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Assessment of lifetime attributable risk (LAR) of cancer incidence from whole-body ^{18}F-FDG PET/CT examinations using established polynomial fittings

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Abstract – The advent of PET/CT examinations has revolutionized cancer treatment, offering greater precision in diagnosis. Nonetheless, the ionizing radiation exposure during the examination could cause radiation cancer risk. Hence, this study aimed to evaluate the radiation dose and radiation-induced risk associated of whole-body PET/CT examinations that includes the ^{18}F-FDG radionuclides. For this retrospective study, 40 participants were studied, with 20 men and 20 women. The average age and weight of the participants were 53.77 ± 15.78 years and 66.59 ± 16.94 kg respectively, and they were administered 424.64 ± 121.19 MBq of ^{18}F-FDG before the PET/CT commenced. The IDAC-Dose 2.1 program was employed to calculate the absorbed dose and effective dose in organs such as the bladder, brain, lung, kidneys, colon, red bone marrow (RBM), stomach, liver, and thyroid. In this study, polynomial regression was used to fit the Lifetime Attributable Risk (LAR) values derived from the BEIR VII phase II report. The effective dose from the ^{18}F-FDG PET/CT examination was 20.1 ± 7.9 mSv, with a ratio of E to the administered activity of 1.612×10^{-2} mSv/MBq, in accordance with ICRP standards. The related risk of cancer in the second part of the work did not include CT component. The estimated average cancer incidence from the PET alone was 7 and 8 cases per 100,000 persons exposed to 0.1Gy for men and women respectively, with PET-related effective doses ranging between 3.2 mSv to 27.3 mSv. In summary, the risk of cancer associated with current whole-body ^{18}F-FDG PET/CT examinations is low, but it is essential to mitigate radiation exposure during these examinations and utilize suitable techniques to prevent stochastic effects from low-dose radiation exposure.

Keywords: Whole-body ^{18}F-FDG PET/CT / lifetime attributable risk (LAR) / cancer risks / organ absorbed dose

1 Introduction

A PET/CT combines the functional imaging of PET with the anatomical resolution of CT through the detection of transmitted and attenuated ionizing radiation. The level of radiation exposure to the patient resulting from PET/CT examinations is subject to various influencing factors, including the injected activity of the radiotracer, the CT acquisition parameters, the patient's size and weight (Alashban *et al.*, 2023; Choi *et al.*, 2020; Lim *et al.*, 2018). For instance, a nationwide survey in Korea estimated the average effective dose from injected ^{18}F-FDG and CT scans was estimated to be 7.6 mSv and 5.2 mSv, respectively (Adeleye & Chetty, 2018; Kwon *et al.*, 2016). Nonetheless, it should be taken into consideration that the values could be subject to variation, depending on the imaging protocols and practices of distinct institutions (Alessio *et al.*, 2015; Li *et al.*, 2019; Masoomi *et al.*, 2021; Velo *et al.*, 2023). Furthermore, the utilization of PET/CT examinations has become indispensable in the care of individuals with cancer, and it has been widely acknowledged as the established norm for diagnosing and monitoring various forms of cancer (Berberoglu, 2019; El-Galaly *et al.*, 2018; Murat *et al.*, 2024).

Investigating potential long-term cancer risks associated with radiation exposure is a continuing concern within low levels of ionizing radiation related to gamma radiation and X-ray in PET/CT examinations. This should be performed in order to weigh the potential radiation risk of the examinations against the other medical risk of not performing the examinations. It is crucial for medical staff and medical physicists to comprehend the amount of radiation a patient is

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Table 1. Demographic of 40 subjects (men and women) included in this study.

Patient characteristics	Gender (Mean ± SD, (Min − Max))	
	Men (n = 20)	Women (n = 20)
Age (years old)	54.55 ± 15.45 (23–85)	53.00 ± 14.45 (17–75)
Weight (kg)	67.22 ± 17.96 (41.1–102.0)	65.97 ± 15.83 (38–89)
BMI (kg m^{-2})	24.36 ± 5.76 (16.90–37.61)	25.85 ± 4.91 (17.8–34.0)

exposed to during a PET/CT examinations. Additionally, it is important for patients undergoing PET/CT to be informed about their radiation dose and the potential risk of long-term development of cancer. The introduction of radiation dose quantities, such as effective dose (E), has allowed for the communication of information regarding radiation levels among medical staff and public (ICRP, 2021, 2022). The E is the most frequently used for estimating the relationship between radiation and stochastic effects, regardless of the type of exposure. The quantity reflects the health impact of radiation exposure on both radiation workers (aged 18–65) and the public regardless of age and gender. Significant gender and age at exposure differences have been recognized as key factors contributing to variations in potential cancer risk related to radiation exposure (Harrison *et al.*, 2016; ICRP, 2007). However, the E concept has been questioned due to its lack of consideration for age at exposure and gender factors (Brenner, 2012). Researchers have proposed Lifetime Attributable Risk (LAR) of cancer incidence as ultimate output to the E, concentrating on estimating cancer incidence from radiation across various age at exposure and genders (Andersson *et al.*, 2017a; Huang *et al.*, 2009; Karim MKA *et al.*, 2017; National Research Council, 2006).

