

Ultra-low dose ^{18}F -FDG PET/CT in pregnant patients with long axial field of view PET/CT system

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Data and images courtesy of Royal Northshore Hospital, Sydney, Australia

Background

Cancer during pregnancy is rare but poses major challenges regarding imaging protocols for minimizing fetal radiation exposure, especially in relation to PET/CT imaging. Although there is no consensus about the maximum radiation exposure considered safe for a fetus, the recommendation is to ensure fetal dose remains below 100 mGy.³ Because pregnant cancer patients may require multiple PET/CT studies, it is critical to optimize the PET/CT protocol to enable as low an injected dose as possible and ultra-low dose (ULD) CT for attenuation correction.

Using long axial field of view (LAFOV) PET/CT systems like Biograph Vision Quadra helps achieve high quality PET/CT acquisition with very low radioactivity due to the extraordinarily high sensitivity leading to high number of detected events. The Biograph Vision Quadra with 106 cm axial field of view and ultrafast 228 ps time of flight (TOF) performance ensures the highest detection rate capability, enabling very low radiopharmaceutical dose for optimized PET/CT imaging without increasing acquisition time.*

History

In routine clinical use, administered radioactivity can be decreased by ~40%-50% while simultaneously decreasing PET acquisition times to 5 minutes for all subjects for static, delayed scans. In standard clinical practice, 150 MBq (~4 mCi) is administered to all subjects independent of patient weight or BMI. The short acquisition time gives more flexibility than a standard field of view PET system to further vary administered radioactivity and acquisition time.

Using ULD protocols, the Fludeoxyglucose F 18 injection (^{18}F -FDG) administered was reduced to around one quarter of the standard amount (40 MBq), while scan time increased fourfold to maintain approximately the same number of total acquired events. A 20-minute scan is similar to the duration of most clinical PET scans and is not overly burdensome

for patients. The radiation dose from the ULD CT protocol was 0.2-0.3 mSv and the radiation dose from 1 mSv/50 MBq. As a result, the total radiation exposure from the ULD protocol was around 1 mSv to both mother and fetus, a level not previously thought possible.

Two clinical case examples below demonstrate ULD imaging in pregnant patients using Biograph Vision Quadra. These patients presented with breast carcinoma and lymphoma and were both approximately 18 weeks into pregnancy.

* Based on bench testing (e.g., improved sensitivity and ToF per NEMA NU-2:2018).
Please refer to the approved PET drug prescribing information for dosing and administration instructions.

Fludeoxyglucose F 18 injection

Indications and usage

Fludeoxyglucose F 18 injection (^{18}F -FDG) is indicated for positron emission tomography (PET) imaging in the following settings:

- **Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- **Cardiology:** For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- **Neurology:** For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

IMPORTANT SAFETY INFORMATION

- **Radiation Risk:** Radiation-emitting products, including Fludeoxyglucose F 18 injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.
- **Blood Glucose Abnormalities:** In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to ensure at least two days of normoglycemia prior to Fludeoxyglucose F 18 injection administration.
- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema, and rash have been reported. Have emergency resuscitation equipment and personnel immediately available.
- **Pediatric Use:** The safety and effectiveness of Fludeoxyglucose F 18 injection in pediatric patients with epilepsy is established on the basis of studies in adult and pediatric patients. In pediatric patients with epilepsy, the recommended dose is 2.6 mCi. The optimal dose adjustment on the basis of body size or weight has not been determined.

In the oncology or cardiology settings, the safety and effectiveness of Fludeoxyglucose F 18 injection have not been established in pediatric patients.

DOSAGE FORMS AND STRENGTHS

Multiple-dose 30 mL and 50 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL)

Fludeoxyglucose F 18 injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 50 mL volume) for intravenous administration.

