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Case Report

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Abstract
A woman in her twenties with cervical cancer underwent conical resection at 13 weeks gestation. The pathological examination showed lymphatic invasion and possible positive margins. A total hysterectomy was recommended; however, the patient strongly desired continuation of the pregnancy. An FDG-PET/MRI was performed at 16 and 27 weeks gestation for cancer staging. No evidence of metastasis was observed. The patient's cancer treatment was delayed until fetal maturity, and a scheduled cesarean section was performed at 30 weeks gestation followed by a modified radical hysterectomy, oophorectomy, and pelvic lymph node dissection with ovarian preservation. Cervical intraepithelial neoplasia was diagnosed 18 months postoperatively and was treated via vaginal wall resection at 19 months postoperatively.
PET/MRI obtains PET and MR images simultaneously and the fused images provide information regarding anatomical and functional relationships. The high contrast resolution of MRI and the functional information provided by PET images render PET/MRI an ideal method for the evaluation of physiological FDG uptake by the fetus.
In this study, we could follow the physiological uptake of FDG by a fetus over time during the gestational weeks by PET/MRI. The FDG uptake by the fetal brain is lower than that in the maternal brain, and the FDG uptake is similar in the left and right cardiac ventricles. In addition, the physiological uptake by the tonsilla, liver, kidneys, and bladder, is reported.

Key words
fetus, fluorodeoxyglucose, PET/MRI, cervical cancer

Ethical comments
A written informed consent was waived because of the case report.
The patient was fully explained about the exposure to the radiation for a diagnostic purpose and was convinced of the benefits and burdens of the FDG PET examinations. A written informed consent for FDG PET/MRI examination was obtained before conducting the scan. This case report was written in accordance with the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Conflict of interest statement
Funding: None.
Conflicts of interest: None.

Introduction

The mechanism of physiological ^{18}F-fluolodeoxyglucose (FDG) uptake by a fetus is unknown. Fused PET/MRI images are obtained simultaneously, providing an ideal modality for determining the exact location of the physiological uptake of FDG by a fetus. In this study, repeated FDG-PET/MRI scans of a pregnant woman are presented and the location and degree of physiological uptake of FDG by the fetus are discussed.

Case Report

A woman in her twenties with cervical cancer (International Federation of Gynecology and Obstetrics (FIGO) stage IA, squamous cell carcinoma) underwent conical resection at 13 weeks gestation. The pathological examination showed lymphatic invasion with possible positive margins. A total hysterectomy was recommended(*1*); however, the patient strongly desired continuation of the pregnancy. Strict management was required to preserve the uterus of this patient, and close follow-up with imaging modalities was considered desirable.

A systemic screening using FDG PET for staging of cervical cancer was required for clinical indication. An FDG-PET/MRI scan was selected because of its higher contrast resolution than CT, higher diagnostic ability for local recurrence and metastases and lower radiation exposure than PET/CT. The patient was fully explained about the exposure to the radiation for a diagnostic purpose and was convinced of the advantages and disadvantages of the FDG PET examinations. A written informed consent for FDG PET/MRI examination was obtained before conducting the scan. An FDG-PET/MRI scan was performed at 16 weeks gestation and revealed no uptake in the cervix and no distant metastasis. Cytology at 23 weeks gestation showed high-grade cervical intraepithelial neoplasia (CIN), and a second FDG-PET/MRI was obtained for re-staging at 27 weeks and two days gestation. The second FDG-PET/MRI scan showed no evidence of local recurrence or metastases.

The patient's treatment was postponed until fetal maturity, and a scheduled cesarean section was performed at 30 weeks gestation followed by a modified radical hysterectomy, oophorectomy, and pelvic lymph node dissection with ovarian preservation. Nine months postoperatively, follow-up cytology revealed a high-grade squamous intraepithelial lesion (HSIL). A biopsy 18 months postoperatively revealed CIN; therefore, a vaginal wall resection was conducted 19 months postoperatively.

