Absorbed ¹⁸F-FDG Dose to the Fetus During Early Pregnancy

Paolo Zanotti-Fregonara¹, Sébastien Jan², David Taieb³, Serge Cammilleri³, Régine Trébossen², Elif Hindié⁴ and Olivier Mundler³

¹Nuclear Medicine Department, St. Antoine Hospital, Paris, France; ²DSV/I²BM/SHFJ, Commissariat à l'Energie Atomique, Orsay, France; ³Service Central de Biophysique et Medecine Nucléaire, Centre Hospitalo-Universitaire de la Timone, Marseille, France; and ⁴Médecine Nucléaire, Hôpital Saint Louis, Assistance Publique-Hôpitaux de Paris, France

We describe a rare case of a woman who underwent ¹⁸F-FDG PET/CT during early pregnancy (fetus age, 10 wk). The fetal absorbed dose was calculated by taking into account the ¹⁸F-FDG fetal self-dose, photon dose coming from the maternal tissues, and CT dose received by both mother and fetus. Methods: The patient (weight, 71 kg) had received 296 MBg of ¹⁸F-FDG. Imaging started at 1 h, with unenhanced CT acquisition, followed by PET acquisition. From the standardized uptake value measured in fetal tissues, we calculated the total number of disintegrations per unit of injected activity. Monte Carlo analysis was then used to derive the fetal ¹⁸F-FDG self-dose, including positrons and self-absorbed photons. Photon dose from maternal tissues and CT dose were added to obtain the final dose. Results: The maximum standardized uptake value in fetal tissues was 4.5. Monte Carlo simulation showed that the fetal self-dose was 3.0×10^{-2} mGv/MBg (2.7×10^{-2} mGv/MBg from positrons and 0.3×10^{-2} mGy/MBg from photons). The estimated photon dose to the fetus from maternal tissues was 1.04×10^{-2} mGy/MBq. Accordingly, the specific ¹⁸F-FDG dose to the fetus was about 4.0×10^{-2} mGy/MBg (11.8 mGy in this patient). The CT scan added a further 10 mGy. Conclusion: The dose to the fetus during early pregnancy can be as high as 4.0×10^{-2} mGy/MBq of ¹⁸F-FDG. Current dosimetric standards in early pregnancy may need to be revised.

Key Words: fetal dosimetry; ¹⁸F-FDG PET/CT; Monte Carlo simulation

J Nucl Med 2010; 51:803–805 DOI: 10.2967/jnumed.109.071878

Several million ¹⁸F-FDG PET examinations are performed annually worldwide, yet dosimetry reports of ¹⁸F-FDG PET examinations accidentally performed during pregnancy are still exceptional (*1*).

Although the photon component of the fetal dose, coming from maternal tissues, can be reliably estimated from phantom measurements, the intensity of fetal tissue uptake—which is essential for deriving the self-dose from positrons—is poorly known.

We describe in the present article a rare case of a woman who underwent ¹⁸F-FDG PET/CT while pregnant. The total fetal dosimetry was calculated by taking into account the fetal ¹⁸F-FDG self-dose, dose coming from the maternal tissues, and CT dose.

MATERIALS AND METHODS

A 30-y-old woman (weight, 71 kg) underwent ¹⁸F-FDG PET/ CT for the follow-up of Hodgkin lymphoma. The lymphoma had been treated by chemotherapy and radiotherapy. The last chemotherapy ended 1 mo before the scan. The scan was required to verify the absence of residual disease.

The patient was examined using a Discovery ST (GE Healthcare) PET/CT hybrid scanner, starting at 1 h after the injection of 296 MBq of ¹⁸F-FDG. Imaging was obtained from the base of the skull to the mid-thigh level. The PET scan, acquired in 3 dimensions, lasted about 20 min (7 table positions, 3 min per position). The images were reconstructed with an iterative (ordered-subset expectation maximization) algorithm using unenhanced CT data for attenuation correction (CT parameters: 140 keV, 80 mAs, and 5-mm section thickness). Coregistered images were displayed on a Xeleris workstation (GE Healthcare).

In the institution where the examination was performed, patients with child-bearing potential are informed that PET/CT cannot be performed in the case of pregnancy. They are asked about the date of their last menstruation, use of contraceptive devices, and other factors. The patient had been in amenorrhea since the end of the chemotherapy. However, she was fully confident that she was not pregnant, because she had an intrauterine device (well visible on the CT images). Therefore, a serum pregnancy test was not done before imaging.

