07	< 0.01	0.00*	< 0.01	0.18
		Female	< 0.01		< 0.01		< 0.01	
	$V_{20\ Gy}$ (%)	Male	24.13 ± 2.79	0.10	21.45 ± 2.53	0.35	21.24 ± 2.57	0.29
		Female	21.78 ± 4.17		20.34 ± 2.98		20.46 ± 5.00	
Liver	D_{mean} (Gy)	Male	25.69 ± 1.19	0.72	29.00 ± 3.63	0.31	28.91 ± 3.55	0.44
		Female	26.90 ± 4.05		30.09 ±2.73		29.71 ± 2.93	
	NTCP (%)	Male	0.56 ± 0.30	0.90	0.79 ± 0.40	0.58	0.77 ± 0.46	0.86
		Female	0.57 ± 0.40		0.85 ± 0.44		0.78 ± 0.39	
Spinal cord	D_{mean} (Gy)	Male	22.53 ± 3.03	0.98	21.64 ± 3.62	0.98	21.26 ± 3.59	0.88
		Female	22.90 ± 4.93		21.95 ± 5.07		21.87 ± 5.06	
	D_{max} (Gy)	Male	55.47 ± 8.30	0.82	55.90 ± 1.54	0.88	53.81 ± 0.96	0.72
		Female	57.16 ± 1.84		56.08 ± 1.59		54.13 ± 1.51	
	NTCP (%)	Male	0.04 ± 0.02	0.72	0.04 ± 0.020	0.72	0.03 ± 0.02	0.54
		Female	0.04 ± 0.03		0.05 ± 0.04		0.04 ± 0.04	

CRT technique, with a D_{max} below 45 Gy, is more effective. Several studies have examined the comparison of radiotherapy outcomes between male and female patients for various organs. Incrocci and Jensen [16] reviewed sexual dysfunction in both male and female patients following pelvic radiotherapy and concluded that pelvic radiotherapy significantly affects sexual function in both genders. Therefore, healthcare professionals should be attentive to sexual dysfunction in patients who have undergone pelvic radiotherapy. Courcy *et al.* [17] conducted a literature review on the effectiveness and outcomes of radiotherapy for both males and females. The results of various studies indicated a small yet significant difference in the responses of the two genders to radiotherapy. Meunier and Marignol [18] conducted a review of various studies, assessing the role of sex as a biological variable in radiotherapy research.

Macdonald *et al.* [19] conducted an evaluation to determine whether gender constitutes a significant prognostic factor and influences outcomes in male and female patients undergoing mastectomy for breast cancer. Their findings indicated that gender did not emerge as a prognostic factor for early-stage breast cancer patients undergoing mastectomy. Page *et al.* [20] evaluated the effects of radiotherapy in male and female patients diagnosed with head and neck cancer. Laaksomaa *et al.* [21] assessed differences in setup accuracy between male and female patients

undergoing radiotherapy for pelvic tumors. Their findings indicated that female patients treated for pelvic tumors exhibited larger positional errors and required larger setup margins compared to their male counterparts.

As a part of our future work, we intend to extend this concept to techniques such as IMRT and VMAT. We will then compare the results with the present study in terms of dose coverage for the PTV and sparing of OARs in both male and female patients for more advanced techniques such as IMRT and VMAT. In this study, we exclusively compared dosimetric and radiobiological parameters in the context of radiotherapy for patients with GE junction cancer. Generally, there were no significant differences observed for most of these parameters. However, it's worth noting that the outcome of radiotherapy may potentially be influenced by gender, and this aspect could serve as a topic for future research in this field.

5. Conclusion

Generally, most dosimetric parameters are similar between male and female patients with GE junction cancer. However, variations were observed in terms of TCP, MU, and certain parameters (such as NTCP and V20Gy for the right lung). Therefore, it is advisable to be more attentive when performing treatment planning for GE junction cancer and to consider the anatomical differences between males and females.

In this study, we exclusively compared dosimetric and radiobiological parameters in radiotherapy for male and female patients with GE junction cancer, and, for the most part, there were no significant differences observed among these parameters. Nevertheless, it's worth considering the possibility that the outcome of radiotherapy may be influenced by gender, making it a potential subject for future research in this field.

Acknowledgments

The authors appreciate Cancer Research Center (Shahid Beheshti University of Medical Sciences) for financial support of this study (with a grant number of: 43003535).

References

1- L. A. Torre, F. Bray, R. L. Siegel, J. Ferlay, J. Lortet-Tieulent, and A. Jemal, "Global cancer statistics, 2012." (in eng), *CA Cancer J Clin*, Vol. 65 (No. 2), pp. 87-108, Mar (2015).

2- Lone Hoffmann *et al.*, "Treatment planning comparison in the PROTECT-trial randomising proton versus photon beam therapy in oesophageal cancer: Results from eight European centres." *Radiotherapy and Oncology*, Vol. 172pp. 32-41, (2022).

