ORIGINAL ARTICLE

Gonads Exposure to Scattered Radiation and Associated Second Cancer Risk from Pelvic Radiotherapy

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Abstract

Purpose: The purpose of this study was to evaluate the risk of gonad cancer induction in adults with pelvic cancer (bladder, rectum, endometriosis) after radiation therapy.

Materials and Methods: In two fractions of radiotherapy, Thermo Luminescence Dosimeters (TLDs) measured the peripheral dose to the testis and ovary. With 3D planning, all patients received a 45 Gy total dose in four fields in the prone position. Researchers investigated the doses produced by linear accelerators operating at 18 MeV.

Results: The mean Excess Relative Risk (ERR) was measured based on the BEIR IIV models. Right pelvic radiotherapy of men was 0.795 ± 0.168 and 0.675 ± 0.134, and for women was 1.015 ± 0.561 and 0.884 ± 0.468 after 5 and 10 years of treatment, respectively. Left pelvic radiotherapy was 0.855 ± 0.172, 0.725 ± 0.138 for men and 0.880 ± 0.464, 0.722 ± 0.342 for women respectively (95% confidence interval). These values for women were higher ($p < 0.05$).

Conclusion: Estimating the second cancer risk of untargeted organs is crucial in radiotherapy. The out-of-field doses can be minimized by using a linear accelerator with a single energy mode and proper shields.

Keywords: Radiotherapy; Cancer Risk; Thermo Luminescence Dosimeters; Organ Dose.

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1. Introduction

Recent developments in Radiotherapy (RT) have improved long-term results for cancer patients. Radiation therapy increases the risk of secondary solid tumor induction compared to the general population [1]. A variety of environmental risk factors, including lifestyle, genetic susceptibility, and chemotherapy contribute to the risk of developing new cancers after treatment [2]. According to a US SEER-based study, radiotherapy is responsible for 8 percent of secondary cancers [3]. There is no doubt that radiotherapy induces cancer. With increasing time since RT and decreasing age at diagnosis, the secondary cancer risk increases. Cervical cancer is one of the most common cancers in women. Globally, 570,000 women were diagnosed with cervical cancer in 2018, while 1,276,106 cases of prostate cancer were reported worldwide based on GLOBOCAN 2018 data [4]. In Iran, prostate cancer is the second most prevalent cancer among men and ovary cancer is the eighth type of cancer among women. Radiation-induced primary cancer risks as well as Normal Tissue Complications Probability (NTCP) should be considered for organs lying within the high-dose gradient. It has been reported that the majority of second malignancies develop near or within the primary treatment site [5]. Photon doses scattered to other organs and dose contamination have probably caused secondary cancers [6].

Adjuvant radiotherapy in 232 patients with stage I testicular seminoma has led to 5 developed second malignancies [7]. Of 12,496 patients with cervix cancer, 12 percent of them developed second cancer after radiotherapy, and no second cancer was found in those who did not receive radiotherapy [8]. A majority of patients who received RT for a previous pelvic cancer represent the long-term radiotherapy risks for rectal cancer [9].

The result of absorbed dose measurements can be used to estimate the risk of second cancers in the irradiated tissues. The risk of out-of-field photons is associated with organs distal to the target volume. The Committee on Biological Effects of Ionizing Radiation (BEIR) VII developed risk models for estimating the risk as a function of exposure, age, sex, and organs based on the Japanese atomic-bomb survivor data [10]. Excess Relative Risk (ERR) is expressed relative to background risk. Decreasing the field edge and moving towards the field center and farther away from the volume target concurrently will reduce the second cancer incidence.

This study aimed to estimate the risk of gonad cancer induction in adults with pelvic cancer (bladder, rectum, endometriosis) after radiation therapy. In order to perform these measurements more conveniently, Thermo Luminescence Dosimeters (TLDs) are used. Their small size allows them to be easily adhered to without causing discomfort [11].

2. Materials and Methods

2.1. Measurement

This study was executed among males and females with pelvic region cancers, including rectum, bladder, and endometriosis cancers. Generally, 10 men and 10 women with pelvic region cancers were randomly assigned. Their treatment was performed with 18 MeV photons in the prone position. Patients treated with a total dose of 45 Gy in 25 fractions (1.8 Gy per fraction) received over 5 days per week by a four-field technique using the TLD only in one fraction.

