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Assessment of radiation-induced cancer risk to patients undergoing computed tomography angiography scans

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► ***Original article***

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ABSTRACT

Background: Computed tomography angiography (CTA) scan is a suitable imaging technique to evaluate the blood vessels. However, one major disadvantage is the potential risk of cancer related to ionizing radiation exposure during the procedures. The aim of this investigation was to estimate the risk of exposure induced cancer death (REID) values for some common computed tomography angiography (CTA) scans. ***Materials and Methods***: The scan parameters and patient gender and age were collected for a total of 251 patients undergoing CTA scans of the head (51), carotid (50), abdomen (50), thoracic (50) and the lower extremities (50). The effective diameter, scan length, effective tube current and the dose-length product (DLP) values were obtained for each patient. The organ doses and the effective dose were calculated by the ImpactDose program. The REID values were estimated for the different CTA scans by the calculated organ doses and corresponding age- and sex- specific risk factors. ***Results:*** The REID values for the CTA scans of head were 17±4 and 20±3 per million, carotid were 35±9 and 67±14 per million, the lower extremities were 60±26 and 64±24 per million, thoracic were 97±28 and 204±72 per million, and for abdomen were 101±25 and 194±72 per million, for males and females, respectively. ***Conclusion:*** The results of this investigation showed that CTA scans are associated with non-negligible risk of exposure induced cancer. A variation in radiation cancer risk as a function of age and gender of the patients was demonstrated and found that the younger female patients were at the highest risk.

Keywords: *Computed tomography angiography, risk of exposure induced cancer death, Monte Carlo simulations.*

INTRODUCTION

Computed tomography angiography (CTA) is a suitable imaging technique to evaluate the blood vessels. The CTA scans are applied for diagnosis of blood vessels diseases in different body parts such as the heart, chest, head, neck, abdomen, pelvis, and upper and lower extremities. As the result of rapid technological evolution especially in multidetector-row CT (MDCT) scanners, the clinical indications for CTA have markedly increased in the last several years. However, one major disadvantage of CT is the potential risk of cancer related to ionizing radiation exposure during the procedures. It was estimated that about 2% of cancers in the United States were attributable to CT scans [1].

For assessing the potential benefit-risk ratio of various CTA scans, the referring physicians, cardiologists and radiologists need to have some knowledge about the magnitude of the radiation risk associated with these procedures. The American College of Radiology [2] has also highlighted this subject. There were some studies that measured effective dose for CTA of brain [3-6], the lower extremities [7], and studies that investigated protocols for reduction of the radiation dose in CTA of carotid [8], abdomen [9],

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and lower extremity [10]. However, effective dose estimates are only valid for comparing doses from different technologies, hospitals, or countries and it cannot be used for the detailed assessment of a specific individual's risk. In this regard, several studies recommended replacing the effective dose by the risk of exposure-induced caner death (REID) values which are based on age and gender [11-16]. The REID values can also be compared with other potential health risks in everyday life, such as car accidents, smoking, alcohol consumption, earthquakes, and air traveling [17]. There were no adequate investigations addressing the REID values of CTA scans and their relationship to the age and gender of patients. Alkhorayef *et al.* [18] calculated the effective dose for CTA of brain, limb, chest, pelvis, and abdomen on the basis of dose length product (DLP) and volume CT dose index (CTDIvol). They also estimated the overall cancer risk per procedure by multiplying effective dose with the risk coefficients (5.5 Sv^{-1}).

The aim of this study was to determine organ doses and effective doses as well as to estimate REID values for some CTA scans with the combination of experimental measurements and Monte Carlo simulations.

