

Estimating risk of exposure induced cancer death in patients undergoing computed tomography pulmonary angiography

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Abstract – The purpose of the study is to estimate the risk of exposure-induced cancer death (REID) values for computed tomography pulmonary angiography (CTPA) examination. During the study period, 152 patients (77 women and 75 men) were referred for evaluation of suspected pulmonary embolism with CTPA examination. Organ doses and the effective dose were calculated by means of Monte Carlo simulations for each patient. The REID values were estimated for CTPA, using models developed in the Biological Effects of Ionizing Radiation VII – Phase 2 report. The REID values varied from 53 to 248 per million depending on the age and gender of patients. These values were considerably higher for females (173 ± 61 per million) than males (82 ± 26 per million) and higher for younger than older patients. The REID values changed with age at exposure by a about factor of 3–5 between the ages of 18 year and 89 year. Results of this study will help the referring physicians to weigh medical benefits of CTPA in clinical practice against possible risks to justify each CTPA decision in order to reduce unnecessary examinations or use alternative imaging modalities with low risk.

Keywords: computed tomography / angiography / Monte Carlo simulations / radiation risk

1 Introduction

Pulmonary embolism (PE) is a considerable cause of mortality. It affects nearly 600,000 persons and may result in approximately 100,000 deaths per year in the United States (Surgeon General, 2008). An accurate procedure for imaging of the pulmonary arteries and diagnosis of PE is computed tomography pulmonary angiography (CTPA). However, the ionizing radiation doses delivered by CT are high and increase the rate of cancer induction and mortality risk (ICRP Publication 60, 1991; NRC, 2006; Preston *et al.*, 2007). The International Commission for Radiological Protection (ICRP) recommends that examinations involving ionizing radiation should fulfill the two basic principles of justification of practice and optimization of protection (ICRP Publication 34, 1982; ICRP Publication 60, 1991; ICRP Publication 73, 1996). Justification is achieved by providing physicians with information about the potential health effects from each medical exposure based on an evaluation of the risk of any detrimental effects that can be weighed against the medical benefits. Also, results of some studies (Wells *et al.*, 2001; Musset *et al.*, 2002; Diederich, 2003; O'Neill *et al.*, 2004, 2005; Costantino *et al.*, 2008; He *et al.*, 2012) have shown that only 9–35% of CTA scans ordered for suspected PE yield

positive findings. Therefore awareness of the potential risks from a CTPA examination is necessary for taking decisions about performing the study in question.

Contrary to the computed tomography coronary angiography that has been studied in detail, few studies described radiation dose associated to CTPA. Heyer *et al.* (2007) calculated the effective dose for CTPA on the basis of dose length product (DLP) and volume CT dose index (CTDI_{VOL}). They compared 16-section multi detector CT at 100 and 120 kVp for image quality and radiation dose. Woo *et al.* (2012) estimated the lifetime attributable risk of cancer mortality due to radiation from CTPA by calculating the estimated effective dose and using gender-specific polynomial equations derived from the Biological Effects of Ionizing Radiation VII (BEIR VII) report. They also calculated benefit-to-risk ratios by dividing the mortality benefit of preventing a fatal PE by the mortality risk of a radiation-induced cancer. Yilmaz *et al.* (2013) evaluated the effectiveness of different tube voltages uses in CTPA in the diagnosis of PE. They also found the optimal tube voltage value and studied the possibility of obtaining appropriate imaging quality with minimal radiation dose.

To date, most studies focused on the calculation of effective dose for CTPA examination. Even in the study conducted by Woo *et al.* (2012), the risk estimation was also based on effective dose. However, the uncertainty in estimated values of the effective dose is about $\pm 40\%$ for a reference

