



Incidence risk assessment of secondary cancer due to radiotherapy of women with rectal cancer using BEIR VII, EPA, and ICRP models

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ABSTRACT

Background: Radiotherapy has a significant side effect known as radiation-induced secondary cancer. This study aims to evaluate the dose and secondary cancer risk for women with rectal cancer treated with three-dimensional conformal radiation therapy (3D-CRT) to the organs at risk (OARs) and some sensitive organs using different types of radiation-induced cancer risk prediction models, including Biological Effects of Ionizing Radiation (BEIRVII), Environmental Protection Agency (EPA) and International Commission on Radiological Protection (ICRP), and compare the results of the different models for same organs.

Materials and methods: Thirty female patients with rectal cancer were considered and dose calculations were based on the PCRT-3D treatment planning system, while the radiotherapy of the patients had been performed using Shinva linear accelerator with a total dose of 45 Gy at 25 fractions. Planning target volume (PTV), OARs, and some sensitive organs were contoured, three models were used to evaluate secondary cancer risk (SCR) using the excess relative risk (ERR) and excess absolute risk (EAR).

Results: The bladder presents the highest risk, in terms of ERR, and the femur head and uterus in terms of EAR from the three models (BEIR VII, EPA, and ICRP).

Conclusion: Based on the obtained results, radiotherapy of rectal cancer is relatively higher for the bladder and femur head, compared to the risk for other organs, the kidney risk is significantly lower. It was observed that the SCR from the ICRP model was higher compared to BEIR VII and EPA models.

Key words: rectal cancer; radiotherapy; secondary cancer risk; BEIR VII; EPA; ICRP

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Introduction

Rectal malignancy is the most prevalent malignancy of the human large intestine and the third most

frequent cancer in women [1, 2] and more than half of all patients receive radiotherapy for treatment [3]. Pelvic irradiation is one of the most important steps in the radiotherapy plan for rectal cancer [4].

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According to previous studies [5–7], most second malignancies related to radiotherapy occur in or close to the radiation-exposed region.

Different organizations have developed prediction models for the incidence or death due to radiation-induced cancer, the most updated data from the atomic bomb survivors' data in Japan has been used to improve these cancer risk models [8]. In 1990 the National Academy of Sciences released its initial report named (BEIR) or BEIR VII — Phase 2 [9, 10]. From 1950 to 2000, there was a noticeable correlation between radiation exposure and rectal cancer in survivors of the atomic bombs in Hiroshima and Nagasaki [11]. Additionally, studies have shown that individuals who undergo long-term radiotherapy have a higher risk of developing second cancers, often located in or near the area where the primary cancer was treated [12]. As a result, various national and international organizations, including the International Committee on Radiation Protection (ICRP), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the Biological Effect of Ionizing Radiation (BEIR VII), and the Environmental Protection Agency (EPA), have developed risk models to estimate the incidence of second rectal cancer. However, there is a significant level of uncertainty associated with each model, with some uncertainty overlapping or even exceeding the differences between the models [13]. The risk calculator utilizes risk models that are largely derived from the BEIR VII committee's work in estimating the lifetime risk of site-specific cancers caused by radiation exposure to the US population [14].

New risk models have been introduced and developed such as ICRP and EPA models [15, 16]. These models enable one to estimate the risk of cancer arising from a specific dose of ionizing radiation. Many studies show that, compared to men, women are more vulnerable to the development of cancer for a given radiation dose [17]. Due to the location of the rectum within the woman's pelvis, the organs inside and near the pelvis can receive a high dose during radiotherapy of the rectum.

Previous research by Birgisson et al. [18] observed an increase in secondary cancer risk (SCR) in patients with rectal cancer receiving 3D-CRT in tissues near the treated volume. Zwahlen et al. [19] in a study on estimated SCR after radiotherapy

for rectal cancer, found that the SCR compared to 3D-CRT and VMAT techniques were not different statistically significantly. The limitation of previous studies is using only one model, while the present study aimed to estimate the dose and the secondary cancer risk induction for OARs and some sensitive organs for women after rectal radiation therapy using BEIR VII, EPA, and ICRP.

Materials and methods

Thirty female patients were evaluated retrospectively and computed tomography (CT) images were acquired for all the patients. Treatment plans and dose calculations were performed using the 3D-CRT treatment planning system (TPS). Radiotherapy irradiation had been conducted using 6-MVshinva linear accelerator machine (SHINVA, China) with a prescription dose of 45 Gy given in 25 fractions of 1.8 Gy. The treatment technique consisted of 4 box fields (4FB) including anterior, posterior, and 2 lateral fields. A summary of the steps for the calculation of the SCR using different models is presented in Figure 1. OARs included the small bowel, bladder, femur head and some other sensitive organs such as the ovaries, uterus, kidney, skin, and bone were also contoured, and dose volume histograms (DVHs) for all patients were obtained. The D_{mean} in Gy to OARs and sensitive organs were extracted, the dose values were introduced into different mathematical equations and the SCR was calculated for all the specified organs, and the results of the three models were compared.

