Technical Note

Embryo/Fetus Doses from ^{18}F-Fludeoxyglucose Radiopharmaceutical in Positron Emission Tomography/Computed Tomography

Nazenin İpek Işıkçı, Mustafa Demir[1]

Department of Electrical and Electronics Engineering, Faculty of Engineering and Architecture, Nisantasi University, [1]Department of Nuclear Medicine, Faculty of Cerrahpasa Medical, Istanbul University-Cerrahpasa, Istanbul, Turkey

Abstract

Aim: The embryo/fetus may be accidentally exposed to ionizing radiation. The aim of this study is to calculate embryo/fetus doses in pregnant women who underwent F-18 fludeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) scan. **Materials and Methods:** Between June 2015 and June 2021, 15 pregnant women underwent F-18 FDG PET/CT applied to the Genetic Research Center (GETAM). The OLINDA/EXM package program was used for internal radiation dosimetry according to the Medical Internal Radiation Dose scheme. FetDose V4 computer software was used to compute the embryo/fetus absorbed dose from CT scan. **Results:** The amount of the injected F-18 FDG activity to patients varied between 333 and 555 MBq. The mean embryo/fetal dose from F-18 FDG was 7.2 ± 2.8 mGy. In addition, the CT component dose to the embryo/fetus dose ranged from 8.5 to 16 mGy with a mean of 12.14 ± 2.05. **Conclusions:** The embryo/fetus dose from F-18 FDG PET/CT was <15 mGy, however, questioning the women's childbearing prior to scintigraphy is the first-line strategy to avoid accidental radiation exposure and stochastic risks.

Keywords: Embryo/fetus dose, F-18 fludeoxyglucose, positron emission tomography/computed tomography, radiation doses

Received on: 06-09-2021 **Review completed on: 12-12-2021** **Accepted on: 28-12-2021** **Published on: 31-03-2022**

Introduction

Nuclear medicine imaging modalities provide important information about disease and pathology and are often a critical component of patient management. F-18 fludeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is an important diagnostic and follow-up method in cancer screening. In pregnant women undergoing PET/CT, the embryo/fetus may be accidentally exposed to ionizing radiation. In this case, ^{18}F-FDG crosses the placental barrier and accumulates in fetal tissues, causing *in vivo* irradiation of the fetus. Therefore, it is important to know the fetal absorbed dose.[1,2]

There are methods developed to calculate embryo/fetal doses retrospectively in PET/CT. Doses from PET can be calculated by the Medical Internal Radiation Dose (MIRD) method, and doses from CT can be calculated using the software.

Recent advances in the fetal dose estimation were driven by Monte Carlo simulations (MCSs). A MCS study showed that the normalized fetal dose estimates ranged from 7.3 to 14.3 mGy/100 mAs, with an average of 10.8 mGy/100 mAs.[3]

In general, prenatal radiation exposure of approximately 10 mGy might enhance the risk of fetal disorders, such as prenatal death, microcephaly, reduced intelligence quotient, organ malformation, mental retardation, intrauterine growth retardation, and childhood cancers. The annual radiation dose limit of 1 mSv was accepted worldwide for general public, and the risk of fetal damage at doses lower than 1 mGy is assumed negligible and riskless.[4] Furthermore, the radiation safety regularities have been established by several local and

Access this article online

Quick Response Code:

Website: www.jmp.org.in

DOI: 10.4103/jmp.jmp_115_21

Address for correspondence: Dr. Nazenin İpek Işıkcı, Department of Computer Engineering, Faculty of Engineering and Architecture, Nisantasi University, Sarıyer, Istanbul, Turkey.
E-mail: nazenin.ipek@nisantasi.edu.tr

How to cite this article: Işıkçı NI, Demir M. Embryo/Fetus doses from ^{18}F-fludeoxyglucose radiopharmaceutical in positron emission tomography/computed tomography. J Med Phys 2022;47:109-13.

global organizations, such as the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection and Measurements. These regularities reported that fetal doses below 100 mGy should not be used as justification for terminating pregnancy.[5] According to the American College of Obstetricians and Gynecologists, potential health risks may arise after cumulative radiation exposure exceeding 50 mSv, depending on the dose and stage of pregnancy.[6]

Since many radiopharmaceutical agents are utilized in nuclear medicine investigations, the variation in the radionuclide biokinetics and excretion rate complicates estimating dose to the embryo/fetus.[7]

The aim of this study is to calculate fetal absorbed doses in pregnant women who were administered F-18 FDG. A further goal was to compare the fetus dose values generated from the mentioned procedures with the risk thresholds reported by ICRP 84.[5]

Materials and Methods

An ethics committee approval numbered 219488 was obtained from Cerrahpasa Medical Faculty for this study. Participants' consent was obtained using an assigned form.