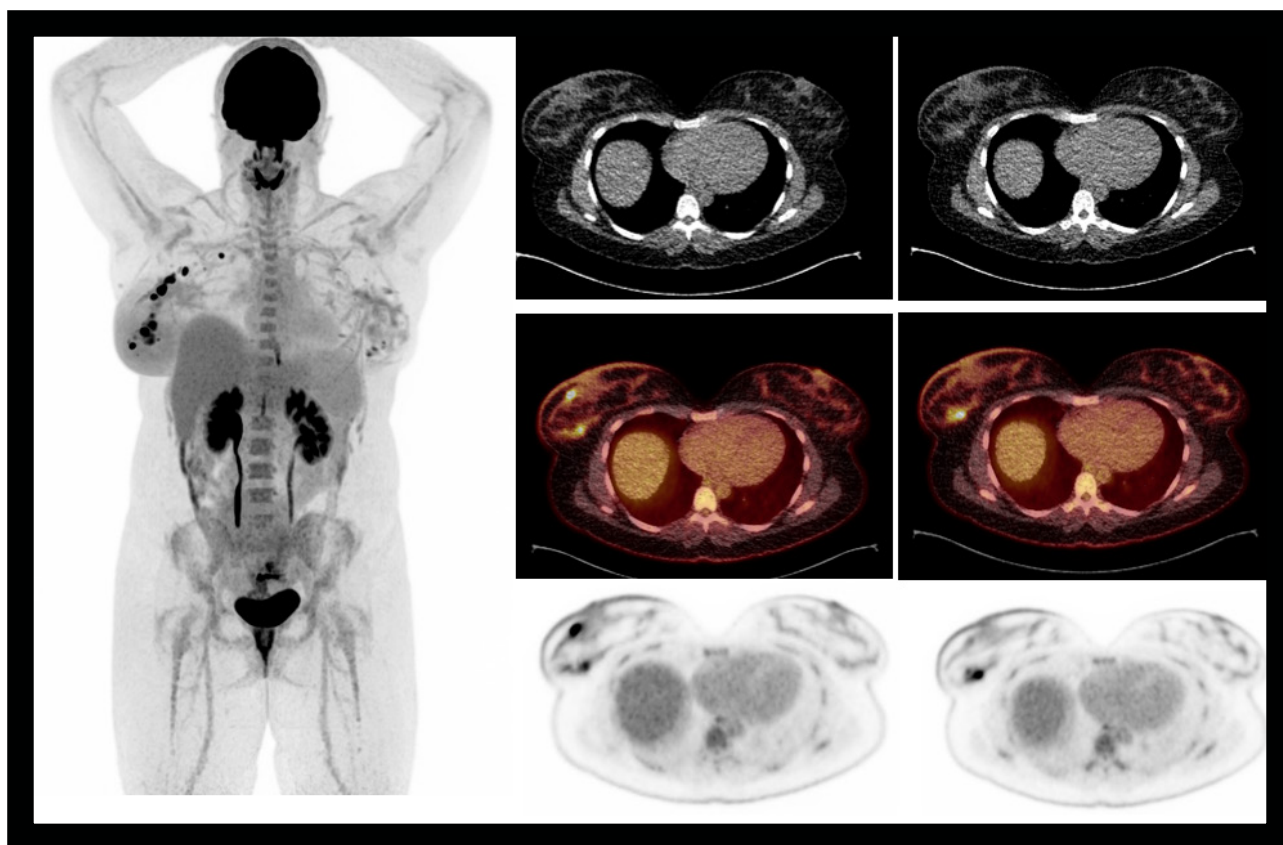
- **Recommended dose for pediatric patients:** Within the neurology setting, the recommended dose for pediatric patients is 2.6 mCi, as an intravenous injection. The optimal dose adjustment on the basis of body size or weight has not been determined.

Fludeoxyglucose F 18 injection is manufactured and distributed by:

PETNET Solutions, Inc.

810 Innovation Drive

Knoxville, Tennessee 37932



1 PET MIP and axial CT, PET, and fused PET/CT images at the primary breast tumor show multiple FDG avid masses in the right breast indicating multifocal primary breast carcinoma with multiple hypermetabolic right axillary lymph node metastases.

Findings

Case 1

A 34-year-old woman in the second trimester of pregnancy (16 weeks gestation) with recently diagnosed HER2 positive breast cancer was sent for ^{18}F -FDG PET/CT study for initial staging. Clinical and ultrasound examination revealed a multifocal right breast mass with enlarged axillary lymph nodes.

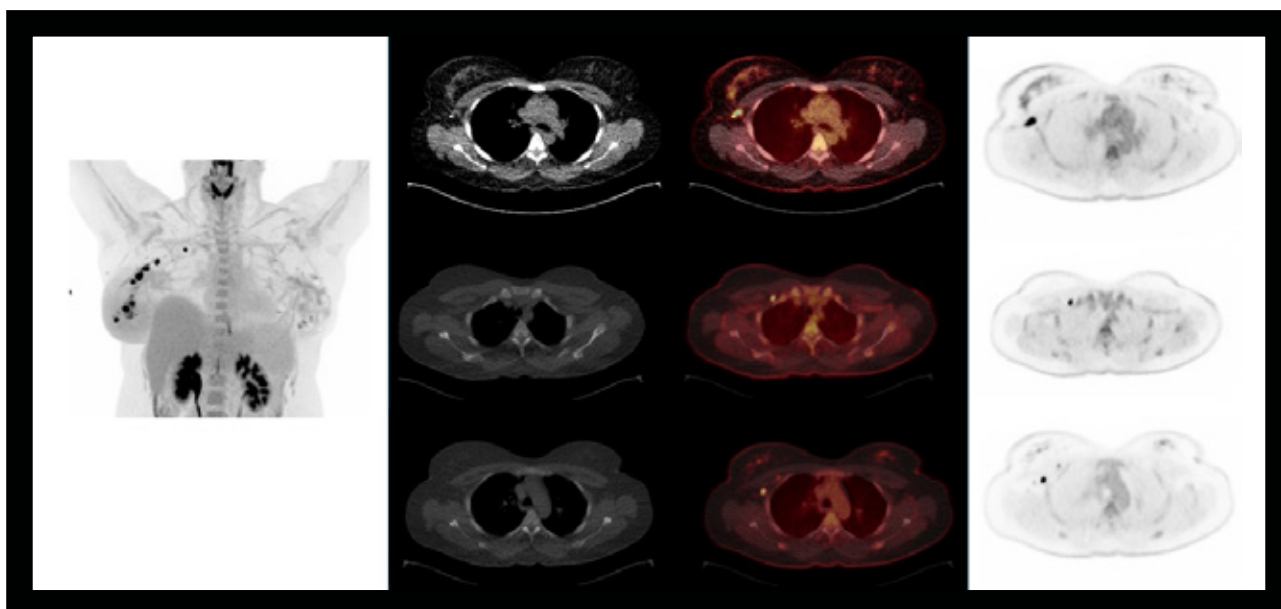
The patient was injected with 56 MBq (~ 1.5 mCi) ^{18}F -FDG (weight 74 kg; ~ 0.75 MBq/kg).^{*} 55 minutes following radiopharmaceutical injection, a

modified whole body PET/CT study was acquired from vertex of skull to mid-thighs, with the arms raised. ULD CT was initially performed for attenuation correction utilizing the Biograph Vision Quadra's Sn filter capability with very low mAs (kVp = Sn140 mAs = 6). PET acquisition was for a single 106 cm axial FOV bed position for 15 minutes. PET was reconstructed using UltraHD PET (PSF+TOF) 4i5s with a post-reconstruction 3D Gaussian filter of FWHM = 2.0.