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patient of 70 kg, since organ doses and tissue weighting factors used for computing effective doses are averaged over all ages and both genders in the general population. The uncertainty in risk of cancer may be a factor of three higher or lower for a reference patient, and will be more variable for an individual (Martin, 2007; McCollough *et al.*, 2010). Since radiation risks and sensitivities for different tissues vary with gender and age at exposure (ICRP Publication 60, 1991; NRC, 2006), the assessment of cancer risk based on effective dose for an individual can lead to an underestimation for children of both genders by a factor of 1.5–4 and an overestimation for adults patients by a factor of 2.5 and 10, respectively (Martin, 2011; Balonov and Shrimpton, 2012). Therefore, the risk assessment should be based on organ dose estimates for the age and gender of the patients concerned. Several investigations (ICRP Publication 103, 2007; Martin, 2007; Brenner, 2008; McCollough *et al.*, 2010; Huda and He, 2012; Pradhan *et al.*, 2012) also suggested that age, gender, and tissue-specific risk coefficients are used instead of effective dose to estimate radiation risk. The purpose of this study was to determine organ doses and to estimate risk of exposure-induced cancer death (REID) values for CTPA examination.

2 Materials and methods

Between June 2014 and July 2015, all consecutive patients who were referred to the computed tomography department of Shohaday-e Kargar hospital (Yazd, Iran) for CTPA examination were considered in this study. All scans were obtained by using a 16-slice multidetector-row CT scanner (Somatom Emotion 16, Siemens AG, Munich, Germany) with spiral technique. Patients were scanned using tube current modulation (reference tube current–time product of 80 mAs), a tube voltage of 110 kV, gantry rotation speed of 0.6 s, collimation of 16×0.6 mm, slice thickness of 0.6 mm and a pitch factor of 1.5. The effective diameter of patients, scan length, effective tube current–time product, and DLP values were recorded from the CT scanner console. The accuracy of the displayed CTDI and DLP values was verified by measuring doses in a Perspex phantom (diameter of 32 cm and length of 15 cm) using a pencil probe solid state dosimeter (Unfors Mult-O-Meter 601, Sweden) according to literature (Shope *et al.*, 1981; IAEA, 2012). The discrepancy between measured and displayed CTDI values was $< \pm 10\%$.

Effective dose (E) is derived from the weighted sum of doses to organs by the equation: $E = \sum W_T \cdot H_T$, where E is the product of the tissue weighting factor (W_T), which represents the relative contribution of that organ or tissue to the overall risk, and the equivalent dose H_T .

Organ doses and effective dose were determined by the ImpactDose program (VAMP GmbH, Erlangen, Germany). Dose calculations in the ImpactDose are based on tabulated Monte Carlo calculation results achieved by the validated Monte Carlo program ImpactMC (Deak *et al.*, 2008; Chen *et al.*, 2012). The ImpactDose program was previously validated in several studies (Kalender *et al.*, 1999; Deak *et al.*, 2008; Chen *et al.*, 2012) by dose measurements for different scan protocols. The dose distributions were simulated and compared with thermoluminescent dosimeters measurements in anthropomorphic phantoms of various sizes.

The calculated dose values were generally within 10% of measurements for all investigated conditions.

Two types of anthropomorphic phantoms are available for the patient model in the ImpactDose program. The user can either use the default voxel phantoms (a standard male and female voxel phantom according to ICRP 110 (2009)) by choosing “voxel phantom” or use the Oak Ridge National Laboratory (ORNL) phantom series (Cristy and Eckerman, 1987) to adapt the calculation to the individual patient’s parameters by choosing “patient data”. If “patient data” is chosen, a linear interpolation is performed between versions of the ORNL phantom series. This interpolation is performed using the “effective diameter” of the patient, which is the square root of the product of lateral (Lat) and anterior-posterior (AP) diameter. The user can either choose to enter the effective diameter directly or give “AP” and “Lat” diameters obtained from CT scans of each patient, which will then be converted to a corresponding effective diameter by the ImpactDose program. For default voxel phantoms, patient gender needs to be specified while the patient data model requires patient age, gender, and diameter (ImpactDose manual). Since it has been shown that organ doses strongly depend on patient size (Turner *et al.*, 2011), in this study, we chose the ORNL phantom series option. The effect of effective diameters on radiation dose has been investigated in several studies (Turner *et al.*, 2010; AAPM, 2011; Li *et al.*, 2011; Sahbaee *et al.*, 2014).

The ImpactDose can calculate effective dose by using both the earlier WT (ICRP 26 and 60) (ICRP Publication 26, 1977; ICRP Publication 60, 1991) and the new ones (ICRP 103) (ICRP Publication 103, 2007). In this investigation, organ doses were calculated in 28 organs and effective dose was obtained using the new tissue weighting factors of ICRP Publication 103 (2007).