Female patients who were administered ^{18}F-FDG radiopharmaceutical may realize afterward that they were pregnant at the time of PET/CT imaging. Therefore, they may approach a health institution to receive support from teratologic counseling services. In Turkey, Genetic Research Center (GETAM) at Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty provides the necessary services to pregnant patients from all other hospitals. One of the services is estimating the fetal absorbed dose by the medical physics department.

Between June 2015 and June 2021, embryo/fetus doses of 15 pregnant women who were administered F-18 FDG radiopharmaceuticals in different regions of Turkey and approached the GETAM were calculated retrospectively. Gestational age was obtained using ultrasound data. The characteristics of pregnant women who underwent PET/CT are shown in Table 1. All of the pregnant women were in the first trimester of pregnancy and their gestational ages ranged from 4 weeks +4 days to 11 weeks +1 day (mean: 7.4 weeks ±2.6 days).

The OLINDA/EXM package program, employing the MIRD method was used to calculate the absorbed radiation dose resulting from radiopharmaceutical application. This code comprises standard reference phantoms for the adult female involving both pregnant and nonpregnant with three trimesters of pregnancy that are suitable for data analysis. Furthermore, it is allowed to modify the standard reference phantom with the patients' corresponding data such as patient weight.[8,9]

Calculation of fetal doses

OLINDA/EXM 1.0 software was used to calculate embryo/fetus dose arising from nuclear medicine practices. All pregnant women were asked to bring the scan documents in order to collect detailed information about the procedure. The following equation[1] introduced by the MIRD for embryo/fetus dose calculation was applied in the current study:

$$D = \tilde{A} \times S = A_0 \times \tau \times S \quad (1)$$

where D: absorbed dose in a target organ (mGy), Ã: cumulated activity in a source organ (MBq • h), A_0: administered activity (MBq), τ: residence time (h), and S is the dose factor provided in the program ($\frac{mGy}{MBq \bullet h}$).

Each radiopharmaceutical has different biokinetics in the human body and thus the effective half-life is also variable and must be derived separately for each patient and examination. Individual embryonal/fetal dosimetry is impossible as no prescan procedures could be tried for dose estimation. Instead, the ^{18}F-FDG kinetic data and the organs' specific residence time were generated from the phantom study reported by Russell *et al*.[10] The early, 3-month pregnant female model was selected for all calculations, and only the patient's weight was replaced in the program. The time-integrated activity coefficients for the fetuses (or the uterus for patient 1) were combined with the standard coefficients of the pregnant organs according to ICRP publication 106.[7] The time-integrated activity coefficients were entered into the residence time page shown in OLINDA/EXM, and then the code was run to generate the fetal doses.

FetDose V4 computer software was used to compute the fetus absorbed dose from CT. A set of equations were used to estimate the CT-related dose following PET/CT scans.[11] The fetal dose (D_f) from CT scans was calculated using the formula (2) as seen below:

$$D_f = \frac{\left(NUD_V \times CTDI_{\text{Soft tissue}} \times \left[\frac{mAs}{100} \right] \right)}{Pitch} \quad (2)$$

where CTDI is CT dose index, $CTDI_{soft\ tissue}$ (mGy/100 mAs) is the $CTDI_{air}$ to ICRU muscle ($CTDI_{soft\ tissue} = CTDI_{air} \times 1.07$) used as approximations for the dose to soft tissue within the body, and NUD_V is the sum of the normalized doses for all 5-mm slabs lying within the scan volume.[12]

The calculated overall doses from CT and ^{18}F-FDG to embryo/fetus were reported in the results section.