As shown in Figure 1, PET/CT images show multiple ^{18}F -FDG-avid lesions within the lateral right breast, corresponding to the biopsy-proven breast carcinoma. The largest lesion just lateral to the nipple measures 1.9 cm maximum diameter with $\text{SUV}_{\text{max}} = 12.9$. Another focal lesion in the lower outer quadrant measures 1.65 cm with $\text{SUV}_{\text{max}} = 14.3$. Several smaller hypermetabolic lesions are visualized in the inner quadrant, with the largest showing $\text{SUV}_{\text{max}} = 8.2$.

^{*} Based on bench testing (e.g., improved sensitivity and ToF per NEMA NU-2:2018).

Please refer to the approved PET drug prescribing information for dosing and administration instructions.



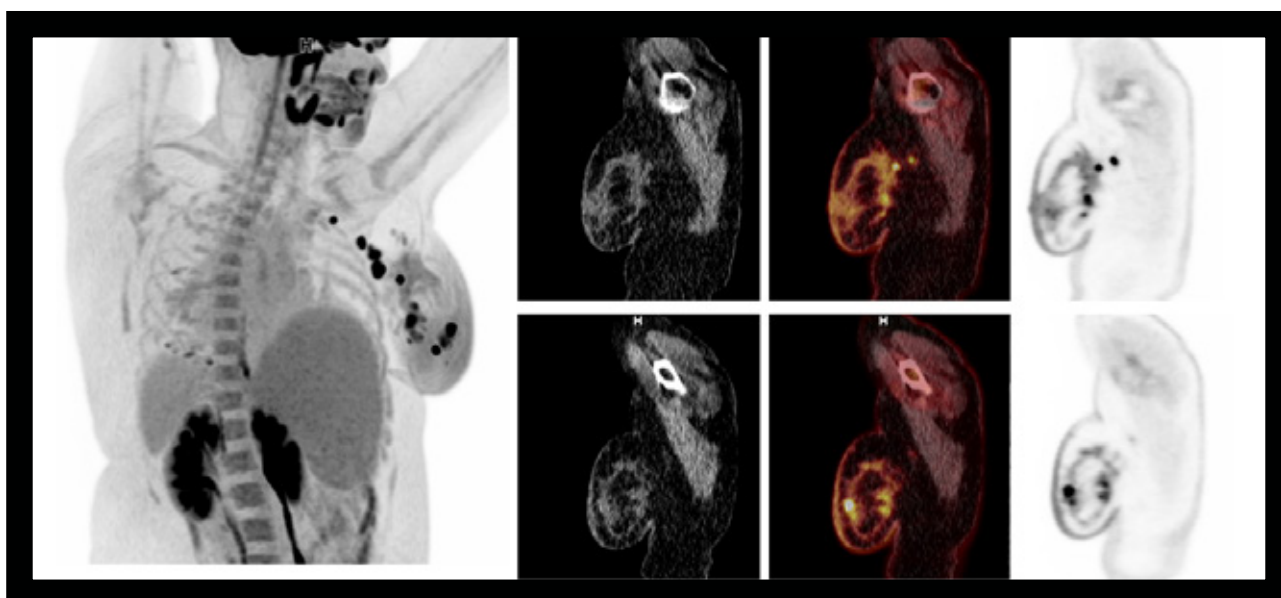
2 Axial CT, PET, and fused PET/CT images at the axilla and upper thorax show multiple hypermetabolic right axillary lymph node metastases.

Figure 2 shows multiple hypermetabolic axillary lymph nodal metastases, with the largest measuring 18 x 9 mm with $SUV_{max} = 14.6$ at level 1. There are multiple hypermetabolic nodes located at level 2 posterior to the pectoralis minor muscle, with the largest and most ^{18}F -FDG-avid with $SUV_{max} = 14.3$. The most superior lymph node is in the