The infant underwent respiratory management in the neonatal intensive care unit after birth and was discharged from the hospital at two months of age (corrected gestational age: 38 weeks and two days). No complications or unexpected developmental delays have been reported.

The patient fasted for six hours before each FDG-PET/MRI and was administered 152 MBq (2.5 MBq/kg) of FDG. The PET was performed on an integrated PET/MRI scanner (SIGNA PET/MR, GE Healthcare, Waukesha, Wisconsin, USA) at a magnetic field strength of 3.0 Tesla. Whole-body simultaneous FDG-PET/MRI of the head to mid-thigh was performed in the arms-down position 60 minutes after FDG administration, followed by a dedicated pelvis FDG-PET/MRI scan 120 minutes after the administration of FDG. The emission time was 2.5 minutes for the whole-body PET scan and 20 minutes for the dedicated pelvis scan. The emission times were reconstructed using the time-of-flight Bayesian penalized likelihood reconstruction algorithm (Q.Clear;, GE Healthcare, Waukesha, Wisconsin, the United States) with β values of 500 and 300 for whole body and pelvis scans, respectively. No antispasmodic or contrast agents were used.

The FDG-PET/MRI revealed physiological FDG uptake by the fetus at 16 and 27 weeks gestation (Table 1). The assessable organs included the brain, tonsilla, myocardium,

liver, kidneys, and bladder, and uptake was measured using the maximum standardized uptake value (SUVmax) normalized using the mother's body weight. The FDG uptake of the fetal brain at 16 weeks gestation (SUVmax=2.5) was lower than that of the maternal brain (SUVmax = 14.2). At 27 weeks gestation, the uptake of the fetal brain (SUVmax = 3.5) remained lower than that of the maternal brain, but was slightly higher than that at 16 weeks gestation. The FDG uptake was similar in the left and right cardiac ventricles of the fetus. The SUVmax measurements for the fetus were obtained using the dedicated pelvis FDG-PET/MRI and those for the mother were obtained using the whole body FDG-PET/MRI.

Discussion

There are few reports of PET scans of fetuses or pregnant women, and little is known about physiological FDG uptake by the fetus. In this study, repeated FDG-PET/MRI scans of the fetus allow for the evaluation of the degree and location of the physiological uptake of FDG with high accuracy.

Low FDG uptake by the fetal brain is consistent with the results of a previous report (*2*), and may be associated with the immaturity of the fetal brain parenchyma, although no evidence for this hypothesis has been reported to date. The assessment of fetal PET/MRI at different gestational ages or with congenital brain disorders is helpful for the understanding of normal FDG metabolism in the fetal brain and the temporal changes with maturity. In this patient, there was a higher level of FDG uptake by the fetal brain at 27 weeks gestation than at 16 weeks gestation, suggesting that brain maturity depends on fetal age. Larger studies are needed to verify these findings regarding the physiological uptake of FDG by the fetal brain. Blanc-Durand et al. reported that symmetrical uptake of FDG by fetal myocardium in both ventricles, which is consistent with the findings in this study (*2*). In the fetus, the systemic and umbilical vein circulations are mixed and flow into the right atrium (*3*). The blood flow continues to the right ventricle and the left atrium through the foramen ovale, then enters the left ventricle. Most of the blood flow from the right ventricle flows to the whole body through the ductus arteriosus, though high pulmonary vascular resistance in the fetus prevents the blood from entering the lungs. Due to the presence of the foramen ovale and ductus arteriosus, the pulmonary artery and the aorta are parallel circuits with the same arterial pressure and blood flow, though the right ventricle ejects slightly more blood than the left ventricle. Therefore, symmetrical myocardial uptake of FDG in both cardiac ventricles of the fetus can be attributed to the similar ventricular metabolism between the right and left ventricles.