MATERIALS AND METHODS

Between August 2014 and December 2015, patients who were referred to the computed tomography department of Shohaday-e Kargar hospital (Yazd, Iran) for CTA of head, carotid, abdomen, thoracic, and the lower extremities were considered in this study. For each examination, four image data sets were collected: scout view, premonitoring images, monitoring images, and CTA scan images. The scout view is taken in order to plan the CTA acquisition. The combination of premonitoring and monitoring images is called bolus tracking technique. This technique is used for monitoring the intensity variation in region of interest (ROI) and triggering the actual CT angiography acquisition series when a threshold (e.g., 100 Hounsfield unit (HU)) is reached. The ROI is selected just before the target region and positioned in the superior region of the neck, the aortic arch, the area above the diaphragm, the aortic arch, and the area before the aortic bifurcation for CTA of head, carotid, abdomen, thoracic, and the lower extremities, respectively.

All scans were performed by using a 16-slice multidetector-row CT scanner (Somatom Emotion 16, Siemens AG, Munich, Germany) with spiral technique. The scan parameters included: Tube voltage (kV), tube current (reference mAs), pitch factor, detector rows, using or non-using of automatic exposure control (AEC), gantry rotation time, and slice thickness (table 1).

The effective diameter, scan length, effective tube current (mAs) (which is lower than the reference tube current when tube current modulation (TCM) is used), and DLP values for each patient were recorded from the displayed ones on the scanner control console. The accuracy of the DLP values were validated by the dose measurement performed in a polymethyl-methacrylate (PMMA) head phantom (16 cm in diameter) and in a body phantom (32 cm in diameter) with a pencil ionization chamber (Unfors Multi-O-Meter 601, Sweden) according to a standard measurement protocol [19].

Organ doses and the effective dose were determined for each patient using the validated program named ImpactDose (VAMP GmbH, Erlangen, Germany) [20, 21]. Dose measurements in this program are based on the Monte Carlo simulations of photon interactions within standard anthropomorphic phantoms. The effective dose can be calculated using both the earlier tissue weighting factors (WT) (ICRP 26 and 60) [22-24] and the new ones (ICRP 103) [11].

Organ doses obtained by the ImpactDose program were used for the REID values assessment. For all patients undergoing CTA scans, the REID values were estimated by the PCXMC program (STUK, Helsinki, Finland) [25]. This program can estimate the REID values based on the models described in the Biological Effects of Ionizing Radiation VII (BEIR VII)–Phase 2 report [26]. For each patient, the specific radiogenic cancer risk was estimated by multiplying organ dose by corresponding age and sex specific risk factor from the BEIR-VII

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report. Site-specific cancer risks were summed to provide the REID estimation for each patient subjected to each CTA. More explanation about the calculation method used in the PCXMC program can be found in a technical program document [25] and in some previous studies [27-29].

Statistical analysis

Statistical analysis was performed using SPSS (version 17, SPSS Inc., Chicago, IL) and Excel 2003 (Microsoft, Redmond, Wash). The data is presented as mean ± standard deviation. The Kolmogorov-Smirnov test was used for normality test of data distribution. Pearson's correlation coefficient (r) was used to determine association between the REID values and age. Independent Samples T tests were used for comparison of the REID values between male and female patients. A value of $P<0.05$ was considered to be significant.

Table 1. The scan parameters for the different CTA scans.

	CTA scan of:				
	Head	**Carotid**	**Thoracic**	**Abdomen**	**Lower Extremities**
Tube voltage (kV)	110	110	110	110	110
Pitch factor	0.8	1.5	1.5	1.5	1.5
Tube current (reference mAs)	70	70	70	90	90
Detector Rows	16 x 0.6	16 X 0.6	16 X 0.6	16 X 0.6	16 X 1.2
using or non-using of AEC	N	Y	Y	Y	Y
Gantry rotation time (s)	0.6	0.6	0.6	0.6	0.6
Slice thickness (mm)	0.6	0.6	0.6	0.6	1.2

RESULTS

A total of 251 patients (137 males, 114 females) who underwent CTA of head, carotid, abdomen, thoracic, and the lower extremities were investigated in this study. The number, age, sex, effective diameter, and scan length of patients undergoing the different CTA scans are shown in table 2.

