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Original Article

Estimating the Radiation-Induced Cancer Risks in Pediatric Computed Tomography

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Abstract

Introduction
One of the central questions in radiological protection is the magnitude of the risks from low doses of radiation, related to the justification and optimization of the diagnostic medical exposures. Therefore, the aim of this study was to estimate the cancer incidence and mortality risks in children of different ages, sizes, and ethnicities undergoing computed tomography examinations.
Materials and Methods
In this study, the risk estimations were performed, using the organ dose data of 16 pediatric voxel phantoms obtained in our previous publications. In addition, we employed the risk models recommended by the committee of biological effects of ionizing radiation for all solid cancers, leukemia, and cancers of several specific sites. Linear interpolation was also applied for the risk estimations of different ages.
Results
According to the results of this study, there are significant differences between the cancer risks for some organs even in the phantoms of the same age. Therefore, it was concluded that using the reference data for all children with anatomical discrepancies would lead to under- or overestimation of the risk values. In addition, only the amount of dose cannot be the appropriate representative of the risk, and parameters like size, age, and gender might have direct impacts on cancer incidence and mortality risks.
Conclusion
The findings of the current study are useful to update the information about the individual and the long-term collective public health risks.

Keywords: Cancer, Computer Simulations, Risk Assessments, X-ray Computed Tomography

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1. Introduction

Computed tomography (CT) is a standard modality in assessing a variety of disorders in pediatric population, including cancer screening and surveillance, trauma, and inflammatory diseases [1]. Although CT scan is not the most common X-ray examination, it is the most important one to the population in terms of the dose [2]. Radiation dose is particularly important in the pediatric patients as it increases lifetime cancer risks. In addition, the organ radio-sensitivity and the effective radiation dose from a single CT examination are higher in children than in adults [3]. The thyroid gland, breasts, and gonads are structures that have an increased sensitivity to radiation in growing children [1].

The risk estimates are mostly derived from the studies conducted on the Japanese citizens, who have been exposed to large amount of radiation during the atomic attacks of Hiroshima and Nagasaki 71 years ago. The results of the prospective dosimetric studies on the patients undergoing CT examinations are not available for a long time. Regarding this, the risks of exposure can be evaluated by estimating the radiation dose to individual organ and applying the organ-specific cancer incidence or mortality rates obtained in the studies of the atomic bomb survivors. These survivors received low-doses of radiation, with effective doses ranging from 5 - 150 mSv and a mean value of almost 40 mSv, which approximates relevant organ dose levels from a typical CT scan in which 2-3 series are performed [4].

Some researchers assessed lifetime cancer risks attributable to the exposure in pediatric CT by the value of the received dose [4-8]. On the other hand, the risk may depend on the type of cancer, the magnitude of the dose, the quality of the radiation, the dose-rate, the age and gender of the exposed person, and the other factors [3]. To the extent of the researcher's knowledge, the large-scale epidemiologic studies conducted by Pearce et al. and Mathews et al., which investigated the cancer risks associated with CT scans, presented the data regarding some cancer sites such as the risks of leukemia and brain tumor [8, 9].

Journy et al. estimated the risks of leukemia, brain, breast, and thyroid cancers, using dose–response models obtained from the Japanese atomic bomb survivors' dataset and medical exposure studies. Their results implied that 5-10% of the CT examinations carried out according to radiological protocols, resulted in much higher potential cancer risks, 1.4-3.6 times higher than the 50th percentile of examinations [10].

However, these studies did not cover all cancer sites for the pediatric patients with different ages, sizes and ethnicities. Considering the importance of evaluating cancer risk, the aim of the present study was to assess the lifetime cancer incidence and mortality risks attributable to pediatric CT radiation based on organ absorbed doses. Despite the existence of reference data for the received doses, these data are still limited because organ doses of the patients vary according to the patient size, CT scanner model, and scan protocols [11]. The size of the patient is a critical issue in the evaluation of the radiation dose used in the pediatric CT examinations [12].

Therefore, for the purpose of risk estimations, the available organ dose data of sixteen whole-body pediatric voxel phantoms, including three Iranian pediatric phantoms recently developed in Ferdowsi University of Mashhad, were used based on the methods described in biological effects of ionizing radiation (BEIR) VII report [13-15].An important task of the BEIR committee was to develop the risk models to estimate cancer risks in the exposed individuals. This task requires determining the dependence of the risk on radiation dose, gender, and age at the time of exposure.

