Short Communication

^{18}F-Fludeoxyglucose Absorbed Dose Estimation in Fetus during Early Pregnancy

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Abstract

The purpose of this study is to assess a rare case of fetal radiation absorbed dose here through ^{18}F-Fludeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) in early pregnancy (5-week-old fetus). The fetal absorbed dose due to the radiation emitted from the mother's body, the fetus self-dose, and the dose received from CT were computed. The 35-year-old patient, weighing 85 kg, was injected with 370 MBq of ^{18}F-FDG. Imaging started at 1 h with CT acquisition followed by PET imaging. The photon and positron self-dose was calculated by applying the Monte Carlo (MC) GATE (GEANT 4 Application for Tomographic Emission) code. The volume of absorbed dose from the mother's body organs and the absorbed dose from the CT were added to the self-dose to obtain the final dose. The volume of self-dose obtained through MC simulation for the fetus was 3.3×10^{-2} mGy/MBq, of which 2.97×10^{-2} mGy/MBq was associated with positrons and 0.33×10^{-2} mGy/MBq was associated with photons. Biologically, the absorbed dose from CT, 7.3 mGy, had to be added to the total dose. The absorbed dose by the fetus during early pregnancy was higher than the standard value of 2.2×10^{-2} mGy/MBq (MIRD DER) because, during the examinations, the mother's bladder was full. This issue was a concern during updating standards.

Keywords: *18F-Fludeoxyglucose, fetus, GATE, maternal dose, Monte Carlo simulation, positron emission tomography/computed tomography, pregnancy*

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Introduction

Several million radiopharmaceutical ^{18}F-Fludeoxyglucose (FDG) are performed annually worldwide for cancer staging, but only very few of them are administered accidentally to pregnant patients who are not aware of their pregnancy or those patients in need of positron emission tomography (PET) scanning for clinical indications.[1,2] As the developing fetus is sensitive to radiation during its growing stage, it requires more specific clinical care. Therefore, it is necessary to evaluate the fetus's absorbed dose. The absorbed dose in the fetus during PET/computed tomography (CT) can be due to photons emitted from the mother's body, self-dose from positrons, photons, and dose from CT.[3] By applying Monte Carlo (MC) dosimetry methods and computational phantoms, the fetal absorbed dose, due to the emitted photons from different mother organs, was estimated. However, for a part of fetal absorbed dose which is related to the absorbed radiopharmaceutical ^{18}F-FDG, information was obtained by *in vivo* method from medical scanned images of the patient. This dose is referred to as self-dose and includes doses due to photons and positrons.[4] The absorbed dose in the fetus through CT was estimated using the CT dose index ($CTDI_{vol}$) recorded in the console device by applying the relevant corrections to each organ.[5,6]

Researchers assessed the fetal absorbed dose volume in a 30-year-old woman weighing 70 kg 7-week pregnant injected with 296 mGy/MBq ^{18}F-FDG subjected to PET/CT scan.[3] She announced that she was not pregnant because of using an intrauterine device, visible in CT image; thus, she was not subjected to a pregnancy test. The standard uptake value (SUV) was calculated through return on investment (ROI). The MC method was applied to estimate the fetus self-dose of

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positron and photon doses which were due to absorption of an estimated 3.0×10^{-2} mGy/MBq including 90% of the positron and 10% of photon. Using the Organ Level Internal Dose Assessment (OLINDA) software,[6] the fetal absorbed dose volume due to photons from different regions of mothers' body was obtained at 4.0×10^{-2} mGy/MBq. Due to partial volume effect, the SUV_{max} was applied to estimate the absorbed activity in the fetus instead of the SUV average.

An exposure case study of a 6-week fetus was assessed by Takalkar *et al*.[7] The patient weighing 68 kg was injected with 583 mGy/MBq ^{18}F-FDG. The fetus SUV volume was calculated through ROI. Although this fetus was not observable, its dose was considered as the equivalent of the uterus dose. Applying the OLINDA (version 1.1), the uptake dose volume in the fetus was 3.14×10^{-2} mGy/MBq. The pregnancy test of the subject before the PET scan was negative. Six cases of fetus exposure, which one of them was 5 weeks old, were assessed by Zanotti-Fregonara *et al*.[8] The weight of this patient was 86 kg, and the injected activity was 296 mGy/MBq of ^{18}F-FDG to scan by PET/CT. Although this fetus was not observable, its dose also was considered as the equivalent of the uterus dose. By applying OLINDA, the fetus uptake dose showed 1.73×10^{-2} mGy/MBq. In this evaluation model, the bladder discharge dynamic was determined through OLINDA.

