Iranian Journal of Medical Physics

ijmp.mums.ac.ir

On Prediction of Cardio-Pulmonary Complications during Hypofractionated versus Conventional Fractionated Regimens of Left Breast Radiation Therapy Using Monte Carlo and Collapsed Cone Convolution Based Algorithms

Sepideh Omidvar[1], Kamal Mostafanezhad[2], Ahad Zeinali[1]*

1. Department of Medical Physics, Urmia University of Medical Sciences, Urmia, Iran
2. Omid Research and Treatment Center, Urmia, Iran

ARTICLE INFO

Article type:
Original Paper

Article history:
Received: Jan 13, 2022
Accepted: July 02, 2022

Keywords:
Breast Neoplasms
Pulmonary Heart Disease
Radiation Dose
Hypofractionation
Radiotherapy Planning
Computer-Assisted

ABSTRACT

Introduction: Due to the challenge of choosing the optimal treatment regimen as well as the accurate dose calculation algorithm (DCA), this study aimed to evaluate the DCAs to compare the conventional fractionation radiotherapy (CFRT) and hypofractionation radiotherapy (HFRT) of breast cancer (BC) in the prediction of cardio-pulmonary complications.

Material and Methods: For 19 patients with left-sided BC, treatment regimens, CFRT (50Gy/25frs) vs. HFRT (42.5Gy/16frs), were simulated. Normal tissue complication probability (NTCP) and tumor control probability (TCP) values for each regimen using radiobiological models were calculated via Monte Carlo (MC) and Collapsed Cone Convolution (CCC) algorithms. For statistical comparison of the results obtained from the regimens and algorithms, the t-test and Wilcoxon test were used in SPSS Statistics. Statistical significance was defined as $p<0.05$.

Results: The mean NTCP and TCP calculated in CFRT and HFRT were as follows: cardiac mortality (MC: CFRT=0.0374±0.0134 vs. HFRT=0.0173±0.0066; $p<0.001$) and (CCC: CFRT=0.0373±0.0134 vs. HFRT=0.0168±0.0064; $p<0.001$), pneumonitis (MC: CFRT=0.1201±0.0322 vs. HFRT=0.0756±0.0221; $p<0.001$) and (CCC: CFRT=0.1131±0.0310 vs. HFRT=0.0697±0.0120; $p<0.010$), and TCP (MC: CFRT=0.9979±0.0087 vs. HFRT=0.9997±0.0092; $p=0.593$) and (CCC: CFRT=0.9982±0.0029 vs. HFRT=0.9986±0.0016; $p=0.821$).

Conclusion: The comparison of CFRT and HFRT using MC and CCC algorithms showed that the risk of cardiac mortality and pneumonitis in CFRT was significantly higher than in HFRT, and TCP was not significantly different in the two regimens. Applications of MC-based DCAs along with suitable biological parameters can help physicists in the prediction of radiation-induced complications accurately and precisely.

►*Please cite this article as:*
Omidvar S, Mostafanezhad K, Zeinali A. On Prediction of Cardio-Pulmonary Complications during Hypofractionated versus Conventional Fractionated Regimens of Left Breast Radiation Therapy Using Monte Carlo and Collapsed Cone Convolution Based Algorithms. Iran J Med Phys 2023; 20: 168-176. 10.22038/IJMP.2022.62939.2066.

Introduction

Breast cancer (BC) is the most common neoplasm among women. Radiotherapy (RT) is effective in treating BC by improving tumor control and survival. In RT of left BC, because of the proximity of breast tissue to the heart and left lung, the absorption of radiation by these tissues is very challenging. The most common lung injury, radiation pneumonitis, is known as early to intermediate toxicity. That corresponds to various pathophysiological in lung tissue and usually occurs 1-6 months after RT with symptoms such as dry cough, fever, chest pain, and in severe cases may lead to death due to respiratory failure. Absorption of radiation by heart tissue may lead to long-term heart damage and increase the risk of cardiac mortality[1-3].

Conventional fractionation radiotherapy (CFRT) is a standard and common regimen in RT for early-stage BC after breast-conserving surgery (BCS) (50Gy/25frs over 5 weeks). In contrast, the hypofractionation radiotherapy (HFRT) regimen (40_44Gy/15_16frs over 3 weeks) has received much attention by reducing the overall dose and overall treatment time. Extensive studies have been conducted to compare the regimens of CFRT and HFRT of patients with BC [4-8]. Normal tissue complication probability (NTCP) and tumor control probability (TCP) are biological-based parameters used as complementary options in many treatment planning systems (TPSs). Using these parameters, radiation oncologists and *radiation* physicists can predict treatment outcomes with better tumor control (TCP close to one) and the fewest

*Corresponding Author: Tel: +98-9143434042; Email: ahadzeinali4042@gmail.com

complications in normal tissues (NTCP close to zero) before starting the treatment process [7-9]. These parameters can be calculated using some equivalents and formulas introduced and used by researchers in experimental studies [9, 10].

Currently, predicting tissue complications after RT is possible more accurately and precisely using powerful model-based dose calculation algorithms (DCAs) in advanced TPSs. However, model-based DCAs do not perform precisely in the field of BCs and RT of the thorax region with the presence of different tissues, such as the bony thorax, muscles, and lungs with different densities and inhomogeneities. Consequently, some corrections are necessary regarding calculation errors, thus alternative DCAs should be used. Recent studies have shown that the application of Monte Carlo (MC)-based DCAs for the evaluation of dose distributions will be useful, especially in the field of inhomogeneities [11, 12].

