

Fetal Dose from Positron Emission Tomography and Computed Tomography in Pregnant Patients

Christiane Sarah Burton^{a)†}, PhD, Kirk Frey^{b)}, MD, Frederic Fahey^{c)}, ScD, Mark S. Kaminski^{d)}, MD, Richard K. J. Brown^{e)}, MD, Judith M. Pohlen^{b)}, MD, Barry L. Shulkin^{a)}, MD

^{a)}St Jude Children's Research Hospital, 262 Danny Thomas Pl, Memphis, TN, 38105, United States

^{b)}Michigan Medicine, 1500 E Medical Center Dr, Ann Arbor, MI, 48109-5028, United States

^{c)}Children's Hospital, 300 Longwood Ave, Boston, MA, 02115, United States

^{d)}University of Michigan, 500 S State St, Ann Arbor, MI, 48109, United States

^{e)}University of Utah School of Medicine, 30 N 1900 E, Salt Lake City, UT, 84132, United States

†christiane.burton@stjude.org

work: 901-595-3927

word count: 6439

Abstract

In cases where pregnancy is discovered during or after a diagnostic examination, the physician or the patient may request an estimate of the radiation dose received by the fetus as per guidelines and standard operating procedures (SOPs). This study provides the imaging community with dose estimates to the fetus in PET/CT with protocols that are adapted to low dose protocols for patients known to be pregnant from the University of Michigan. There were nine patients analyzed with data for the first, second and third trimester, the availability of which is quite rare. These images were used to calculate the size-specific dose estimate (SSDE) from the CT scan portion, and the standard uptake value (SUV) and ^{18}F -FDG uptake dose from the PET scan portion using the Medical Internal Radiation Dose (MIRD) formulation. The fetal dose estimates were tested for correlation with each of the following independent measures: gestational age, fetal volume, average water-equivalent diameter of the patient along the length of the fetus, size-specific dose estimate (SSDE), SUV, percentage of dose from FDG . Stepwise multiple linear regression analysis was performed to assess the partial correlation of each variable. This is the first study where fetal doses have been determined from CT and PET images. Fetal self-doses from ^{18}F for the 1st, 2nd and 3rd trimester range from 2.18 mGy (single data point), 0.74-1.82 mGy and 0.017-0.0017 mGy. The combined SSDE and fetal self dose ranges from 1.2-8.2 mGy. These types of images from pregnant patients are rare. Our data indicate that the fetal radiation exposure from ^{18}F -FDG PET and CT performed, when medically necessary, in pregnant women with cancer is low. All efforts should be made to minimize the fetal radiation exposure by modifying the protocol appropriately.

Introduction

Diagnostic imaging that uses ionizing radiation may sometimes be necessary for a pregnant patient despite the potential risk to the fetus. Typically, when such diagnostic information is needed, it is relating to the health of the mother. When a radiologist or nuclear medicine physician needs to decide if the diagnostic benefits will outweigh the risks of radiation, it is important they have a reasonable estimate of radiation dose to the fetus. In cases where pregnancy is discovered during or after a diagnostic examination, the physician or the patient may request an estimate of the radiation dose received by the fetus. The risks of fetal adverse outcomes, including childhood cancer induction, are small at a dose of 100 mGy and negligible at doses of less than 50 mGy. [1,2] In the case of hybrid imaging where both modalities involve radiation, the fetal dosimetry resulting from both modalities should be considered. One example is positron emission tomography/computed tomography (PET/CT) where the CT scan provides anatomic information, and the PET scan provides information on radionuclide uptake at the tumor site. Fetal dose estimates from CT have been primarily based on Monte Carlo simulations of geometric patient models. [3-5] PET studies of pregnant patients are extremely uncommon, and even ^{18}F -FDG PET studies accidentally performed in pregnant patients are rare. [6-11] Therefore, providing fetal dose estimates from CT and ^{18}F -FDG PET images where the dose can be estimated from the image itself and from dose reports would be helpful to the medical imaging community. In this study, fetal dose estimates for PET/CT scans that are based on a series of pregnant patients in their first, second and third trimester. These images were used to calculate the size-specific dose estimate (SSDE) [12] from the CT scan portion, and the standard uptake value (SUV) and ^{18}F -FDG uptake dose from the PET scan portion using the Medical Internal Radiation Dose (MIRD) formulation. This study will provide the imaging community with dose estimates to the fetus in PET/CT based on patient data, the availability of which is quite rare.

Methods and materials

Pregnant Patient Population

A total of nine ^{18}F -FDG PET/CT scans performed in pregnant patients over an 11 year period at the University of Michigan were analyzed. The axial range of these scans covered the full uterus. The gestational ages of the fetuses of these patients ranged from 3 to 40 weeks. The cohort included two patients in the first trimester of pregnancy, two in the second trimester, and five in the third trimester. Some patients were scanned multiple times during pregnancy and post-partum to ascertain diagnostic information pertaining to the patient. The post-partum scans were included in this study as a way of comparing what dose a fetus might get from a PET/CT scan using standard protocols for non-pregnant patients.

CT Fetal Dose Estimation

The CT portion of the scans were acquired with 120-kVp and 130-kVp acquisition protocols, with the slice thickness varying from 2 to 5 mm. The patients were originally scanned with one of the following scanners: Siemens Biograph Vision 6 PET/CT, Siemens Biograph 40 True Point PET/CT and Siemens Emotion Duo CT/CPS 1062 PET. No oral contrast agent was used for the CT examinations. The PET/CT images of the pregnant mothers' anatomy were at least from the top of the cranium to the upper thigh of the mother. The gestational age was estimated from the clinical data.

CT axial scans of the same nine patients were collected on SIEMENS systems. These images were analyzed retrospectively and the scan parameters were obtained from the DICOM header shown in Table 1. There are two patients that were scanned twice with the fetus at different gestational ages.

Patient#	System	kV, mA, ms	Slice thickness (mm)	Pitch	CTDI _{vol}	Weight (kg)	Kernel Recon	DW fetus/overall (cm)	Gestational age (weeks)	Patient perimeter (cm)	Topogram (kV/mA)
1**	Emotion Duo	130, 79, 800	5	1.0	6.74	74.5	B40s	34.9/33.6	17	92.5	130/30
2**	Emotion Duo	130, 47, 800	5	1.0	4.01	66.7	B40s	37.0/35.3	33	102.4	130/30
3	Emotion Duo	130, 47, 800	5	1.0	4.01	53.9	B40s	33.0/32.4	12	81.4	N/A
4	Emotion Duo	130, 47, 800	5	1.0	4.01	72.6	B40s	36.5/32.4	36	99.2	N/A
5 ^δ	Biograph 6	130, 75, 600	5	1.0	4.79	58.6	B30s	35.1/32.4	28	84.3	N/A
6	Biograph 40	120, 60, 500	5	1.0	2.45	54.4	B30s	35.4/33.0	36	87.8	120/29
7 [†]	Biograph 40	120, 40, 500	2	1.0	1.63	69.0	I31f\5	37.4/33.6	14	99.2	120/20
8 [†]	Biograph 40	120, 40, 500	2	1.0	1.63	79.8	I31f\5	38.5/34.8	26	85.6	120/20
9 [§]	Biograph 40	120, 40, 500	3	1.0	1.46	88.9	I30f\3	39.1/33.5	20	109.0	120/20
10**	Emotion Duo	130, 156, 800	5	1.0	13.35	68.1	B40s	0/35.43	post-partum	92.1	130/30
11 [§]	Biograph 6	130, 164, 600	4	1.0	12.65	88.53	B31s	0/37.42	post-partum	111.1	N/A
12 [†]	Biograph 40	120, 84, 500	3	1.0	2.98	74.39	I30f\3	0/37.10	post-partum	103.2	120/35
13 ^δ	Biograph 6	130, 162, 600	4	1.0	9.73	62.4	B30s	0/34.97	post-partum	92.09	N/A
14 ^δ	Biograph 6	130, 182, 600	4	1.0	10.49	59.9	B30s	0/34.66	post-partum	86.94	N/A

Table 1. Data collection of human patient routine cases performed for pregnant patients. Patient #8 and patient #9 are the same patient that came in for two separate scans.