The demographic and characteristics of patients, as well as the prescribed dose (Gy), are listed in Table 1.

Treatment planning

Computed tomography (CT) images were taken using a 16-slice CT unit with 5 mm axial plane slice. Treatment plans and dose calculations were performed using PCRT-3D TPS (version 6.0.2.14, Spain), using a superposition algorithm. With a 3 mm dose grid, differential DVHs for all 30 female patients were obtained and dose delivery was performed with the prescription dose of 45 Gy given in 25 fractions of 1.8 Gy. The treatment technique consisted of 4 fields box including anterior, posterior, and 2 lateral fields.

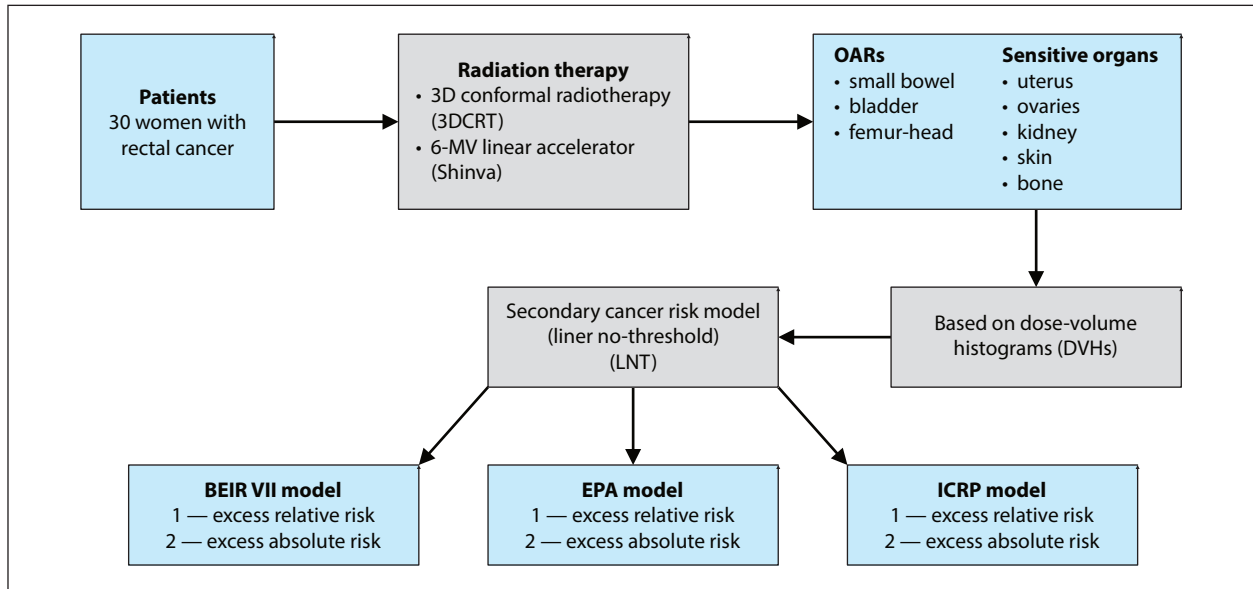


Figure 1. A summary of the steps for calculation of Biological Effects of Ionizing Radiation (BEIR VII), Environmental Protection Agency (EPA), and International Commission on Radiological Protection (ICRP) models

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

Characteristics	Number
Number of female patients	30
Age [range in years]	37–75
Prescribed dose [Gy]	45.00
PTV volume [cc]	558.60
Small bowel volume [cc]	458.99
Bladder volume [cc]	179.52
Right femur head [cc]	132.34
Left femur head [cc]	130.71
Right ovary [cc]	7.06
Left ovary [cc]	9.35
Uterus [cc]	102.57

Here, the OARs, including the small bowel, bladder, femur head, and some sensitive organs, such as ovaries, uterus, kidney, skin, and bone, were contoured. The planning was performed to cover the PTV within 95–107% of the prescribed dose. For the PTV, a 10 mm margin was added to the CTV to consider patient movement. From the DVHs, the mean absorbed dose in Gy was obtained for the OARs and sensitive organs during the 3D-CRT conformal radiotherapy treatment of the thirty patients. Figure 2. shows sample DVH curves for the PTV and OARs. Then the D_{mean} val-

ues were introduced into different mathematical equations, the SCR was calculated for all the specified organs, and the results of these three risk models were compared.