In nuclear medicine, LAR could be used to assess radiation-related health risks. It quantifies the risk of cancer incidence per 100,000 persons exposed to a single dose of 0.1 Gy. This method utilizes a risk model derived from epidemiological studies such as excess relative risk (ERR) and excess absolute risk (EAR). ERR represents the relative increase in cancer rates in an exposed population compared to an unexposed population, while EAR measures the additional absolute risk of developing cancer due to exposure over a specified period. These models are applied in presenting the foundation of the linear non-threshold (LNT) model into practical in epidemiological studies. In the LNT model, there is no threshold dose below which the risk is eliminated. These estimates are important for understanding the specific risks associated with radiation doses used in PET/CT examinations (National Research Council, 2006). The significance of LAR is highlighted in the BEIR VII phase II report, published in 2006 by the United States National Research Council Committee. This report focused on determining the risks of exposure to low levels of ionizing radiation drawing on data from the life span study of atomic bomb survivors (Karim MKA *et al.*, 2017; National Research Council, 2006). This approach was notably reflecting its relevance and application in evaluating radiation-related health risks (Fahey *et al.*, 2016; Huda *et al.*, 2011; Karim MKA *et al.*, 2017; Murat *et al.*, 2023).

The LAR method can predict cancer risk generated from different variables such as gender, age at exposure, and absorbed dose. However, there are relatively few studies based on LAR has focused on PET/CT examinations. Furthermore, past studies indicated that there is absence of age-specific LAR coefficients in the BEIR VII Phase II report for adjacent age at exposure groups, necessitating the use of an interpolation method (Halid *et al.*, 2018). This interpolation method which is a type fitting method is useful for bridging gaps in the data, inherently introduces a degree of uncertainty (Kessara *et al.*, 2023). This limitation underscores the need for cautious interpretation of interpolated risk, especially when utilizing risk assessments. Therefore, this study aimed to evaluate organ doses and LAR of cancer incidence risk associated with whole-body ^{18}F-FDG PET/CT examinations.

2 Materials and methods

2.1 Subjects demography

This retrospective study was conducted at a one oncology center in the Klang Valley, with approval from the Research and Ethics Committee (identification number NMRR-18-1176-41991). Informed consent was waived for this study. A total of 40 individuals participated in whole-body ^{18}F-FDG PET-CT examinations. Only those patients who had imaging records at the center were included in the analysis, resulting in a final sample size of 20 men and 20 women. The sample has a median age at exposure of 55 years, and an age at exposure range spanning from 17 to 85 years. All data collection and processing were done in accordance with institutional ethical standards. The data collected comprised of administrated activities, A, in megabecquerel (MBq), volume weighted CT dose index ($CTDI_{vol}$), dose length products (DLP), as well as patient age, gender, weight and height.

Table 1 presents the characteristics of both men and women participants in this study. Men had an average age of 54 years, with a standard deviation of 15 years and a range of 23 to 85 years, while women had an average age of 53 years, with a standard deviation of 14 years and a range of 17 to 75 years, suggesting that there is a similar age distribution in both groups. It has been found that, on average, women tend to have slightly higher Body Mass Index (BMI) values than men. This can lead to an increased requirement for administered activity of radiopharmaceuticals to achieve sufficient image quality, resulting in higher radiation exposure (Halpern *et al.*, 2004). Furthermore, higher BMI values may lead to attenuation of the emitted radiation, which can affect image quality and require

longer scan times or higher radiation doses (Bouchareb *et al.*, 2023).

2.2 Acquisition protocols

All examinations were conducted on PET/CT system (DST Discovery, GE, USA) that was equipped with BGO crystal-based detector. The scanner was calibrated in accordance with the guidelines for clinical and research studies. Patients were required to fast for a minimum of 6 hours prior to the injection of ^{18}F-FDG, and their glucose levels had to be lower than 10 mmol/L (180 mg/dL). The mean amount of ^{18}F-FDG injected was 443.8 MBq, ranging from 200.7 to 646.3 MBq. Patients were instructed to empty their bladder and occupy the uptake room before the PET/CT examination, which was usually conducted in three-dimensional mode for increased sensitivity. After CT acquisition with an automatic tube current modulation (AEC) protocol, PET images were acquired at three minutes per bed position to match the same anatomical extent as the CT images. A low-dose CT scan was often performed for PET attenuation correction and anatomical localization (Boellaard *et al.*, 2015; Koopman *et al.*, 2016)

2.3 PET/CT Dosimetry

In this study, we employed IDAC-Dose 2.1, a Monte-Carlo based software, to compute both the absorbed and effective dose linked to PET imaging. To perform PET dosimetry, we entered the specific activity of the radiopharmaceuticals used, as well as patient-specific parameters in order to accurately model the distribution of radiation dose in different organs. The input data also necessitates the cumulated activity, $\tilde{A}$ in a source region r_s, relative to the administered activity as outlined in Eq. (1) (Andersson *et al.*, 2017b).

$$\frac{\tilde{A}}{A_o} = \frac{\int_0^{T_D} A(r_s, t) \cdot dt}{A_o}, \tag{1}$$

where $A(r_s,t)$ is the activity of the radiopharmaceutical in source region r_s at time t, and A_o is the administered activity. This cumulated activity per administered activity for a biokinetic model of ^{18}F-FDG provided by ICRP Publication 128 (ICRP, 2015).