With the effectiveness of HFRT in reducing the total dose to patients and diminishing total treatment time and costs, the HFRT will be a more attractive approach for researchers, physicians, and patients in the case of maintaining acceptable treatment results. The purpose of this study evaluated the DCAs of MC and CCC to compare the CFTR and HFRT of the left BC in the prediction of cardio-pulmonary complications and tumor control. This study was conducted due to the lack of studies on the prediction of cardio-pulmonary complications during left breast RT using MC in HFRT. Different biological models introduced by researchers were used for predicting NTCP for cardio-pulmonary complications and TCP in two regimens, HFRT and CFRT [9,10]. Consequently, some dosimetric parameters are derived from TPS for the completion of the calculation of NTCP and TCP. Dosimetric parameters derived from MC and Collapsed Cone Convolution (CCC) DCAs used in Monaco TPS were segregated here. A homemade code was developed in MATLAB for calculating NTCP and TCP by biological and dosimetric parameters for each algorithm, followed by analyzing and comparing the results.

Materials and Methods

Patients' characteristics

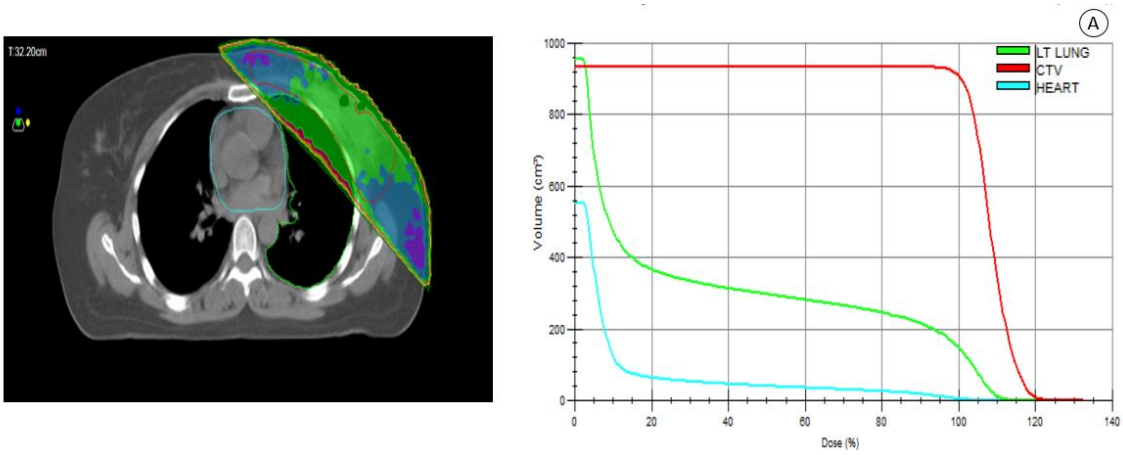
Computed tomography (CT) scan data of 19 female patients with early-stage left-sided BC were used. Selected patients underwent a mastectomy or BCS. Patients were chosen from those referred to the Radiation Oncology Department of Omid Hospital in Urmia, Iran, from January 2019 to September 2020. The research ethics committee of Urmia University of Medical Sciences approved the study protocol and the research team considered the confidentiality of patient information.

Contouring of the tumor and organs at risk (OARs)

Contouring target and non-target volumes, such as clinical target volume (CTV), heart, and left lung, was performed according to the criteria of the International Commission of Radiation Units (ICRU) and Measurements Reports 50 and 62 [13,14]. All the contours were delineated by a radiation oncologist who collaborated with a qualified radiation physicist on patients' CT images, which were transferred from archive software to MONACO-5 (version 5.11.03, Crawley, UK) TPS.

Treatment planning

A 6 MV X-ray photon beam was used by considering two tangential fields. Two administered doses for two RT regimens, CFRT vs. HFRT, were simulated for each patient's plan. The administered dose for CFRT and the second dose for HFRT were 50Gy/25frs and 42.5Gy/16frs, respectively. Calculations were performed using two DCAs, MC vs. CCC, and dosimetric data were derived from the dose-volume histogram (DVH) (Figure 1).