The REID values were estimated for CTPA, using models developed in the BEIR VII – Phase 2 report (NRC, 2006). Organ doses calculated by the ImpactDose program were used for the assessment of the REID values. The PCXMC Monte Carlo code developed by STUK (Radiation and Nuclear Safety Authority in Finland) was used for the calculation of REID values. The PCXMC program is able to calculate organ doses, and effective doses of patients in X-ray projection radiographies. Also, this program has the ability to estimate the risk of exposure-induced cancer from organ dose files of X-ray examinations simulated in the program and similarly from the organ dose files of arbitrary irradiation cases. Thus, for REID estimation of the CTPA examinations in this study, we manually changed the format and font of the organ dose files calculated by the ImpactDose to be compatible with the input files of the PCXMC. The risk of exposure-induced cancer assessment in PCXMC is performed according to the sex- and age-dependent risk model of the BEIR VII Committee. Risk models are available for leukemia, cancers in colon, stomach, lung, urinary bladder, prostate, uterus, ovaries, breast, liver, thyroid, and for all other solid cancers combined. For all cancer types, the BEIR VII had obtained absolute and relative risk models. Excess cancer risk from radiation is independent of the background cancer risk (*i.e.*, cancers from other causes than radiation) in the absolute risk model, but in the relative risk model, the radiation risk is proportional to the background cancer risk. Both models were combined in the BEIR VII for

Table 1. The characteristics of patients including number, age, effective diameter and length of the scanning area.

Number of patients			Age			Effective diameter (cm)			Scan length (mm)		
All	Male	Female	All	Male	Female	All	Male	Female	All	Male	Female
152	75	77	52±18 (18–89)	53±18 (18–89)	51±18 (18–89)	28±2.8 (19.5–36.3)	27±2.6 (20.0–33.3)	28±3.0 (19.5–36.3)	296±33 (219–390)	312±32 (240–390)	280±24 (219–336)

Table 2. The effective tube current–time product, CTDI_{VOL} and DLP values used for CTPA examination.

Tube current–time product (mAs)			CTDI _{VOL} (mGy)			DLP (mGy cm)		
All	Male	Female	All	Male	Female	All	Male	Female
51.9±15.6 (30–100)	52.5±14.7 (30–85)	60.5±15.5 (30–100)	4.6±1.4 (2.4–11.5)	4.2±1.2 (2.5–6.8)	5.0±1.6 (2.4–11.5)	139.8±42.3 (12.1–353.9)	136.7±35.6 (73.3–224.9)	142.8±48.1 (12.1–353.9)

Table 3. The effective dose values (mSv) calculated for CTPA examinations.

Effective dose values (mSv)											
All				Male				Female			
Mean	SD	Maximum	Minimum	Mean	SD	Maximum	Minimum	Mean	SD	Maximum	Minimum
2.04	0.61	4.1	0.92	1.61	0.33	2.49	0.92	2.46	0.53	4.1	1.41

risk estimation. For the REID estimation of a given patient in the PCXMC, data include the ‘Age’, ‘Gender’ and mortality “Statistics” (Euro-American) of the patient were selected in the program. A more thorough explanation of the PCXMC program and its calculation method can be found in the technical program document (Tapiovaara and Siiskonen, 2008).

3 Results

The characteristics of patients include number, age, effective diameter and length of the scanning area are shown in Table 1 for both genders separately. In this study, CTPA examinations were equally performed among female (77/152, 51%) and male (75/152, 49%) patients.

Maximum, minimum, mean, and standard deviation of the effective tube current–time product (mAs), CTDI_{VOL}, and DLP values are separately shown in Table 2 for all patients and for male and female patients separately.

Table 3 shows maximum, minimum, mean, and standard deviation of the effective dose values for all patients. The effective dose was much higher in females (2.46 mSv) than in males (1.61 mSv). This is explained by the fact that the effective dose depends not only on the scanning parameters but also on the radiosensitivity of the tissues irradiated. In particular, breast is highly radiosensitive in young females.