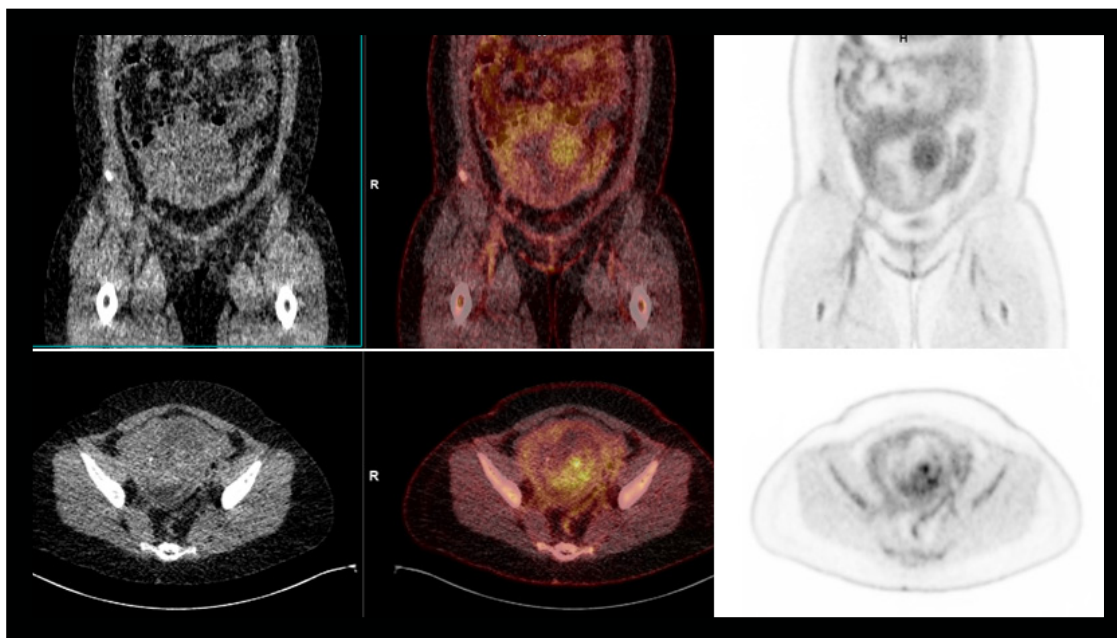
level 3 station (medial and just superior to pectoralis minor) and is immediately anterolateral to the head of the first rib with SUV_{max} of 10.5.

Both breasts also show physiological proliferation of parenchyma as is expected during pregnancy. No other abnormal distant foci were visualized.

The study was performed with extremely low injected dose with a 15-minute vertex-to-mid-thigh acquisition. The acquisition time was adequate for producing very high-quality images without undue patient motion despite such low injected activity.



3 Oblique PET MIP and coronal CT, PET, and fused PET/CT images at the right breast (bottom row) and right axilla (top row) show multifocal primary breast lesions with multiple focal hypermetabolic axillary nodal metastases.



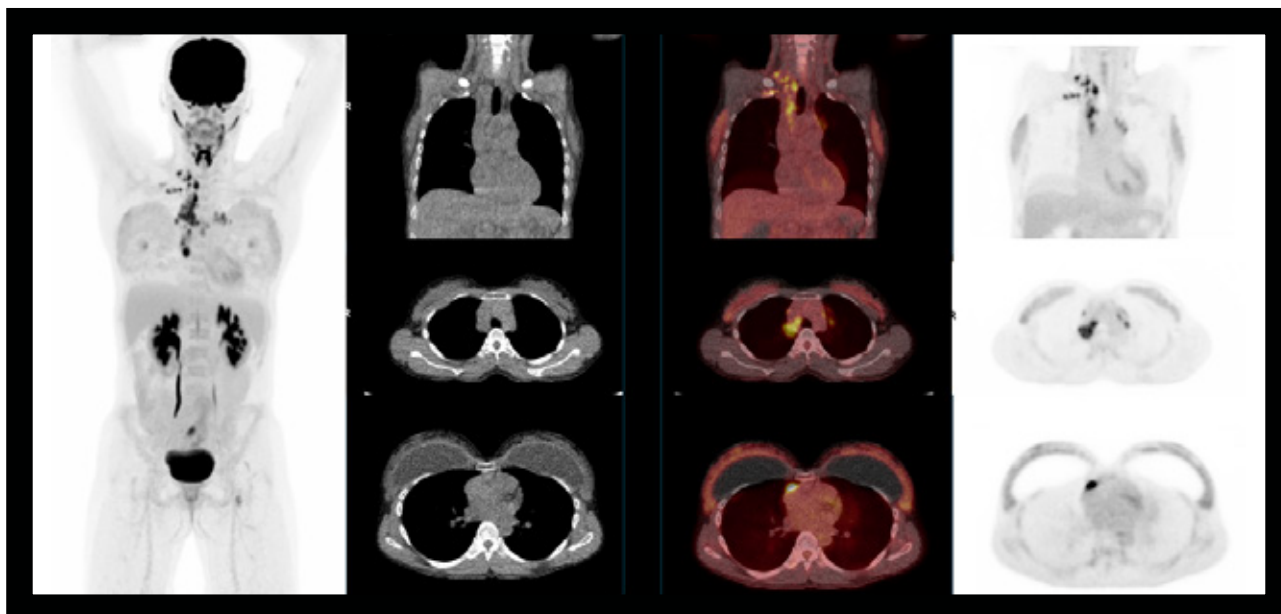
4 Coronal and axial CT, PET, and fused PET/CT images at the uterine level shows ^{18}F -FDG uptake in the fetal brain and heart.

Case 2

A 37-year-old female patient with newly diagnosed Hodgkin's lymphoma who was in her second trimester of pregnancy (18 weeks gestation) was referred for ^{18}F -FDG PET/CT for initial staging.