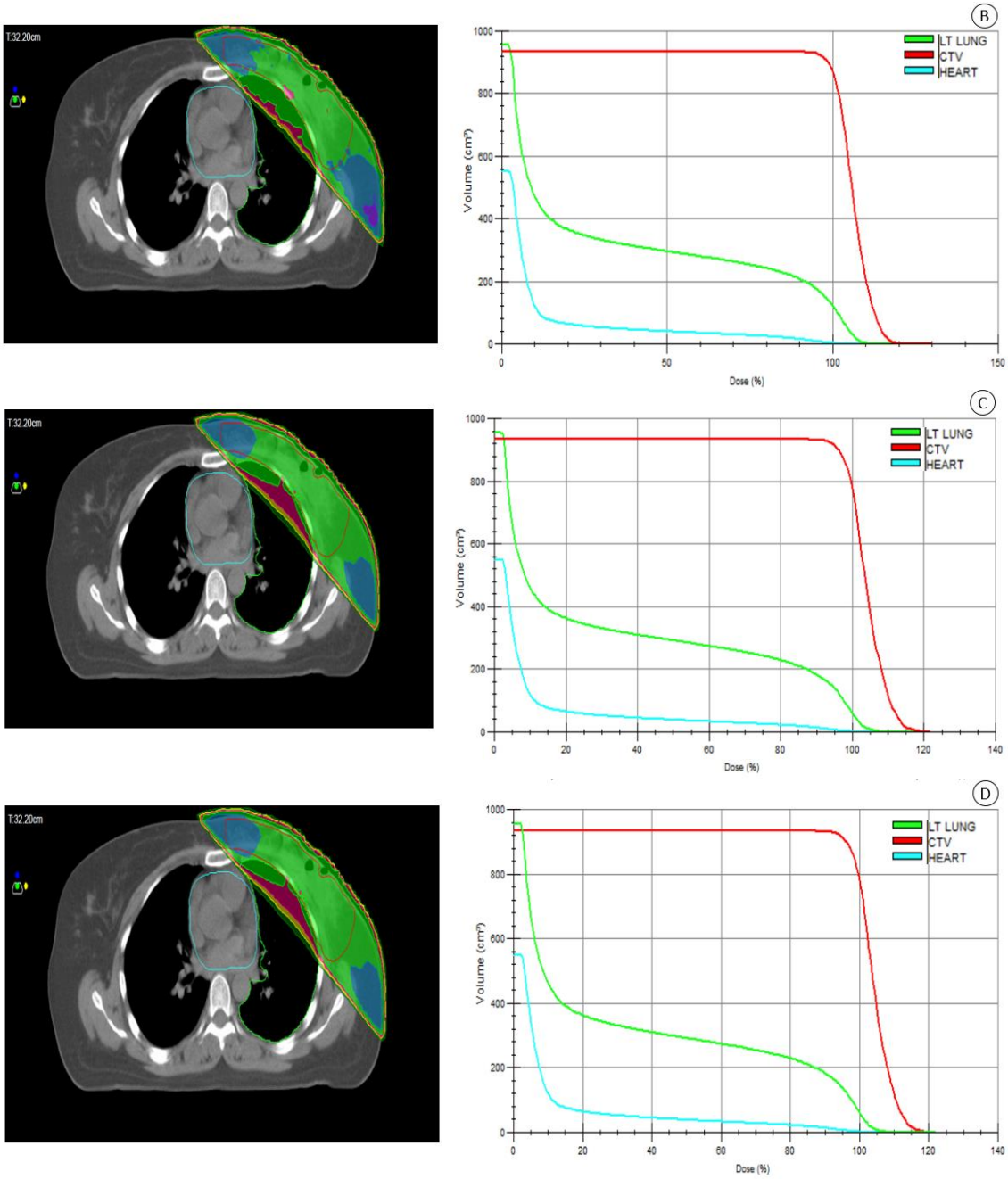


Figure 1. The plans of two tangential fields in the RT of left-sided BC and the related DVHs; (A) CFRT used in MC; (B) the HFRT used in MC; (C) CFRT used in CCC; (D) HFRT used in CCC.

TCP and NTCP calculation

For calculating NTCP and TCP, a homemade computer code was developed in MATLAB (MATLAB-Rb 2018). In addition to dosimetric data extracted from TPS, two radiobiological-based models, the Niemierko model [9] and the Relative Seriality (RS) model [10] were used to calculate TCP and NTCP (cardiac mortality and pneumonitis), respectively. The mathematical formulas correspond to each radiobiological model accompanied by dosimetric parameters used in the developed code for the calculation of NTCP and TCP and the results were derived for each patient's plan.

The following formulas were used for the calculation of NTCP according to the RS model:

$$\mathrm{NTCP} = \{1 - \prod_{i=1}^{n}[1 - P(D_i)^s]^{\Delta v_i}\}^{\frac{1}{s}} \quad (1)$$

$$\mathrm{P(Di)} = 2^{-\exp\left\{e\gamma\left(1-\frac{D_i}{D_{50}}\right)\right\}} \quad (2)$$

In equations (1) and (2), n is the number of DVH dose bins, γ is the maximum slope of the dose-response curve, D_{50} is the dose leading to 50% of complications, and Di is the absorbed dose in each dose bin, $\Delta Vi = Vi/V$ where Vi is the volume of each dose bin that receiving dose D_i, V is the total volume of the organ, and P(Di) is the probability of complication due to the

irradiation of the relative volume Vi at the dose Di described by an approximation of Poisson statistics. The value of the relative seriality factor, s (0≤s≤1), depends on the structure of the organ. In an organ that has a secret structure, it is close to one, in which case the whole organ loses its function by damaging one of the functional units. These parameters in the NTCP calculation were pneumonitis (D_{50}=34Gy, γ=0.9, s=0.06) [15] and cardiac mortality risk (D_{50}=52.3Gy, γ=1.28, s=1) [10].

The following formula was used for the calculation of TCP according to the Niemierko model:

$$TCP = \frac{1}{1+\left(\frac{TCD_{50}}{EUD}\right)^{4\gamma_{50}}} \quad (3)$$

In the Niemierko model, the equivalent uniform dose (EUD) [9] is defined as:

$$EUD = \left(\sum_{i=1}(v_i D_i^a)\right)^{\frac{1}{a}} \quad (4)$$

In equations (3) and (4), the TCD_{50} is the tumor dose to control 50% of the tumors when the tumor is homogeneously irradiated [9], γ_{50} describes the slope of the dose-response curve in D_{50}, and a is a parameter that is specific to the normal structure or tumor, which is a large negative number for the tumor, v_i is unitless and represents the i'th partial volume receiving dose Di in Gy. Since the relative volume of the whole structure of interest corresponds to 1, the sum of all partial volumes vi will equal 1. These parameters in the TCP calculation were (γ_{50}=1.3, TCD_{50}=30.89Gy, a=-7.2) [16].

Statistical analysis

Statistical significance was defined as p<0.05. SPSS Statistics (version 17.0; IBM) was used for the analysis of data. The hypothesis of normality of the data was examined in the inferential statistics. Based on the null hypothesis, "data have a normal distribution=H0", against the alternative hypothesis "data do not have a normal distribution=H1". The paired sample t-test was used when H0 was established, and if H1 was established the nonparametric test (Wilcoxon signed-rank test) was used to compare the mean value of the extracted data. The normality of the data was tested by the Shapiro–Wilk test and the value of the skewness coefficient was also calculated here.

Flowchart related to material and methods is described in Figure 2.