In the meantime, IDAC-Dose 2.1 was used to compute the effective dose, E for PET by summing up these organ doses and applying tissue weighting factors according to the latest ICRP publications, as outlined in equation (2) (ICRP, 2008, 2021).

$$E = \sum\nolimits_T w_T D_T, \tag{2}$$

where w_T is the tissue weighting factor, D_T is organ absorbed dose.

In order to calculate the E from the CT component, we first obtained the dose length product (DLP) values from the CT control console. Subsequently, the contribution of E from CT was calculated using the following equation (3).

$$E = k \cdot DLP. \tag{3}$$

k is a conversion factor that is based on the body part being scanned and the patient age at exposure as stipulated in ICRP Publication 103, and AAPM Report No. 96, respectively and it is expressed in mSv mGy^{-1} cm^{-1} (AAPM, 2008; ICRP, 2007).

2.4 Organ cancer risk based on LAR of cancer incidence

The organ doses were converted into organ cancer risks by utilizing patient age at exposure and gender-specific data from BEIR VII phase II report (Huda *et al.*, 2011; ICRP, 2022; Karim MKA *et al.*, 2016; National Research Council, 2006). The main process involved tabulating the b coefficients based on Table 12 D-1 in the report through a 3rd order polynomial fitting. Subsequently, the LAR was calculated based on b coefficients and the age of exposure for specific organs and gender as given in equation (4) (Halid *et al.*, 2018; Huda & He, 2012).

$$\mathrm{LAR} = b_0 + b_1 Y + b_2 Y^2 + b_3 Y^3, \tag{4}$$

where b is the curve fit coefficient, and Y is the patient's age at exposure.

The estimation of organ cancer risk was determined by multiplying the organ dose and adjusted LAR according to age at exposure and gender, as listed in Table 1. To ensure that the organ cancer risk values correspond to the actual organ dose, we adjusted the organ dose based on the actual dose received compared to the standard dose of 0.1 Gy. Therefore, the organ doses for each patient were converted into organ cancer risks by utilizing the given equation (5). An independent t-test was conducted to test any differences that existed between two groups. The summary elements for predicting the LAR of cancer incidence are shown in Figure 1.

$$\text{Organ cancer risk} = \frac{D_T}{0.1} \times \mathrm{LAR}, \tag{5}$$

where D_T organ absorbed dose by specific organ calculated in unit Gy, and LAR is the probability per unit dose (Gy) of developing cancer in that specific organ over a lifetime.

2.5 Statistical analysis and AI tools

The data obtained was recorded and analyzed using Excel spreadsheet with XrealStats plugin. In this study, the data variables were expressed as mean values ± standard deviation. The normality of the data was assessed using the Shapiro–Wilk test, and differences were tested using t-test with significance level of <0.05. The LAR in the selected radiosensitive organs was then analyzed using the Kruskal–Wallis test. The test compared the mean ranks of LAR values across the different organs to determine if at least one organ's LAR was significantly different from the others.