The mean and standard deviation values (range) of the effective tube current-time product (mAs), DLP (mGy.cm), and effective dose (mSv) values for different CTA scans are shown in table 3. The highest effective tube current-time product was 67±17.5 mAs for the abdomen CTA. In head CTA, due to non-use of TCM program, the reference tube current-time product of 70 mAs was applied for all patients. The effective doses were significantly higher in females than those in males for all scans except for the CTA of lower extremities. The highest and lowest values of effective dose occurred for CTA scans of the abdomen and head, respectively.

According to ICRP 103 [11], organ dose are divided in main and remainder organs. Mean and standard deviation of organ dose values (mSv) from the different CTA scans for both sexes are summarized in table 4 for the 14 main organs and in table 5 for an additional 14 remainder organs.

In head CTA, the highest mean organ doses in main organs and highest mean organ dose in remainder organs were 10.05±1.05 mSv, 9.62±1.27 mSv, and 9.42±0.30 mSv for salivary glands, oral mucosa, and brain, respectively. In carotid CTA, the highest mean organ doses in main organs and highest mean organ dose in remainder organs were 7.51±1.64 mSv, 5.32±1.34 mSv, and 5.20 ±1.30 mSv for thyroid, salivary glands, and extra thoracic area, respectively. In thoracic CTA, the highest mean organ doses in main organs and highest mean organ dose in remainder organs were 6.77±1.44 mSv, 8.94±1.75 mSv, and 5.88±1.32 mSv for lung, thymus, and breast (for female patients), respectively. In abdomen CTA, the highest mean organ doses in main organs and highest mean organ dose in remainder organs were 6.62±1.90 mSv, 6.61±1.29 mSv, and 7.16±1.41 mSv for bladder, stomach, and kidneys, respectively. In lower extremities CTA, the highest mean organ

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doses in main organs and highest mean organ dose in remainder organs were 5.36±1.30 mSv, 5.08±0.81 mSv, 4.92±1.05 mSv, and 4.77±0.68 mSv for skeletal system, bladder, prostate (for male patients) and uterus (for female patients), respectively.

Figure 1 shows the results of the REID (per million) due to different CTA scans for male and female patients as a function of age. There was a significant inverse correlation between the REID values and age for head CTA (in both males and females: r = -0.893, P<0.01), abdomen CTA (in female: r = -0.629, P<0.01 and in male: r = -0.456, P<0.05), and thoracic CTA (in female: r = -0.760, P<0.01). There was no significant correlation between patient age and REID values for thoracic CTA (in male: r= -0.341, P=0.095), carotid CTA (in female: r= -0.263, P=0.185 and in male: r=-0.323, P=0.133), and lower extremities CTA (in female: r=0.321, P=0.194 and in male: r= -0.180, P=0.325).

In table 6, the mean and standard deviation (range) of the REID for different CTA scans are shown in two forms, cases per million and odds. The REID values were significantly higher in females than those in males for all CTA scans except for the CTA of lower extremities. The highest REID values occurred for CTA scans of the thoracic and abdomen.

Table 2. The number, age, sex, effective diameter, and scan length of patients undergoing the different CTA scans.

		CTA scans of:				
		Head	Carotid	Thoracic	Abdomen	Lower Extremities
Patient population	All	51	50	50	50	50
	Male	27	24	25	28	33
	Female	24	26	25	22	17
Age (y)	All	46±16	49±14	51±15	46±16	53±16
	Male	44±15	52±15	53±15	51±15	53±16
	Female	45±10	47±14	48±15	40±16	51±13
Effective diameter (cm)	All	16±0.6	16±1.1	29±2.8	28±3.1	26±2.0
	Male	16±0.6	16±1.4	29±2.8	28±2.8	26±2.1
	Female	16±0.6	16±0.6	28±2.8	28±3.6	26±1.9
Scan length (mm)	All	166±11	268±24	319±55	437±35	1119±106
	Male	168±10	273±30	345±62	437±63	1134±117
	Female	164±12	263±16	293±29	439±55	1090±68

Table 3. Mean and standard deviation of effective tube current-time product, DLP, and effective dose values for different CTA scans.