** Same patient scanned at 17, 33 weeks and post-partum.

† Same patient was scanned at 14, 26 weeks and post-partum.

§ Same patient was scanned at 20 weeks and post-partum.

δ Same patient was scanned at 28 weeks and twice post-partum.

These CT scans were performed using techniques yielding low doses as shown in Table 1. For all nine cases there was no automatic tube current modulation (ATCM), therefore a constant tube current and kilovoltage was used. For patient numbers 1-5 scanned prior to 2011, the CTDI_{vol} was not reported since this quantity was not an FDA requirement at the time. The CTDI_{vol} was calculated using the output values for a 32 cm phantom of 6.7 mGy/100 mAs in the center and 12.8 mGy/100 mAs at the periphery for the Emotion Duo[13] and Biograph 6[14] scanners. The pitch factor could not be located in the DICOM header for scans from these scanners, so we assumed it to be 1.0.

The CT dose to the fetus was calculated based on the size specific dose estimate (SSDE) method used to calculate organ dose. [15-24] A recent study by Hardy et al.[25] showed a reasonable accuracy ($\pm 25\%$) with the use of SSDE as a surrogate of fetal dose. The normalized dose coefficient (NDC) scales the

CTDI_{vol} to make it reflect the dose the patient actually receives. The NDC is calculated directly from the patient size surrogates, which include the effective diameter or water-equivalent diameter (D_w). The preferred patient size surrogate is the water equivalent diameter since it directly incorporates attenuation properties from the patient scan. The water-equivalent diameter (D_w) represents the diameter of a cylinder of water that contains the same total x-ray attenuation as that contained within the patient's axial cross section and depends on both the cross-sectional area of the patient and the attenuation of the contained tissues. The method of calculating D_w described in AAPM Report 220[12] was implemented using the following equation

$$D_w = \sqrt{\frac{4}{\pi} \left(\frac{CT(x,y)}{1000} + 1 \right) \times A_{ROI}} \quad (\text{equation 1})$$

where D_w is the water-equivalent diameter, CT represents the mean CT number within the reconstructed field of view (FOV), and A_{ROI} is the product of the number of pixels in the ROI and the pixel area. Our ROI was inscribed inside the reconstructed DICOM images for each patient. Since the DICOM images are square matrices, we inscribed a circle inside each DICOM image with a diameter equal to the entire width of the image. D_w was calculated from CT axial images as previously described. Corrections were applied to images that were not reconstructed at isocenter.[26] In some cases, when the reconstructed image center was not at isocenter, this ROI could contain "padding" values of -3024 HU. Therefore, we applied a remapping of all of the values inside the circle used to calculate the mean CT number which mapped all signals equal to -3024 to -1000 HU to simulate air. The use of padding values is common to most CT vendors, but the padding value may differ. Failure to correct for this would decrease the D_w values. We did not perform any thresholding or connected component analysis of the axial image data prior to calculating D_w . The D_w uses the mean Hounsfield units of the patient habitus taking into consideration the attenuation properties of the patient. The D_w was then used to calculate the normalized dose coefficient (NDC) using equation A-1 from the AAPM TG Report 204 replicated in equation 2 here as

$$NDC = a \times \exp(-b \times D_w) \quad (\text{equation 2})$$

where constants $a = 3.70469$ and $b = 0.03671937$, the water-equivalent diameter is denoted as D_w , and the normalized dose coefficient is denoted as NDC. The SSDE is simply the product of the NDC and CTDI_{vol} as shown in equation 3,

$$SSDE = NDC \times CTDI_{vol} \quad (\text{equation 3})$$

where the CTDI_{vol} for a 32 cm phantom was taken from the patients' dose reports. The average SSDE was taken along the length of the fetus. The absorbed dose to the uterus was used as a surrogate for the absorbed dose to the embryo/fetus as is common practice in medical radiation dosimetry.[23,24] The CT localizer radiographs (or topograms) technique (kVp, mA) is reported in table 1. The dose ranges for the topograms ranges from 0.08-0.13 mGy.

¹⁸F FDG Fetal Dose Estimation

The ¹⁸F-FDG dose administered for all nine patients in this study was 130 MBq (3.5 mCi). At the time of the injection, it was known to the physician that the patients were pregnant, which is the reason for

such a low injection dose. All pharmacokinetic and dosimetric estimates for ¹⁸F-FDG including placental crossover as shown in Table 2.[27]

Patient #	Gestational age (weeks)	SSDE (mGy)	FDG fetus self-dose (mGy)	FDG fetus total dose (mGy)	SSDE + FDG self-dose fetus (mGy)	Fetal self-dose to total fetal dose (%)
1	17	6.9	1.28	1.38	8.2	92.8
2	33	3.8	0.0063	0.0099	3.8	63.6
3	12	4.4	2.18	2.35	6.6	93.6
4	36	3.9	0.0017	0.0034	3.9	50.0
5	28	4.9	0.014	0.021	4.9	67.6
6	36	2.0	0.0017	0.0034	2.0	50.0
7	14	1.2	1.82	1.96	3.0	92.9
8	26	1.2	0.0017	0.025	1.2	68.0
9	20	1.0	0.74	0.80	1.7	92.2
10	post-partum	13.47	4.9 (12) 0.045 (24) 0.0038 (36)	5.2 (12) 0.065 (24) 0.0075 (36)	18.37 (12) 13.52 (24) 13.47 (36)	92.8 (12) 68.5 (24) 51.2 (36)
11	post-partum	11.87	9.2 (12) 0.085 (24) 0.0073 (36)	9.9 (12) 0.12 (24) 0.014 (36)	21.07 (12) 11.96 (24) 11.88 (36)	92.8 (12) 68.5 (24) 51.2 (36)
12	post-partum	2.83	5.0 (12) 0.046 (24) 0.0039 (36)	5.4 (12) 0.067 (24) 0.0077 (36)	7.83 (12) 2.88 (24) 2.84 (36)	92.8 (12) 68.5 (24) 51.2 (36)
13	post-partum	9.99	5.1 (12) 0.047 (24) 0.0040 (36)	5.4 (12) 0.068 (24) 0.0078 (36)	15.09 (12) 10.04 (24) 9.99 (36)	92.8 (12) 68.5 (24) 51.2 (36)
14	post-partum	10.89	5.3 (12) 0.049 (24) 0.0042 (36)	5.7 (12) 0.071 (24) 0.0082 (36)	16.19 (12) 10.94 (24) 10.89 (36)	92.8 (12) 68.5 (24) 51.2 (36)

Table 2. The patient number (year of exam), the gestational age (weeks), the ¹⁸F-FDG uptake MIRD calculation using RADAR with interpolation for weeks between 12, 24 and 36 weeks. The injection activity for the post-partum scans were used to calculate the fetus dose at 12, 24 and 36 weeks as indicated in parentheses.

For ¹⁸F-FDG dose calculations the fetuses in the first, second and third trimester were rounded to the gestational age at 3, 6, and 9 months. The ¹⁸F-FDG fetal self-dose and total dose from both maternal organs and the fetal self-dose were calculated using a table of specific absorption fractions[28] for the following organs: adrenals, brain, breasts, gallbladder wall, LLI wall, small intestine, stomach, ULI wall, heart wall, kidneys, liver, lungs, muscle, ovaries, pancreas, red marrow, bone surfaces, skin, spleen, thymus, thyroid, urinary bladder wall, uterus, fetus and placenta.