Results

PET/CT scans were made at different nuclear medicine centers in Turkey. The amount of F-18 FDG activity injected into patients varied between 333 and 555 MBq. The mean embryo/fetal dose from F-18 FDG was 7.2 ± 2.8 mGy. The embryo/fetus dose from the CT component ranged from 8.5 to 16 mGy, with a mean of 12.14 ± 2.05 [Table 2].

Table 1: Characteristics of patients and ^{18}F-FDG residence time

Patient number	Age (years)	Weight (kg)	Stage of gestation (week + day)	Time-integrated activity (Bq-h/Bq)
1	28	61.7	7+3	0.0041
2	27	79.2	11+0	0.0015
3	31	62.0	6+3	0.0032
4	27	57.3	5+2	0.0028
5	27	71.1	8+3	0.0052
6	23	58.0	4+4	0.0022
7	32	63.3	5+2	0.0027
8	29	67.0	7+6	0.0048
9	30	71.1	7+2	0.0051
10	24	81.2	11+1	0.0075
11	24	76.3	7+4	0.0054
12	25	67.0	6+1	0.0039
13	24	86.6	10+3	0.0062
14	27	81.9	9+2	0.0055
15	28	75.4	8+3	0.0067
Mean±SD	27.06±2.71	70.6±9.2	7.4±2.6	0.04453±0.001734

SD: Standard deviation, ^{18}F-FDG: ^{18}F-fludeoxyglucose

Table 2: ^{18}F-FDG activities, PET/CT embryo/fetus doses, and normalized doses of per unit activity (MBq)

Patient number	Activity (MBq)	Embryo/fetus dose from F-18 FDG (mGy)	Embryo/fetus dose per unit activity (mGy/MBq)	Embryo/fetus dose from CT (mGy)
1	555	9.60	0.017	11.3
2	518	6.73	0.013	13.1
3	555	7.21	0.013	16.0
4	555	13.87	0.025	8.5
5	518	6.73	0.013	10.0
6	333	8.32	0.025	12.3
7	518	12.95	0.013	13.1
8	481	6.25	0.013	14.2
9	518	6.73	0.013	9.8
10	370	4.81	0.002	11.0
11	407	5.29	0.002	12.2
12	370	4.81	0.002	13.2
13	370	4.81	0.002	15.1
14	407	5.29	0.002	11.9
15	370	4.81	0.002	10.5
Mean±SD	456.3±82.3	7.2±2.8	0.0104±0.0081	12.14±2.05

SD: Standard deviation, ^{18}F-FDG: ^{18}F-fludeoxyglucose, PET: Positron emission tomography/, CT: Computed tomography

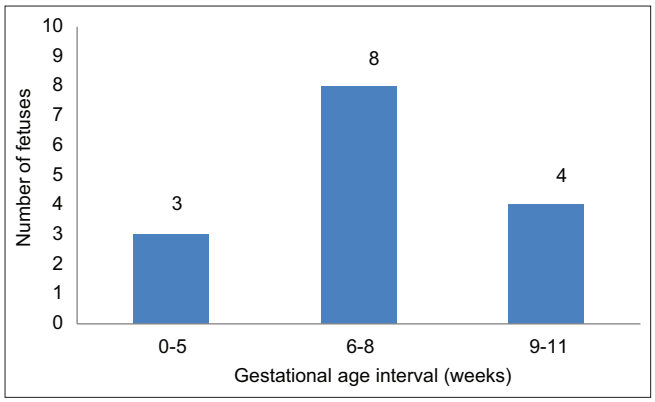

Figure 1: Number of fetuses corresponding to the pregnant women's gestational age intervals

The number of fetuses corresponding to the pregnant women's gestational age intervals is shown in Figure 1. The relation between absorbed dose interval and the number of fetuses is shown in Figure 2.