Mean and standard deviation of organ dose values from CTPA scans are summarized in Table 4. Directly irradiated organs, like the lung, heart, thymus and esophagus, received doses of 5.98, 5.96, 6.2 and 4.52 mGy, respectively. For female patients, breast doses were relatively high at 5.53 mGy. Doses to thyroid, liver, stomach, adrenal, pancreas and spleen positioned in the proximity of the scan range were 2.00, 2.77, 2.00, 3.96, 2.66, and 2.45 mGy, respectively.

Table 4. Organ dose values (mGy) obtained in CTPA examinations.

Organ or tissue	Mean	SD	Organ or tissue	Mean	SD
Bladder	0.01	0.01	Adrenal	3.96	1.31
Brain	0.04	0.02	Extra thoracic area	0.54	0.22
Breast ¹	5.53	1.34	Gall bladder	0.90	0.54
Colon	0.09	0.06	Heart	5.96	1.21
Esophagus	4.52	0.87	Kidneys	0.98	0.71
Gonads ²	0.00	0.00	Lymphatic node	1.39	0.31
Gonads ¹	0.04	0.02	Muscle	1.39	0.31
Liver	2.77	1.01	Oral mucosa	0.20	0.11
Lung	5.98	1.18	Pancreas	2.66	1.16
Red bone marrow	0.55	0.12	Prostate ²	0.00	0.00
Salivary glands	0.24	0.09	Small intestine	0.11	0.08
Skeleton	3.85	0.86	Spleen	2.45	1.09
Skin	1.30	0.36	Thymus	6.91	1.33
Stomach	2.01	0.87	Uterus ¹	0.03	0.02
Thyroid	2.00	1.18			

¹ For female.

² For male.

Each graph in Figures 1 and 2 shows results of the REID (per million) due to CTPA scans for male and female patients as a function of age. The REID values were considerably higher in females than in males. In both genders, the radiation risk decreased with patient age, with the decrease being much steeper for women. The REID value for a 20-year-old woman was 1 in 4032 (248 per million). For a 40-year-old woman, the REID value was 1 in 5025 (199 per million); for a 60-year-old, the REID value was 1 in 6536 (153 per million); and for an 80-year-old, the REID value was 1 in 13,513 (74 per million).

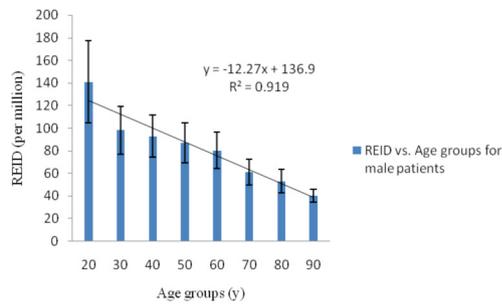


Fig. 1. The results of the REID (per million) due to CTPA scans for male patients as a function of age, with error bars showing the corresponding standard deviations.

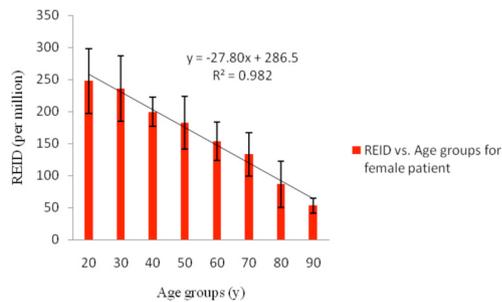


Fig. 2. The results of the REID (per million) due to CTPA scans for female patients as a function of age, with error bars showing the corresponding standard deviations.

For a 20-year-old man, the REID value was 1 in 7092 (141 per million), equivalent to the risk to a 66-year-old woman. Risks to men also decreased as a function of age, to 1 in 10,753 (93 per million) for a 40-year-old, 1 in 12,453 (80 per million) for a 60-year-old, and 1 in 18,867 (53 per million) for an 80-year-old.

4 Discussion

The major findings of the current study are as follows: (1) the mean effective dose for a CTPA scan was 1.61 ± 0.33 mSv in men and 2.46 ± 0.53 mSv in women. (2) The REID values ranged from 248/1000,000 for a 20-year-old female patient to 53/1000,000 for an 80-year-old male patient.