3- Yinan Chen, Lei Hu, Hexin Lin, Huangdao Yu, and Jun You, "Serum metabolomic profiling for patients with adenocarcinoma of the esophagogastric junction." *Metabolomics*, Vol. 18 (No. 5), pp. 1-12, (2022).

4- Ruixi Wang, Shiliang Liu, Baoqing Chen, and Mian Xi, "Recent Advances in Combination of Immunotherapy and Chemoradiotherapy for Locally Advanced Esophageal Squamous Cell Carcinoma." *Cancers*, Vol. 14 (No. 20), p. 5168, (2022).

5- G. Mehri-Kakavand *et al.*, "Assessment of Field-in-Field, 3-Field, and 4-Field Treatment Planning Methods for Radiotherapy of Gastro-Esophageal Junction Cancer." (in eng), *J Biomed Phys Eng*, Vol. 12 (No. 5), pp. 439-54, Oct (2022).

6- Abraham J Wu *et al.*, "Expert consensus contouring guidelines for intensity modulated radiation therapy in esophageal and gastroesophageal junction cancer." *International Journal of Radiation Oncology Biology Physics*, Vol. 92 (No. 4), pp. 911-20, (2015).

7- R. Baskar, K. A. Lee, R. Yeo, and K. W. Yeoh, "Cancer and radiation therapy: current advances and future directions." (in eng), *Int J Med Sci*, Vol. 9 (No. 3), pp. 193-9, (2012).

8- Anurag Chandra *et al.*, "Feasibility of using intensity-modulated radiotherapy to improve lung sparing in treatment planning for distal esophageal cancer." *Radiotherapy and Oncology*, Vol. 77 (No. 3), pp. 247-53, (2005).

9- Yi-Jen Chen *et al.*, "Helical tomotherapy for radiotherapy in esophageal cancer: a preferred plan with better conformal target coverage and more homogeneous dose distribution." *Medical Dosimetry*, Vol. 32 (No. 3), pp. 166-71, (2007).

10- Liam Van Benthuysen, Lee Hales, and Matthew B Podgorsak, "Volumetric modulated arc therapy vs. IMRT for the treatment of distal esophageal cancer." *Medical Dosimetry*, Vol. 36 (No. 4), pp. 404-09, (2011).

11- Nagarajan Vivekanandan, Padmanaban Sriram, S. A. Syam Kumar, N R Bhuvaneswari, and K. Saranya, "Volumetric modulated arc radiotherapy for esophageal cancer." *Medical dosimetry: official journal of the American Association of Medical Dosimetrists*, Vol. 37 1pp. 108-13, (2012).

12- Farzaneh Allaveisi and Amir Nami Moghadam, "Comparison between the four-field box and field-in-field techniques for conformal radiotherapy of the esophagus using dose–volume histograms and normal tissue complication probabilities." *Japanese journal of radiology,* Vol. 35pp. 327-34, (2017).

13- Yuchuan Fu *et al.*, "Dosimetric effect of beam arrangement for intensity-modulated radiation therapy in the treatment of upper thoracic esophageal carcinoma." *Medical Dosimetry,* Vol. 42 (No. 1), pp. 47-52, (2017).

14- C-Y Lin *et al.*, "Dosimetric and efficiency comparison of high-dose radiotherapy for esophageal cancer: volumetric modulated arc therapy versus fixed-field intensity-modulated radiotherapy." *Diseases of the Esophagus,* Vol. 27 (No. 6), pp. 585-90, (2014).

15- Ziad Simon Fawaz *et al.*, "What is the optimal radiation technique for esophageal cancer? A dosimetric comparison of four techniques." *Cureus,* Vol. 10 (No. 7), (2018).

16- Luca Incrocci and Pernille Tine Jensen, "Pelvic radiotherapy and sexual function in men and women." *The journal of sexual medicine,* Vol. 10pp. 53-64, (2013).

17- Louis De Courcy, Eva Bezak, and Loredana G Marcu, "Gender-dependent radiotherapy: The next step in personalised medicine?" *Critical Reviews in Oncology/Hematology,* Vol. 147p. 102881, (2020).

18- Armelle Meunier and Laure Marignol, "The radiotherapy cancer patient: female inclusive, but male dominated." *International Journal of Radiation Biology,* Vol. 96 (No. 7), pp. 851-56, (2020).

19- G Macdonald, C Paltiel, IA Olivotto, and S Tyldesley, "A comparative analysis of radiotherapy use and patient outcome in males and females with breast cancer." *Annals of oncology,* Vol. 16 (No. 9), pp. 1442-48, (2005).

20- BR Page *et al.*, "Gender differences in radiation therapy effects in male and female patients with head and neck cancer." *International Journal of Radiation Oncology, Biology, Physics,* Vol. 100 (No. 5), pp. 1400-01, (2018).