The Standard Uptake Volume (SUV) is a simple metric for assessing the amount of activity present in the fetus. The SUV was determined using HERMES software by drawing a contour region of interest (ROI) about the fetus in all slices of the PET image where the fetus is present. The mean, maximum and peak (95% percentile) values were determined over the entire volume of the fetus.

Statistical Analysis

The fetal dose estimates were tested for correlation with each of the following independent measures: gestational age, fetal volume, average water-equivalent diameter of the patient along the length of the fetus, size-specific dose estimate (SSDE), SUV, and percentage of dose from FDG. Stepwise multiple linear regression analysis was performed to assess the partial correlation of each variable.

Results

All data were collected under an IRB-approved protocol in a retrospective manner in which the patient consent was waived. Table 3 shows the following information gathered from the PET scan: mean SUV, standard deviation, the maximum SUV and the 95th percentile SUV, all over the entire volume of the fetus. Table 2 shows the SSDE for 4 cases after 2011, the ¹⁸F fetus self-dose, ¹⁸F fetus total dose, total dose from SSDE and ¹⁸F to fetus and percentage of fetus self-dose to total dose. Figure 1 shows the ¹⁸F-FDG fetal self-dose to fetal total dose from organs, including the fetus, of the patient.

Patient #	Gestational age (weeks)	Mean SUV	Standard Deviation	Maximum SUV	95 th percentile SUV
1	17	2.30	0.98	7.67	4.20
2	33	4.61	0.98	9.13	6.51
3	12	1.28	0.31	2.64	1.8
4	36	2.71	1.02	9.36	5.18
5	28	2.11	1.01	6.61	4.08
6	36	2.50	1.18	11.71	4.80
7	14	1.24	0.73	7.83	2.66
8	26	1.73	1.45	15.03	4.49
9	20	1.62	0.85	7.28	3.27

Table 3 shows information from the PET images: gestational age, mean SUV over entire fetal volume with standard deviation summed in quadrature, the maximum SUV over the entire fetal volume and 95th percentile SUV over the entire volume.

Figure 1. ¹⁸F-FDG fetal self-dose to fetal total dose from organs of patient.

Discussion

To our knowledge, this is the largest series of pregnant patients for whom fetal radiation dose from ¹⁸F-FDG and SSDE was calculated. Our data adds considerably to the existing literature about fetal radiation exposure from ¹⁸F-FDG PET and CT dose studies of pregnant patients. These patients were not accidentally exposed to ¹⁸F-FDG during their pregnancy but rather underwent intentional studies that were performed after adequate consideration of the risks and benefits of ¹⁸F-FDG PET in these pregnant patients with malignancy. ¹⁸F-FDG is known to cross the placental membrane and accumulate in the fetus[8,23,29-32] and we were able to clearly identify ¹⁸F-FDG activity in the fetus inside the gravid uterus, confirming the ability of ¹⁸F-FDG to cross the placenta and accumulate in the fetus. There is no scientific literature documenting fetal toxicity associated with ¹⁸F-FDG in pregnant women or nonhuman primates. All our patients delivered healthy babies at term.

For visual inspection, figure 2 shows examples of a single CT and corresponding PET image of the fetus for pregnant patients in the first, second and third trimester.

Figure 2. Examples of a single PET, CT and PET/CT fused image for 6 patients in the cohort at gestational age of a) 12 weeks with high concentration of ^{18}F -FDG in the fetal heart b-c) 20 weeks, d-f) 36 weeks to demonstrate 1st trimester, 2nd trimester, and 3rd trimester pregnancy, respectively. The ^{18}F -FDG uptake in the fetus is seen in the PET images.

Our results show that fetal doses from a combined dose from ^{18}F -FDG and SSDE ranges from 1.2 to 8.2 mGy and the SSDE alone ranges from 1.0 to 2.0 mGy, shown in Table 2. These doses are significantly below the threshold of 50-100 mGy considered for deterministic effects to the fetus although fetal dose in this range does not conclusively result in adverse impact to the fetus.[33] Generally, most of the diagnostic studies performed during a mother's pregnancy are below this threshold. However, there is no threshold for stochastic effects, but a discussion about the probability of various deterministic and stochastic effects occurring because of fetal exposure to radiation from CT or ^{18}F -FDG PET in pregnancy is beyond the scope of this article.

It is not uncommon for a pregnant mother to be imaged using CT by itself. According to a large, multicenter study of advanced medical imaging in pregnancy CT, the imaging rates in the United States increased from 2.0 examinations per 1000 pregnancies in 1996 to 11.4 per 1000 pregnancies in 2007, remained stable through 2010, and decreased to 9.3 per 1000 pregnancies by 2016.[32] Fetal dose estimates from CT have been primarily based on Monte Carlo simulations of geometric patient models. One method is the CTExpo software (version 1.5.1; Medizinische Hochschule, Hannover, Germany) [34,35], which estimates organ dose based on simulations performed by Zankl et al at the German National Research Center with the Eva geometric phantom model to represent a standard-size female patient [3,4]. Felmlee et al. demonstrated estimates of CT dose index using Monte Carlo on an anthropomorphic phantom.[5] Using Monte Carlo, Ratnapalan et al.[36] and Lazarus et al.[37] reported that normalized fetal CT dose ranges from 7.3-14.3 mGy/100 mAs and mean dose of 17.1 mGy (range of 8–44 mGy), respectively. Goldberg-Stein et al. looked at a series of 54 patients and estimated mean fetal dose to be 24.8 mGy (range of 6.7–56 mGy).[38] Doses to the fetus from a single-acquisition abdominal-pelvic CT examination have ranged between 10-50 mGy in phantom and clinical studies. Hurwitz et al.[39] estimated fetal dose by using physical measurements from internal dosimeters in an anthropomorphic phantom that was modified to represent a newly pregnant patient and a patient who was 3 months pregnant from 1.52 to 3.22 cGy. Since the patients in our study were known to be pregnant prior to the scan, the technique on the scanner may have been set to give the lowest possible CTDI_{vol} which was indicative of the AEC being turned off. While CTDI_{vol} is often provided, the uniform cylindrical phantom does not represent the gross anatomy of a pregnant patient. The SSDE is a quantity that describes the absorbed dose to the patient that scales the CTDI_{vol} with a scaling factor based on the patient's size and attenuation.[12,40] This metric will be required to be reported by vendors soon, though it will likely be an average SSDE over the entire patient range. Hardy et al.[25] calculated the CTDI_{vol}-to-fetal-dose coefficients for tube current modulated and fixed tube current CT examinations of pregnant patients of various gestational ages and reported the SSDE. Moore and Brady et al.[24] provided a method for estimating SSDE to an organ where the conversion factor for the uterus was utilized in this study. Existing methods for the estimation of fetal dose for pregnant patients undergoing CT examinations assume early term pregnancy in a single-size patient model with an average, non-varying maternal anatomy. These dose estimates do not consider natural variations, such as fetal

presentation and gestational age. Differences in these attributes can cause overestimation or underestimation of up to 100%.[41] Angel et al.[42] used Monte Carlo simulations to estimate fetal dose in CT for a range of gestational age and patient sizes and found no significant correlation between gestational age and fetal dose. The fetal age, and maternal body habitus, fetal estimated doses using patient data between 1.1 and 21.9 mGy have been reported for CT.