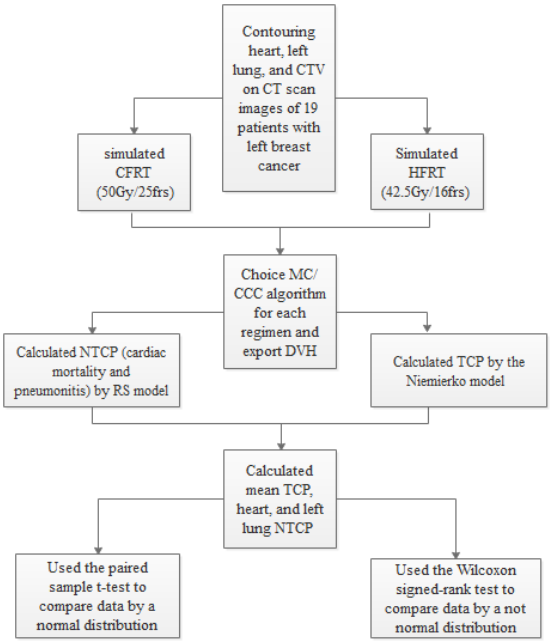
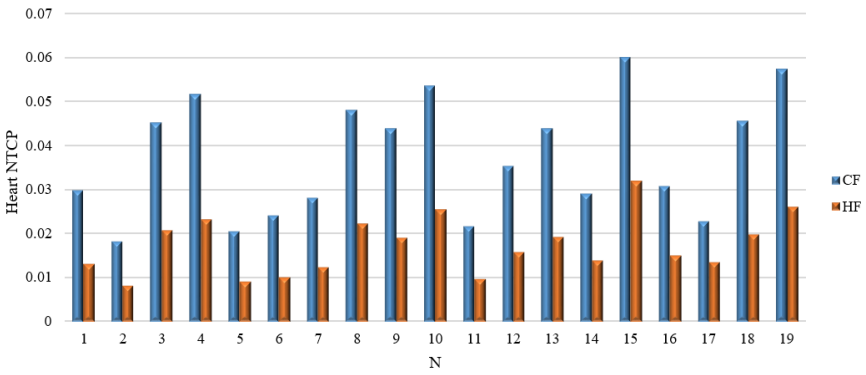


Figure 2. The flowchart related to methods and materials.

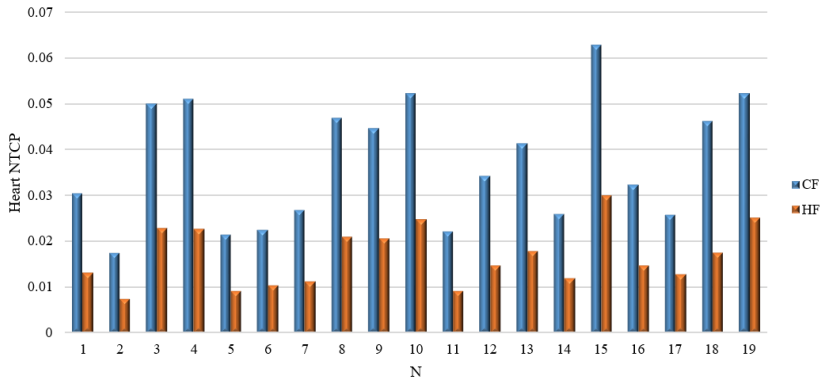
Results

The NTCP and TCP values of 19 patients based on the CFRT and HFRT in the MC and CCC algorithms are depicted in Figure 3. The median and also mean values of heart NTCP, lung NTCP, and TCP in two algorithms for CFRT and HFRT calculated. Then the normality test of data considering standard deviation (SD), and standard error (SE) was performed and listed in Table 1. Table 2 described the Shapiro–Wilk, and the skewness coefficient to test the data normality in the MC and CCC algorithms. Based on this test for (p>0.05) and small values of the skewness coefficient, the data have a normal distribution. In Table 3, the t-test and Wilcoxon test were used to compare the mean value of NTCP and TCP for data with normal distribution and non-normal distribution. In this table, t stat and z stat are the values of statistics in the t-test and Wilcoxon test.