Calculation of secondary cancer risk

Both excess relative risk (ERR) models for the relative change in rates and excess absolute risk (EAR) models for the absolute difference in rates for exposed values for OARs and some sensitive organs were calculated using BEIR VII, EPA and ICRP models. Mathematical equations were used and specific parameters such as sex, age at exposure, and the attained age were applied. The method of calculating the ERR and EAR of SCR is presented in the sections which follow

BEIR VII model

The ERR and EAR for SCR were calculated by mathematical equations and according to the parameters, which were selected based on the patient's gender, body organs, and age at exposure. The parameter β_s , γ , and η are listed in Table 2. ERR and EAR can be calculated using the following formulas:

$$\text{EAR} = \beta_s D \text{Exp}(\gamma e^*) \left(\frac{a}{60}\right)^\eta \quad (1)$$

$$\text{ERR} = \beta_s D \text{Exp}(\gamma e^*) \left(\frac{a}{60}\right)^\eta \quad (2)$$

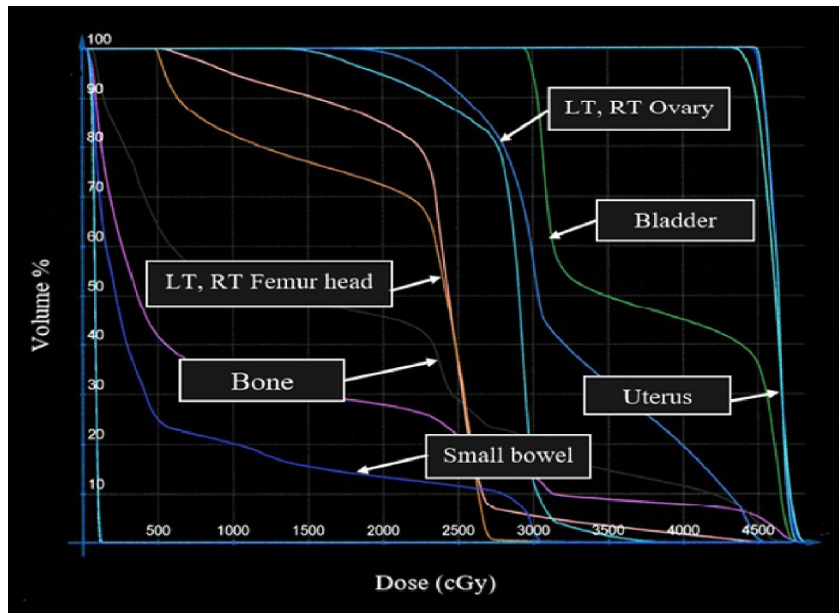


Figure 2. A sample of dose volume histogram (DVH) curves and organs at risk (OARs) for rectal cancer radiotherapy patient

Table 2. β_{Male} , β_{Female} , γ , and η parameters for calculation of risk of excess relative risk (ERR) and excess absolute risk (EAR) using Biological Effects of Ionizing Radiation (BEIR VII) and Environmental Protection Agency (EPA) models

Cancer type	ERR				EAR			
	β_{Male}	β_{Female}	γ	η	β_{Male}	β_{Female}	γ	η
Colon	0.63	0.43	-0.3	-1.4	3.2	1.6	-0.41	2.8
Uterus	-	0.055	-0.3	-1.4	-	1.2	-0.41	2.8
Ovary	-	0.38	-0.3	-1.4	-	0.7	-0.41	2.8
Bladder	0.5	1.65	-0.3	-1.4	1.2	0.75	-0.41	6.0
Other tumors	0.27	0.45	-0.3	-2.8	6.2	4.8	-0.41	2.8

β_s , γ , and η are changed based on the type of EER and EAR, where β_s is referred to β for males or females, which means the risk type per Gy at the age of exposure 30 and attained age 60, β_s differs depending on the patient’s sex.

D is the D_{mean} to organs in Gy, the γ value suggests that the risk of cancer at age e decreases for each decade that the age of exposure is increased.

η suggests that at the attained age, the absolute level of risk is decreased.

$$e^* = \frac{e - 30}{10}$$

and $e^* = zero$ if $e \geq 30$, α is the attained age (years) and is equal to $\alpha = e + L$.

EPA model

Similar to the BEIR VII model, EAR and ERR were calculated. In addition, additional mathemat-

ical models for specific types of cancers were used in the EPA model, where the risk of kidney, bone, and skin cancers was calculated using the new models which are presented below:

First, for kidney cancer as

$$EAR_{\text{kidney cancer}} = \frac{\lambda_{i, \text{kidney}}(s, a)}{\lambda_{i, \text{residual}}(s, a)} EAR_{\text{residual}} \quad (3)$$

Where $\lambda_{i, \text{kidney}}$ is the kidney cancer incidence rate, and $\lambda_{i, \text{residual}}$ is the incidence rate of other solid tumors.