The BEIR report employed in this study was the seventh in the series of the reports from the Board on Radiation Effects Research from National Research Council of the National Academies, which focuses on the relationship between the exposure to ionizing radiation and human health. The primary objective of this report was to develop the best possible risk estimate for exposure to low-dose and low linear energy transfer (LET) radiation in human subjects, using information from epidemiologic and experimental studies accumulated since

1990. To this aim, they developed appropriate risk models for all cancer sites, which would help to determine and update the regulations for the exposed radiation workers and the general population [3].

2. Materials and Methods

16 different whole-body pediatric phantoms with different ages, sizes and ethnicities were used for radiation-induced cancer assessments. These phantoms were modeled based on the reference data of ICRP publication 89 [16] or non-reference anatomical data of a volunteer patient. These phantoms were ranged from newborn (0 year-old) to 15 years old in both genders to consider various pediatric patients undergoing CT examinations. The information about their ages, genders, and ethnicities, which were needed for risk estimations, will be provided in this section.

2.1. Computational Model of Anthropomorphic Phantoms

2.1.1. Iranian Pediatric Voxel Phantoms

Three different Iranian pediatric voxel phantoms(including two 8- and11-year-old males andone11-year-old female) were developed based on the whole-body magnetic resonance imaging of a volunteer and CT images of pediatric patients(further information about these phantoms can be found in our previous publications) [14, 15].

GSF pediatric models

In 1988, Zankl et al. created two different phantoms based on the CT data of two Caucasian females [17]. BABY was developed from a whole-body scan of an 8-week-old cadaver and CHILD was created from a 7-year-old female undergoing whole-body radiation therapy for leukemia [18].

2.1.2. Virtual Population of Pediatric Phantoms

The Virtual Population Program at the Foundation for Research on Information Technologies in Society (IT'IS) in Switzerland created six detailed anatomical whole-body pediatric models of both genders including: Roberta (a 5-year-old female), Thelonious (a 6-year-old male), Eartha (an 8-year-old female), Dizzy (an 8-year-old male), Billie (an 11-year-old female), and Louis (a 14-year-old male) [19, 20].

2.1.3. UF Series B Pediatric Voxel Phantom

The reference voxel phantoms of UF Series B include five children: a 9-month-old male, a 4-year-old female, an 8-year-old female, an 11-year-old male, and a 14-year-oldmale. The UF Series B phantoms were developed from their predecessors, UF Series A phantoms, which were in turn constructed through image segmentation of the head and chest-abdomen-pelvis (CAP) CT scans of the patients [21].

2.2. Dose Data

In our previous studies, organ doses from axial scans (mGy/mAs) were provided for the head, chest, abdomen–pelvis, and CAP examinations for all the 16 phantoms in different tube voltages. These data were obtained through simulation of SOMATOM Sensation 16 multi-slice CT scanner (Siemens Medical Solutions, Erlangen, Germany) by general purpose Monte Carlo radiation transport code, MCNPX. The information about the X-ray spectra and scanner filters were provided by the manufacturer. To model CT scanner and fan beam, the same method described by Khursheed et al. was applied [22]. The absorbed doses were recorded, using F6:p tally. It should be mentioned that the accuracy of the simulation was verified with an error less than 9% by comparing the measured and simulated dose values [13-15]. In order to assess attributable risk of cancer incidence and mortality, in this study, organ doses (in mGy) were calculated for a common tube loading of 200 mAs.

2.3. Radiation-Induced Risk Estimation

The lifetime risks of cancer incidence and mortality for children of different ages were evaluated, using the models recommended by BEIR VII committee. Addressing low-LET radiations like X-rays, the BEIR VII report provided the estimates for all solid cancers, leukemia, and cancers of several specific sites. This report defines low doses within the range of near zero up to about 100 mSv (0.1 Sv) of low-LET radiation. Linear interpolation as explained later was applied for risk estimations

of the age, which was not determined in the BEIR VII report.

The BEIR VII preferred models prepared lifetime risk estimates for cancer incidence and mortality, resulting from a single dose of 0.1 Gy at several specific ages for all cancers. The following example illustrates how these data may be used to obtain estimates for other exposure scenarios.

A 10-year-old male receives a dose of 0.01 Gy (10 mGy) to the colon from a CT scan. Based on BEIR VII, the estimated lifetime risk of being diagnosed with colon cancer for a male exposed to 0.1 Gy at age 10 is 241 per 100,000. By linear interpolation, the estimate for a male exposed at 0.01 Gy is obtained as (0.01 / 0.1) ×□241 = 24.1 per 100,000 (about 1 in 4000). The risk of dying of colon cancer can be obtained in a similar manner.