Doses to organs were measured using TLDs. A total of 60 TLDs were used. The TLDs LiF: Mg, Cu, P (GR-200) with a diameter of 1.8 mm and a thickness of 9.3 mm were used for organ dose measurements [12]. Readouts were recorded over the 5~15-sec interval from 135 ˚C to 240 ˚C. GR-200 TL detector set to a heating rate of 6~20 ˚C /sec. Dosimeter sensitivity is compared to the mean sensitivity of the population through a factor called the element correction coefficient (ECC). In the second step, TLDs were divided into seven groups and exposed to 1, 2, 4, 8, 16, 32, and 64 cGy, respectively, with one group acting as a control. Each group includes 3 TLDs in the badge. Doses were estimated based on Equation 1:

$$Dose = (TL_i).ECC_i.C_F \quad (1)$$

The TL represents the number of readings read by the device (nC), the C_F represents its calibration coefficient, and the ECC represents the correction factor for each crystal that has no unit [13].

2.2. Second Cancer Risk Model

Risk refers to a relative risk, which represents how many times a certain factor increases the risk of an individual being exposed. Modifying factors of risk are

sex, age at exposure, and attained age. The BEIR VII report used the linear no-threshold model to calculate ERR. The uncertainties in estimated ERR based on the models presented in the BEIR VII report are high and this is dominated by the β parameter. ERR (D,e,a) is described by Equation 2.

$$ERR\ or\ EAR\ (D.s.e.a)\ =\ D.\beta s.exp(\gamma e*).(\frac{a}{60})^{\eta} \quad (2)$$

Where D is the dose (Sv); β_s, γ, and η are ERR-specific parameters for different organs for each sex; a is the attained age (years); e is the age at exposure (years); e* for e < 30 equal to (e-30)/10 and zero for e > 30 [14]. Table 1 outlines the committee's preferred ERR model for site-specific cancer incidence and mortality.

A total of 20 patients were randomly selected. These patients were treated for pelvic cancers (bladder, rectum, endometriosis). TLDs were located in at least two regions each region included 3 TLDs in the badge including right and left ovaries and testis in every four treatment fields (Anterior-posterior, Posterior anterior, Left lateral, and right lateral) on every patient.

Testis and ovary dose measurements were used to estimate the risk of induction of gonad cancer in adults. All risk evaluations in the current study were explained as excess relative risk values [15].

Table 1. Committee's Preferred ERR and EAR Models for Estimating Site-Specific Solid Cancer Incidence and Mortality (Table 12-2 BEIR VII page 272) [10]

Cancer Site	ERR Models		
	βs	γ	η
Ovary	0.38	-0.3	-1.4
Prostate	0.12	-0.3	-1.4

3. Results

The risk of second cancer among patients treated by RT is an area of debate in the clinic. Every person has his own treatment planning with the same field size (17 * 18 cm), so the risk of secondary cancer was investigated based on gender, age, and the distance between the target and gonad. Evaluating the risk of secondary cancer is challenging due to the latency period of onset radiotherapy [16]. The time of this recurrence makes the risk difficult to be measured.

Table 2 presents the dose of gonads from radiotherapy delivery findings of 20 patients. The background output of TLD was deducted. The data are stratified into two levels for men and women. Data from Table 2 are used to calculate the ERR of gonads 5 and 10 years after pelvic radiotherapy. The mean excess relative risk of men's right testicular measured by the BEIR VII report were 0.795 ± 0.168, 0.675 ± 0.134, and left testicular were 0.855 ± 0.172 and 0.725 ± 0.138 and the mean ERR of women's right ovaries were 1.015 ± 0.561 and 0.884 ± 0.468 and for left ovary were 0.880 ± 0.464 and 0.722 ± 0.342 after 5 and 10 years of radiotherapy treatment, respectively. Patients are between the ages of 30 and 45. A decrease in ERR with increasing age at exposure is observed. Furthermore, both males and females' ERRs decrease with age.

Coefficients in Equation 2 explain how the risk of these critical organs varies with age and sexuality during radiotherapy.

4. Discussion

This study evaluated the secondary cancer risk associated with pelvic irradiations in 20 patients, ages 30 to 45 years old. Fouad [17] has reported that the occurrence of cancer in sensitive organs such as the testis and ovary is growing and incidence and mortality are more prevalent in males than females. Men are prone to left-sided higher severity tumors while women disclosed the tumor more on the right side [18]. Its accuracy was also investigated in this study.

In this study, ERR estimates are higher for males than females, and ERR increases with organ dose regardless of gender.

Mazonakis *et al.* [19] measured the dose received by the gonads with rectal cancer with a total dose of 45 Gy in 25 fractions. In their study, the testicular dose was 0.076 Gy in each fraction of 1.8 Gy. They reported that the testicular dose depended on the field dimensions and distance from the isocenter. In this study, the testicular dose is 0.038 Gy in each fraction. The treatment plan and patient set-up probably account for the slight difference. However, the good agreement between the measured and the calculated gonadal doses gives strong evidence of the reliability and accuracy of the proposed method. Ahmadloo *et al.* [20] reported that the dose of scattered

radiation on the testis in rectal cancer is 0.163Gy in each fraction of 2Gy with a total dose of 50Gy.