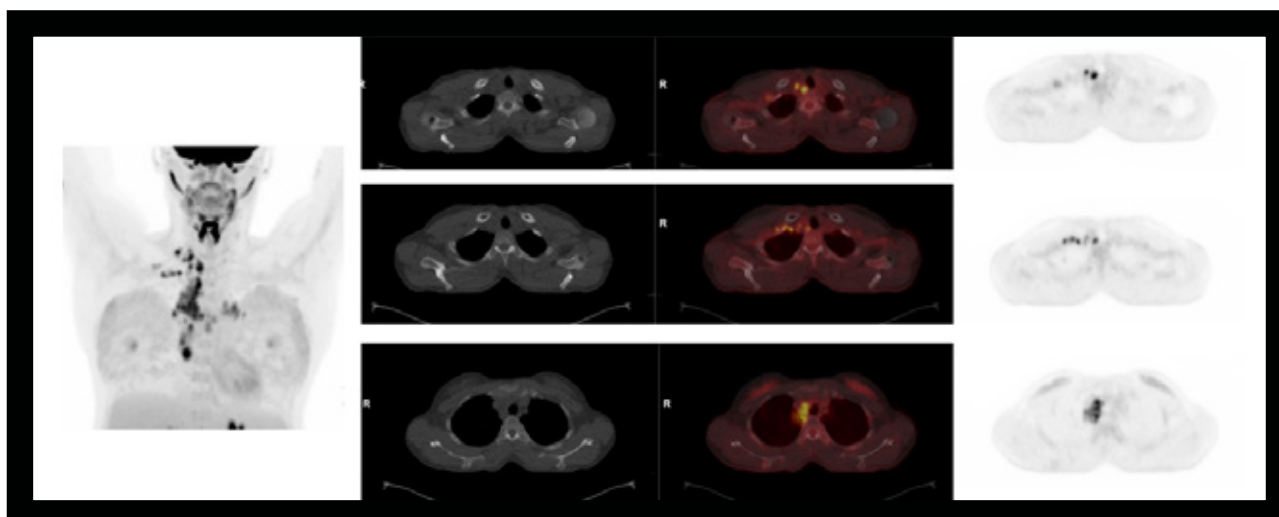
The patient was injected with 39.1 MBq (1.0 mCi) ^{18}F -FDG (weight 60 kg; 0.65 MBq/kg). * 60 minutes following radiopharmaceutical injection, a whole body PET/CT study was acquired from vertex of skull to

mid-thighs with the arms raised. ULD CT was initially performed for attenuation correction utilizing the Sn filter capability of the CT in Biograph Vision Quadra with very low mAs (kVp = Sn140 mAs = 6).

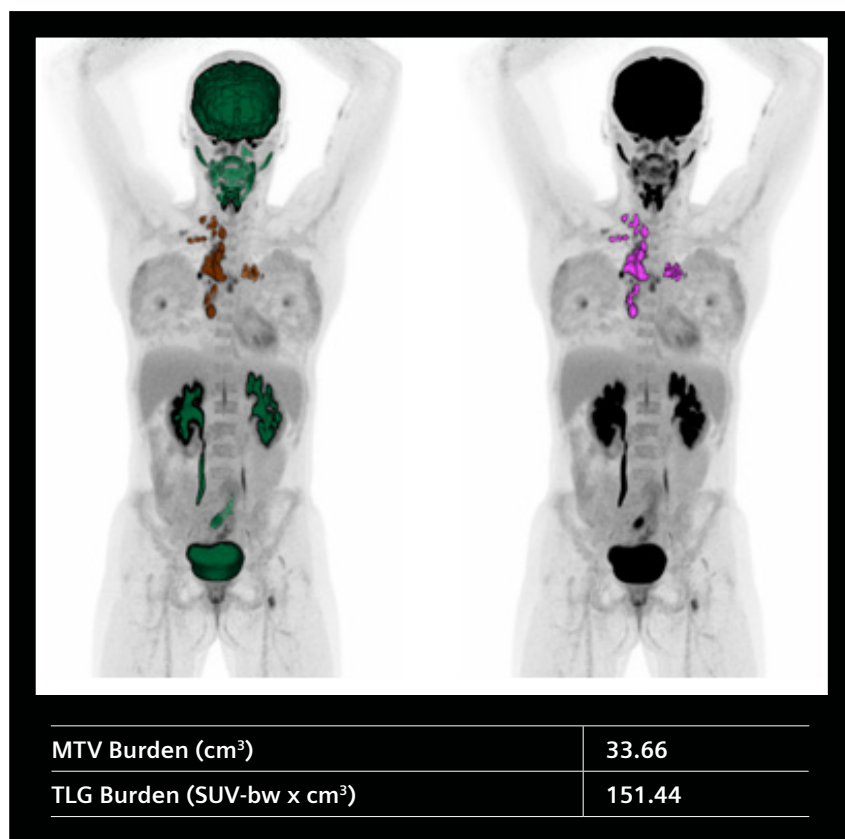


5 PET MIP and coronal and axial CT, PET, and fused PET/CT images at the hilar and lower thoracic level show ^{18}F -FDG-avid enlarged mediastinal lymph nodal lesions involving right and left hilar and right paratracheal and anterior paracardiac lymph nodes. Coronal images also reveal multiple upper mediastinal lymph nodes.

* Based on bench testing (e.g., improved sensitivity and ToF per NEMA NU-2:2018).
Please refer to the approved PET drug prescribing information for dosing and administration instructions.



6 Axial CT, PET, and fused PET/CT images show multiple hypermetabolic upper mediastinal lymph nodes involving right upper paratracheal as well as supraclavicular nodes.