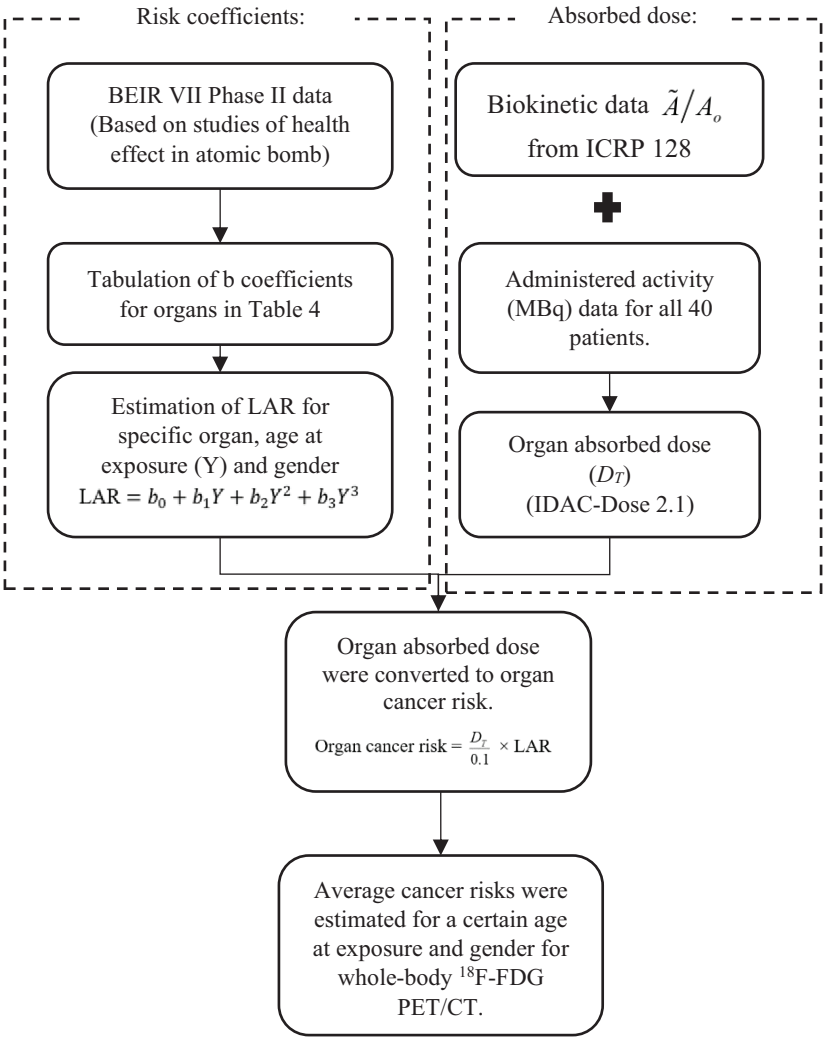

Fig. 1. A schematic diagram of the fundamental elements for predicting LAR cancer incidence.

In this paper, we have polished the text by using AI Stork's Writing Assistant (https://www.storkapp.me/writeassistant/) and significantly improved the coherence of the writing. Notably, the use of this AI tool did not influence the originality of the manuscript and its scientific facts.

3 Results

3.1 PET/CT dosimetry

The mean absorbed doses (D_T) and their standard deviations across different organs were quantified for whole-body ^{18}F-FDG PET imaging using internal dose assessment software, IDAC-Dose 2.1. Table 2 provides a detailed breakdown of the results. The analysis revealed that the bladder received the highest absorbed dose, while the thyroid received the lowest among the organs studied for both genders.

In this study, E was calculated separately for PET and CT in accordance with the ICRP recommendation. The distribution of the administered activity, A and E for PET, as well as $CTDI_{vol}$, DLP, and E for CT, were analyzed to gain a better understanding of the distribution of radiation dose received by all 40 patients. Table 3 provides a summary of patient doses for whole body ^{18}F-FDG PET/CT examinations. It is apparent from this table that the mean E for PET was 6.85 ± 1.82 mSv, while for CT it was substantially higher at 13.24 ± 6.10 mSv, resulting in a combined mean total E of 20.09 ± 7.85 mSv for PET/CT examinations.

3.2 Organ cancer risk based on LAR of cancer incidence

Table 4 outlines b coefficients for various organs, obtained by fitting data from BEIR VII phase II report as indicated in equation (5), and used to calculate the LAR. These coefficients allow for a detailed assessment of the cancer risks associated with specific organ dose and age at exposure from PET/CT examinations.

The absorbed doses and corresponding LAR for various organs in men and women during ^{18}F-FDG PET/CT

Table 2. Internal dose assessment for whole body ^{18}F-FDG PET examinations.

Organ	Absorbed dose, mGy (mean ± SD)	
	Men	Women
Bladder	21.72 ± 6.05	25.25 ± 7.18
Brain	13.77 ± 3.83	16.72 ± 4.75
Lung	7.61 ± 2.11	9.76 ± 3.44
Liver	7.26 ± 2.02	9.66 ± 2.74
RBM	5.14 ± 1.43	6.34 ± 1.84
Colon	4.35 ± 1.21	5.95 ± 1.69
Kidneys	4.33 ± 1.19	5.47 ± 1.60
Stomach	4.33 ± 1.20	5.20 ± 1.48
Thyroid	3.81 ± 1.06	4.94 ± 1.44
Mean ± SD	8.04 ± 5.66	9.92 ± 6.47

examinations are presented in Table 5, showing significant differences in LAR between the gender. It has been observed that women have a slightly increased risk of developing cancer when exposed to radiation compared to men. Further analysis reveals that the LAR for bladder, lung, stomach, and liver cancer vary significantly between genders. However, there were no significant differences found between men and women in relation to brain, kidney, colon, red bone marrow (RBM), and thyroid cancer.

Figure 2 illustrates the adjusted of LAR from the BEIR VII phase II report using 3rd order polynomial approach. This figure shows how the LAR of cancer incidence due to PET examinations varies as a function of age at exposure for different genders and organs. It is already known that LAR is an important metric for cancer risk assessment associated with low-dose radiation exposure. It consists of two components: (1) the radiation dose received from the imaging procedure and (2) its potential long-term effects on cancer. In this study, LAR values for organs such as RBM, stomach, bladder, and colon are higher in men than women of similar age of exposure. However, LAR for kidneys and brain tend to be higher in women than men.