In the study by Hermann *et al.* among 11 patients with rectal cancer, the mean cumulative dose received by the gonads was 3.56 (0.7–8.4) Gy. They concluded that

A study by Haddad [22] found that the mean scrotal radiation dose, measured by TLD, for 33 patients was 3.77 Gy, or 7.5% of the total dose, which is higher than the dose measured in the present study for the testis. It can be explained by the fact that in the Haddad study, the total dose received was higher (50 Gy) than in the

Table 2. Patient (No=20) dosimetry and Excess Relative Risk (ERR) of males and females

Number	Age	Sex	Testicular /Ovarian dose (cGy)		5 years		10 years	
			Right	Left	Right	Left	Right	Left
1	30	M*	3.925	4.078	1.009	1.049	0.842	0.875
2	31	M	3,901	3.931	0.957	0.964	0.803	0.809
3	33	M	3.954	4.515	0.906	1.034	0.766	0.875
4	34	M	4.371	4.834	0.958	1.060	0.814	0.901
5	35	M	3.625	3.898	0.778	0.836	0.650	0.699
6	35	M	3.792	3.889	0.814	0.835	0.680	0.698
7	37	M	3.788	4.144	0.749	0.819	0.643	0.704
8	41	M	3.891	4.270	0.685	0.752	0.586	0.643
9	45	M	3.093	3.603	0.481	0.561	0.423	0.493
10	45	M	3.992	4.109	0.621	0.640	0.546	0.562
MEAN	**36.6**	**M**	**3.833**	**4.127**	**0.795**	**0.855**	**0.675**	**0.725**
SD	**±5.37**	**M**	**±0.306**	**±0.331**	**±0.168**	**± 0.172**	**±0.134**	**±0.138**
11	31	F*	2.436	1.906	1.892	1.761	1.588	1.243
12	33	F	2.804	2.217	2.034	1.069	1.721	1.361
13	34	F	1.744	1.368	0.960	0.950	1.029	0.807
14	35	F	1.362	1.095	0.926	0.744	0.774	0.622
15	35	F	1.815	1.488	1.234	1.012	1.032	0.846
16	38	F	0.977	0.970	0.600	0.595	0.607	0.503
17	40	F	0.976	0.969	0.555	0.551	0.481	0.478
18	43	F	1.012	0.955	0.526	0.496	0.460	0.414
19	45	F	1.953	1.377	0.963	0.679	0.846	0.597
20	45	F	0.945	0.825	0.466	0.407	0.409	0.357
MEAN	**37.9**	**F**	**1.563**	**1.310**	**1.015**	**0.880**	**0.884**	**0.722**
SD	**±5.10**	**F**	**±0.662**	**±0.454**	**±0.561**	**±0.464**	**±0.468**	**±0.342**

*M: Male *F: Female

Radiation therapy for rectal cancer may cause severe gonadal injury, with the gonadal dose being delivered primarily by the posterior field due to its divergence towards the testicles and penetration of the whole body before reaching the scrotum, resulting in high scattered radiation doses [21].

present study (45 Gy). Limited information has been reported about ovary dose reduction during radiotherapy for pelvic cancer. Gonad dose depends upon the field arrangement used, field dimensions, distance from the irradiated area, the introduction of wedges, and tumor dose. In our study the ERR measured for right pelvic radiotherapy in men after 5 and 10 years of treatment

was 0.795 ± 0.168, 0.675 ± 0.134, and for women was 1.015 ± 0.561, and 0.884 ± 0.468 and for left pelvic radiotherapy was 0.855 ± 0.172, 0.725 ± 0.138 for men and 0.880 ± 0.464 and 0.722 ± 0.342 for women, respectively. Females with an increase in gonadal dose were at a higher risk of developing second cancer. This might be due to decreasing distance of the inferior border of the fields. A high scattered dose was observed in the gonad, the most sensitive organ near the pelvic treatment field. Generally, data indicate that treatment of a primary tumor increases the development of second cancer due to radiation carcinogens.

Our measurements show that the development of second cancer must be a real concern for patients that been cured of the first treatment. In fact, the development of a second malignancy is related to the efficacy of the first treatment.

5. Conclusion

In conclusion, we found a dose of about 2.7 Gy received by gonads from a total prescribed dose of 45 Gy in pelvic radiotherapy. For survivors of pelvic tumors, it is important to follow up for years to determine whether or not they develop pelvic cancer. In pelvic lesions, it is essential to use different treatment methods to reduce out-of-field doses to the sensitive organs. An external shield can help to deduct the scattering doses.

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