3. Results

The values of organ absorbed doses were calculated for all the 16 phantoms at tube loading of 200 mAs. Table 1 contains the results of the absorbed doses (mGy) at tube voltage of 120 kVp and tube loading of 200 mAs. The lifetime attributable risks of cancer incidence and mortality in CAP scan at tube voltage of 120 kVp and tube loading of 200 mAs are presented in Table 2 and Table 3, respectively, for 8 male and 8 female phantoms that are arranged by age. In order to be comparable with BEIR VII, the risks were reported per 100,000; therefore, if there is a need to calculate the risk for person undergoing CT imaging, the results reported in the table should be divided by 100,000.

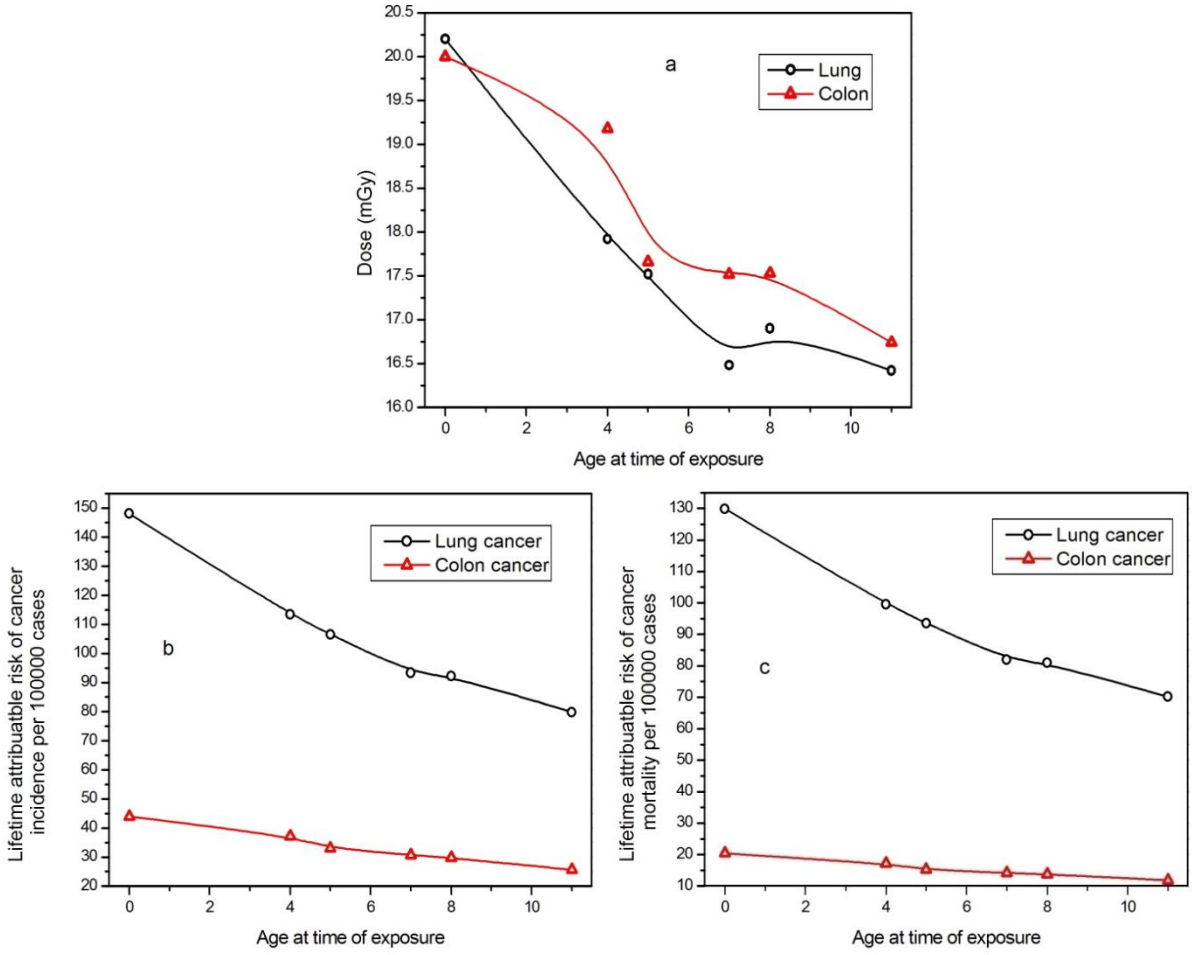

Figure 1.a) Dose [11-13] and, lifetime attributable risk of cancer b) incidence and c) mortality per 10000 cases in pediatric CAP CT examination.