^{18}F -FDG PET studies of pregnant patients are extremely uncommon, and even ^{18}F -FDG PET studies accidentally performed in pregnant patients are rare.[6-11] Because adequate and accurate data regarding ^{18}F -FDG uptake by the fetus are not available other than the very few case reports of accidental exposure, it is difficult to get an estimate of fetal radiation exposure from ^{18}F -FDG PET in pregnant patients. As a result, most estimates of fetal dose from ^{18}F -FDG PET are based on models of exposure to the fetus from radiation from the mother, and do not consider self-dose from the fetus itself. Those studies that have been published are mostly based on data from either nonhuman primates and mathematic models.[8-11] Recent case reports by Zanotti-Fregonara et al.[29,43] have raised the possibility that ^{18}F -FDG dose to the fetus in early pregnancy may be higher than estimated by current dosimetric standards. Hence, there is a need to have more data to establish the accurate fetal dose exposure. There have been a few studies that have looked at fetal dose from mothers having a PET scan using ^{18}F -FDG [44-47]. The Society of Nuclear Medicine and Molecular Imaging (SNMMI) has provided a Nuclear Medicine Radiation Dose Tool for ^{18}F -FDG exams for different patient models including pregnant women in early stage of pregnancy, 3, 6 and 9 months into their pregnancy. This model provides two dosimetry tables [48,49] to perform these calculations and user inputs the initial activity. The first is the ICRP 128 (2015) that bases their dosimetry model on anthropomorphic phantoms and effective doses are based on organ weighting factors from ICRP 60. Their tables contain a mix of published estimates from ICRP (Publications 53, 80, 106) and dosimetry provided by Stabin et al.[27] The second is RADIATION Dose Assessment Resource (RADAR 2017) generated dose estimates using a set of anthropomorphic phantoms[27], which are based on the recommended body and organ masses given in ICRP Publication 89 (ICRP 2003). This study uses PET scans of pregnant patients to calculate the SUV, fetal self-dose and total fetal dose from the organs of the patient from and based on our findings we determined that ^{18}F -FDG dose is exceedingly low. The fetal heart contains the highest concentration of uptake of ^{18}F -FDG as shown in Figures 3-7. Figure 3-7 show examples of ^{18}F -FDG in the fetal heart for patients in their 2nd and 3rd trimester, respectively. Supplemental Figure 1 shows a patient that is well into their third trimester with ^{18}F -FDG in the fetal heart, like that shown in Figure 7. Figure 2a shows a higher concentration of ^{18}F -FDG uptake in the fetal heart.

Figure 3 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients in their 2nd trimester at 20 weeks.

Figure 4 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients in their 2nd trimester at 26 weeks.

Figure 5 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients in their 2nd trimester at 28 weeks.

Figure 6 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients well into their 3rd trimester at 33 weeks.

Figure 7 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients well into their 3rd trimester at 36 weeks.

For PET/CT, the total fetal estimate radiation dose is the sum of CT exposure, maternal gamma irradiation, fetal beta and fetal gamma irradiation. One method for calculating the fetal dose estimates for CT is the ImPACT CTDosimetry dose calculator (CTDosimetry.xls, version 0.99; ImPACT, London, England) [50], which is based on Monte Carlo simulations performed by the National Radiological Protection Board [51] with the use of a geometric Medical Internal Radiation Dose (MIRD) phantom model [52].

A limitation to our study is that, despite our sample of pregnant patients being the largest ever reported, it is still relatively small. Another limitation is that we considered the fetus to be an oval shape in PET images for calculating SUV. It was difficult to contour the perimeter of the fetus especially for first trimester, however this oval was confined as much as possible to the fetus for each PET slice. We also rounded the gestational age upwards to 3, 6 and 9 months for the MIRD calculations. Lastly, we did not attempt to estimate the dose uncertainties for this study.

Conclusion

This is the first study where fetal doses have been determined from CT and PET images of pregnant patients. These types of images from pregnant patients are rare. Fetal self-dose from ^{18}F for the 1st, 2nd and 3rd trimester range from 2.18 mGy, 0.74-1.82 mGy and 0.017-0.0017 mGy, respectively. The range of SSDE for the CT scan and fetal self-dose for the PET scan ranges from 1.2-8.2 mGy. Our data indicate that the fetal radiation exposure from ^{18}F -FDG PET and CT performed, when medically necessary, in pregnant women with cancer is low. All efforts should be made to minimize the fetal radiation exposure while maintaining diagnostic accuracy by modifying the protocol appropriately.

Disclosure

No potential conflicts of interest relevant to this article exist.

Key Points

Question: Is there a risk to the fetus for pregnant patients undergoing a positron emission tomography (PET) and computed tomography (CT) scan?

Pertinent findings: In a study involving 9 pregnant patients who underwent PET/CT, our data suggests that the fetal radiation exposure from ^{18}F -FDG PET and CT performed, when medically necessary, in pregnant women with cancer is low. The fetal self-dose from ^{18}F -FDG for the 1st, 2nd and 3rd trimester range from 2.18 mGy, 0.74-1.82 mGy and 0.017-0.0017 mGy, respectively, and the range of SSDE and fetal self-dose ranges from 1.2-8.2 mGy.

Implications for patient care: While it is not encouraged for pregnant patients to undergo PET/CT scans, the data suggests that if a scan was needed to assess the health of the patient, the dose to the fetus would not put the fetus at risk. All efforts should be made to minimize the fetal radiation exposure by modifying the protocol appropriately.

References

1. Brent, R., F. Mettler, L. Wagner, Berry M. Streffer, S. He, and T. Kusama. "ICRP publication 84: pregnancy and medical radiation." ICRP 30 (2001): 1.
2. Atkinson, William. Epidemiology and prevention of vaccine-preventable diseases. Department of Health & Human Services, Centers for Disease Control and Prevention, 2006.
3. Kramer, Richard. "The calculation of dose from external photon exposures using reference human phantoms and Monte Carlo methods." Part I: the male (ADAM) and female (EVA) adult mathematical phantoms (1982).
4. Zankl, M., W. Panzer, and G. Drexler. The calculation of dose from external photon exposures using reference human phantoms and Monte Carlo methods. Pt. 6. No. GSF--30/91. GSF-Forschungszentrum fuer Umwelt und Gesundheit GmbH, 1991.
5. Felmlee, Joel P., J. E. Gray, M. L. Leetzow, and J. C. Price. "Estimated fetal radiation dose from multislice CT studies." AJR. American journal of roentgenology 154, no. 1 (1990): 185-190.
6. Hutchins E, Wallis J. Diagnosis: metastatic melanoma in a pregnant patient. MIR teaching file. Case no. pt114. 2004. Available at: <http://gamma.wustl.edu/pt114te198.html>. Accessed June 2, 2011.
7. ten Hove, C. H., J. M. Zijlstra-Baalbergen, E. F. I. Comans, and R. M. van Elburg. "An unusual hotspot in a young woman with Hodgkin's lymphoma." Haematologica 93, no. 1 (2008): e14-e15.
8. Benveniste, Helene, Joanna S. Fowler, William D. Rooney, Daryn H. Moller, W. Walter Backus, Donald A. Warner, Pauline Carter et al. "Maternal-fetal in vivo imaging: a combined PET and MRI study." Journal of Nuclear Medicine 44, no. 9 (2003): 1522-1530.
9. Stabin, Michael G. "Proposed addendum to previously published fetal dose estimate tables for 18F-FDG." Journal of Nuclear Medicine 45, no. 4 (2004): 634-635.
10. Russell, Joy R., M. G. Stabin, and R. B. Sparks. "Placental transfer of radiopharmaceuticals and dosimetry in pregnancy." Health physics 73, no. 5 (1997): 747-755.
11. Russell, Joy R., Michael G. Stabin, Richard B. Sparks, and Evelyn Watson. "Radiation absorbed dose to the embryo/fetus from radiopharmaceuticals." Health physics 73, no. 5 (1997): 756-769.
12. Boone, John M. "Reply to "Comment on the 'Report of AAPM TG 204: Size-specific dose estimates (SSDE) in pediatric and adult body CT examinations'" [AAPM Report 204, 2011]." Medical physics 39, no. 7 (2012): 4615.
13. Centers for Disease Control and Prevention. (2020). Radiation and pregnancy: information for clinicians.
14. <https://5.imimg.com/data5/SELLER/Doc/2020/12/YA/LW/WZ/7182657/emotion-duo-dual-slice-siemens-ct-scan-machines.pdf>
15. Wang, Jia, Xinhui Duan, Jodie A. Christner, Shuai Leng, Lifeng Yu, and Cynthia H. McCollough. "Attenuation-based estimation of patient size for the purpose of size specific dose estimation in CT. Part I. Development and validation of methods using the CT image." Medical physics 39, no. 11 (2012): 6764-6771.
16. Leng, Shuai, Maria Shiung, Xinhui Duan, Lifeng Yu, Yi Zhang, and Cynthia H. McCollough. "Size-specific dose estimates for chest, abdominal, and pelvic CT: effect of inpatient variability in water-equivalent diameter." Radiology 276, no. 1 (2015): 184-190.