The above-mentioned effective doses were comparable to those reported in Heyer *et al.* (2007) study (1.37–2.44 mSv) and Yilmaz *et al.* (2013) (1.2–4.7 mSv). However, the effective doses computed by Woo *et al.* (2012) (8.4 mSv for females and 9.7 mSv for males) were higher than those calculated in our study. Higher effective dose values in Woo *et al.* (2012) study may be due to the higher exposure factors (120 kVp and 100–250 mA) in that study compared with those in other investigations. Another reason for this difference is that Woo *et al.* (2012) calculated the effective dose by multiplying the total DLP by the chest-specific conversion coefficient of $0.017 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$ determined from Monte Carlo simulations of chest CT (European Commission, 1996). Because calculations based on DLP reduces the effective dose estimates for women and increases it for men in comparison to ImpactDose estimates, this method is not appropriate. Also, the

mentioned chest-specific conversion coefficient is a composite value for female and male patients, thereby underestimating breast dose in women but overestimating it in men (Einstein *et al.*, 2008).

Comparison of the REID values of this survey with other studies was difficult. Because to date, only one study (Woo *et al.*, 2012) has estimated the REID values for CTPA. As shown in Figures 1 and 2, the REID values were markedly higher in females (53–248 per million) than in males (40–141 per million). This is consistent with the results of Woo *et al.* (2012) who also reported higher radiation risks for women, but the magnitude of radiation risks in their results were higher than those estimated in the present study. This may also be attributed to the use of different methodology and higher exposure factors in that study.

Effects of age at exposure and attained age are important modifiers of the radiation risks and BEIR VII (NRC, 2006) reported an association between age at exposure and/or attained age and the risk of radiation induced cancer. In our study, also the radiation risk increased with decreasing age at time of exposure for both genders. This is attributed to the inclusion of radiosensitive organs such as the female breast, thyroid gland, and lung in the scan field. These organs in young adults are highly radiosensitive; their radiosensitivity drop abruptly with age (NRC, 2006).

Our study had several limitations. First, the cancer risk models, which were based on the linear no-threshold (LNT) model for low-dose radiation risk, have inherent uncertainty. However, most surveys (Pierce and Preston 2000; Cardis *et al.*, 2007) agree that the LNT model is a reasonable assumption for low-dose radiation risk estimation. Second, another important aspect that has to be considered is limitation in the epidemiologic data that contributes to the uncertainty of the cancer risk estimation. For assessment of REID values, PCXMC uses the Euro-American mortality data which are available from ICRP Publication 103 (2007). These data do not necessarily correspond to the average mortality statistics of all countries in the world, but fortunately Iranian population has similar mortality data with Euro-American population (Vatandoost *et al.*, 2016). Third, calculation methods for organ doses were based on the mathematical phantoms (ORNL series). Although several aspects in this study were matched to those in individual patient scans, including age, gender, effective diameter of patients, scan length, effective tube current–time product, tube voltage, scan range, gantry rotation time, pitch, CTDI and DLP values, it was not possible to precisely simulate all aspects of patient anatomy. For further investigations, we suggest to use the Monte Carlo-based simulation program ImpactMC (Deak *et al.*, 2008) for dose calculations. With this program, the organ doses are calculated from the CT images obtained for each patient; therefore, dose calculations are specific to patient anatomy.

5 Conclusion

This study was set out to determine the REID values associated with CTPA. The REID values varied from 53 to 248 per million depending on the age and gender of patients. The REID values were considerably higher for females than males,

and higher for younger compared to older patients. An approach for minimizing the radiation risk is to reduce the number of CT examinations. Awareness of referring physicians about the REID values obtained in this study will help them to better evaluate radiation exposure risk, before ordering a CTPA examination. Also, the REID values can be comprehensible and easily understandable for referring physicians and radiologists to justify each CTPA examination in order to reduce unnecessary examinations or use alternative imaging modalities with lower risk. Other alternative modalities for imaging of the pulmonary arteries and diagnosis of PE are magnetic resonance angiography, Doppler ultrasound, Ventilation-perfusion (V/Q) scanning and each has its advantages and disadvantages. For example, while CTPA is regarded as a highly sensitive and specific test for PE (Fedullo and Tapson, 2003), the total effective dose from CTPA is about 5 times greater than that from V/Q scans (Jones *et al.*, 2012).

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