Table 1. Organ absorbed doses (in mGy) in CAP scan at tube voltage of 120 kVp and tube loading of 200 mAs.

Organ	Phantom														
	BABY	**UF9m**	**UF4y**	**Roberta**	**Thelonious**	**CHILD**	**UF8y**	**Eartha**	**Dizzy**	**IR8y**	**UF11y**	**Billie**	**IRb11y**	**IRg11y**	**UF14y**	**Louis**
Stomach	20.6	18.96	18.02	17.6	17.02	17.74	18.52	16.92	17.66	17.7	16.64	16.64	17.44	16.94	15.46	16.06
Colon	20	19.46	19.18	17.66	17.22	17.52	17.88	17.18	16.3	18.6	17.06	15.96	17.68	17.52	16.12	15.64
Liver	21	19.52	18.3	18.34	17.22	17.78	18.02	17.34	17.86	17.86	16.84	16.68	17.84	17.6	15.96	16.56
Lung	20.2	18.94	17.92	17.52	16.44	16.48	17.64	16.16	17.5	17.28	16.72	15.32	17.4	17.52	17.26	14.94
Prostate/ Uterus	20	15.52	16.72	14.88	13	14.82	14.92	14	5.62	14	13.36	11.5	12.98	12.28	12	11.68
Ovary	21.8	N.A.	17.22	16.32	N.A.	16.56	15.42	14.16	N.A.	N.A.	N.A.	12.34	N.A.	13.64	N.A.	N.A.
Bladder	22	19.12	18.12	16.86	15.72	16.58	15.1	14.42	14.54	18.16	15.64	13.22	15.7	14.68	15.24	14.48
Thyroid	3.96	6.1	5.62	N.A.	N.A.	4.86	6.18	N.A.	N.A.	4.58	14.5	3.48	5.48	4.02	13.24	2.7
Red bone marrow	9.52	8.78	8.36	4.66	0.346	7.26	8.74	4.22	4.7	9.08	8.16	1.714	10.16	9.42	7.4	2.7

N.A. Not available

It should be mentioned that in some phantoms, thyroid gland has not been considered in the models; as a result, there are no data for its doses and consequently its risks. According to Table 1 and 2, a 7-year-old female (CHILD) received a dose of 17.52 mGy to the colon from a CAP CT scan. Based on BEIR VII, an estimated lifetime risk of being diagnosed with colon cancer for a female exposed to 0.1 Gy at the age of 5 years is187 per 100,000, whereas the evaluated risk for exposure at the age of 10 years is 158 per 100,000. To calculate the comparable risk of exposure at the age of 7, linear interpolation was used. As known, "$y - y_1 = \frac{y_2 - y_1}{x_2 - x_1}(x - x_1)$" is the standard form of a linear equation. For risk estimates, "y" is used for unknown risk at age 7, and "y_1" and "y_2" display the risks at age 5 and age 10, respectively.

Table 2. Lifetime attributable risk of cancer incidence per 100000 cases in CAP scan at tube voltage of 120 kVp and tube loading of 200 mAs.

	Phantom															
Cancer site	**BABY**	**UF9m**	**UF4y**	**Roberta**	**Thelonious**	**CHILD**	**UF8y**	**Eartha**	**Dizzy**	**IR8y**	**UF11y**	**Billie**	**IRb11y**	**IRg11y**	**UF14y**	**Louis**
Stomach	20.81	14.10	15.89	14.96	10.72	14.16	14.30	13.06	10.42	10.44	8.85	11.61	9.28	11.82	7.39	7.68
Colon	44.00	63.90	37.13	33.02	47.56	30.73	30.32	29.14	42.15	48.10	39.85	24.45	41.30	26.84	34.08	33.06
Liver	5.88	11.59	4.39	4.22	8.37	3.88	3.82	3.68	8.18	8.18	7.01	3.20	7.42	3.38	5.97	6.19
Lung	148.07	57.97	113.43	106.52	41.43	93.34	96.24	88.17	40.95	40.44	34.91	74.55	36.33	85.25	32.31	27.97
Prostate/ Uterus	10.00	14.13	7.29	6.25	10.06	5.87	5.73	5.38	4.06	10.11	8.68	4.00	8.44	4.27	7.08	6.89
Ovary	22.67	N.A.	15.57	14.20	N.A.	13.48	12.12	11.13	N.A.	N.A.	N.A.	8.69	N.A.	9.60	N.A.	N.A.
Bladder	46.64	39.04	33.78	30.35	26.98	27.99	24.64	23.53	23.38	29.20	22.74	19.49	22.83	21.64	20.06	19.06
Thyroid	25.11	6.66	25.96	N.A.	N.A.	22.39	29.75	N.A.	N.A.	2.77	6.76	15.80	2.55	18.25	4.82	0.98
Leukemia	17.61	19.65	10.58	5.22	0.50	7.38	8.43	4.07	6.19	11.95	9.55	1.44	11.89	7.91	7.99	2.92