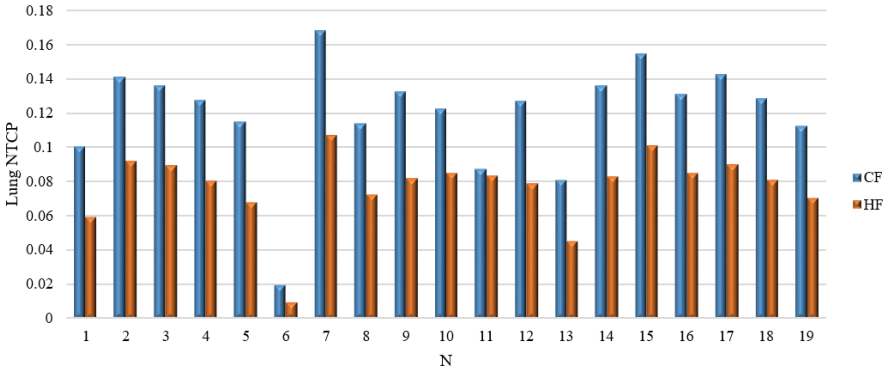
A



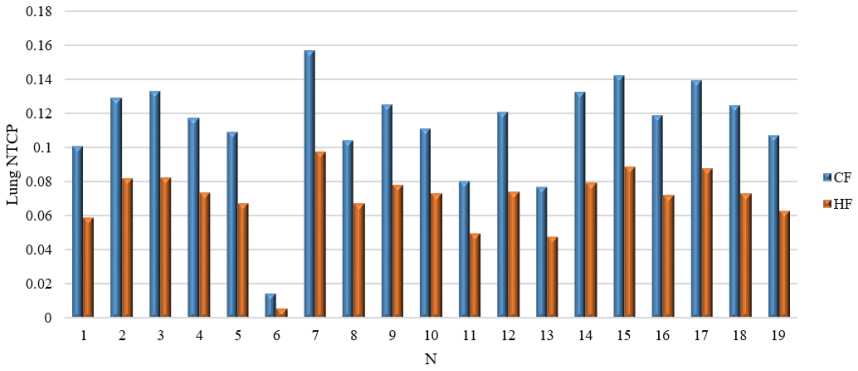
B


Heart NTCP
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
N
CF
HF

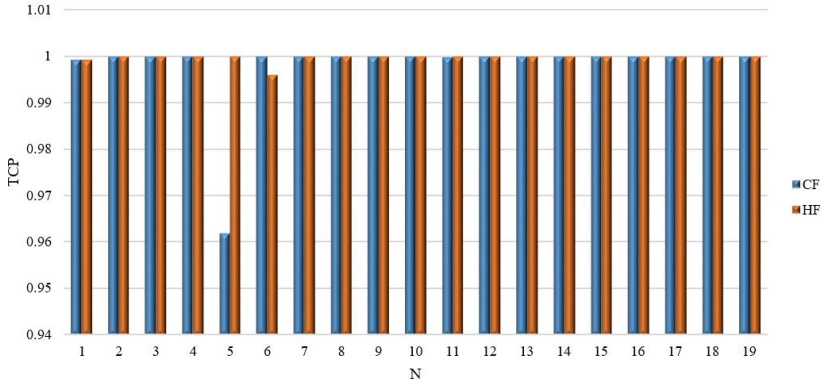
C


Lung NTCP
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
N
CF
HF

D


Lung NTCP
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
N
CF
HF

E


TCP
1.01
1
0.99
0.98
0.97
0.96
0.95
0.94
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
N
CF
HF

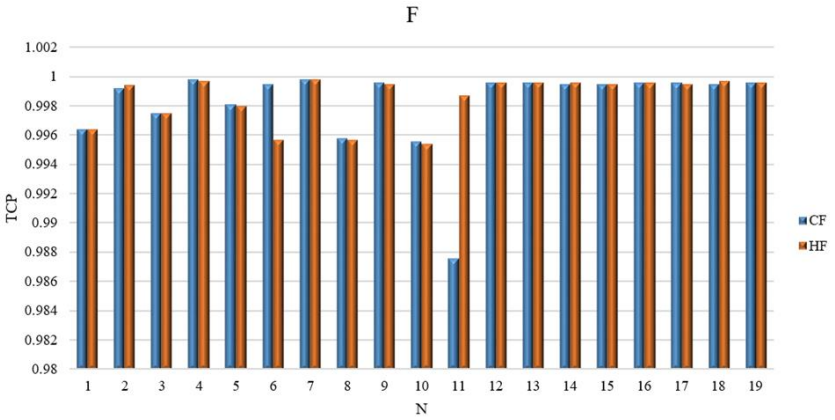


Figure 3. Comparison of NTCP and TCP in CFRT and HFRT using MC and CCC algorithms in 19 patients; (A) Heart NTCP using MC algorithm; (B) Heart NTCP using CCC algorithm; (C) Left lung NTCP using MC algorithm; (D) Left lung NTCP using CCC algorithm; (E) TCP using MC algorithm; (F) TCP using CCC algorithm. The horizontal axis is the number of patients, and the vertical axis is the mean NTCP and TCP.

Table 1. The values of mean ±SD, median, and SE of cardiac mortality, pneumonitis, and TCP

	Heart NTCP (cardiac mortality)				Left lung NTCP (pneumonitis)				TCP			
	MC		CCC		MC		CCC		MC		CCC	
	CFRT	HFRT	CFRT	HFRT	CFRT	HFRT	CFRT	HFRT	CFRT	HFRT	CFRT	HFRT
Mean	0.0374	0.0173	0.0373	0.0168	0.1201	0.0756	0.1131	0.0697	0.9979	0.9997	0.9982	0.9986
SE	0.0031	0.0015	0.0031	0.0015	0.0074	0.0051	0.0071	0.0045	0.0020	0.0002	0.0007	0.0004
Median	0.0355	0.0158	0.0343	0.0148	0.1277	0.0822	0.1190	0.0732	1	1	0.9995	0.9995
CI (95%) $\frac{Lower}{Upper}$	$\frac{0.0310}{0.0439}$	$\frac{0.0142}{0.0205}$	$\frac{0.0308}{0.0437}$	$\frac{0.0137}{0.0168}$	$\frac{0.1046}{0.1356}$	$\frac{0.0649}{0.0862}$	$\frac{0.0981}{0.1280}$	$\frac{0.0601}{0.0793}$	$\frac{0.9937}{1.0021}$	$\frac{0.9993}{1.0002}$	$\frac{0.9968}{0.9996}$	$\frac{0.9978}{0.9993}$

Table 2. Data normality test in CFRT and HFRT using MC and CCC algorithms

	Regimens and		Shapiro-Wilk Test	Skewness
Heart NTCP (cardiac mortality)	MC	CFRT	0.184	0.167±0.524
	CCC	CFRT	0.192	0.204±0.524
Lung NTCP (pneumonitis)	MC	CFRT	<0.050	-1.718±0.524
	CCC	CFRT	<0.010	-1.842±0.524
TCP	MC	CFRT	<0.001	-4.356±0.524
	CCC	CFRT	<0.001	-2.960±0.524

Table 3.Comparison of the regimens (CFRT vs. HFRT) and algorithms (MC vs. CCC) for the mean values of NTCP (heart and left lung) and TCP by the paired sample t-test and Wilcoxon signed-rank test.

			t-test			Wilcoxon test				
			Heart NTCP (cardiac mortality)			Lung NTCP (pneumonitis)			TCP	
Algorithms and Regimens			Mean±SD	t stat	p-value	Mean±SD	z stat	p-value	Mean±SD	z stat	p-value
MC	CFRT	HFRT	(0.0374±0.0134) (0.0173±0.0066)	12.257	<0.001	(0.1201±0.0322) (0.0756±0.0221)	-3.823	<0.001	(0.9979±0.0087) (0.9997±0.0092)	-0.535	0.593
CCC	CFRT	HFRT	(0.0373±0.0134) (0.0168±0.0064)	12.499	<0.001	(0.1131±0.0310) (0.0697±0.0120)	-3.058	<0.010	(0.9982±0.0029) (0.9986±0.0016)	-0.227	0.821
CFRT	MC	CCC	(0.0374±0.0134) (0.0373±0.0134)	0.317	>0.050	(0.1201±0.0322) (0.1131±0.0310)	-3.783	<0.001	(0.9979±0.0087) (0.9982±0.0029)	-3.073	<0.010
HFRT	MC	CCC	(0.0173±0.0066) (0.0168±0.0064)	2.309	<0.050	(0.0756±0.0221) (0.0697±0.0120)	-2.938	<0.010	(0.9997±0.0092) (0.9986±0.0016)	-3.834	<0.001