The risk of radiation exposure due to PET imaging in pregnant women cannot be ignored. During organogenesis (4 - 10 weeks gestation), the fetus is at risk for congenital fetal malformations (*4*). The increased incidence of malformations due to exposure to more than 100 mGy radiation is controversial (*5*). The International Commission of Radiological Protection guidelines state that fetal doses of less than 100 mGy at any stage of pregnancy should not be considered a reason for pregnancy interruption (*6*). The American College of Obstetricians and Gynecologists (ACOG) guidelines also state that exposure to 50 mGy does not cause adverse events such as fetal infertility or fetal death (*7*). Although the exact radiation exposure to the fetus cannot be calculated, unlike in adult patients, the irradiated dose to be the maternal bladder wall seems to be correlated with that of the fetus, and the fetus's radiation exposure is most affected by FDG excretion in the mother's bladder due to the spatial relationship between the bladder and the uterus. The estimated radiation at the bladder wall after the administration of 185 MBq of FDG is estimated to be 30 mGy. Therefore, the fetal dose is expected to be less than 50 mGy, which is lower than the dose recommended by the ACOG guidelines.

Contrast-enhanced MRI is considered to be hazardous to the fetus during early pregnancy (5 - 10 weeks gestation) (*8*), while 1.5 Tesla non-contrast-enhanced MRI is not harmful or within the acceptable range. However, the fetal safety of 3 Tesla MRI, which is used in FDG-PET/MRI systems, has yet to be established. More studies are needed to determine the fetal safety of MRI.

Conclusion

FDG-PET/MRI scans of a pregnant patient and fetus at 16 and 27 weeks gestation revealed temporal changes in the physiological uptake of FDG. Simultaneously acquired PET/MRI leads to an understanding of the exact location of the uptake in a fetus during the gestational weeks.

Table 1 Physiological uptake of FDG by the fetus

	16 weeks gestation		27 weeks gestation	
	Fetus	Mother	Fetus	Mother
Brain	2.6	14.4	4.2	12.3
Tonsilla	2.5	10.7	5.2	7.6
Myocardium (Left/Right)	3.9/3.2	9.1/1.6	8.8/8.2	2.5/1.1
Liver	1.6	2.9	2.0	2.6
Kidney	2.9	6.4	6.5	31.3
Bladder	5.3	13.7	3.9	19.4

Data are shown as SUVmax values, which were normalized based on the maternal weight.