		CTA scans of:				
		Head	Carotid	Thoracic	Abdomen	Lower Extremities
Effective tube current-time product (mAs)		70 ± 0	37.48 ± 9.44	58.96 ± 18.36	67 ± 17.5	36.58 ± 8.09
DLP (mGy.cm)		238 ± 14	93 ± 23	176 ± 56	251 ± 64	316 ± 78
Effective dose (mSv)	All	0.44 ± 0.03	0.90 ± 0.22	2.49 ± 0.70	3.39 ± 0.82	1.82 ± 0.72
	Male	0.42 ± 0.02	0.80 ± 0.18	2.08 ± 0.55	2.94 ± 0.52	1.79 ± 0.72
	Female	0.45 ± 0.03	0.98 ± 0.23	2.91 ± 0.58	3.98 ± 0.76	1.87 ± 0.72

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Table 4. Mean and standard deviation of main organ dose (mSv) obtained for the different CTA scans.

CTA scan	Bladder	Brain	Breast*	Colon	Esophagus	Gonads^	Gonads *	Liver	Lung	Red bone marrow	Salivary glands	Skeletal system	Skin	Stomach	Thyroid
Head	0.00± 0.00	9.42± 0.30	0.02± 0.00	0.00± 0.00	0.04± 0.05	0.00± 0.00	0.00± 0.00	0.00± 0.00	0.04± 0.01	0.24± 0.01	10.05± 1.05	3.40± 0.27	0.86± 0.08	0.00± 0.00	0.46± 0.16
Carotid	0.00± 0.00	0.82± 0.42	0.51± 0.45	0.00± 0.00	1.60± 0.34	0.00± 0.00	0.00± 0.00	0.08± 0.04	1.76± 0.47	0.29± 0.08	5.32± 1.34	2.56± 0.62	0.87± 0.22	0.04± 0.02	7.51± 1.64
Thoracic	0.02± 0.01	0.03± 0.02	5.88± 1.32	0.29± 0.52	5.08± 1.05	0.00± 0.00	0.07± 0.04	4.04± 1.20	6.77± 1.44	0.66± 0.15	0.20± 0.08	4.53± 1.05	1.58± 0.67	3.32± 1.21	1.09± 0.48
Abdomen	6.62± 1.90	0.00± 0.00	1.20± 1.33	6.00± 1.79	2.54± 1.07	2.06± 2.18	6.28± 1.31	6.34± 1.20	1.99± 1.18	0.88± 0.21	0.01± 0.00	4.35± 1.27	2.16± 0.57	6.61± 1.29	0.02± 0.01
Lower Extremities	5.08± 0.81	0.00± 0.00	0.34± 1.14	4.03± 0.84	0.49± 0.95	4.90± 1.10	4.37± 0.61	1.53± 1.76	0.48± 1.15	0.50± 0.15	0.00± 0.01	5.36± 1.30	2.94± 0.66	1.90± 1.86	0.01± 0.03

*=for female ^=for male

Table 5. Mean and standard deviation of remainder organ dose (mSv) obtained for the different CTA scans.