For skin cancer the corresponding formula for ERR is as below:

$$EAR_{\text{skin cancer}} = 0.2D \times 0.88e^{-7} \quad (4)$$

Where D is D_{mean} to the skin, e is the age at the time of exposure

The related EAR formula for bone cancer is shown below, it is based on data on radiation-induced bone sarcoma from the BEIR IIV calculation methods by Nekolla et al. [16].

$$\text{EAR}_{\text{bone cancer}} = \alpha D \times g(e) \times h(t) \quad (5)$$

$$g(e) = e^{-0.0532(e-30)} \quad (6)$$

$$h(t) = (2\pi\sigma^2)^{-0.5} \times e^{\frac{[\ln(t)-\ln(t_0)]^2}{2\sigma^2}} \times \frac{1}{t} \quad (7)$$

Where $\alpha = 178 \times 10^{-1} \text{ Gy}^{-1}$, $t = 12.3$, $t_0 = 12.72$, $\sigma = 0.61$

D is the D_{mean} to the bone, $g(e)$ shows the risk variance. e is the exposure age, and $h(t)$ shows the change over time following exposure.

ICRP model

The third model is the ICRP model with different mathematical equations and different parameters which are defined as follows:

$$\text{ERR} = g_s D \times e^{-g_e(e-30)+g_a \cdot \ln(\frac{a}{70})} \quad (8)$$

$$\text{EAR} = g_s D \times e^{-g_e(e-30)+g_a \cdot \ln(\frac{a}{70})} \quad (9)$$

Where D is D_{mean} to organs, g_s, g_e, g_a parameters for the ICRP model are listed in Table g_s is risked per Gy at age of 70 for exposure at age of 30, g_e the age at exposure 100% change in ERR or EAR per decade increase g_a is the parameter by which the EAR or ERR differs: the power of attained age.

Statistical analysis

The statistical analyses were performed using Statistical Package for the Social Sciences (SPSS)

software (version 25, SPSS Inc., Chicago, United States). The Kolmogorov-Smirnov test was applied to the dosimetric data to evaluate if the data has normal distribution or not. The independent t -test was used to analyse the data having a normal distribution. Whereas the Mann-Whitney U test for those data that had not normally distributed. A significant difference between the two models that were compared was defined as $p < 0.05$.

Results

Organ doses

For 30 women who received rectal cancer treatment with 3D-CRT, the absorbed dose in different organs was evaluated. These values were obtained for each organ using the DVHs curves. The D_{mean} in Gy for PTV and OARs including small bowel, bladder, and femur head were 18.12 Gy, 44.44 Gy, and 22.99 Gy, respectively. The D_{mean} for ovaries, uterus, kidney, skin, and bone was 44.56 Gy, 45.37 Gy, 2.20 Gy, 16.65 Gy, and 22.20 Gy, respectively. Table 4 lists these doses compared to the tolerance dose of normal tissues to therapeutic radiation based on the study by Emami et al. [21].

Secondary cancer risk using BEIR, EPA, and ICRP models

Our results for ERR and EAR to OARs and sensitive organs in unit per 100,000 persons-year from the BEIR VII model are presented in Table 5. The average value of ERR for the small bowel bladder and femur head is 3.77, 37.91, and 6.11, respectively, while the ERR for sensitive organs such as ovaries, uterus, kidney, skin, and bone are: 8.83, 1.27, 0.52, 4.20, and 5.89, respectively. The EAR for OARs including the small bowel, bladder, and fe-

Table 3. g_s, g_e, g_a coefficients from the International Commission on Radiological Protection (ICRP) cancer risk model for calculation of excess relative risk (ERR) and excess absolute risk (EAR)

Cancer type	ERR				EAR		
	Sex	g_s	g_e	g_a	g_s	g_e	g_a
Colon	Male	0.68	-0.017	-1.65	5.76	0.024	2.38
	Female	0.33	-0.017	-1.65	2.40	0.024	2.38
Ovary	Male	-	-	-	-	-	-
	Female	0.32	-0.017	-1.65	1.47	0.024	2.38
Bladder	Male	0.67	-0.017	-1.65	2.77	0.011	1.38
	Female	0.10	-0.017	-1.65	7.45	0.024	1.38
Other tumors	Male	0.22	0.017	-1.65	7.45	0.024	2.38
	Female	0.17	-0.017	-1.65	10.40	0.024	2.38

Table 4. Average D_{mean} (Gy) to organ at risk (OAR) and sensitive organs and comparing these doses to tolerance doses of normal tissues based on Emami et al. [22]

Organ	D_{mean} [Gy]	Tolerance dose [Gy]
Small bowel	18.12	40.00
Bladder	44.44	65.00
Femur head	22.99	52.00
Ovaries	44.56	–
Uterus	45.37	–
Kidney	2.20	28.00
Skin	16.56	55.00
Bone	22.20	55.00

mur head is 10.19, 14.80, and 38.61, respectively. EAR for sensitive organs such as the ovaries, uterus, kidney, skin, and bone is 11.19, 19.08, 3.71, 27.87, and 37.43, respectively. The highest risk is related to the bladder in terms of ERR and the femur head in terms of the EAR. The risk for the kidney is considerably lower in terms of ERR and EAR compared to the other organs.