The pregnancy was first suspected at review of imaging. The fetus was at about 10 wk of gestational age on the day of PET/CT examination.

The fetal self-dose, photon dose coming from maternal tissues, and CT dose were independently assessed.

Self-Dose

We first calculated the weight-based maximum standardized uptake value (SUV_{max}), using circular regions of interest drawn around the fetus on multiple slices, encompassing the entire fetal volume. Then, we derived the total number of disintegrations per

Received Oct. 22, 2009; revision accepted Jan. 26, 2010.

For correspondence or reprints contact: Paolo Zanotti-Fregonara, Nuclear Medicine Department, St. Antoine Hospital, 184 Rue du Fbg St. Antoine, 75571 Paris Cedex 12, France.

E-mail: fregonara@hotmail.com

COPYRIGHT © 2010 by the Society of Nuclear Medicine, Inc.

unit of injected activity. Because the cumulated activity in the fetus is not known, we assumed an instantaneous tracer uptake and no biologic removal.

We considered that the fetus, on the day of the ¹⁸F-FDG study, had the average dimensions of a normal fetus at 10 wk (2). The fetus was thus represented by a cylinder capped with hemispheres, with a total length of 6 cm and a diameter of 1.13 cm (volume, 21 cm^3).

Monte Carlo analysis, performed with GATE (3), was used to derive the positron and the photon self-dose. In a previous case report (I), the photon self-dose was neglected because the fetus in that case was smaller (4.8 cm³). The pregnancy was more advanced in the present case, and photons needed to be considered.

Photon Dose

We calculated an average photon dose to the fetus using the 3-mo pregnant woman anthropomorphic phantom included in the OLINDA software (4). Because we did not know the pharmacokinetics in maternal tissues for this specific patient, we used published average data on the pharmacokinetics of ¹⁸F-FDG (5).

CT Dose

We calculated the CT dose using the whole-body volumetric CT dose index, as displayed on the operator's console. The volumetric CT dose index is a close estimation of the fetal dose in early pregnancy (6,7).

RESULTS

On the PET images, the fetus was visualized in the middle of the uterine cavity (Fig. 1). It was seen as a C-shaped structure—which evokes the idea of the classic fetal position—several centimeters in length and with one end bigger than the other (the head and the feet, respectively).

The fetus, as compared with maternal tissues, showed a high ¹⁸F-FDG uptake. The SUV_{max} in the fetus, found in 2 successive slices in the region of the head, was 4.5. We thus used this value to derive the total number of disintegrations occurring in the fetus. Low variability of SUV_{max} across the different fetal slices, with a mean of 4.1 ± 0.4 , was observed. However, given the poor spatial resolution of PET machines, the radioactivity distribution was likely to be more heterogeneous than it appeared on PET images. Thus, our study did not address the possibility of heterogeneous dose distribution at a microscopic level.

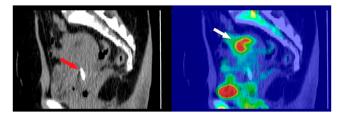


FIGURE 1. Sagittal CT (left) and fused ¹⁸F-FDG PET and CT (right) slices through uterus. Fetus is indicated by white arrow. Red arrow points to portion of intrauterine device visible in this CT slice.

The PET scan did not show any pathologic focus that could be linked to the lymphoma. The patient has been disease-free since the time that this scan was obtained (4 y before publication of this report).

Fetal Self-Dose

The total number of disintegrations occurring in the fetus was 12,623,000/MBq injected to the mother. Monte Carlo simulation showed that the total energy released and absorbed in fetal tissues was about 3.9×10^6 MeV/MBq injected, composed of 3.5×10^6 MeV from positrons $(2.7 \times 10^{-2} \text{ mGy/MBq})$ and 3.8×10^5 MeV from photons $(0.3 \times 10^{-2} \text{ mGy/MBq})$. Thus, the total fetal self-dose was $3.0 \times 10^{-2} \text{ mGy/MBq}$ (90% from positrons and 10% from photons).

Photon Dose

The photon cross-dose to the fetus, coming from maternal tissues, was 1.04×10^{-2} mGy/MBq.

In total, the average dose to the fetus per unit of ¹⁸F-FDG activity administered to the mother was estimated at about 4.0×10^{-2} mGy/MBq (11.8 mGy in this patient, who received 296 MBq).