CTA scan	Adrenal	Extra thoracic area	Gall bladder	Heart	Kidneys	Lymphatic node	muscle	Oral mucosa	Pancreas	Prostate^	Small intestine	Spleen	Thymus	Uterus *
Head	0.00± 0.00	5.58± 0.52	0.00± 0.00	0.01± 0.00	0.00± 0.00	0.35± 0.05	0.35± 0.05	9.62± 1.27	0.00± 0.00	0.00± 0.00	0.00± 0.00	0.00± 0.00	0.03± 0.01	0.00± 0.00
Carotid	0.08± 0.03	5.20± 1.30	0.02± 0.01	0.47± 0.20	0.02± 0.01	0.87± 0.18	0.87± 0.18	4.68± 1.24	0.06± 0.03	0.00± 0.00	0.00± 0.00	0.06± 0.02	3.98± 1.48	0.00± 0.00
Thoracic	5.13± 1.32	0.36± 0.13	1.98± 1.22	6.52± 1.45	2.37± 1.46	1.68± 0.41	1.68± 0.41	0.16± 0.06	4.03± 1.19	0.01± 0.04	0.38± 0.75	3.85± 1.29	8.94± 1.75	0.06± 0.03
Abdomen	6.29± 1.16	0.01± 0.01	6.75± 1.25	2.52± 1.21	7.15± 1.41	2.93± 0.72	2.93± 0.72	0.00± 0.00	5.88± 1.11	5.42± 1.98	6.28± 1.30	6.04± 1.21	0.28± 0.11	6.86± 1.42
Lower Extremities	1.14± 1.92	0.00± 0.01	2.59± 2.02	0.65± 1.51	2.41± 2.25	3.10± 0.75	3.10± 0.75	0.00± 0.00	1.37± 1.80	4.92± 1.05	4.100± 0.97	1.26± 1.66	0.30± 1.21	4.77± 0.68

***=for female ^=for male**

Table 6. The REID values for the different CTA scans.

		CTA scans of:														
		Head			Carotid			Thoracic			Abdomen			Lower Extremities		
		All	Male	Female	All	Male	Female	All	Male	Female	All	Male	Female	All	Male	Female
Cases per million	**Mean ± SD**	19 ± 4	17 ± 4	20 ± 3	52 ± 20	35 ± 9	67 ± 14	150 ± 76	97 ± 28	204 ± 72	142 ± 69	101 ± 25	194 ± 72	62 ± 25	60 ± 26	64 ± 24
Odds	**Mean**	1 :526 32	1:58823	1:50000	1:19 230	1:28571	1:14925	1:6667	1:10309	1:4901	1:7042	1:9900	1:5154	1:16 129	1:166 66	1:15625