Fetal absorbed dose of 19 pregnant women with fetuses within 5–34-week age range was estimated by Zanotti-Fregonara.[9] In 15 cases, the fetus inside the uterus was clearly detectable, and the fetal absorbed dose of ^{18}F-FDG in the fetal tissues could be directly estimated. Mathematical modeling of human data was performed by extrapolating human data and real voxel-based phantoms,[10] with the new standardized values for estimating fetal dose by Stabin. Due to the importance of the subject of fetal radiation absorbed dose during pregnancy, simulation and experimental works have been performed. Since the real cases are rare, most of the work is based on simulation which some of them were reviewed in this section. The importance of our study is that it is an Iranian rare case that underwent an ^{18}F-FDG with PET/CT scan that has occurred in the world, and it could improve the last proposed new fetal radiation doses for ^{18}F-FDG in early pregnancy. We obtained real and experimental information and obtained an accurate fetal dose estimate with a new PET/CT device and compared it with other results. The absorbed dose, in our case at early pregnancy (5-week-old fetus), includes photons absorbed from the mother's organs, self-dose, and dose absorbed from the CT were calculated separately using actual data and MC methods.

Materials and Methods

The case study in the present work was a pregnant woman aged 35, weighing 85 kg, diagnosed with non-Hodgkin Lymphoma B-cell (high grade) disease that underwent FDG PET/CT imaging. Seven months before PET/CT scanning, the patient underwent chemotherapy twice and radiotherapy once. The patient was scanned through the Philips Ingenuity TF mode PET/CT scanner, with 64 slices, injected with 370 MBq of ^{18}F-FDG 1 h before scanning. The scanning covers the whole body (Skull to the mid-thigh level) in 3D imaging for 22 min in 11-bed positions, each for 2 min. To improve image quality, the image reconstruction method OS-EM, BLOB-OS-TF algorithm, and the CT data were applied. The CT parameters consisted of 100 mAs 120 keV and a slice thickness of 5 mm. According to the hospital rules, the patient was asked about her last menstruation, contraceptive use, or other related issues. Considering that she has been infertile for 10 years following marriage. She was trustful that she was not pregnant, and no pregnancy test was performed. After scanning and reviewing the images, her pregnancy with a fetus of 5 weeks becomes evident. Here, the fetal absorbed dose from the photons emitted from the mother body, the self-dose, and the CT dose were all evaluated.

Self-dose

The mean volume of average concentrated activity in the fetus was computed by drawing ROI around the fetus. For calculation of the absorbed, cumulated activity in the fetus was multiplied by the fetus mass using the fetus's shape, and mass was estimated through accessible features in DICOM image reading software. Here, it was assumed that the absorbed radiopharmaceutical was not removed biologically. The photon self-dose and the fetus position were computed by applying the MC GATE code.[11] GATE is a well-known MC simulation platform based on GEANT4 dedicated to nuclear imaging and dosimetry applications. Using GATE code, it can be possible to simulate time-dependent problems such as the movement of the detector, phantom, and the radioactive decay of the source. The physics instructions in the GATE code have been written based on the Geant4 library. A variety of outputs such as binary image, dose, and fluency can be obtained from GATE simulations. In this study, we applied output dose to our simulation, and the designed phantom for our simulation was a cylinder with 7.13 mm height and 3.21 mm diameter. Cylinder material was set equivalent to fetus material in density and composition. The source was defined as a mono-energy 120 keV photons.

Photon dose

So long as there is no change in the abdominal organs, usually, the uterus replaces fetus photon dose during early pregnancy for calculation purposes.[5] Since the single static imaging began 1 h after radiopharmaceutical injection, the cumulated activity in the mother's organs was unknown. The ^{18}F-FDG radiopharmaceutical data (Standard Time Integrated Activities) were applied based on ICRP No. 106.[12] The average photon dose from the mother's organs to the uterus was obtained through the MIRD scheme, Eq. 1:

$$D = \Sigma\widetilde{A} \times S = \Sigma A_o \times \tau \times S \qquad (1)$$

where, the S-factors for ^{18}F-FDG were provided through the radiation dose assessment resource group.[13]

Computed tomography dose

When the uterus image appears in FOV of CT imaging, the fetus doses are the same as the $CTDI_{vol}$ value. The CT dose value was obtained by applying the $CTDI_{vol}$ recorded on the device console.[13,14] Thus, the CT dose to the fetus can be calculated using Eq. 2:

$$D = \Gamma_T^{CT}\ CTDI_{vol} \qquad (2)$$

where Γ_T^{CT} is an organ-specific dose coefficient for each tissue which can be estimated using the TLD measurements dosimetry method on the Alderson phantom that relates $CTDI_{vol}$ to dose as pursued by.[5,15]