The CT acquisitions added a further 10 mGy. Thus, the final absorbed dose for this fetus was 21.8 mGy.

DISCUSSION

The present case is, to our knowledge, only the second ever reported in the literature. Our results suggest that the dose received by a 10-wk-old fetus is about 4.0×10^{-2} mGy/MBq of ¹⁸F-FDG injected to the mother. This figure is higher than currently reported standard values for early pregnancy (2.2×10^{-2} mGy/MBq) (8). These standard values were extrapolated from PET images of monkeys in late pregnancy, which showed a similar ¹⁸F-FDG uptake between maternal and fetal tissues (9).

The present case showed a much higher 18 F-FDG uptake in human fetal tissues. One likely explanation, besides species differences, is that early pregnancy is characterized by rapid cell proliferation (*10*), which is generally associated with high glucose consumption.

The fetal absorbed dose in the present case was also higher than that of the previously reported case (at a different institution), which had an estimated fetal absorbed dose of 3.3×10^{-2} mGy/MBq (1). This difference could be due not only to the normal interindividual variability but also to the larger dimensions of the fetus in the present case, so that the SUV_{max} was less influenced by partial-volume effect.

Because the measure of radioactivity concentration in the fetus is likely to be influenced by partial-volume effect, we chose to use the SUV_{max} as the most accurate and conservative value to represent the average concentration in the fetus. Moreover, it is possible that even the SUV_{max} underestimates the real activity concentration, because at this age the fetus still has nonnegligible mobility inside the uterine cavity.

In the previous case (11), the placenta was seen as a thin layer of activity lining the inner portion of most of the uterine wall. However, in the present case, we did not observe any placental ¹⁸F-FDG uptake. Data from other case reports are needed to clarify this issue.

After the discovery of this nonplanned pregnancy, the woman chose to abort.

CONCLUSION

In agreement with a previously published case report (1), ¹⁸F-FDG fetal uptake in early pregnancy is higher than current dosimetric standards, mainly because of a high positron self-dose. Current dosimetric standards in early pregnancy may need to be revised.

ACKNOWLEDGMENTS

We thank Dr. Michael G. Stabin for helpful discussion and Dr. Christina S. Hines for editorial assistance.

REFERENCES

- Zanotti-Fregonara P, Champion C, Trébossen R, Maroy R, Devaux JY, Hindié E. Estimation of the β+ dose to the embryo resulting from ¹⁸F-FDG administration during early pregnancy. *J Nucl Med.* 2008;49:679–682.
- International Commission on Radiological Protection (ICRP). Basic Anatomical and Physiological Data for Use in Radiological Protection: Reference Values—A Report of Age- and Gender-Related Differences in the Anatomical and Physiological Characteristics of Reference Individuals. ICRP publication 89. Oxford, U.K.: Elsevier Science Ltd.; 2003.
- Jan S, Santin G, Strul D, et al. GATE: a simulation toolkit for PET and SPECT. *Phys Med Biol.* 2004;49:4543–4561.
- 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;46:1023–1027.
- Hays MT, Watson EE, Thomas SR, Stabin M. MIRD dose estimate report no. 19: radiation absorbed dose estimates from ¹⁸F-FDG. J Nucl Med. 2002;43:210–214.
- Helmrot E, Pettersson H, Sandborg M, Alten JN. Estimation of dose to the unborn child at diagnostic x-ray examinations based on data registered in RIS/ PACS. *Eur Radiol.* 2007;17:205–209.
- Jaffe TA, Neville AM, Anderson-Evans C, et al. Early first trimester fetal dose estimation method in a multivendor study of 16- and 64-MDCT scanners and low-dose imaging protocols. AJR. 2009;193:1019–1024.
- Stabin MG. Proposed addendum to previously published fetal dose estimate tables for ¹⁸F-FDG. J Nucl Med. 2004;45:634–635.
- Benveniste H, Fowler JS, Rooney WD, et al. Maternal-fetal in vivo imaging: a combined PET and MRI study. J Nucl Med. 2003;44:1522–1530.
- O'Rahilly R, Muller F. Human Embryology and Teratology. New York, NY: Wiley-Liss; 2001.
- Zanotti-Fregonara P, Jan S, Champion C, et al. In vivo quantification of ¹⁸F-FDG uptake in human placenta during early pregnancy. *Health Phys.* 2009;97:82–85.