17. Anam, Choirul, Freddy Haryanto, Rena Widita, Idam Arif, Geoff Dougherty, and Donald McLean. "The impact of patient table on size-specific dose estimate (SSDE)." *Australasian physical & engineering sciences in medicine* 40, no. 1 (2017): 153-158.
18. Kalra, Mannudeep K., Michael M. Maher, Thomas L. Toth, Bernhard Schmidt, Bryan L. Westerman, Hugh T. Morgan, and Sanjay Saini. "Techniques and applications of automatic tube current modulation for CT." *Radiology* 233, no. 3 (2004): 649-657.
19. Anam, Choirul, Freddy Haryanto, Rena Widita, Idam Arif, Geoff Dougherty, and Donald McLean. "Estimation of eye radiation dose during nasopharyngeal CT examination for an individual patient." *Information (Japan)* 19 (2016): 3951-3962.
20. Burton, Christiane S., and Timothy P. Szczykutowicz. "Evaluation of AAPM Reports 204 and 220: estimation of effective diameter, water-equivalent diameter, and ellipticity ratios for chest, abdomen, pelvis, and head CT scans." *Journal of applied clinical medical physics* 19, no. 1 (2018): 228-238.
21. Nickel, Mattias. "Pharmacokinetic modeling for optimization of radioimmunotherapy—macroscopic and microscopic approach." (2005).
22. Benveniste, Helene, Joanna S. Fowler, William D. Rooney, Daryn H. Moller, W. Walter Backus, Donald A. Warner, Pauline Carter et al. "Maternal-fetal in vivo imaging: a combined PET and MRI study." *Journal of Nuclear Medicine* 44, no. 9 (2003): 1522-1530.
23. Adelstein, S. James. "Administered radionuclides in pregnancy." *Teratology* 59, no. 4 (1999): 236-239.
24. Moore, Bria M., Samuel L. Brady, Amy E. Mirro, and Robert A. Kaufman. "Size-specific dose estimate (SSDE) provides a simple method to calculate organ dose for pediatric CT examinations." *Medical physics* 41, no. 7 (2014): 071917.
25. Hardy, Anthony J., Erin Angel, Maryam Bostani, Chris Cagnon, and Michael McNitt-Gray. "Estimating fetal dose from tube current-modulated (TCM) and fixed tube current (FTC) abdominal/pelvis CT examinations." *Medical physics* 46, no. 6 (2019): 2729-2743.
26. American College of Radiology. "ACR practice guideline for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation." Reston, VA: ACR (2008).
27. Stabin, Michael G., X. George Xu, Mary A. Emmons, W. Paul Segars, Chengyu Shi, and Michael J. Fernald. "RADAR reference adult, pediatric, and pregnant female phantom series for internal and external dosimetry." *Journal of Nuclear Medicine* 53, no. 11 (2012): 1807-1813.
28. Stabin, Michael G. "Internal dosimetry in pediatric nuclear medicine." In *Pediatric nuclear medicine*, pp. 556-581. Springer, New York, NY, 1995.
29. Zanotti-Fregonara, Paolo, Sébastien Jan, David Taieb, Serge Cammilleri, Régine Trébossen, Elif Hindié, and Olivier Mundler. "Absorbed 18F-FDG dose to the fetus during early pregnancy." *Journal of Nuclear Medicine* 51, no. 5 (2010): 803-805.
30. Alibazoglu, Haluk, Richard Kim, Amjad Ali, Alexander Green, and Gregory La Monica. "FDG uptake in gestational sac." *Clinical nuclear medicine* 22, no. 8 (1997): 557.
31. Zanotti-Fregonara, Paolo, Sébastien Jan, David Taieb, Serge Cammilleri, Régine Trébossen, Elif Hindié, and Olivier Mundler. "Absorbed 18F-FDG dose to the fetus during early pregnancy." *Journal of Nuclear Medicine* 51, no. 5 (2010): 803-805.
32. Zanotti-Fregonara, Paolo, Sebastien Jan, Christophe Champion, Régine Trébossen, Renaud Maroy, Jean-Yves Devaux, and Elif Hindié. "In vivo quantification of 18F-FDG uptake in human placenta during early pregnancy." *Health physics* 97, no. 1 (2009): 82-85.

33. Kwan, Marilyn L., Diana L. Miglioretti, Emily C. Marlow, EJ Aiello Bowles, Sheila Weinmann, Stephanie Y. Cheng, Kamala A. Deosaransingh et al. "Trends in medical imaging during pregnancy in the United States and Ontario, Canada, 1996 to 2016." *JAMA network open* 2, no. 7 (2019): e197249-e197249.
34. Stamm, Georg, and Hans Dieter Nagel. "CT-expo--a novel program for dose evaluation in CT." *RoFo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin* 174, no. 12 (2002): 1570-1576.
35. Nagel HD. Radiation exposure in computed tomography, fundamentals, influencing parameters, dose assessment, optimisation, scanner data, terminology. COCOR European Coordination Committee of the Radiological and Electromedical Industries, 2nd ed (in English, revised and translated by Nagel HD and Shrimpton PC). Hamburg, Germany: Paul Hartung Druck, 2000.
36. Ratnapalan, Savithiri, Nicole Bona, Kiran Chandra, and Gideon Koren. "Physicians' perceptions of teratogenic risk associated with radiography and CT during early pregnancy." *American journal of roentgenology* 182, no. 5 (2004): 1107-1109.
37. Lazarus, Elizabeth,Carolynn DeBenedictis, David North, Patricia K. Spencer, and William W. Mayo-Smith. "Utilization of imaging in pregnant patients: 10-year review of 5270 examinations in 3285 patients—1997–2006." *Radiology* 251, no. 2 (2009): 517-524.
38. Goldberg-Stein, Shlomit, Bob Liu, Peter F. Hahn, and Susanna I. Lee. "Body CT during pregnancy: utilization trends, examination indications, and fetal radiation doses." *American Journal of Roentgenology* 196, no. 1 (2011): 146-151.
39. Hurwitz, Lynne M., Terry Yoshizumi, Robert E. Reiman, Philip C. Goodman, Erik K. Paulson, Donald P. Frush, Greta Toncheva, Giao Nguyen, and Lottie Barnes. "Radiation dose to the fetus from body MDCT during early gestation." *American Journal of Roentgenology* 186, no. 3 (2006): 871-876.
40. McCollough, Cynthia, Donovan M. Bakalyar, Maryam Bostani, Samuel Brady, Kristen Boedeker, John M. Boone, H. Heather Chen-Mayer et al. "Use of water equivalent diameter for calculating patient size and size-specific dose estimates (SSDE) in CT: the report of AAPM task group 220." *AAPM report 2014* (2014): 6.
41. Osei, E. K., and K. Faulkner. "Fetal position and size data for dose estimation." *The British journal of radiology* 72, no. 856 (1999): 363-370.
42. Angel, Erin, Clinton V. Wellnitz, Mitchell M. Goodsitt, Nazanin Yaghmai, John J. DeMarco, Christopher H. Cagnon, James W. Sayre et al. "Radiation dose to the fetus for pregnant patients undergoing multidetector CT imaging: Monte Carlo simulations estimating fetal dose for a range of gestational age and patient size." *Radiology* 249, no. 1 (2008): 220-227.
43. Zanotti-Fregonara, Paolo, Christophe Champion, Régine Trébossen, Renaud Maroy, Jean-Yves Devaux, and Elif Hindié. "Estimation of the $\beta+$ dose to the embryo resulting from 18F-FDG administration during early pregnancy." *Journal of Nuclear Medicine* 49, no. 4 (2008): 679-682.
44. Takalkar, Amol M., Alok Khandelwal, Stephen Lokitz, David L. Lilien, and Michael G. Stabin. "18F-FDG PET in pregnancy and fetal radiation dose estimates." *Journal of Nuclear Medicine* 52, no. 7 (2011): 1035-1040.
45. Zanotti-Fregonara, Paolo, Richard Laforest, and Jerold W. Wallis. "Fetal radiation dose from 18F-FDG in pregnant patients imaged with PET, PET/CT, and PET/MR." *Journal of Nuclear Medicine* 56, no. 8 (2015): 1218-1222.