Results

The accurate observation of the fetus due to being 5 weeks in the PET image was difficult. Still, due to the large size of the uterus, the fetus was visualized in the uterine cavity [Figure 1]. The fetus's shape was considered in a cylindrical structure, located behind the mother's bladder. The average concentration activity in the fetus as estimated through the ROI method was 6901 Bq/cm^3, which was multiplied by the fetal mass volume concentration to yield the cumulated activity. The dimensions of the fetus were 7.13 mm in length and 3.21 mm in average diameter, thus a volume of 58 mm^3, with 40,026 Bq cumulative activities. Furthermore, the resolution of the PET/CT device was 4 mm, and as to the fetus volume, there exists no partial volume effect in the case.[16]

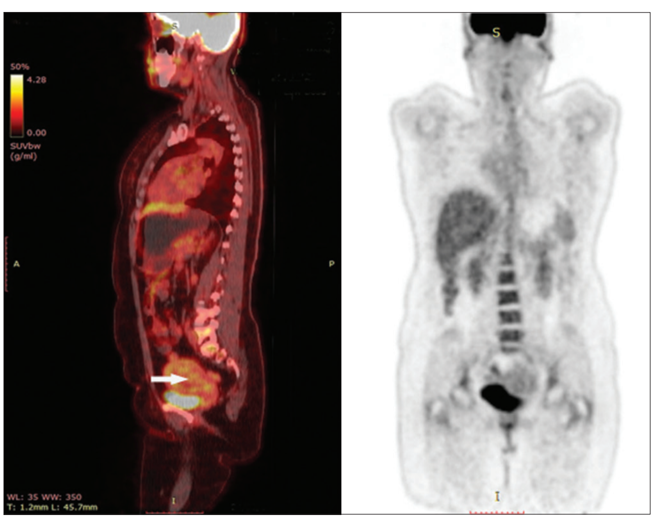

Figure 1: Sagittal ^{18}F-Fludeoxyglucose positron emission tomography/computed tomography (left) and coronal (right) positron emission tomography image of the patient with Hodgkin Lymphoma B cell (high grade) disease. The patient had been pregnant for 5 weeks, and the embryo is indicated by the white arrow

Because the patient's bladder was not completely voiding at the time of imaging, the volume of fetal absorbed dose from the mother's bladder compared to other mother organs was higher. The average concentration activity in the bladder of this patient obtained through ROI whole bladder was 18,892 Bq/cm^3, which according to the average volume of 350 cm^3.[17] Here, the cumulative activity was 6,612,200 Bq, respectively. The patient's images indicate that she responds to treatment as to her "Non-Hodgkin lymphoma B-cell (high grade)" disease.

Self-dose

The total disintegrations in the fetus were 3.87×10^6/MBq due to injected activity to the mother. The volume of energy released and absorbed in the fetus was 1.2×10^6 MeV/MBq estimated through MC simulation computation, from which the fetal absorbed dose was 3.3×10^{-2} mGy/MBq. The 2.97×10^{-2} mGy/MBq of this value was related to the positrons, and 0.33×10^{-2} mGy/MBq was related to the photons.

Photon dose

The photon-dose volume released from different organs of the mother to the fetus was 1.07×10^{-2} mGy/MBq. The total absorbed dose by this fetus was about 4.37×10^{-2} mGy/MBq, but from this patient, concerning the 370 MBq injection of the ^{18}F-FDG radiopharmaceutical, it was 16.2 mGy.

Computed tomography dose

Based on $CTDI_{vol}$ value recorded through the device console, 6.5, and the correction coefficient obtained through Birx, which was (1.11 ± 0.04), the absorbed dose by fetus through CT was 7.3 mGy. This, in turn, made the total absorbed dose by the fetus 23.5 mGy (16.2 + 7.3).[9] The results of the fetus absorbed dose in early pregnancy in this study together, with the results of available related studies, were tabulated and compared in Table 1.

Discussion

Estimating the fetal absorbed dose due to ^{18}F-FDG injections to the mother because of the skeleton nonformation, as all drawing contour around the fetus, is one of the most controversial issues in fetal dose in early pregnancy, due to it is not being observed accurately. This issue included photon emission from the mother's body, self-absorption dose, and dose emitted through the CT.