For the EPA model (Tab. 5), including all average values of ERR and EAR in unit per 100,000 persons-year, the average value of ERR for the small bowel and bladder are 3.77 and 37.91, respectively. ERR for sensitive organs such as the ovaries, uterus, and skin is 8.83, 1.27, and 0.01, respectively. The EAR for the small bowel, bladder, and femur head is 10.19, 14.80, and 24.23, respectively. For sensitive organs such as the ovaries, uterus, kidney, and bone are 11.19, 19.08, 0.06, and 24.35, respectively. According to these data, the highest SCR is related to the bladder in terms of ERR

and bone in terms of the EAR. In comparison to the risk for the other organs, the kidney risk is considerably lower in terms of ERR and EAR.

For the ICRP model, ERR and EAR for OARs and sensitive organs in unit per 100,000 persons-year are presented in Table 5. The average value of ERR for the small bowel bladder and femur head is 5.11, 42.88, and 3.30, respectively. For sensitive organs such as the ovaries, uterus, kidney, skin, and bone it is 12.64, 6.67, 0.30, 2.21, 3.33, respectively. While EAR for the small bowel, bladder, and femur head is: 16.69, 55.26, 92.19, respectively. For sensitive organs such as the ovaries, uterus, kidney, skin, and bone it is 11.09, 19.08, 3.71, 27.87, and 37.43, respectively. The results show that the highest secondary cancer risks are related to the bladder in terms of ERR and the uterus in terms of EAR. The average risk for the kidney in terms of ERR and EAR is considerably lower compared to the other organs.

Discussion

The SCR was evaluated for 30 women with rectal cancer after radiotherapy using BEIR VII, EPA, and ICRP risk prediction models. The D_{mean} in Gy for PTV, OARs, and sensitive organs is presented in Table 4. The D_{mean} in Gy is the highest for the uterus, ovaries, and bladder: 45.37, 44.56, and 44.44 Gy, respectively, D_{mean} for other organs such as the small bowel, femur head, skin, and bone is 18.12, 22.99, 16.56 and 22.20 Gy, respectively. The D_{mean} of the kidney is lower compared to the other organs. As it is clear from mathematical

Table 5. Mean excess relative risk (ERR) and excess absolute risk (EAR) per 100,000 persons-year for rectal cancer patients from Biological Effects of Ionizing Radiation (BEIR VII), Environmental Protection Agency (EPA), and International Commission on Radiological Protection (ICRP) models

Organ	BEIR VII		EPA		ICRP	
	ERR	EAR	ERR	EAR	ERR	EAR
Small bowel	3.77	10.19	3.77	10.19	5.11	16.69
Bladder	37.91	14.80	37.91	14.80	42.88	55.26
Femur head	6.11	38.61	–	24.23	3.30	92.19
Ovaries	8.83	11.19	8.83	11.19	12.64	25.49
Uterus	1.27	19.08	1.27	19.08	6.67	182.12
Kidney	0.52	3.71	–	0.06	0.30	11.75
Skin	4.20	27.87	0.01	–	2.21	66.14
Bone	5.89	37.43	–	24.35	3.33	89.88