Discussion

PET/CT embryo/fetus dosimetry is performed in two stages: first, the calculation of dose resulting from ^{18}F-FDG, and then, the CT dose contribution is estimated. The fetal dose from F-18 FDG has been reported as 0.81 mGy/mCi (0.0219 mGy/MBq) in the early and 3-month period of pregnancy.[10,13-15] In our study, the embryo/fetal dose per unit activity was found to be 0.0104 ± 0.0081 mGy/MBq. Zanotti-Fregonara *et al.* calculated the total fetal dose of 21.0 mGy for a pregnant

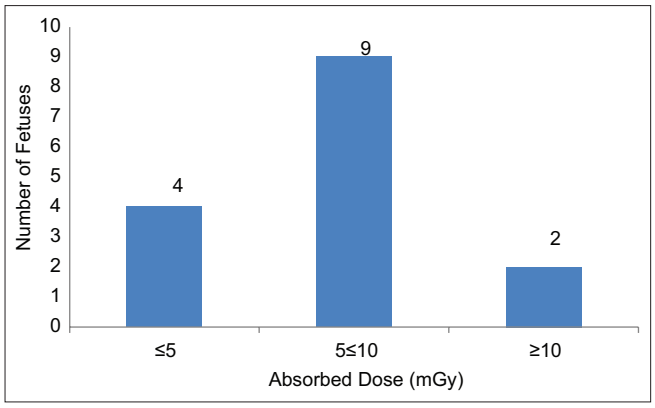

Figure 2: Distribution of embryo/fetus doses according to the number of fetuses

woman undergoing PET/CT, and reported that 10 mGy of that dose arose from CT scan.[14] The present results showed that an average radiation dose of 8.19 ± 0.83 mSv and 13.44 ± 5.14 mSv from PET and CT components, respectively, resulted in a total dose of 21.64 ± 5.20 mSv.[15] The total effective dose ranged from 8.0 to 24.05 mSv using General Electric Healthcare (Discovery STE, 16, BGO) and 8.35–26.85 mSv using Philips Medical Systems (Gemini TF 16, LYSO) scanner, resulting in differences of 4.3%–15% for the low-dose scan and 4.1%–11% for standard-dose scans. The CT component contribution to the total dose was between 32% and 77% for GE, and 35% and 79% for Philips.[16] Huang *et al*.[17] reported that the fetal dose from 328 MBq ^{18}F-FDG was 6.25 mSv, and Liu *et al*.[18] likewise reported fetal dose from 370 MBq ^{18}F-FDG as 6.28 mSv. Zanotti-Fregonara *et al*.[1] reported that fetal doses from 328 MBq F-18 FDG ranged from 6.29 x 10-3 to 2.46 x 10-2 mGy/MBq mGy/MBq in six cancer women with known pregnancy.[1] Takalkar *et al*.[19] reported that the fetal dose from 173.9 to 340.4 MBq F-18 FDG was estimated to be 9.04 mGy in five women with known pregnancy.

In our study, the mean embryo/fetus dose from F-18 FDG was found to be 7.2 ± 2.8 mGy. In general, 6–16-slice diagnostic CT is used in PET/CT equipment ensuring a relatively low dose from CT. However, the dose level may change in CT scan according to the CTDIvol value for each patient.[20]

Hsieh *et al*.[21] reported in 2012 that patients in their first trimester had a fetal dose of 6.3 mGy from F-18 FDG, and a CT dose as low as 3.6 mGy leading to a total dose of 9.9 mGy. In contrast, our study showed that the mean embryo/fetus dose from CT scan was 12.14 ± 2.05 mGy, while the mean embryo/fetal dose from 456.3 ± 82.3 MBq F-18 FDG activity was 7.2 ± 2.8 mGy. The total embryo/fetus dose resulting from PET/CT procedure was 19.34 ± 3.5 mGy.

Conclusions

ICRP Publication 84 states that radiation-induced malformations have a threshold of 50–100 mGy (5–10 rad). Accordingly, the diagnostic nuclear medicine examinations often induce fetal dose less than the dose threshold (50–100 mGy) of the teratogenic effects reported by ICRP 84. Thus, fetal doses below 100 mGy should not be considered a reason for terminating a pregnancy after radiation exposure.