4 Discussion

The current principles on radiation protection emphasizes that the use of radiation must be justified by a clear net benefit. The principle also applies to PET/CT examinations, ensuring that the benefits to a patient from the examinations are greater than any potential risks involved. Examinations satisfying this criterion are considered clinically necessary. Typically, professional judgment is essential in weighing the "benefits" against the "radiation risks", which can be difficult to compare directly. The determination of clinically indicated examinations requires professionals with expertise in both the effects of ionizing radiation and the clinical advantages of nuclear medicine. Nevertheless, it is crucial to have a clear understanding of the magnitude of risk a patient is exposed to during a particular examination. Moreover, it is crucial to understand how these risks vary depending on factors such as age at exposure, gender, and the amount of radiation exposure from nuclear medicine procedures. The findings of this study offer valuable insights into these factors for patients who are undergoing whole-body PET/CT examinations using ^{18}F-FDG radiotracer.

This study reported three important findings from the patient organ dose, effective dose, and LAR of cancer incidence. We assessed the effective dose for both the PET and CT components, along with the corresponding organ cancer risk for the PET component only. We focused on assessing the organ dose from the PET component, and we acknowledge the significance of considering additional external exposure from the CT component in comprehensive cancer risk evaluations. However, because of limited data from CT and the specific objectives of this study, which aimed to isolate the direct contributions of the internal exposure from PET component to the overall radiation burden, the CT component was not included in our organ dose analysis. This approach likely underestimates the total patient risk, as the CT component exposes patients to relatively higher doses that significantly contribute to organ cancer risk. We utilized IDAC-Dose 2.1 to calculate the organ and effective doses for patients undergoing whole-body ^{18}F-FDG PET/CT examinations. Table 3 in the results section indicates that the mean dose from the CT component is nearly 50% higher than that from PET (Alameen *et al.*, 2021; Andersson *et al.*, 2017a; Masoomi *et al.*, 2020). Consequently, it can be inferred that the patient cancer risk associated PET/CT examinations could be approximately 50% higher than the estimates provided in this study.

The variation in absorbed doses across different organs can be attributed to the differential uptake and metabolism of ^{18}F-FDG. In this study, the bladder exhibits the highest radiation dose at 23.483 mGy, which is significantly higher than other organs. This relatively higher dose can be attributed to the metabolic and excretory pathways of ^{18}F-FDG, which accumulate in the urinary tract (Quinn *et al.*, 2016). The brain follows with a dose of 15.244 mGy, likely due to its high glucose uptake and metabolism, which is a characteristic behavior of ^{18}F-FDG as a glucose analog (Boellaard *et al.*, 2015). Murat *et al.* (2023) reported high bladder doses, but with a slightly lower average, suggesting potential variations in scanning techniques (Murat *et al.*, 2023). The high dose in the brain aligns with previous findings, which similarly highlighted the brain's high metabolic activity and resultant dose concentrations (Breustedt *et al.*, 2018; Grimes & Celler, 2014; Masoomi *et al.*, 2020).

Table 3 clearly shows that the mean E for PET/CT examinations in this study is 20.09 ± 7.85 mSv, which could be lower than the values reported in previous studies (Alameen *et al.*, 2021; Huang *et al.*, 2009; Kessara *et al.*, 2023a; Khamwan *et al.*, 2010; Salah *et al.*, 2020). Noting that, the ratio of E to A is 1.61×10^{-2} mSv/ MBq is compliant with the recommendations of the International Commission on Radiological Protection (ICRP, 2008). These findings consistent with prior studies that suggest CT is a major contributor to the overall E in PET/CT scans (Alameen *et al.*, 2021; Andersson *et al.*, 2017a; Khamwan *et al.*, 2010; Masoomi *et al.*, 2020; Salah *et al.*, 2020). Additionally, it has been established that radiation dose observed in CT scans is indicated by the $CTDI_{vol}$ and DLP values. In this study, the imaging protocol used may have a significant impact on the $CTDI_{vol}$ and DLP, as higher tube currents and longer scan

Table 3. Statistical analysis of patient dose information.

Statistics	PET		CT			PET-CT
	A (MBq)	*E* (mSv)	$CTDI_{vol}$ (mGy)	DLP (mGy cm)	*E* (mSv)	*E Total* (mSv)
Min	200.70	3.23	4.40	401.94	6.03	9.26
25th percentile	329.39	5.32	5.01	516.35	7.75	13.07
Median	416.25	6.71	8.24	786.31	11.80	18.51
75th percentile	514.53	8.30	11.90	1223.85	18.36	26.66
Max	646.39	10.40	17.50	1821.73	27.33	37.73
Mean ± SD	424.64 ± 121.19	6.85 ± 1.82	8.82 ± 3.92	882.97 ± 406.91	13.24 ± 6.10	20.09 ± 7.85

Table 4. LAR coefficients for various organs based on BEIR VII Phase II data.