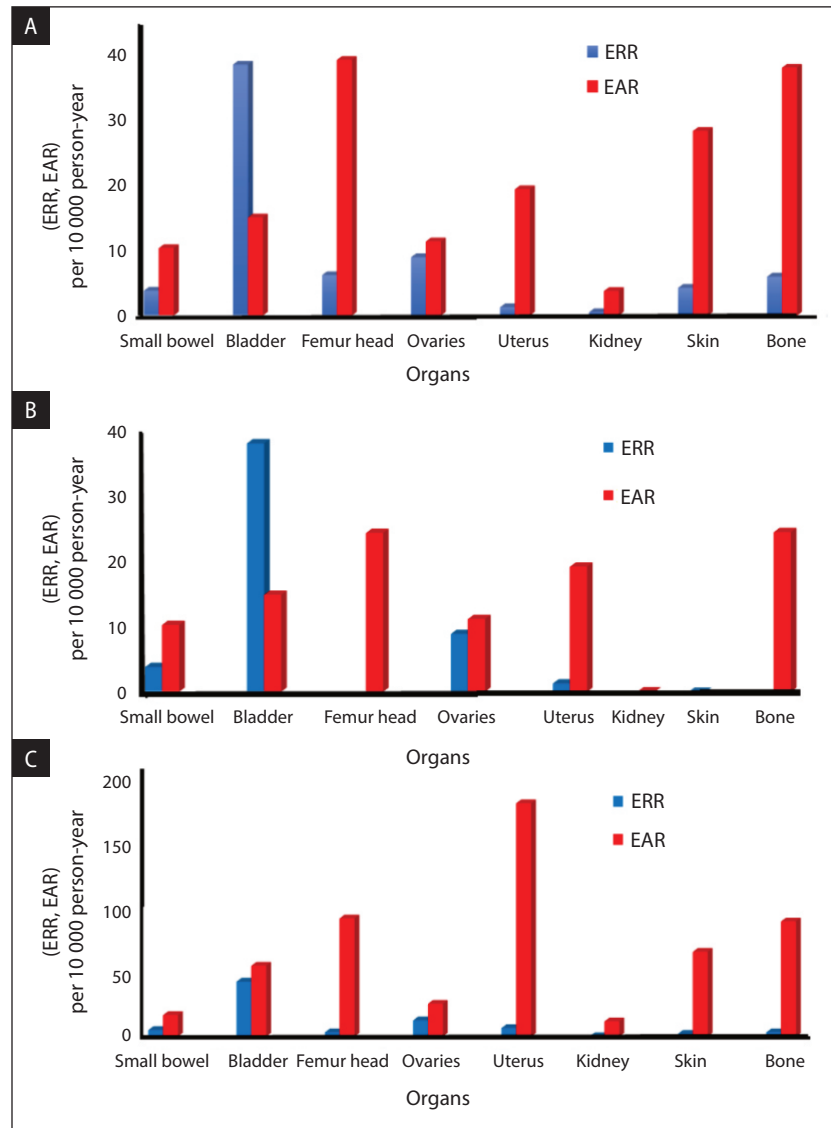


Figure 3. The excess relative risk (ERR) and excess absolute risk (EAR) (per 100,000 persons-year for organs at risk (OARs) and sensitive organs of patients treated with radiotherapy of rectal cancer using: Biological Effects of Ionizing Radiation (BEIR VII) (A); Environmental Protection Agency (EPA) (B); and International Commission on Radiological Protection (ICRP) (C) models

equations for risk calculation, the ERR and EAR are directly proportional to organ dose, in the BEIR VII, EPA, and ICRP models. It was observed that SCR increases with increasing doses to the organs. Due to this effect, the highest D_{mean} was for the uterus, ovaries, and bladder. These organs have a higher risk compared to the risks for the kidneys and skin, which received a lower dose. In this study, the SCR was the highest in organs inside or near the treatment field such as the bladder, femur head, and uterus while the kidneys and skin had less risk. These results are in agreement with the studies by Dorr et al. [22] and Boice et al. [23] who noted that

the highest SCR is observed in organs or tissues that are placed close to or on the edges of the PTV.

As can be seen from the data in Figure 3A the average risks from the BEIR VII model for all 30 patients which were calculated using the EAR and ERR risk in unit per 100,000 persons-year are for the small bowel, bladder, femur head, ovaries, uterus, kidney, skin, and bone. According to ERR, the bladder presents the greatest risk, which is 37.91. The highest risk in EAR is 38.61, and 37.43 for the femur head, and bone, respectively. On the other hand, the average risk for a kidney is significantly lower compared to the other organs

which are: 0.52 and 3.71 in terms of ERR and EAR, respectively.

According to the EPA model, the present results in Figure 3B show that the cancer risks using the ERR, and EAR in unit per 100,000 persons-year for the small bowel, bladder, ovaries, and uterus are equal to the corresponding values from the BIER VII model. This is because the same methodology is used for both quantities with the same mathematical equations for these two models. But the risks for bone, kidney, skin, and femur head are considerably lower in the EPA model, which is, on the other hand, due to applying new mathematical equations developed in the EPA report. As it is clear that there is no ERR formula for some organs such as the kidney, femur head, and bone in the EPA model, ERR was not calculated for them. As regards the ERR values, the highest cancer risk is related to the bladder which is: 37.91, while the highest risk in EAR is 24.35, 24.23 for bone and femur head, respectively. These results are similar to those from the BIER VII model. The average risk for the kidney is lower: 0.06 in terms of the EAR and 0.01 in terms of ERR for skin due to applying the new mathematical equation in the EPA report.

As shown in Figure 3C, the highest average ERR value for the bladder was 42.88 which is estimated using the ICRP model. Similar to the previous two models, the femur and bone were the highest estimation risk in EAR with values of 92.19, and 89.88, respectively. And the highest risk is related to the uterus with a value equal to 182.12, and this is because the uterus had a higher g_s value in the ICRP model [15] compared to the other organs. This means that the uterus is more sensitive to radiation. The average risk for the kidney is considerably lower compared to the other organs which are: 11.75 and 0.30 in terms of ERR and EAR, respectively.

By using BEIRVII, EPA, and ICRP models in radiotherapy of rectum cancer it was observed that in ERR and EAR the bladder and femur head, respectively, are associated with the highest SCR. This is mostly due to the location of the bladder and femur head within the irradiated volume, and because the SCR increases with the therapeutic dose of OARs which was 44.44 and 22.89 for the bladder and femur, respectively. According to the BEIR VII report in comparison to other organs, the bladder's β_s value was higher, indicating that it is more ra-

diation-sensitive. These results are consistent with the study reported by Guan et al. [24] who reported that radiation-treated rectal cancer patients had a greater SCR for the bladder than the general population. Another study by Nangia et al. [25] on the estimation of SCR after treatment of rectal cancer has shown that uterine cancer incidence is higher than expected in people who receive pelvic radiation used for treating rectal cancer.