The embryo/fetus dose from F-18 FDG PET/CT was less than 50 mGy which is the threshold dose for teratogenic effects dose, however, questioning the women's childbearing prior to scintigraphy is the first-line strategy to avoid accidental radiation exposure and the arising stochastic effects.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Zanotti-Fregonara P, Laforest R, Wallis JW. Fetal radiation dose from 18F-FDG in pregnant patients ımaged with PET, PET/CT, and PET/MR. J Nucl Med 2015;56:1218-22.
2. Stabin MG. New-generation fetal dose estimates for radiopharmaceuticals. J Nucl Med 2018;59:1005-6.
3. Sensakovic WF, Royall I, Hough M, Potrebko P, Grekoski V, Vicenti R. Fetal dosimetry at CT: A primer. Radiographics 2020;40:1061-70.
4. Ozbayrak M, Cavdar I, Seven M, Uslu L, Yeyin N, Tanyildizi H, *et al.* Determining and managing fetal radiation dose from diagnostic radiology procedures in Turkey. Korean J Radiol 2015;16:1276-82.
5. International Commission on Radiological Protection. Pregnancy and medical radiation. Ann ICRP 2000;30:iii-viii, 1-43.
6. ACOG Committee on Obstetric Practice. ACOG Committee Opinion. Number 299, September 2004 (replaces No. 158, September 1995). Guidelines for diagnostic imaging during pregnancy. Obstet Gynecol 2004;104:647-51.
7. International Commission on Radiological Protection. Radiation dose to patients from radiopharmaceuticals. Ann ICRP 2008;38:1-2.
8. Stabin MG, Sparks RB, Crowe E. OLINDA/EXM: The second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med 2005;46:1023-7.
9. Pandit-Taskar N, Dauer LT, Montgomery L, St. Germain J, Zanzonico PB, Divgi CR. Organ and fetal absorbed dose estimates from 99mTc-sulfur colloid lymphoscintigraphy and sentinel node localization in breast cancer patients. J Nucl Med 2006;47:1202-8.
10. Russell JR, Stabin MG, Sparks RB, Watson E. Radiation absorbed dose to the embryo/fetus from radiopharmaceuticals. Health Phys 1997;73:756-69.
11. Osei EK, Kotre CJ. Equivalent dose to the fetus from occupational exposure of pregnant staff in diagnostic radiology. Br J Radiol 2001;74:629-37.
12. ICRP. Doses to the embryo and fetus from ıntakes of radionuclides by the mother. A report of the International Commission on Radiological Protection. ICRP Publication 88 Ann ICRP 2001;31:19-515.
13. Stabin MG. Proposed addendum to previously published fetal dose estimate tables for 18F-FDG. J Nucl Med 2004;45:634-5.
14. Zanotti-Fregonara P, Jan S, Taieb D, Cammilleri S, Trébossen R, Hindié E, *et al.* Absorbed 18F-FDG dose to the fetus during early pregnancy. J Nucl Med 2010;51:803-5.
15. Li Y, Jiang L, Wang H, Cai H, Xiang Y, Li L. Effective radiation dose of 18F-FDG PET/CT: How much does dıagnostıc CT contrıbute? Radiat Prot Dosimetry 2019;187:183-90.
16. Adeleye B, Chetty N. Radiation dose from 18F-FDG PET/CT procedures: İnfluence of specific CT model and protocols. Radioprotection 2018;53:107-13.

17. Huang B, Law MW, Khong PL. Whole-body PET/CT scanning: Estimation of radiation dose and cancer risk. Radiology 2009;251:166-74.
18. Liu Y. The role of 18F-FDG PET/CT in the follow-up of well-differentiated thyroid cancer with negative thyroglobulin but positive and/or elevated antithyroglobulin antibody. Nucl Med Commun 2016;37:577-82.
19. Takalkar AM, Khandelwal A, Lokitz S, Lilien DL, Stabin MG. 18F-FDG PET in pregnancy and fetal radiation dose estimates. J Nucl Med 2011;52:1035-40.
20. Inoue Y, Nagahara K, Tanaka Y, Miyatake H, Hata H, Hara T. Methods of CT dose estimation in whole-body ^{18}F-FDG PET/CT. J Nucl Med 2015;56:695-700.
21. Hsieh TC, Wu YC, Sun SS, Chu LY, Yen KY, Kao CH. FDG PET/CT of a late-term pregnant woman with breast cancer. Clin Nucl Med 2012;37:489-91.