N.A. Not available

In this regard, "x", "x_1", and "x_2" illustrate the ages of the exposed individuals, which are 7, 5, and 10, respectively. So, the risk equation is: (risk at the age of $7 - 187 = \frac{158-187}{10-5}(7-5) = 175.4$). Given the outcome, 175.4 is the risk of diagnosing with colon cancer per 100,000 for a 7 years old girl exposed to colon dose of 0.1 Gy. According to table 1, a 7-year-old girl receives a colon dose of 17.52 mGy (0.01752 Gy) in CAP CT scan at tube voltage of 120 kVp and tube loading of 200 mAs. Therefore, the risk of exposure to 0.01752-Gy is estimated as: (0.01752/ 0.1) × 175.4 = 30.73 per 100,000 cases.

Table 3. Lifetime attributable risk of cancer mortality per 100000 cases in CAP scan at tube voltage of 120 kVp and tube loading of 200 mAs.

	Phantom																			
Cancer site	**BABY**	**UF9m**	**UF4y**	**Roberta**	**Thelonious**	**CHILD**	**UF8y**	**Eartha**	**Dizzy**	**IR8y**	**UF11y**	**Bilie**	**IRb11y**	**IRg11y**	**UF14y**	**Louis**
Stomach	11.74	7.57	8.97	8.45	5.65	8.02	8.11	7.41	5.58	5.59	4.83	6.59	5.06	6.71	4.02	4.18
Colon	20.40	31.02	17.11	15.19	23.18	14.16	13.98	13.43	20.51	23.40	19.35	11.30	20.05	12.40	16.54	16.05
Liver	5.04	8.38	3.81	3.67	6.16	3.34	3.28	3.16	5.97	5.97	5.09	2.74	5.39	2.89	4.44	4.60
Lung	129.89	58.70	99.60	93.56	41.92	81.94	84.46	77.37	41.48	40.95	35.38	65.42	36.82	74.81	32.69	28.30
Prostate / Uterus	2.20	2.59	1.71	1.49	1.87	1.36	1.31	1.23	0.74	1.85	1.55	0.90	1.51	0.96	1.25	1.21
Ovary	11.99	N.A.	8.37	7.67	N.A.	7.25	6.51	5.98	N.A.	N.A.	N.A.	4.69	N.A.	5.18	N.A.	N.A.
Bladder	12.98	8.40	9.53	8.60	5.79	7.93	6.98	6.66	5.00	6.25	4.85	5.50	4.87	6.11	4.27	4.05
Leukemia	5.05	6.23	4.36	2.42	0.25	3.80	4.60	2.22	3.34	6.45	5.78	0.91	7.19	4.97	5.19	1.90

N.A. Not available

According to the findings, in a given organ of a phantom, the risk of cancer mortality is less than that of cancer incidence. As expected, the highest risk of cancer incidence and mortality belongs to the lungs. On the other hand, even the phantoms of the same age showed significantly different amount of risks regarding some cancers. For instance, the incidence risk of leukemia for the UF 8-year-old phantom, Dizzy, Eartha, and the Iranian 8-year-old phantom were 8.43, 4.07, 6.19, and 11.95 per 100,000 cases, respectively.

The doses and the risks of cancer incidence and mortality of two of the highly prevalent cancers for the pediatric females are presented in Figure 1 (a-c). In addition, similar data are provided for the male phantoms. For children of the same age, the average values were reported. According to this figure, increasing the age at the time of exposure leads to reduction of dose as well as risk.