Heart NTCP (cardiac mortality)

Based on Table 1 the mean values of heart NTCP in MC and CCC algorithms were respectively 0.0374±0.0134 and 0.0373±0.0134 for CFRT, and 0.0173±0.0066 and 0.0168±0.0064 for HFRT. The results of a normality hypothesis test of data in the CCC and MC algorithms were p>0.05 for the CFRT and HFRT in the Shapiro-Wilk test. Moreover, data had a natural distribution due to the small values of the skewness coefficient (Table 2), which confirmed H0. Hence, we used the t-test to compare the mean values of heart NTCP in CFRT and HFRT via MC and CCC algorithms and presented the results in Table 3. In this table, the mean values of heart NTCP in CFRT vs. HFRT were 0.0374±0.0134 vs. 0.0173±0.0066 for MC

(p<0.001), and 0.0373±0.0134 vs. 0.0168±0.0064 for CCC (p<0.001) and the mean values of heart NTCP in MC vs. CCC algorithms were 0.0374±0.0134 vs. 0.0373±0.0134 for CFRT (p>0.050), and 0.0173±0.0066 vs. 0.0168±0.0064 for HFRT (p<0.050).

Left lung NTCP (pneumonitis)

Based on Table 1 the mean values of left lung NTCP in MC and CCC algorithms were respectively 0.1201±0.0322 and 0.1131±0.0310 for CFRT, and 0.0756±0.0221 and 0.0697±0.0120 for HFRT. The results of the normality test of data in all cases were p<0.05 (Table 2), therefore data had a non-normal distribution, thus confirming H1. We used the nonparametric test (Wilcoxon test) to compare the mean values of left lung NTCP in CFRT and HFRT via MC and CCC algorithms and presented the results in Table 3. In this table, the mean values of left lung NTCP in CFRT vs. HFRT were 0.1201±0.0322 vs. 0.0756±0.0221 for MC (p<0.001), and 0.1131±0.0310 vs. 0.0697±0.0120 for CCC (p<0.01) and the mean values of left lung NTCP in MC vs. CCC algorithms were 0.1201±0.0322 vs. 0.1131±0.0310 for CFRT (p<0.001), and 0.0756±0.0221 vs. 0.0697±0.0120 for HFRT (p<0.01).

TCP

Based on Table 1 the mean values of TCP in MC and CCC algorithms were respectively 0.9979±0.0087 and 0.9982±0.0029 for CFRT, and 0.9997±0.0092 and 0.9986±0.0016 for HFRT. The results of the normality test of data were significant in all cases p<0.001 (Table 2). Besides, high values of the skewness coefficient (Table 2) revealed a non-normal distribution of data. Therefore, confirmed H1. We used the nonparametric test (Wilcoxon test) to compare the mean values of TCP in CFRT and HFRT via MC and CCC algorithms and represented the results in Table 3. In this table, the mean values of TCP in CFRT vs. HFRT were 0.9979±0.0087 vs. 0.9997±0.0092 for MC (p=0.593), and 0.9982±0.0029 vs. 0.9986±0.0016 for CCC (p=0.821) and the mean values of TCP in MC vs. CCC algorithms were 0.9979±0.0087 vs. 0.9982±0.0029 for CFRT (p<0.01), and 0.9997±0.0092 vs. 0.9986±0.0016 for HFRT (p<0.001).

Discussion

Recent studies have shown that TCP and NTCP are well-known tools as radiobiological indices for the evaluation of tumor control and the prediction of normal tissue complications during RT. During the last decade, extensive studies indicated that DCAs using appropriate organ-specific biological models and parameters in TPSs have a considerable role in the calculations of NTCP and TCP [7, 8,17,18].

The main goal of this study was the prediction of cardio-pulmonary complications during HFRT versus CFRT of left breast radiation therapy using MC and CCC-based algorithms. The MC algorithm is more accurate and precise than the CCC, especially in dose calculation in heterogeneous environments; however, the CCC algorithm is especially preferred in clinics because CCC calculations take less time than the MC [19]. In addition, we tried to evaluate the effects of different radiobiological models along with dosimetric parameters in TCP and NTCP calculations. For this purpose, two biological models, the RS model and the Niermieko model used to estimate NTCP and TCP. Because of the non-normal distribution nature of data in the calculation of left lung NTCP, the Wilcoxon test was used to compare mean left lung NTCP in the CFRT and HFRT and the MC and CCC algorithms. Our results showed that the mean values of left lung NTCP for the MC algorithm were: CFRT=0.1201 vs. HFRT=0.0756 (p<0.001) and for the CCC algorithm were: CFRT=0.1131 vs. HFRT=0.0697 (p<0.01) (Figure 4A). Our results confirmed that the predicted values for RT-induced pneumonitis, for all DCAs and biological models in HFRT are lesser than CFRT. So in the field of RT-induced pulmonary complications, HFRT is less complicated and safer than CFRT. These results are well compared to the results reported by: Li et al. (2004), and Astudillo et al. (2015) [7,8].