The comparison of the risk for the other organs shows that the kidney has a lower risk. This is because the location of the kidney is outside the irradiated volume and a low dose is received by the kidney. Similar findings were reported by Horwich et al. [26] on the estimate of the SCR in patients receiving radiation therapy in stage I seminoma who found that treatment does not substantially increase SCR for organs outside the radiation field.

This study aimed to compare the results of cancer risk from three models, therefore, there are three comparisons: the first between BIER VII and EPA, the second between BEIR VII and ICRP and, finally, between EPA and ICRP. As indicated in Table 6, there are significant differences between these models in some cases. As can be seen from the data in this Table, for the ERR quantity, there is no statistically significant difference ($p > 0.05$) for secondary cancer risk between BEIR VII and EPA models for the small bowel, bladder, ovaries, and uterus. Therefore, SCR values using BEIR VII are equal to the corresponding values from the EPA model, except for the risks for the bone, kidney, skin, and femur head, for which the SCR values are considerably lower from the EPA model. According to the ERR data from BEIRVII and ICRP models, there are statistically significant differences ($p < 0.05$) between two models for the OARs and sensitive organs. In other words, SCR using the ICRP model is significantly higher when comparing BEIR VII and ICRP models. For EPA and ICRP models, there is a statistically significant difference ($p < 0.05$) between these models for the OARs and sensitive organs, and it was observed that the risk using the ICRP model is significantly higher compared to the EPA model.

As can be seen from the data in Table 7, according to the EAR data from BEIR VII and EPA models, there is no statistically significant difference ($p > 0.05$) between these two models. Therefore, SCR using BEIR VII are equal to the correspond-

Table 6. Excess relative risk (ERR) (per 100,000 persons-year) and p-values for comparison of cancer risk from Biological Effects of Ionizing Radiation (BEIR VII), Environmental Protection Agency (EPA), and International Commission on Radiological Protection (ICRP) models

Organ	BEIR VII vs. EPA			BIER VII vs. ICRP			EPA vs. ICRP		
	BEIR VII	EPA	p-value	BIER VII	ICRP	p-value	EPA	ICRP	p-value
Small bowel	3.77	3.77	0.99	3.77	5.11	0.01*	3.77	5.11	0.01*
Bladder	37.91	37.91	0.99	37.91	42.88	0.04*	37.91	42.88	0.04*
Femur head	5.89	–	–	5.89	3.30	0.02*	–	3.30	–
Ovaries	8.83	8.83	0.99	8.83	12.64	0.01*	8.83	12.64	0.00*
Uterus	1.27	1.27	0.99	1.27	6.67	0.00*	1.27	6.67	0.00*
Kidney	0.52	–	–	0.52	0.30	0.01*	–	0.30	–
Skin	4.20	0.01	0.00*	4.20	2.21	0.05*	0.01	2.21	0.00*
Bone	5.89	–	–	5.89	3.21	0.02*	–	3.21	–

*p < 0.05 means a significant difference between two models

Table 7. Excess absolute risk (EAR) (per 100,000 persons-year) and p-values for comparison of cancer risk from Biological Effects of Ionizing Radiation (BEIR VII), Environmental Protection Agency (EPA), and International Commission on Radiological Protection (ICRP) models

Organ	BEIR VII vs. EPA			BIER VII vs. ICRP			EPA vs. ICRP		
	BEIR VII	EPA	p-value	BIER VII	ICRP	p-value	EPA	ICRP	p-value
Small bowel	10.20	10.20	0.99	10.20	16.69	0.00*	10.20	16.69	0.00*
Bladder	14.81	14.81	0.99	14.81	55.27	0.02*	14.81	55.27	0.01*
Femur head	38.62	24.24	0.00*	38.62	92.20	0.00*	24.24	92.20	0.00*
Ovaries	11.10	11.10	0.99	11.10	25.49	0.02*	11.10	25.49	0.01*
Uterus	19.08	19.08	0.99	19.08	182.1	0.00*	19.08	182.1	0.00*
Kidney	3.71	0.06	0.00*	3.71	11.75	0.00*	0.06	11.75	0.04*
Skin	27.87	–	–	27.87	66.15	0.00*	–	66.15	–
Bone	37.43	24.35	0.00*	37.43	89.31	0.01*	24.35	89.31	0.00*

*p < 0.05 means a significant difference between two models

ing values from the EPA model. This trend is due to applying the same methodologies for both quantities with the same mathematical equations. However, for the bone, and kidney there are statistically significant differences ($p < 0.05$) between BEIR VII and EPA models. Therefore, generally speaking, SCR using BEIR VII is equal to the corresponding values from the EPA model, on the other hand, for BEIR VII and ICRP models there are statistically significant differences ($p < 0.05$) between these models and the same results were obtained when comparing the EPA and ICRP models for SCR for the OARs and sensitive organs.