4. Discussion

The most important aspect of this study was the attempt to estimate the incidence and mortality risks of radiation-induced cancers in the pediatric patients undergoing CT examinations. The results were obtained, using the BEIR VII incidence and mortality risk models for children exposed to CT radiations. The reason of not using the whole-body effective dose was that the dose was non-homogeneous even for a specific organ. Therefore, the cancer incidence and mortality risks for different organs were assessed organ-by-organ. It should be mentioned that tube loading has a linear relationship with dose and consequently the risk. Therefore, by linear scaling, the risk levels reported in Tables 2 and 3 (for 200 mAs) could be used for other tube loadings.

According to the findings of the current study, one parameter of the dose magnitude could not be representative of the cancer risk since cancer type, dose-rate, age, and gender are also important in this regard. For instance, as indicated in Figure 1, the colon dose is greater than the lung dose; however, the lung risks are higher. In addition, aging decreases the risks of lung cancer more drastically than those of colon cancer. On the other hand, the reason for the shape of Figure 1b and 1c is that younger patients have longer lifetime ahead to develop a cancer; moreover, they are inherently more sensitive to radiation due to their dividing cells.

Consequently, according to the dose data and the results of the cancer incidence and mortality, considering only the dose value for displaying the amount of risks in medical procedures does not suffice. It should be noticed that not only do age, gender, and size have direct effects on the dose values, but also they have notable impacts on the cancer risks. It could be said that, despite the existence of the dose data, developing a library of cancer risks for different genders, ages, and cancer sites in various medical and occupational exposures is a critical issue.

The data presented in Figure 1 can be compared with the risk values reported in other studies. Brenner et al. [23] provided the lifetime attributable risk of mortality based on the data derived from CT scan, using the BEIR VII models. Despite the differences in the methods of dose estimation, the results of this study are in line with those reported by Brenner et al. For instance, the risks of lung cancer mortality for a new born exposed to dose of 10 mGy were almost 64 and 52 per 100,000 cases in this study and the report of Brenner et al., respectively.

Journy et al. [10] investigated the risks of cancer per 100,000 cases in the children younger than 10 years of age, using the dose data of BABY and CHILD. Based on the scan protocols and CT scans, the dose values for thyroid varied between 3 and 25 mGy, and the average scores were 8 and 7 mGy for BABY and CHILD, respectively. The dose values reported in this study were located within the estimated range. Moreover, in the report of Brenner et al., the average scores for risk of thyroid cancer incidence were 46 and 31 in 1-month- and 5-year-old children, respectively. Considering the interpolation method and the average values of 8 mGy for BABY and 7 mGy for CHILD, the risks of thyroid cancer based on this study would be 50.70 and 32.24 for BABY and CHILD, respectively. The observed discrepancies are due to the differences between the procedure of determining organ absorbed doses and the CT scanners.

Regarding the low risk level for any individual patient, the benefits of an appropriate CT scan always outweighs the risks. Nevertheless, the collective public health risk is another issue. To evaluate the collective risk for a large exposed pediatric population, the small individual risk is multiplied by the number of children, the result of which would cause a significant public health concern [2].

The risk estimates of this study are subjected to several sources of uncertainty. In addition to the fact that the BEIR models are based on the epidemiologic data of atomic bomb survivors,

there is still a limitation regarding the limited number of the pediatric computational phantoms of different ages, genders, and ethnicities. However, these data are useful to update the information about the individual patient risks as well as long-term collective public health risks.

Moreover, these data highlight the need for a better understanding of radiation-induced cancer incidence and mortality and provide better dose estimates [2]. CT accounts for a large portion of overall medical exposure, between 20% and 70% depending on the country [24, 25]. According to the literature, about one third of all CT scans are not justified by medical need [23]. Regarding this, the immediate outcome of this study and the similar investigations is attracting attentions to the importance of reducing CT exposure, especially in pediatric examinations.

5. Conclusion

Given the significance of estimating the cancer risks of low-dose radiation, the aim of this study was to investigate the cancer incidence and mortality risks for children, using the risk models recommended in BEIR report. To this aim, this study employed the dose data of 16 pediatric phantoms with different genders, ages, and sizes along with the BEIR VII models.

According to the findings, concerning the anatomical discrepancies, using the reference data for all the children, results in underestimation or overestimation of cancer risk values, which increases concerns, especially in public health. Up to now, there is no large-scale epidemiologic study on the radiation risks associated with CT scans for all cancer sites. Therefore, these data are useful to update the information about individual patient risks as well as the long-term collective public health risks.

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