Because of the normal distribution of data in the calculation of heart NTCP, the t-test was used to compare mean values of NTCP in the CFRT and HFRT and the MC and CCC algorithms. Our results demonstrated that the mean values of heart NTCP using MC algorithm were: CFRT=0.0374 vs. HFRT=0.0173 and for CCC algorithm were: CFRT=0.0373 vs. HFRT=0.0168 (Figure 4B). So in the field of RT-induced cardiac complications similar to pulmonary complications, the HFRT is less complicated and safer than CFRT (p<0.001). Our results are consistence with the results reported by James et al. (2018) and Applet et.al (2013) [4-5]. James et.al compared the risks of cardiac complications in RT from BCS or mastectomy in CFRT (50Gy/25frs) and HFRT (42.5Gy/16frs) in 220 and 281 patients, respectively. After 10 years of follow-up, they reported 27 RT-induced cardiac events. They eventually reported that cardiac risks were equally low in HFRT groups [4]. Applet et al. Compared CFRT (50Gy/25frs) with four different HFRTs (40Gy/15frs, 39Gy/13frs, 42.5Gy/16frs, and 41.6Gy/13frs) in patients with left BC after RT. Cardiac toxicity was lower than CFRT in all HFRT regimens, which confirms our results [5]. Also, research by Nozaki et al. Showed that HFRT is a standard and safe treatment for fibrosis, pneumonitis, and heart damage [6].

Although the TCP values in both RT regimens for MC and CCC calculations are about the same, however in each regimen alone, the calculated TCPs for different algorithms are different. According to our results listed in Table 3, in the CFRT, the mean TCP in the CCC is higher than the MC (p<0.010), and in the HFRT, the mean TCP in the MC algorithm is higher than the CCC algorithm (p<0.001). Based on the results listed in table 3, in CFRT, no significant difference was observed between MC and CCC algorithms in terms of mean heart NTCP (p>0.050). However, in HFRT, the mean heart NTCP in the MC is higher than in the CCC (p<0.050). Also, the values listed in Table 3 show that

in the CFRT, the mean left lung NTCP in the MC is higher than in the CCC ($p<0.001$), and in the HFRT, the mean lung NTCP in the MC is higher than the CCC ($p<0.010$). These differences may be because the NTCP and TCP are dependent on biological parameters. Some studies have suggested that there may be other biologically effective parameters in the calculation of TCP and NTCP to achieve a model with more accurate biological optimization and evaluation to predict tissue biophysical response and thus Calculated TCP and NTCP more accurately [19]. On the other hand, the MC and CCC algorithms in compared CFRT and HFRT provide similar performance and results. According to the results, the use of these algorithms is unobstructed and both work carefully in calculating the dose and reducing cardio-pulmonary complications.

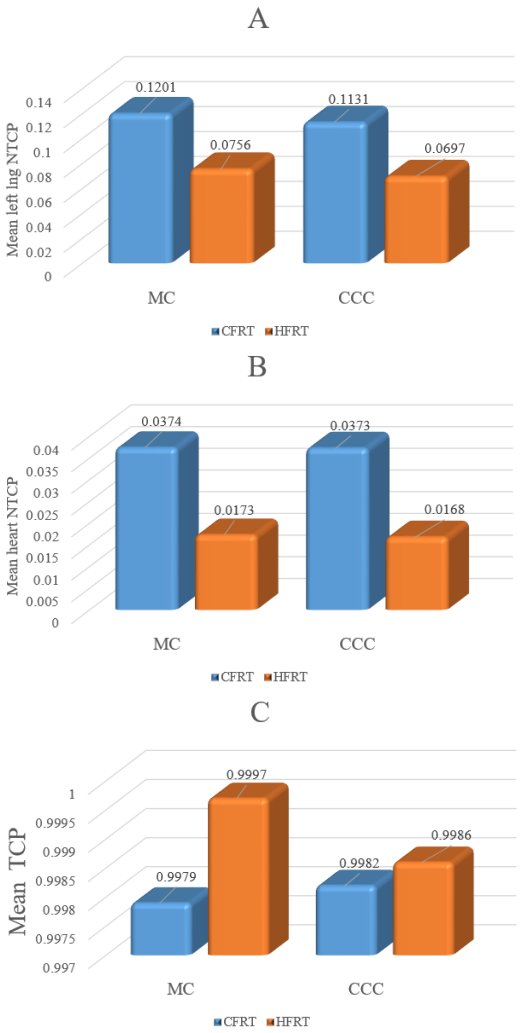


Figure 4. Comparison of the mean TCP and NTCP in CFRT and HFRT using MC and CCC algorithms; (A) Mean of Left lung NTCP for CFRT and HFRT using MC and CCC algorithms; (B) Mean of heart NTCP for CFRT and HFRT using MC and CCC algorithms; (C) Mean of TCP for CFRT and HFRT using MC and CCC algorithms.

Our results showed that the mean values for TCPs for the MC algorithm were: CFRT=0.9979 vs. HFRT=0.9997 and for CCC were: CFRT: 0.9982 vs. HFRT: 0.9986 (Figure 4C). According to these results, there are no significant differences in the TCP values between the CFRT and HFRT using MC and CCC (MC: $p=0.593$ vs. CCC: $p=0.821$). According to a study by Goli A.M, the reason for the lack of significant differences in TCP between CFRT and HFRT treatment regimens is related to the α/β ratio. In this study, the results of TCP calculations using the Poisson model are highly dependent on the tissue radiosensitivity, so with decreasing α/β, the TCP values in CFRT and HFRT increase. In our study, there was no significant difference between the two regimes due to the choice of the Niemierko model for calculating the TCP which is less dependent on tissue radiosensitivity, and the selection of a specific endpoint (tumor control) and a constant α/β value [20].

As the prevalence of cancer in the world increases, its treatment strategies are constantly evolving, including RT aimed at devising and implementing techniques to further control the tumor and better maintain OARs. Therefore, non-conventional radiation techniques, such as fractionated RT to provide a high therapeutic index and deal with possible challenges in the treatment of patients have been developed [21]. According to the results of this study, the results of clinical studies are consistent with the results of our research, which expresses the appropriate and reliable performance of MC and CCC algorithms in predicting the dose distribution in tissues and OARs.