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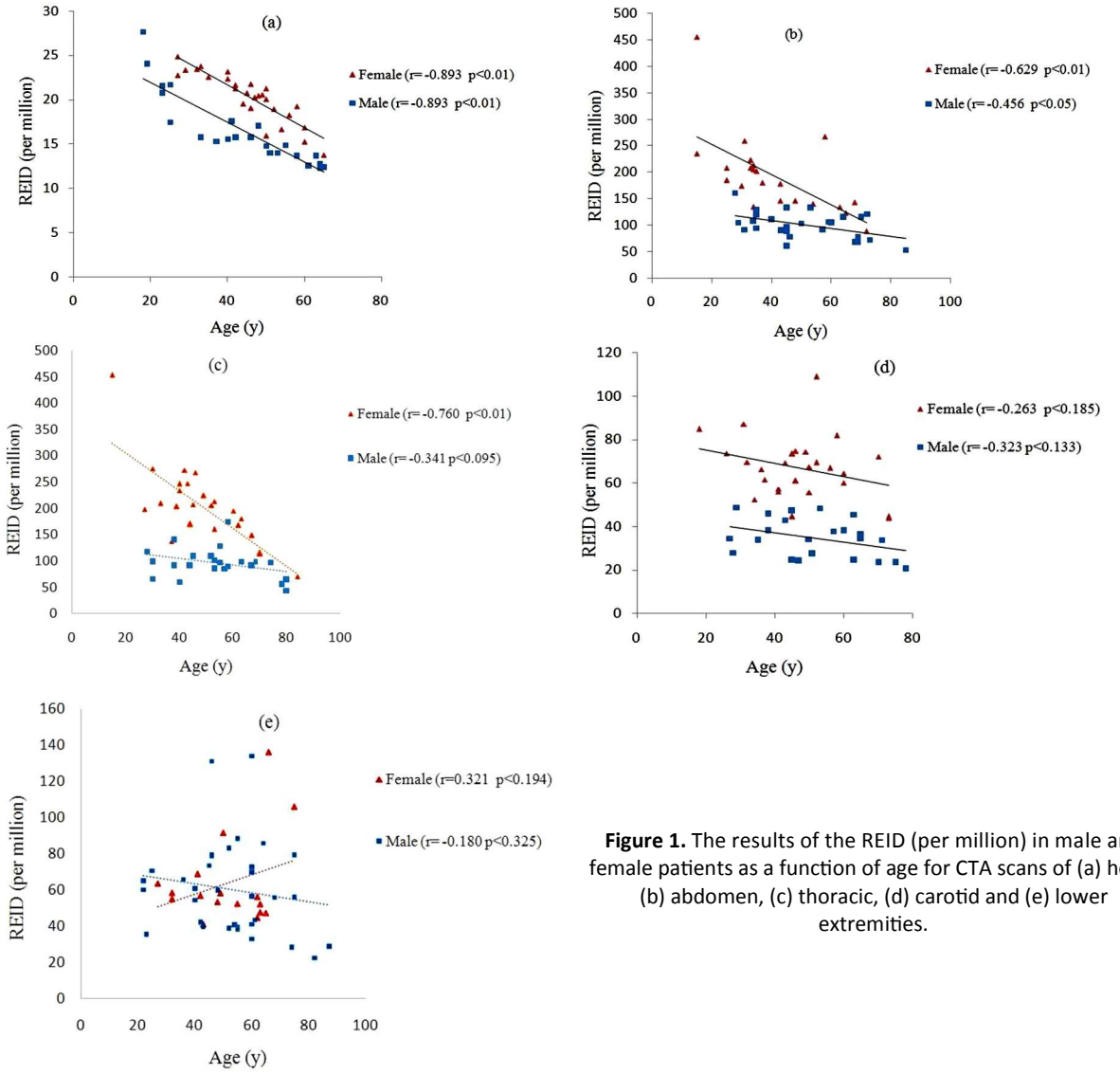

Figure 1. The results of the REID (per million) in male and female patients as a function of age for CTA scans of (a) head, (b) abdomen, (c) thoracic, (d) carotid and (e) lower extremities.

DISCUSSION

To date, there is little information about the radiation-induced cancer risk values of patients undergoing the different CTA scans. The present study was designed to determine organ doses, effective doses, and in particular the REID values for patients undergoing CTA scans of head, carotid, abdomen, thoracic, and the lower extremities. The results were obtained with the combination of experimental measurements and Monte Carlo simulations. The REID values were separately displayed for male and female patients as a function of age.

In this study, organ doses and effective doses were obtained by the ImpactDose program. This Monte Carlo simulation program was validated in several studies [20, 21, 30] and used in other studies [7, 14, 31] for dose calculation of CT scans. Some previous studies [32, 33] calculated the effective dose by multiplying the DLP by the relevant conversion factors. Those factors were based on old scanners and the tissue weighting factors from ICRP 60 [24, 34, 35], while the new tissue weighting factors introduced in ICRP Publication 103 [11] were used in our study. While, the obtained effective doses in our investigation for CTA scan of the head was 0.44 ± 0.03 mSv, this was 0.03 to 4.1 mSv in study of Yamauchi-Kawara *et al.* [3]. The calculated