21- Marko Laaksomaa, Mika Kapanen, Tapio Tulijoki, Seppo Peltola, Simo Hyödynmaa, and Pirkko-Liisa Kellokumpu-Lehtinen, "Evaluation of overall setup accuracy and adequate setup margins in pelvic image-guided radiotherapy: comparison of the male and female patients." *Medical Dosimetry,* Vol. 39 (No. 1), pp. 74-78, (2014).

22- Clifton D Fuller *et al.*, "Prospective randomized double-blind pilot study of site-specific consensus atlas implementation for rectal cancer target volume delineation in the cooperative group setting." *International Journal of Radiation Oncology Biology Physics,* Vol. 79 (No. 2), pp. 481-89, (2011).

23- J Chavaudra and A Bridier, "Definition of volumes in external radiotherapy: ICRU reports 50 and 62." *Cancer radiotherapie: journal de la Societe francaise de radiotherapie oncologique,* Vol. 5 (No. 5), pp. 472-78, (2001).

24- Mohamad Pursamimi, Mahdi Ghorbani, Wrya Parwaie, Ahmad Shakeri, and Ali Soleimani Meigooni, "Evaluation of field-in-field, three-field, and four-field techniques for treatment planning of radiotherapy of pancreatic cancer." *Journal of Cancer Research and Therapeutics,* Vol. 18 (No. 1), pp. 190-99, (2022).

25- Hiram A Gay and Andrzej Niemierko, "A free program for calculating EUD-based NTCP and TCP in external beam radiotherapy." *Physica Medica,* Vol. 23 (No. 3-4), pp. 115-25, (2007).

26- Kazuhiro Ohtakara, S Hayashi, and H Hoshi, "The relation between various conformity indices and the influence of the target coverage difference in prescription isodose surface on these values in intracranial stereotactic radiosurgery." *The British journal of radiology,* Vol. 85 (No. 1014), pp. e223-e28, (2012).

27- Kunzhi Chen *et al.*, "Application of auto-planning in radiotherapy for breast cancer after breast-conserving surgery." *Scientific Reports,* Vol. 10 (No. 1), p. 10927, (2020).

28- Lu Wang *et al.*, "Dosimetric and radiobiological comparison of external beam radiotherapy using simultaneous integrated boost technique for esophageal cancer in different location." *Frontiers in oncology,* Vol. 9p. 674, (2019).

29- Behnam Ghadimi, Nasrollah Jabbari, Laya Karimkhani, and Kamal Mostafanezhad, "Field-in-field technique improves the dosimetric outcome of treatment plans compared with the three-dimensional conformal radiation therapy for esophageal cancer radiotherapy." *International Journal of Hematology and Oncology,* Vol. 32 (No. 3), pp. 079-85, (2018).

30- Duygu Baycan, Didem Karacetin, Ayben Y Balkanay, and Yücel Barut, "Field-in-field IMRT versus 3D-CRT of the breast. Cardiac vessels, ipsilateral lung, and contralateral breast absorbed doses in patients with left-sided lumpectomy: a dosimetric comparison." *Japanese journal of radiology,* Vol. 30pp. 819-23, (2012).

31- Masahiro Sasaoka and Tomoyuki Futami, "Dosimetric evaluation of whole breast radiotherapy using field-in-field technique in early-stage breast cancer." *International journal of clinical oncology,* Vol. 16pp. 250-56, (2011).

32- Andrzej Niemierko, "A generalized concept of equivalent uniform dose (EUD)." *Med Phys,* Vol. 26 (No. 6), p. 1100, (1999).

33- Francisco Cutanda Henríquez and Silvia Vargas Castrillón, "A quality index for equivalent uniform dose." *Journal of medical physics/Association of Medical Physicists of India,* Vol. 36 (No. 3), p. 126, (2011).

34- Suresh Rana *et al.*, "Dosimetric study of uniform scanning proton therapy planning for prostate cancer patients with a metal hip prosthesis, and comparison with

volumetric-modulated arc therapy." *Journal of applied clinical medical physics*, Vol. 15 (No. 3), pp. 335-48, (2014).

35- A Shanei, A Amouheidari, I Abedi, A Kazemzadeh, and A Jaafari, "Radiobiological comparison of 3D conformal and intensity modulated radiation therapy in the treatment of left-sided breast cancer." *International Journal of Radiation Research*, Vol. 18 (No. 2), pp. 315-22, (2020).

36- A Mesbahi, N Rasouli, and M Mohammadzadeh, "Comparison of radiobiological models for radiation therapy plans of prostate cancer: Three-dimensional conformal versus intensity modulated radiation therapy." *Journal of biomedical physics & engineering*, Vol. 9 (No. 3), p. 267, (2019).

37- Hatice Erdem, Timur Koca, Nina Tunçel, and Aylin Fidan Korcum, "Comparison of three dimensional conformal, intensity modulated and hybrid intensity modulated planning techniques for thorasic esophageal cancer." *Turkiye Klinikleri Journal of Medical Sciences*, Vol. 40, (2020).