46. Zanotti-Fregonara, Paolo, Thomas M. Koroscil, Joseph Mantil, and Martin Satter. "Radiation dose to the fetus from [18F]-FDG administration during the second trimester of pregnancy." *Health physics* 102, no. 2 (2012): 217.
47. Gill, Manpreet, Winnie Sia, Michael Hoskinson, Erin Niven, and Rshmi Khurana. "The use of PET/CT in pregnancy: a case report of malignant parathyroid carcinoma and a review of the literature." *Obstetric medicine* 11, no. 1 (2018): 45-49.
48. Mattsson, S., L. Johansson, J. Linięcki, D. Noßke, K. Å. Riklund, M. Stabin, D. Taylor et al. "Radiation dose to patients from radiopharmaceuticals: a compendium of current information related to frequently used substances." *Annals of the ICRP* 44, no. 2 Suppl (2015): 7-321.
49. Stabin, Michael G., and Jeffrey A. Siegel. "RADAR dose estimate report: a compendium of radiopharmaceutical dose estimates based on OLINDA/EXM version 2.0." *Journal of Nuclear Medicine* 59, no. 1 (2018): 154-160.
50. CTDosimetry, ImPACT. "Imaging performance assessment of CT Scanners: a medical devices agency evaluation group." CT scanner matching data, tables of CTDI values in air, CTDI_w, and phantom factor values', (ImPACT Internet home page. Available on [http://www. ImPACTscan.org](http://www.ImPACTscan.org) (2000).
51. Jones, D. G., and P. C. Shrimpton. "Survey of the Practice in the UK. III. Normalized Organ Doses Calculated Using Monte Carlo Techniques." (1991).
52. Snyder, W. S. "Estimates of absorbed fractions for monoenergetic photon sources uniformly distributed in various organs of a heterogeneous phantom. Medical Internal Radiation Dose Committee (MIRD). Pamphlet No. 5." *J. Nucl. Med.* 10, no. 3 (1969).

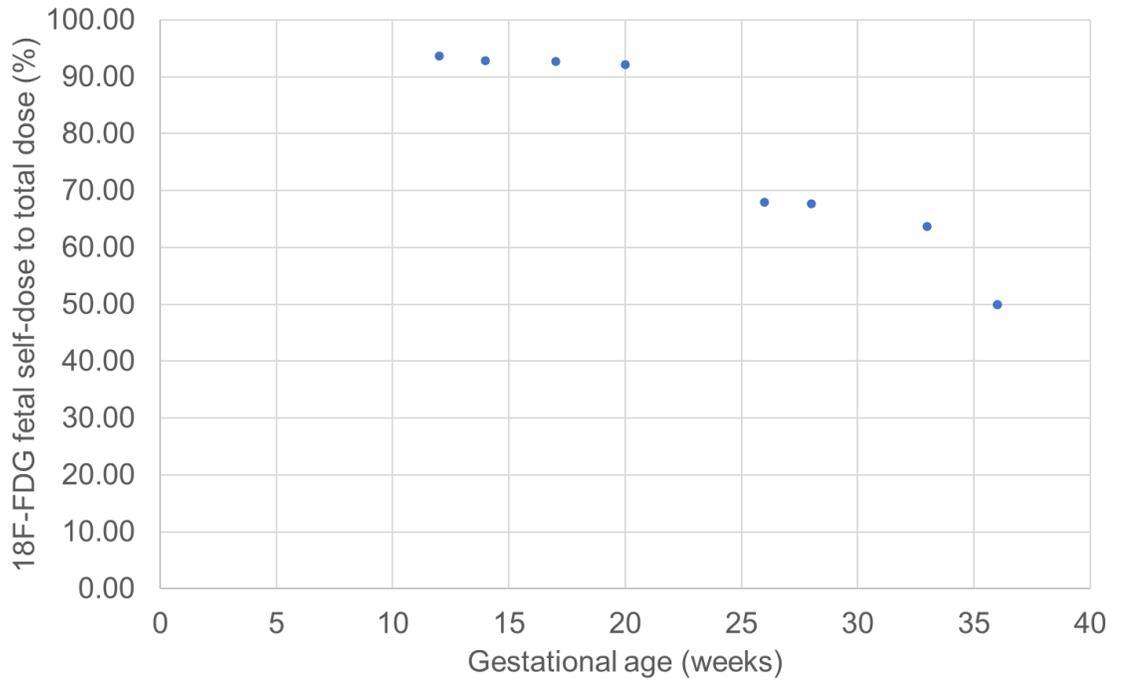


Figure 1. ^{18}F -FDG fetal self-dose to fetal total dose from organs of patient.

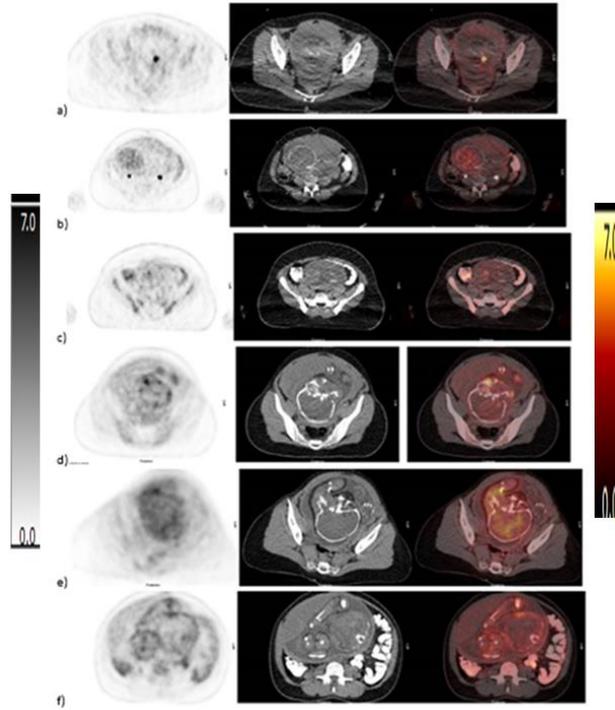


Figure 2. Examples of a single PET, CT and PET/CT fused image for 6 patients in the cohort at gestational age of a) 12 weeks with high concentration of ^{18}F -FDG in the fetal heart b-c) 20 weeks, d-f) 36 weeks to demonstrate 1st trimester, 2nd trimester, and 3rd trimester pregnancy, respectively. The ^{18}F -FDG uptake in the fetus is seen in the PET images.