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effective dose in the current study for CTA scan of the carotid was 0.90 ± 0.22 mSv, which was lower than results of Beitzke *et al.* [36] and Jo *et al.* [37] that were 1.29 ± 0.21 mSv and 2.15 ± 0.35 mSv, respectively. The calculated effective dose for CTA scan of the thoracic was 2.49 ± 0.7 mSv in the current study, which was consistent with that reported by Arthurs *et al.* [38]. The calculated effective dose for CTA scan of the abdomen was 3.39 ± 0.82 mSv in the current study, which was lower than results of Van der Molen *et al.* [39] and Hart *et al.* [40] that were 7.8 and 5.2 mSv, respectively. While, the obtained effective dose for CTA scan of the lower extremities was 1.82 ± 0.72 mSv in our study, this was 1.6–3.9 mSv in study of Willmann *et al.* [41]. The reasons of some discrepancies between different studies can be attributed to the use of different scanners and scan parameters for the different CTA scans. Another reason for these differences may be due to the use of different tissue weighting factors and different methods for calculation of the effective dose.

According to literature [42], the reported effective doses for conventional angiography of the head, carotid, and thoracic were 5 mSv and for conventional angiography of abdomen and the lower extremities were 12 and 11 mSv, respectively. Therefore, the obtained effective doses from CTA examinations in our study were between 2 to 12 times lower than ones from corresponding conventional angiography examinations.

In this study, the REID values were estimated for the different CTA scans by the PCXMC program based on the calculated organ doses. This validated program had been used in previous studies [29, 43, 44] for risk assessment in conventional radiography. Comparison of the REID values in this study with other studies was difficult, because there were no adequate investigations addressing the REID values of CTA scans and their relationship to the age and gender of patients. While, the estimated REID values of CTA scans of the head, thoracic, abdomen, and lower extremities was 19, 150, 142, and 62 per million, respectively in our study, the overall patient risk in study of Alkhorayef *et al.* [18] were 130, 450, 410, and 210 per million, respectively. The reason for the discrepancy between our results and Alkhorayef's was probably due to the different methods employed: while, in our study, the specific radiogenic cancer risk was estimated by multiplying organ dose by corresponding age and sex specific risk factor from the BEIR-VII report and site-specific cancer risks were summed to provide the REID estimation for each patient subjected to each CTA, Alkhorayef *et al.* [18] estimated the overall cancer risk per procedure by multiplying effective dose with the risk coefficients (5.5 Sv^{-1}). In addition, in our study, we used of low tube voltage (110 kV vs. 120 kV) and low tube current (70-90 mAs vs. 100-250 mAs) in comparison with study of Alkhorayef *et al.* [18].

In this study, a variation in cancer risk as a function of age and gender of the patients was displayed and demonstrated that younger females were at higher risk. These variations can be explained by the different organ distributions and the significantly greater radiosensitivity and cancer risks per unit dose for some organs, particularly breast in younger women. The REID variation with gender wasn't significant for CTA scans of the lower extremities and head, because of very low contribution dose in tissues such as breast, as well as cancer risks for exposed organs in these scans do not vary greatly with sex. Generally, the variation in radiation cancer risk with age and sex described in the present study are consistent with that reported in previous studies [26, 43-48].

The major limitation of the current study was that the cancer risk estimation has inherent uncertainty and there is no clinical experimental study to prove that the linear no-threshold model for low-dose radiation risk is valid. However, the REID estimation is based on large studies on atomic bomb survivors and nuclear workers [49, 50]. Another limitation of the present study was that a single 16-slice scanner was investigated. Nevertheless, the results of this study can be applied for various scanner models by normalizing the associated CTDI and DLP values.

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CONCLUSION

Awareness of the REID values is essential for referring physicians, cardiologists and radiologists to better evaluate the radiation exposure risk of CTA scans. The results of this investigation showed that CTA scans are associated with non-negligible risk of exposure induced cancer. A variation in radiation cancer risk as a function of age and gender of the patients was demonstrated and found that the younger female patients were at the highest risk. Physicians' knowledge about the REID values can hinder either overestimation or underestimation of radiation cancer risks. The REID values can be used to provide a more objective basis for weighing predictable benefits against potential radiation cancer risks. These findings also encourage practitioners to optimize scan parameters in order to keep exposures to patients as low as reasonably achievable.

***Conflicts of interest*:** *Declared none.*

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