Generally, as can be seen when comparing between BEIR VII, EPA, and ICRP models using both ERR and EAR values, there are different results between them. It was observed that the risk using the ICRP model was significantly higher

when comparing BEIR VII, and EPA models as shown the data in Figure 4 which show three models of ERR and EAR values. This is consistent with the study by Amaoui et al. [27] on the evaluation of SCRs in breast cancer using the EAR and ERR from the ICRP models. They reported that the results are much higher (by around 19 times) than those calculated by Elgendy et al. [28] on the estimation of SCRs in breast cancer. A limitation of the current study was that the results were based on 3D-CRT. However, in applying BEIR VII or any other model to predict secondary cancer risk it's critical to reduce the doses to surrounding organs as much as achievable, and it is suggested to select IMRT techniques instead of 3D-CRT and it is predicted that the doses to OARs and SCR by IMRT will be less and this would be a subject of a future study.

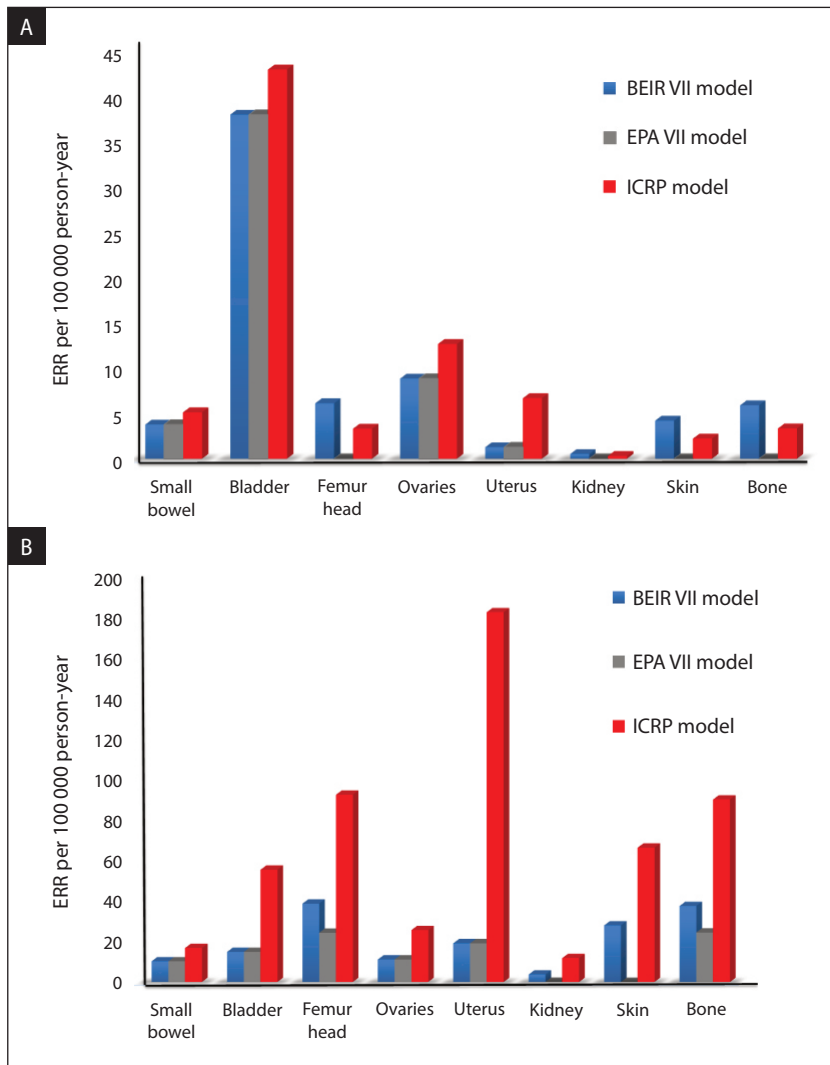


Figure 4. Mean excess relative risk (ERR) and excess absolute risk (EAR) per 100,000 persons-year for three models obtained from Biological Effects of Ionizing Radiation (BEIR VII), Environmental Protection Agency (EPA), and International Commission on Radiological Protection (ICRP) risk calculation models including ERR (A); EAR (B)

Conclusion

It was observed that there is a higher SCR in organs near the volume target, and the highest secondary cancer risks are related to the bladder in terms of ERR, and to the femur head and uterus in terms of EAR from BEIR VII, EPA, and ICRP models. Compared to the risk for other organs, the kidney risk is significantly lower. It was observed that the SCR from the ICRP model was higher compared to BEIR VII and EPA models.

Conflict of interests

There is not any relationship that might lead to a conflict of interest.

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