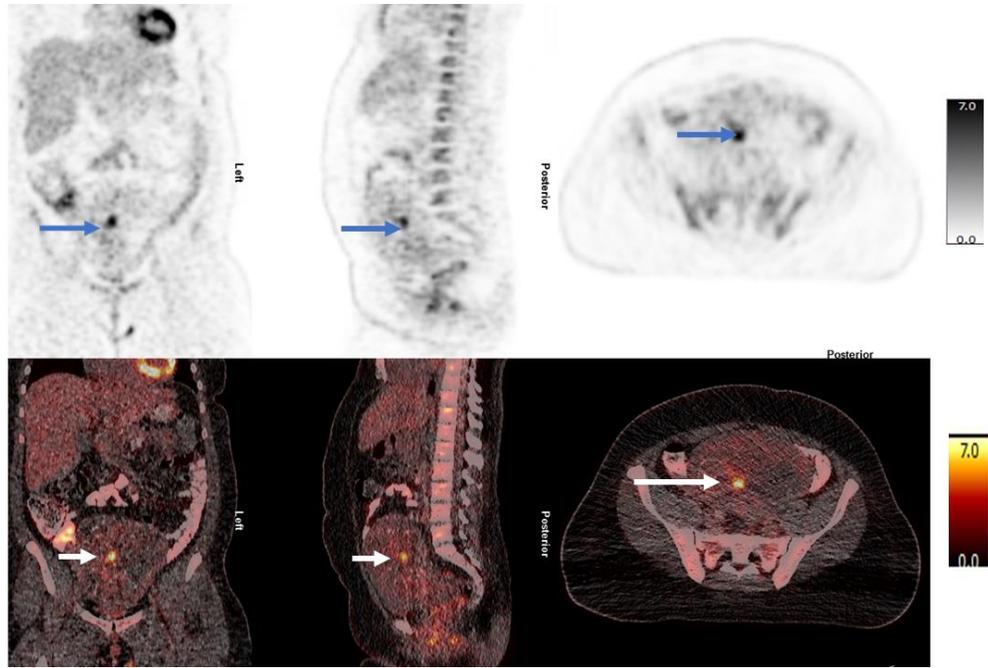


Figure 3 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patient in the second trimester at 20 weeks.

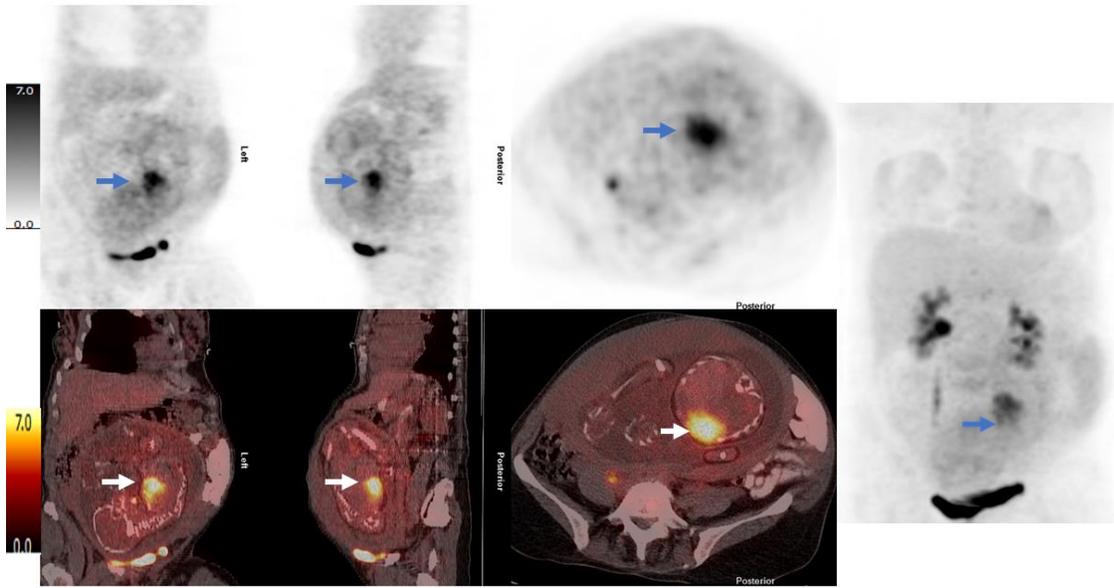


Figure 4 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patient in the second trimester at 26 weeks.

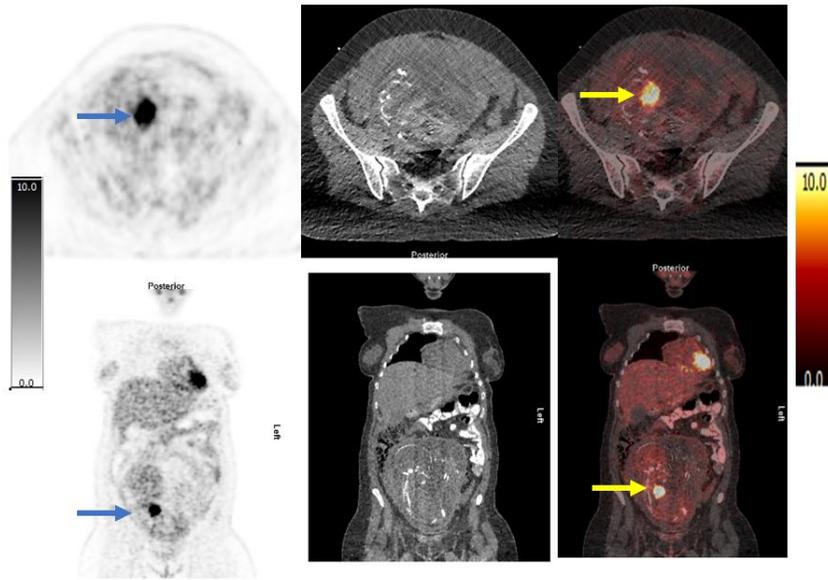


Figure 5 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patient in the second trimester at 28 weeks (entering third trimester).