Conclusion

Given the widespread prevalence of BC in the world and the use of RT to treat patients, any process that reduces the risk of possible complications from RT in these patients is of great importance. The CFRT and HFRT can be simulated by changing the treatment parameters, such as the number of fractions, fraction sizes, and the overall treatment time. Due to the challenge of choosing the optimal treatment regimen as well as the accurate DCA, this study was performed. According to the results of this study and other similar studies, the use of HFRT in medical centers is guaranteed and due to reduced time, cost Treatment, and complications of left chest RT in heart and lung tissues is recommended. The HFRT brings significant therapeutic benefits to patients and treatment centers and is a safe and cost-effective treatment method by provides acceptable treatment results. Among these, the role of DCAs in predicting the dose distribution of vital organs and heterogeneous areas and planning an ideal treatment plan is essential.

Acknowledgment

We would like to express our special thanks to the staff of the physics department of the Urmia Omid Oncology Center in Urmia, Iran, for their cooperation and participation in this research.

References

1. Mehnati P, Ghorbanipoor M, Mohammadzadeh M, Motlagh BN, Mesbahi A. Predicting the Risk of Radiation Pneumonitis and Pulmonary Function Changes after Breast Cancer Radiotherapy. J Biomed Phys Eng. 2021;11(4):459.
2. Vasiljevic D, Arnold C, Neuman D, Fink K, Popovscaia M, Kvitsaridze I. Occurrence of pneumonitis following radiotherapy of breast cancer–A prospective study. Strahlenther Onkol. 2018;194(6):520-32.
3. Mondal D, Jhawar SR, Millevoi R, Haffty BG, Parikh RR. Proton versus photon breath-hold radiation for left-sided breast cancer after breast-conserving surgery: a dosimetric comparison. Int J Part Ther. 2020;7(3):24-33.
4. James M, Swadi S, Yi M, Johansson L, Robinson B, Dixit A. Ischaemic heart disease following conventional and hypofractionated radiation treatment in a contemporary breast cancer series. J Med Imaging Radiat Oncol. 2018;62(3):425-31.
5. Appelt AL, Vogelius IR, Bentzen SM. Modern hypofractionation schedules for tangential whole breast irradiation decrease the fraction size-corrected dose to the heart. Clin Oncol. 2013;25(3):147-52.
6. Nozaki M, Kagami Y, Shibata T, Nakamura K, Ito Y, Nishimura Y, et al. A primary analysis of a multicenter, prospective, single-arm, confirmatory trial of hypofractionated whole breast irradiation after breast-conserving surgery in Japan: JCOG0906. Jpn J Clin Oncol. 2019;49(1):57-62.
7. Li J, Xiong W, Freedman GM, Anderson P, Ma C. Comparison of TCP and NTCP between conventional and hypofractionated breast treatment. Int J Radiat Oncol Biol Phys. 2004;60(1):S395.
8. Astudillo V A, Paredes G L, Resendiz G G, Posadas V A, Mitsoura E, Rodriguez L A, et al. TCP and NTCP radiobiological models: conventional and hypo fractionated treatments in radiotherapy. 2015.
9. Gay HA, Niemierko A. A free program for calculating EUD-based NTCP and TCP in external beam radiotherapy. Phys Med. 2007;23(3-4):115-25.
10. Gagliardi G, Lax I, Soderstrom S, Gyenes G, Rutqvist LE. prediction of excess risk of long-term cardiac mortality after radiotherapy of stage I breast cancer. Radiother Oncol. 1998;46(1):63-71.
11. Sheng Y, Wang W, Huang Z, Wu X, Schlegel N, Zhang Q, et al. Development of a Monte Carlo beam model for raster scanning proton beams and dosimetric comparison. Int J Radiat Biol. 2020;96(11):1435-42.
12. Hasani M, Mohammadi K, Ghorbani M, Gholami S, Knaup C. A Monte Carlo evaluation of dose distribution of commercial treatment planning systems in heterogeneous media. J Cancer Res Ther. 2019;15(8):127.
13. Jones D. ICRU Report 50: Prescribing, recording, and reporting photon beam therapy. International Commission of Radiation Units and Measurements. 1994: 833-4.
14. Wambersie A. ICRU Report 62: Prescribing, recording, and reporting photon beam therapy (supplement to ICRU Report 50). International Commission of Radiation Units and Measurements. 1999.
15. Seppenwoolde Y, Lebesque JV, de Jaeger K, Belderbos JS, Boersma LJ, Schilstra C, et al. Comparing different NTCP models that predict the incidence of radiation pneumonitis. Normal tissue complication probability. Int J Radiat Oncol Biol Phys. 2003;55(3):724-35.
16. Okunieff P, Morgan D, Niemierko A, Suit HD. Radiation dose-response of human tumors. Int J Radiat Oncol Biol Phys. 1995;32(4):1227-37.
17. Bufacchi A, Caspiani O, Rambaldi G, Marmiroli L, Giovinazzo G, Polsoni M. Clinical implication in the use of the AAA algorithm versus the AXB in nasopharyngeal carcinomas by comparison of TCP and NTCP values. Radiat Oncol. 2020;15(1):1-8.
18. Chaikh A, Khamphan C, Kumar T, Garcia R, Balosso J. What should we know about photon dose calculation algorithms used for radiotherapy? Their impact on dose distribution and medical decisions based on TCP/NTCP. Int J Cancer Ther Oncol. 2016;4(4):4418.
19. Liang X, Penagaricano J, Zheng D, Morrill S, Zhang X, Corry P, et al. Radiobiological impact of dose calculation algorithms on biologically optimized IMRT lung stereotactic body radiation therapy plans. Radiat Oncol. 2016;11:10.
20. Gloi AM. A broad evaluation of left breast radiotherapy. Am J Biomed Sci. 2019;11(3).
21. Moghaddasi L, Reid P, Bezak E, Marcu LG. Radiobiological and Treatment-Related Aspects of Spatially Fractionated Radiotherapy. Int J Mol Sci. 2022;23(6):3366.