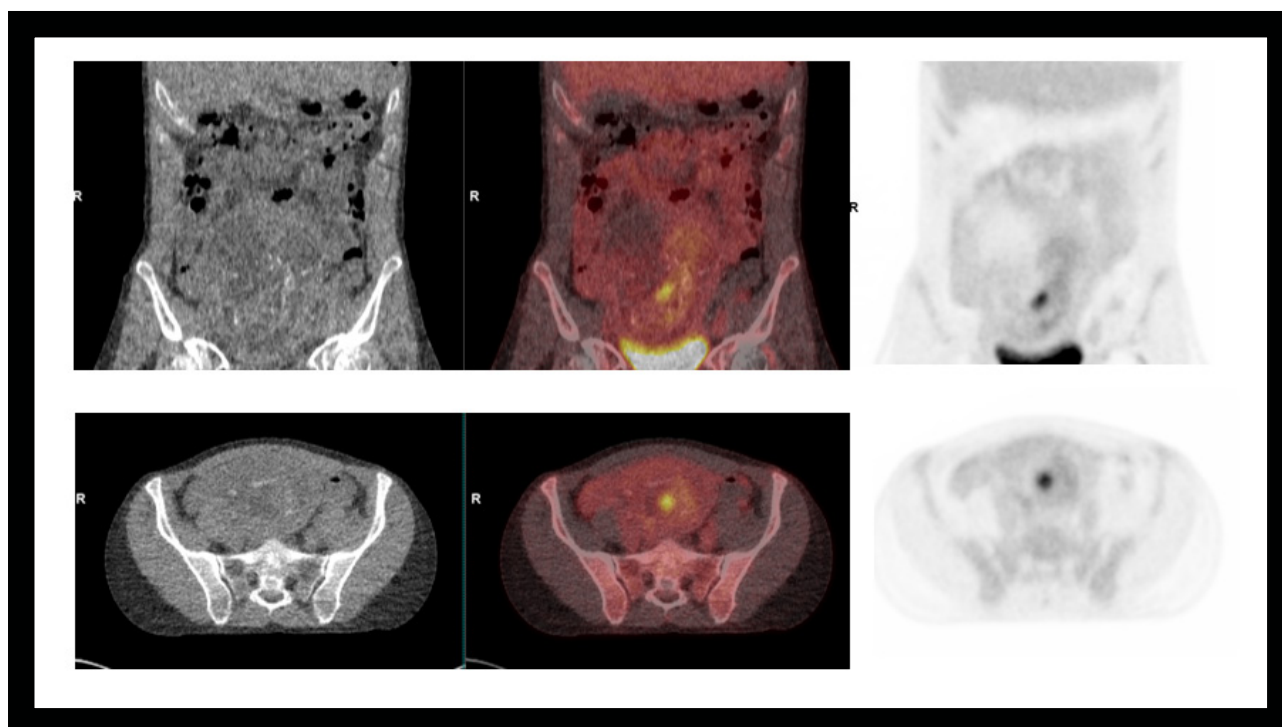
7 Estimation of metabolic tumor volume from ¹⁸F-FDG PET/CT using *syngo.via* shows MTV of 33.6 cc and a high TLG of 151.44, data which can be valuable to evaluate therapy response from post therapy PET/CT studies.

PET acquisition was for a single 106 cm PET axial FOV bed position for 20 minutes. UltraHD PET reconstruction using 4i5s with a post-reconstruction 3D Gaussian filter of FWHM = 2.0 mm.

As shown in Figures 5 and 6, ¹⁸F-FDG PET/CT shows multiple moderate to intensely avid upper thoracic and mediastinal lymph nodal lesions involving right supraclavicular, right paratracheal, and right and left hilar, with the largest lesion in the right hilum measuring 39x24 mm with $SUV_{max} = 9.7$. The largest upper paratracheal node measured 1.4 cm in diameter with $SUV_{max} = 8.3$. The right epicardiac node shown in Figure 5 had $SUV_{max} = 10.5$, which is the highest among thoracic nodal lesions.

No ¹⁸F-FDG-avid nodes were visualized below the diaphragm. Bone marrow uptake was within normal limits. Liver and splenic uptake and size within normal limits. No hypermetabolic extra-lymphatic sites were visualized.

Bilateral breast prostheses visualized with mild diffuse bilateral breast tissue uptake reflecting pregnancy related proliferation.



8 Coronal and axial CT, PET, and fused PET/CT studies show physiological ^{18}F -FDG uptake in the fetus especially the fetal heart.

Discussion

The study was consistent with extensive lymphomatous involvement in mediastinal and supraclavicular nodal groups but without involvement of any other distinct nodal groups including bilateral axillary or nodes on the other side of diaphragm. Total tumor burden and metabolic tumor volume estimations (Figure 7) were performed as a benchmark for post therapy evaluation of response.

High overall image quality with high lesion contrast in the lymph nodal lesions was obtained with 20-minute head-to-mid-thigh PET/CT study despite the very low injected dose due to the high sensitivity of the Biograph Vision Quadra with ultrafast time of flight capability and 106 cm FOV.

These two cases illustrate the capability of the Biograph Vision Quadra system to deliver high quality PET/CT imaging with extremely low injected dose without unduly increased acquisition time. The 15- and 20-minute scan times for head-to-mid-thigh acquisition in a single bed position with injected dose of approximately 40-60 MBq (1-1.5 mCi) achieved high image quality within acquisition times, which were acceptable to the departmental workflow and reduced undue patient motion. The high lesion contrast evident from the PET images and the SUV_{max} values reflects the high count statistics and high resolution of the 3.2 mm x 3.2 mm LSO detectors, as well as the ultrafast time of flight performance of the

system. Generating high quality images at extremely low dose opens the possibility of imaging pregnant patients without serious risk of excessive fetal radiation dose and performing routine low dose evaluation of at-risk populations.