Organ	Sex	b_0	b_1	b_2	b_3	r^2
Stomach	Men	13.43	0.95	–0.01	6.00×10^{-5}	0.9992
	Women	18.81	1.13	–0.02	0.01×10^{-2}	0.9991
Colon	Men	78.86	2.81	–0.04	-1.00×10^{-16}	0.9997
	Women	73.62	0.53	–0.01	-0.01×10^{-2}	0.9999
Liver	Men	–1.72	1.58	–0.03	0.01×10^{-2}	0.9978
	Women	3.00	0.45	–0.01	0.03×10^{-3}	0.9986
Bladder	Men	53.05	1.24	–0.01	0.01×10^{-2}	0.9944
	Women	64.43	0.67	–0.001	-0.02×10^{-2}	0.9998
RBM	Men	152.95	–4.99	0.12	-0.01×10^{-1}	0.9983
	Women	80.64	–1.35	0.03	-0.03×10^{-2}	0.9998
Brain	Men	150.12	5.66	–0.16	0.01×10^{-1}	0.9998
	Women	197.83	3.12	–0.11	0.01×10^{-1}	1.0000
Thyroid	Male	56.80	–2.61	0.04	-0.02×10^{-2}	0.9968
	Female	257.12	–11.77	0.18	-0.01×10^{-1}	0.9982
Lung	Male	88.48	0.52	0.01	-0.03×10^{-2}	0.9987
	Female	190.12	2.30	–0.004	-0.01×10^{-1}	0.9993
All solid	Male	426.00	13.28	–0.27	0.01×10^{-1}	0.9994
	Female	1772.50	–35.13	0.39	-0.03×10^{-1}	0.9998

Table 5. Calculated LAR of cancer incidence based on gender.

Organ	Lifetime attributable risk (no. of cases per 100,000 persons exposed to 0.1 Gy)		
	Mean ± SD		*p*-value
	Men (n = 20)	Women (n = 20)	
Bladder	23.98 ± 5.00	14.90 ± 5.92	<0.05
Lung	6.95 ± 2.92	20.18 ± 7.40	<0.05
Stomach	1.91 ± 0.40	1.41 ± 0.53	<0.05
Liver	0.50 ± 0.99	0.77 ± 0.28	<0.05
Brain	17.04 ± 11.69	22.47 ± 9.37	0.122*
Kidneys	5.42 ± 3.73	7.32 ± 3.05	0.094*
Colon	4.27 ± 2.12	4.06 ± 1.30	0.711*
RBM	3.91 ± 1.57	3.73 ± 1.07	0.670*
Thyroid	0.13 ± 0.23	0.51 ± 0.98	0.107*
Mean ± SD	7.12 ± 7.63	8.37 ± 8.09	0.755*

*Red bone marrow (RBM) indicates leukemia.