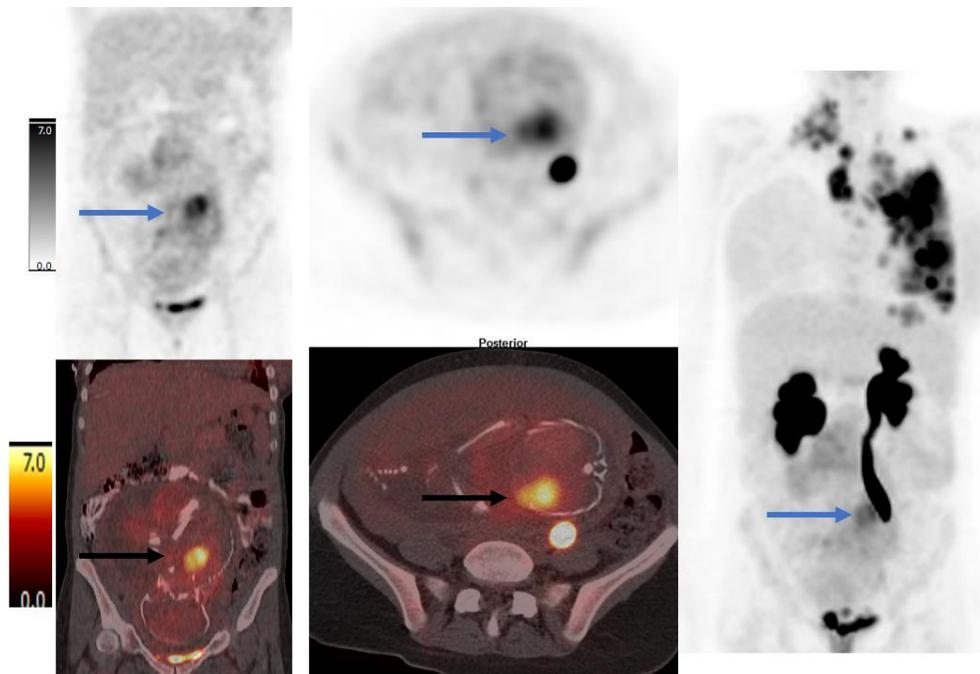


Figure 6 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients well into the third trimester at 33 weeks.

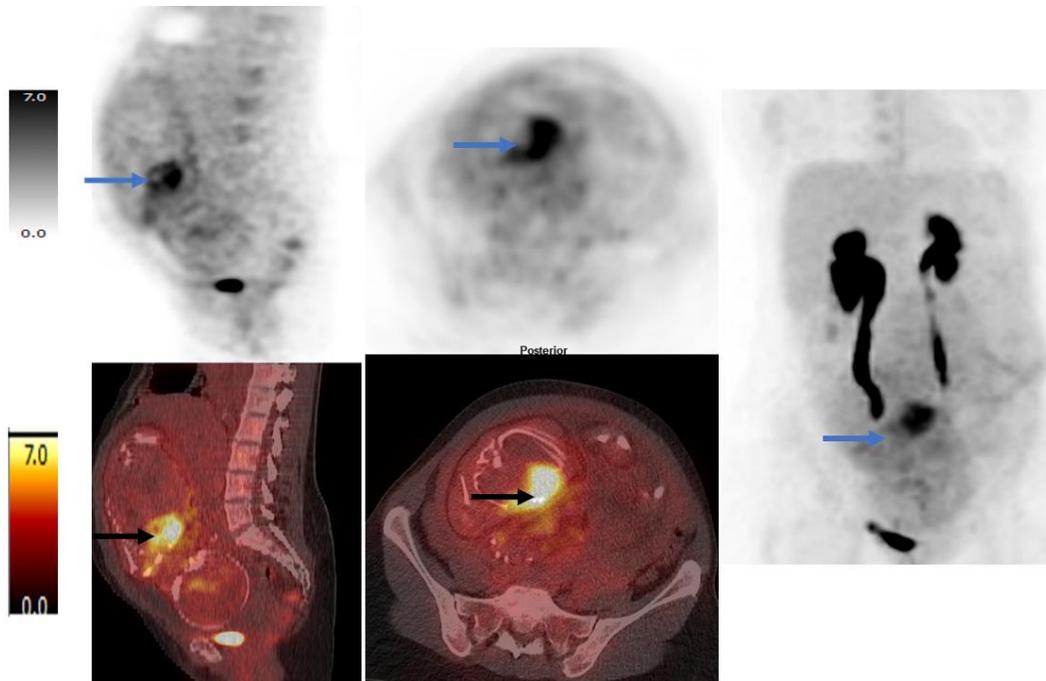
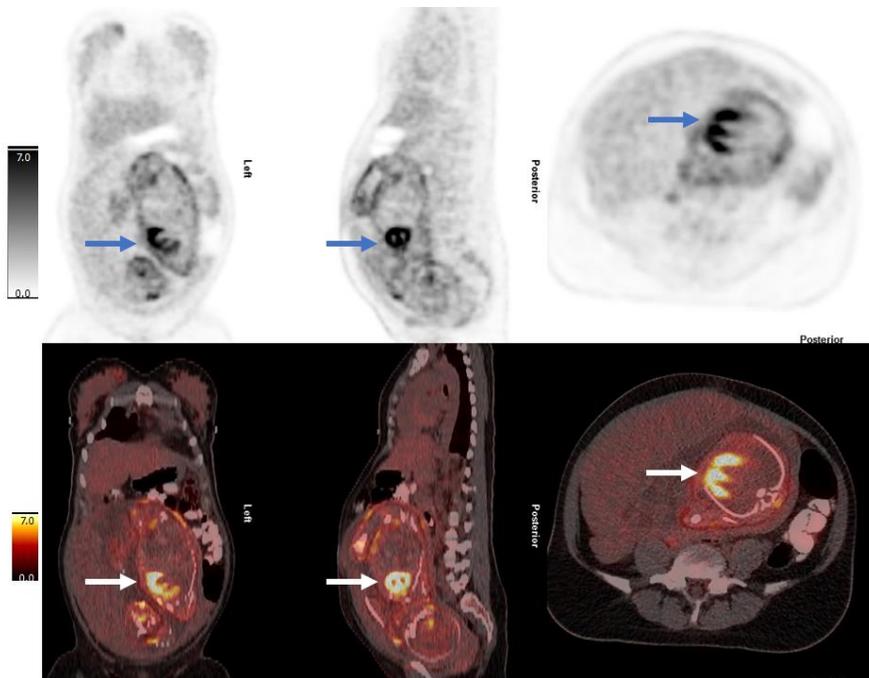
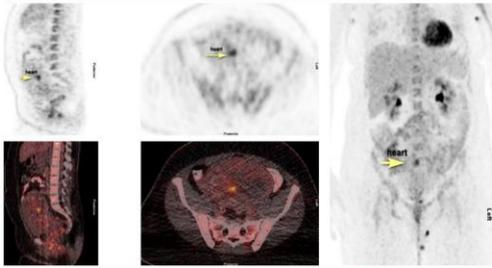


Figure 7 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients well into the third trimester at 36 weeks.

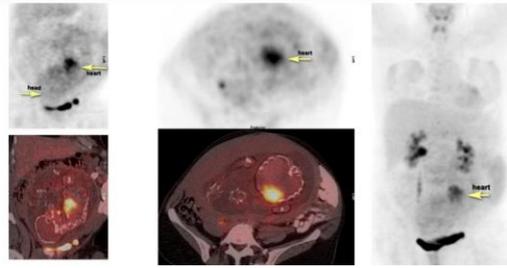


Supplemental figure 1 shows example of concentrated uptake of ^{18}F -FDG in the fetal heart for patients well into the third trimester at 36 weeks.

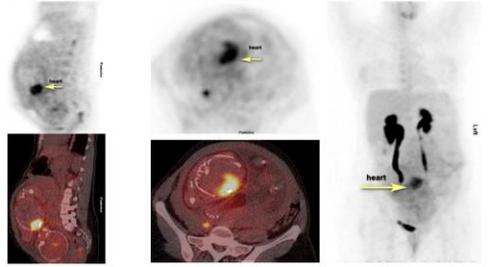
18F-FDG uptake in fetal heart at 20 weeks



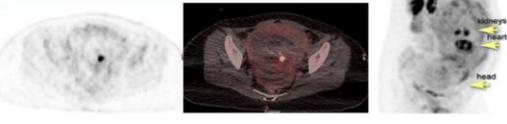
18F-FDG uptake in fetal heart at 36 weeks



18F-FDG uptake in fetal heart at 33 weeks



18F-FDG uptake in fetal heart at 12 weeks



Graphical Abstract