Here, it was observed that the volume of absorbed dose by this fetus of 5 weeks was approximately 4.37×10^{-2} mGy/MBq as a result of injected ^{18}F-FDG into the mother. This volume was higher than the standard for early pregnancy.[18] Concerning the injection of 370 MBq to the mother, the fetal absorbed dose was 16.2 mGy, and the same through PET/CT was 7.3 mGy due to the attenuation correction issue, which should be added to the absorbed

Table 1: Comparison of fetal absorbed dose in early pregnancy due to ^{18}F-FDG radiopharmaceutical with available related studies

Stage of gestation (weeks)	Weight (kg)	Injected activity (MBq)	Machine	Phantom (trimester)	Dose olinda1 (mGy/MBq)	Dose olinda2 (mGy/MBq)	Our study	References
5	86	296	PET/CT	Nonpregnant	1.73×10^{-2}	1.92×10^{-2}	-	[8]
6	68	583	PET	Nonpregnant	3.14×10^{-2}	3.29×10^{-2}	-	[7]
10	70	296	PET/CT	Nonpregnant	2.08×10^{-2}	2.26×10^{-2}	-	[3]
5	85	370	PET/CT	Nonpregnant	-	-	4.37×10^{-2}	Our study

^{18}F-FDG – Fluorodeoxyglucose; PET/CT – Positron Emission Tomography/Computed Tomography

dose from the ^{18}F-FDG radiopharmaceutical by the fetus, to have a total fetus absorbed dose of 23.5 mGy. At this stage of pregnancy, the threshold for deterministic effects for definitive outcomes such as fetus *Lethality* was 250–500 mGy; fetus head size reduction was 200 mGy, and growth retardation rate was 50–250 mGy.[19] As observed, the findings here were well below the threshold for deterministic effects. These findings indicated that, upon necessity, becoming exposed to PET/CT has no reason for hesitation. This by no means discounts the notion of taking appropriate measures in reducing fetus radiation absorption through a reduction in activity injection and applying the protocols in low-dose CT scanning.

Regarding this subject, few points are of the essence: (a) in the past decade, according to the turned in documents by the patients claiming, they are not pregnant, pregnancy tests are not run, (b) despite the constant notifications from the nuclear medicine department physicist on having empty bladder during the tests, this subject is with a full bladder, and (c) though the patient weight and the proportional injection volume activity increase per/kg does not have a significant effect on image quality,[20] in the case of being aware of her pregnancy, she would have had less volume of FDG that would yield the same image quality.

The fetal absorbed doses due to ^{18}F-FDG activity injected to the mother at 5, 6, and 10 weeks according to OLIND2 software were 1.92×10^{-2} mGy/MBq, 3.29×10^{-2} mGy/MBq, and 2.26×10^{-2} mGy/MBq, respectively, which were higher than previously obtained volume in Table 1. The volume of fetus doses was based on the temporal activity of human volumes obtained from the four patients in the early pregnancy period based on OLIND2 indicated 2.6×10^{-2} mGy/MBq, which was less than the volume obtained in the case. The higher dose of this fetus is due to the reasons such as (1) the fetal absorbed dose constituted 75.5% self-dose, and 68% was from the positron, due to the larger size and dimension of the fetus in this case compared to the normal case and therefor more radiopharmaceutical absorption, and (2) the image obtained from this patient revealed that, due to the patient's full bladder, the absorbed dose from the mother's bladder was higher than that of the other cases. The entire bladder, in this case, was one of the critical factors in fetal absorbed dose increase, which was confirmed in studies run by Zanotti-Fregonara and Takalkar.[8,18]

There were existed uncertainties in estimating the fetal absorbed dose that should be of concern. Uncertainty in the fetus shape in the womb when drawing ROI, single static imaging only 1 h after injection (cumulative activity estimation), and applying the stabilizer or voxel-based phantom or maternal volumetric or hybrid phantom, constituted uncertainties in fetal dose estimation at early pregnancy. The dosimetry data were involved in deciding on a PET/CT scan for a pregnant woman. When staging cancer in a pregnant woman, PET/CT is run, some measures through more accurate dosimetry data of the fetus can be done without any fetus does increase.[21] These measures include abdominal dynamic scanning at different periods to obtain the amount of cumulative activity absorbed in the fetus and encourage the patient to an empty bladder, reduce fetal absorbed dose half without altering the image quality. Applying low-dose CT imaging protocols is another practical, viable approach in reducing the fetal absorbed dose. These results related to a fetus with high absorption dose from the mother's bladder could be used, revising the standard fetus radiation dosimetry.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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