In a recent study from University Medical Center Groningen,⁴ 10 pregnant patients were evaluated on the Biograph Vision Quadra with approximately 20 MBq ^{18}F -FDG injection with 15-minute head-to-mid-thigh single bed position acquisition. All patients reported excellent image quality. A simulation study was performed to determine if the injected dose could be lowered while still achieving acceptable image

quality without increasing scan time. The study showed that for a 15-minute scan time on the Biograph Vision Quadra, the injected dose could be reduced by around 40% without losing any clinical diagnostic confidence. The fetal dose calculated from an approximately 20 MBq ^{18}F -FDG dose was 0.18 mGy, while the low dose CT with kVp Sn 140 and reference mAs of 10 delivered a fetal dose of 0.3 mGy, which together was deemed very low.

Using very low dose CT for attenuation correction is also key for fetal dose reduction. The Sn filter available in the Biograph Vision Quadra can absorb lower energy photons from the x-ray beam and can reduce radiation dose by around 25% in adults with BMI around 25 and up to 45% in adults with BMI>40. This was recently demonstrated in a series of obese patients from MD Anderson Medical Center.⁵

The combination of high sensitivity PET acquisition and ULD CT with Sn filter makes the Biograph Vision Quadra ideal for achieving high image quality with very low injected dose. This opens possibilities for imaging a wide range of patient populations including pregnant patients and pediatric patients with high radiosensitivity, as well as for patients with a high risk of cancer. ●

Examination protocol

Scanner: Biograph Vision Quadra

Case 1

PET	
Injected dose	55.9 MBq (1.5 mCi) ^{18}F -FDG
Post-injection delay	55 minutes
Acquisition time	1 bed position/15 minutes per bed
Reconstruction	UltraHD PET (PSF+TOF) 4i5s Gauss 2.0
CT	
Tube voltage	140 KvP Sn
Tube current	6 mAs

Case 2

PET	
Injected dose	39.1 MBq (1.05 mCi) ^{18}F -FDG
Post-injection delay	60 minutes
Acquisition time	1 bed position/20 minutes per bed
Reconstruction	UltraHD PET (PSF+TOF) 4i5s Gauss 2.0
CT	
Tube voltage	140 KvP Sn
Tube current	6 mAs

The outcomes achieved by the Siemens Healthineers customers described herein were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that others will achieve the same results.

References

- ¹ Siemens Healthineers Molecular Imaging, Hoffman Estates, Illinois, USA
- ² Royal North Shore Hospital and University of Sydney, Sydney, Australia
- ³ Yoon I and Slesinger TL. Radiation exposure in pregnancy. *StatPearls*. 2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551690/>.
- ⁴ Deurloo IS, et al. Smart scanning for two: [^{18}F]FDG dose optimization for pregnant patients using LAFOV PET/CT technology. *EJNMMI Phys*. 2026;13(41). doi : 10.1186/s40658-026-00855-7.
- ⁵ Hemmati et al. Large-scale patient evaluation of SN-filtered CT dose reduction in long axial field-of-view PET/CT. *Journal of Nuclear Medicine*. 2026;67(1).

- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to Fludeoxyglucose F 18 Injection facilitates localization of cardiac ischemia.

2.4 Radiation Dosimetry

The estimated human absorbed radiation doses (rem/mCi) to a newborn (3.4 kg), 1-year old (9.8 kg), 5-year old (19 kg), 10-year old (32 kg), 15-year old (57 kg), and adult (70 kg) from intravenous administration of Fludeoxyglucose F 18 Injection are shown in Table 1. These estimates were calculated based on human² data and using the data published by the International Commission on Radiological Protection⁴ for Fludeoxyglucose ¹⁸F. The dosimetry data show that there are slight variations in absorbed radiation dose for various organs in each of the age groups. These dissimilarities in absorbed radiation dose are due to developmental age variations (e.g., organ size, location, and overall metabolic rate for each age group). The identified critical organs (in descending order) across all age groups evaluated are the urinary bladder, heart, pancreas, spleen, and lungs.

Table 1. Estimated Absorbed Radiation Doses (rem/mCi) After Intravenous Administration of Fludeoxyglucose F 18 Injection^a

Organ	Newborn (3.4 kg)	1-year old (9.8 kg)	5-year old (19 kg)	10-year old (32 kg)	15-year old (57 kg)	Adult (70 kg)
Bladder wall ^b	4.3	1.7	0.93	0.60	0.40	0.32
Heart wall	2.4	1.2	0.70	0.44	0.29	0.22
Pancreas	2.2	0.68	0.33	0.25	0.13	0.096
Spleen	2.2	0.84	0.46	0.29	0.19	0.14
Lungs	0.96	0.38	0.20	0.13	0.092	0.064
Kidneys	0.81	0.34	0.19	0.13	0.089	0.074
Ovaries	0.80	0.8	0.19	0.11	0.058	0.053
Uterus	0.79	0.35	0.19	0.12	0.076	0.062
LLI wall *	0.69	0.28	0.15	0.097	0.060	0.051
Liver	0.69	0.31	0.17	0.11	0.076	0.058
Gallbladder wall	0.69	0.26	0.14	0.093	0.059	0.049
Small intestine	0.68	0.29	0.15	0.096	0.060	0.047
ULI wall **	0.67	0.27	0.15	0.090	0.057	0.046
Stomach wall	0.65	0.27	0.14	0.089	0.057	0.047
Adrenals	0.65	0.28	0.15	0.095	0.061	0.048
Testes	0.64	0.27	0.14	0.085	0.052	0.041
Red marrow	0.62	0.26	0.14	0.089	0.057	0.047
Thymus	0.61	0.26	0.14	0.086	0.056	0.044
Thyroid	0.61	0.26	0.13	0.080	0.049	0.039
Muscle	0.58	0.25	0.13	0.078	0.049	0.039
Bone surface	0.57	0.24	0.12	0.079	0.052	0.041
Breast	0.54	0.22	0.11	0.068	0.043	0.034
Skin	0.49	0.20	0.10	0.060	0.037	0.030
Brain	0.29	0.13	0.09	0.078	0.072	0.070
Other tissues	0.59	0.25	0.13	0.083	0.052	0.042