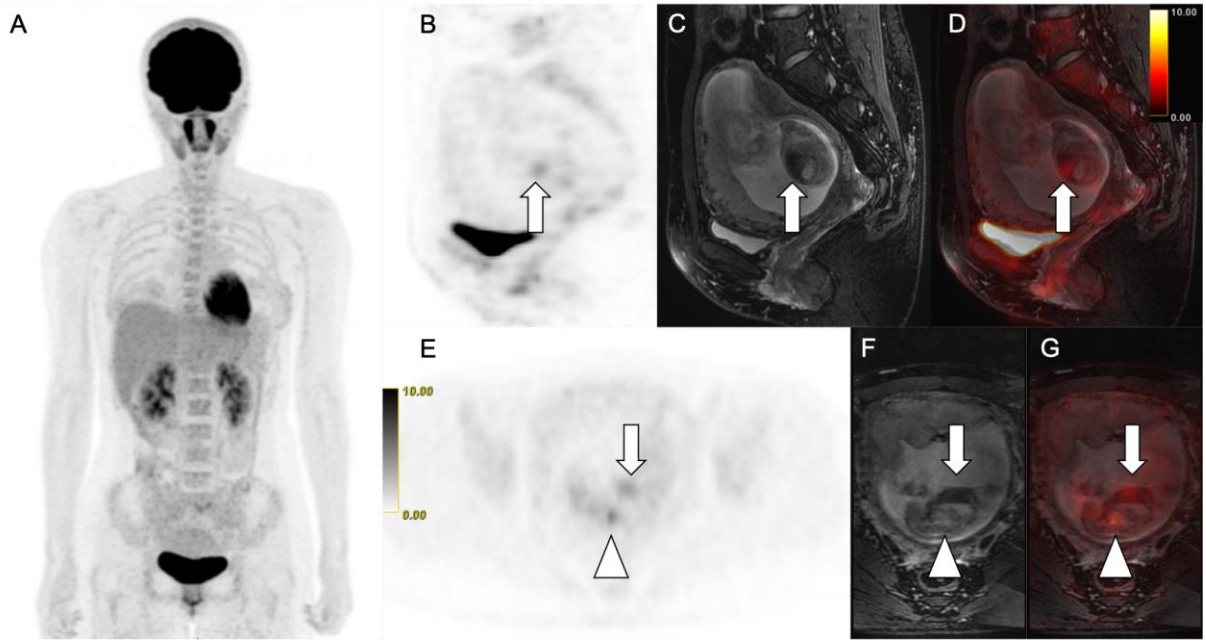

Figure legends

Figure 1. FDG-PET/MRI at 16 weeks gestation

The FDG uptake by the fetal liver (arrows) and kidney (arrowheads) are lower than the uptake by the maternal organs (A). PET images are shown in panels (B) and (E) while MRIs are shown in panels (C) and (F). The fused image is shown in panel (G).

Abbreviations: FDG, fluorodeoxyglucose; PET, positron emission tomography; MRI, magnetic resonance imaging.

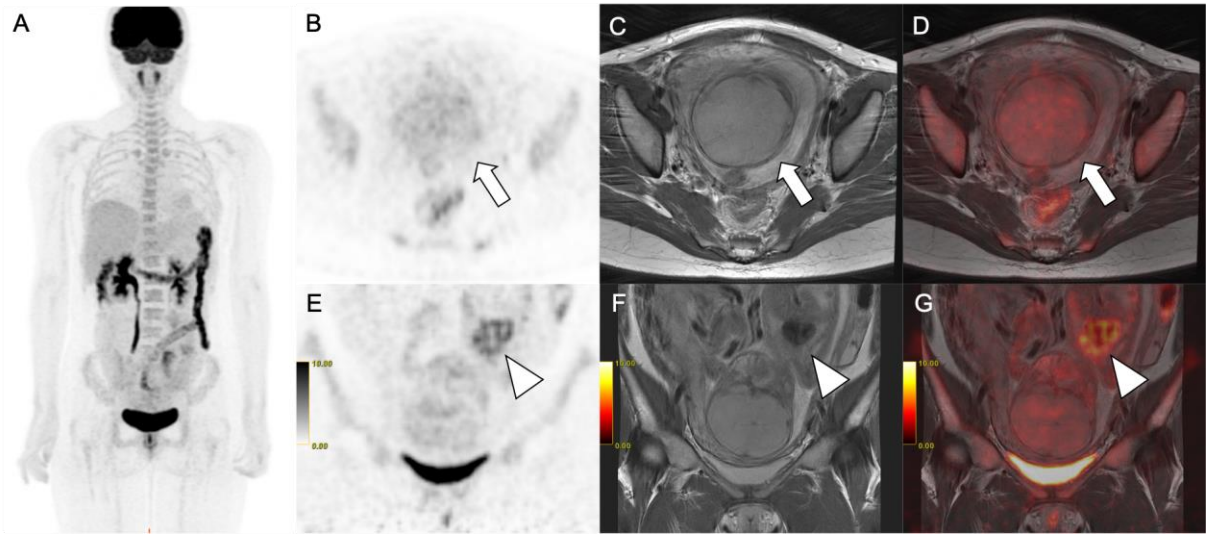

Figure 2. FDG-PET/MRI at 27 weeks gestation
The FDG uptake by the fetal brain (arrows) is lower than that by the maternal brain (A). The PET image is shown in panel (B), the MRI in panel (C), and the fused image in panel (D). The physiological uptake of FDG by the fetal myocardium is similar in the right and left ventricles (arrowheads). The PET image is shown in panel (E), the MRI in panel (F), and the fuse image in panel (G). Abbreviations: FDG, fluorodeoxyglucose; PET, positron emission tomography; MRI, magnetic resonance imaging.

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