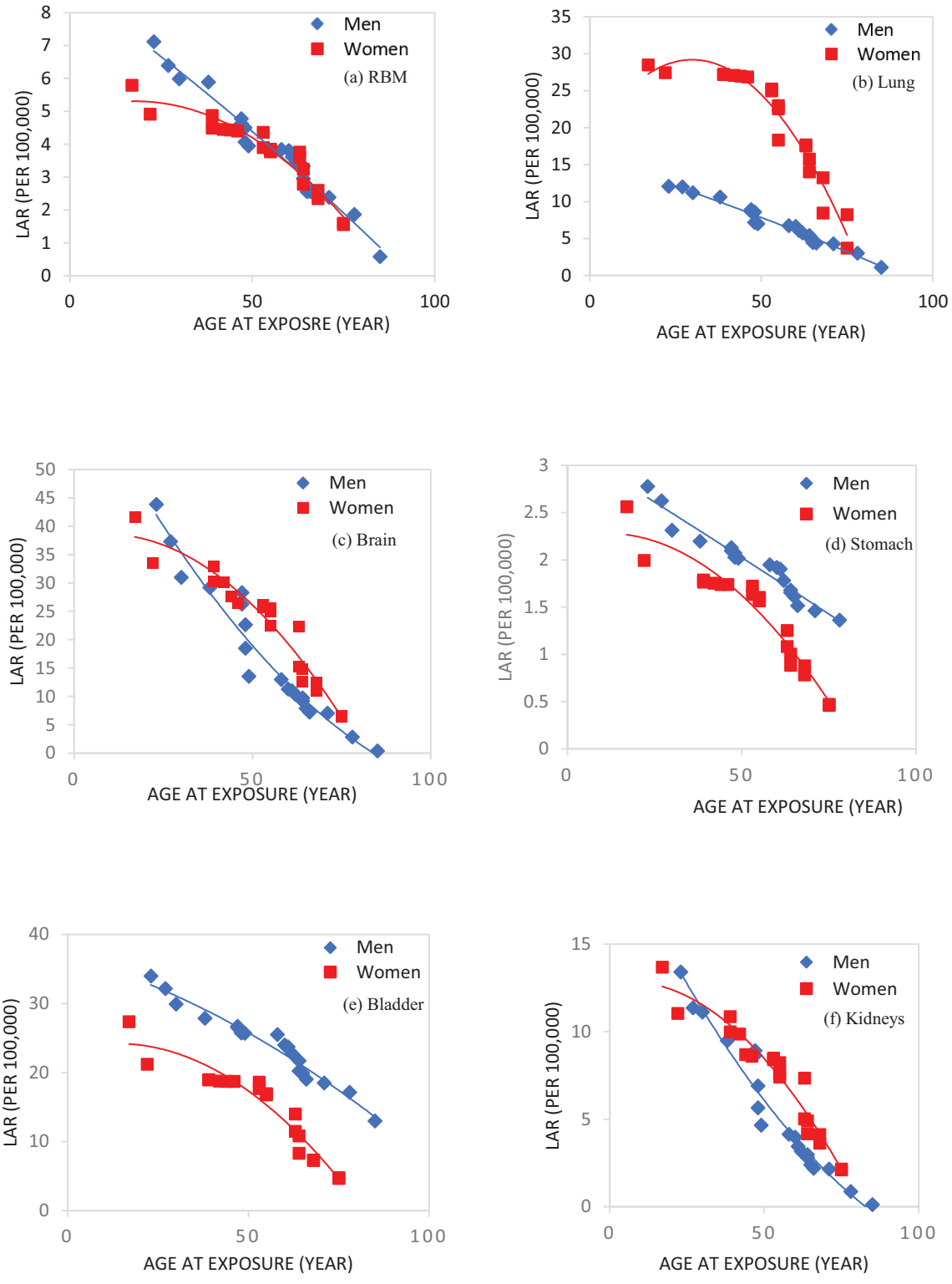

Fig. 2. LAR based on the gender and age at exposure of selected organs: (a) RBM, (b) Lung, (c) Brain, (d) Stomach, (e) Bladder, (f) Kidneys, (g) Thyroid, (h) Liver, and (i) All Solid.

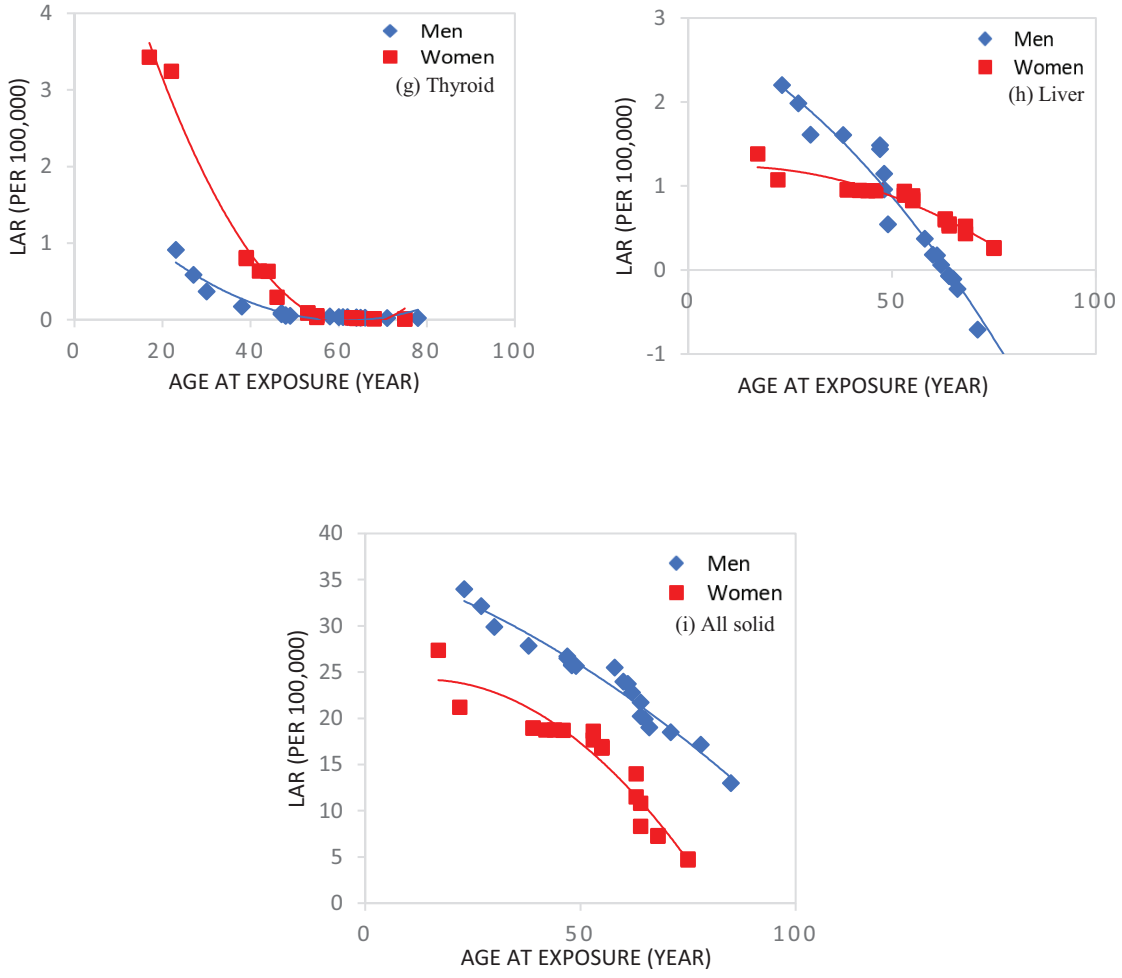

Fig. 2. Continued.

durations typically lead to higher dose (Karim MKA *et al.*, 2017). The imaging protocol and patient's characteristics has been identified as major contributing factor in optimization of CT dose (Harun *et al.*, 2020).

According to ICRP Publication 106, PET/CT examinations conducted in this study are deemed safe, as the E to A ratio does not exceed 1.9×10^{-2} mSv/MBq (ICRP, 2008). However, the E to A ratio depends on the radiopharmaceutical, imaging procedure, and patient characteristics. Factors such as patient age at exposure, body weight, and imaging protocols also play crucial roles in determining the effective dose. It is therefore essential to assess the ratio of effective dose to administered activity across different nuclear medicine procedures to maintain patient radiation safety.

The stochastic risks associated with PET examinations involving the injection of radionuclides into a patient's body generally involve the potential development of cancer and genetic effects that could be seen in those who have been exposed to radiation (ICRP, 2022). However, the radiation dose in PET examinations is generally lower than in other imaging techniques like CT or nuclear medicine therapy (Andersson *et al.*, 2017b; ICRP, 2015; Murat *et al.*, 2023). In this study, we calculated the LAR of cancer incidence and analyzed how different organs contribute to this risk. Organ dose for PET examinations can be estimated by using IDAC-Dose 2.1 by utilizing equation (1) and biokinetics data from ICRP Publication 128 and summarized in results section Table 2. Table 4 present the b coefficient used to calculate LAR, as outlined in equation (4) derived from a 3rd order polynomial generated from the data in the BEIR VII phase II report (ICRP, 2015; National Research Council, 2006). In addition to the radiation dose, estimating LAR involves taking into account factors such as cancer baseline rates from population data, risk models, and survival functions (ICRP, 2022; National Research Council, 2006). In our analysis, we have utilized the BEIR VII phase II report cancer baseline rates as the foundation for estimating LAR associated with radiation exposure. These American cancer baseline rates are derived from extensive epidemiological data collected and maintained by reputable institutions, providing a thorough understanding of cancer incidence across diverse demographics (Kessara *et al.*, 2023; National Research Council, 2006). This makes them a valuable benchmark for risk assessment in this study. However, incorporating local cancer baseline rates such as Asian population, into radiation risk assessment models could provide a more tailored approach to understanding the LAR of the Malaysian population (Halid *et al.*, 2018; Karim MKA *et al.*, 2016).

The differences in LAR values observed in different organs and between men and women are consistent with the patterns seen in the BEIR VII phase II report. For instance, our findings indicate higher LAR values in thyroid and lung tissues, particularly in women, which is consistent with the gender-specific susceptibilities discussed in the BEIR VII phase II report. These observations are reinforced by the age at exposure and gender demographics of our cohort, where differences in metabolic activity and hormonal influences at different age at exposure might affect radionuclide distribution in organs (Alameen *et al.*, 2021; Sprinz *et al.*, 2018). Furthermore, research has demonstrated that some organs are more radiosensitive, such as the thyroid and breast, particularly in females (National Research Council, 2006). Figure 2 in the results section shows a more detailed understanding of the relationship between PET examinations and LAR cancer incidence risk. This figure highlights the importance of age at exposure and gender as key factors in evaluating radiation risk. The used of the 3rd order polynomial approach is justified in providing a closer approximation to the observed data patterns where risk changes from younger to older age at exposure. Studies like (Brenner, 2012) have shown that age at exposure significantly impacts radiation-related cancer risks, particularly in younger populations, where the cancer risk can be significantly higher (Brenner, 2012).

We acknowledge the limitation of our study due to the lack of baseline cancer rates data for Asian populations that could substitute the American population data. Future research should strive to incorporate the local population data to analyze the impact of demographic factors on radiation risks. Furthermore, our analysis of the radiation risks from PET examinations did not include data on organ absorbed doses from the CT component which are crucial for a comprehensive evaluation of total radiation exposure. The lack of this data might compromise the precision of our risk assessment, as the CT component often accounts for a significant contribution for the total dose. To address these limitations, future studies should focus on obtaining detailed measurements of organ absorbed doses from both PET and CT components and also evaluate the LAR of cancer incidence by considering the local cancer baseline rates.

5 Conclusion

In summary, our findings show that the *E* of whole-body ^{18}F-FDG PET/CT examinations vary from 3.2 mSv to 27.3 mSv, and the LAR of cancer incidence among men and women is 7 and 8 cases per 100,000 persons exposed to 0.1 Gy, respectively. It is important to note that these data only represent the PET component, and the radiation risk may be higher when taking into account the organ dose from the CT component. Despite this, there is an increasing demand for whole-body ^{18}F-FDG PET/CT examinations in oncology studies. To ensure radiation safety and improve image quality, protocols should be optimized with advanced image processing techniques, and appropriate image reconstruction parameters.

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Conflicts of interest

The author(s) declare(s) that there is no conflict of interest.

Data availability statement

The data are not publicly accessible as they contain information that could compromise the privacy of research participants.

Ethics approval

This study was approved by the Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia (MOH), which waived patient consent forms for the retrospective analysis with the approval ID; NMRR-18-1176-41991.

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