^a MIRDOSE 2 software was used to calculate the radiation absorbed dose.

^b The dynamic bladder model with a uniform voiding frequency of 1.5 hours was used.

*LLI = lower large intestine; **ULI = upper large intestine

2.5 Radiation Safety – Drug Handling

- Use waterproof gloves, effective radiation shielding, and appropriate safety measures when handling Fludeoxyglucose F 18 Injection to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel and other persons.
- Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.
- Calculate the final dose from the end of synthesis (EOS) time using proper radioactive decay factors. Assay the final dose in a properly calibrated dose calibrator before administration to the patient [see [Description \(11.2\)](#)].
- The dose of Fludeoxyglucose F 18 used in a given patient should be minimized consistent with the objectives of the procedure, and the nature of the radiation detection devices employed.

2.6 Drug Preparation and Administration

- Calculate the necessary volume to administer based on calibration time and dose.
- Aseptically withdraw Fludeoxyglucose F 18 Injection from its container.
- Inspect Fludeoxyglucose F 18 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.
- Do not administer the drug if it contains particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.
- Use Fludeoxyglucose F 18 Injection within 12 hours from the EOS.

2.7 Imaging Guidelines

- Initiate imaging within 40 minutes following Fludeoxyglucose F 18 Injection administration.
- Acquire static emission images 30 to 100 minutes from the time of injection.

3 DOSAGE FORMS AND STRENGTHS

Multiple-dose 50 mL and 100 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 Injection, USP and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 100 mL volume) for intravenous administration.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Radiation Risks

Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker [*see [Dosage and Administration \(2.5\)](#)*].

5.2 Blood Glucose Abnormalities

In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.

6 ADVERSE REACTIONS

Hypersensitivity reactions with pruritus, edema and rash have been reported in the post-marketing setting. Have emergency resuscitation equipment and personnel immediately available.

7 DRUG INTERACTIONS

The interactions of Fludeoxyglucose F 18 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Data from published case series and case reports describe Fludeoxyglucose F 18 Injection crossing the placenta with uptake by the fetus (see Data). All radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. However, published studies that describe Fludeoxyglucose F 18 Injection use in pregnant women have not identified a risk of drug-associated major birth defects, miscarriage, or adverse maternal or fetal outcomes. If considering Fludeoxyglucose F 18 Injection administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes based on the radiation dose from Fludeoxyglucose F 18 Injection and the gestational timing of exposure.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

Data

Human Data

Data from published case series and case reports describe Fludeoxyglucose F 18 Injection crossing the placental barrier and visualization of radioactivity throughout the body of the fetus. The estimated fetal absorbed radiation dose from the maximum

labeled dose (370 MBq) of Fludeoxyglucose F 18 was 10 mGy with first trimester exposure to PET alone and 20 mGy with first trimester exposure to PET/CT scan combination. Long-term adverse radiation effects to a child exposed to Fludeoxyglucose F 18 Injection in utero are unknown. No adverse fetal effects or radiation-related risks have been identified for diagnostic procedures involving less than 50 mGy, which represents less than 20 mGy fetal doses.

8.2 Lactation

Risk Summary

A published case report and case series show the presence of Fludeoxyglucose F 18 Injection in human milk following administration. There are no data on the effects of Fludeoxyglucose F 18 Injection on the breastfed infant or the effects on milk production. Exposure of Fludeoxyglucose F 18 Injection to a breastfed infant can be minimized by temporary discontinuation of breastfeeding (see Clinical Considerations). The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Fludeoxyglucose F 18 Injection, any potential adverse effects on the breastfed child from Fludeoxyglucose F 18 Injection or from the underlying maternal condition.

Clinical Considerations

To decrease radiation exposure to the breastfed infant, advise a lactating woman to pump and discard breastmilk and avoid close (breast) contact with the infant for at least 9 hours after the administration of Fludeoxyglucose F 18 Injection.

8.4 Pediatric Use

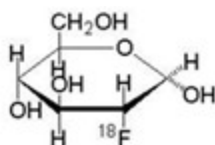
The safety and effectiveness of Fludeoxyglucose F 18 Injection in pediatric patients with epilepsy is established on the basis of studies in adult and pediatric patients. In pediatric patients with epilepsy, the recommended dose is 2.6 mCi. The optimal dose adjustment on the basis of body size or weight has not been determined.

In the oncology or cardiology settings, the safety and effectiveness of Fludeoxyglucose F 18 Injection have not been established in pediatric patients.

11 DESCRIPTION

11.1 Chemical Characteristics

Fludeoxyglucose F 18 Injection, USP is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. The active ingredient 2-deoxy-2- ^{18}F fluoro-D-glucose has the molecular formula of $\text{C}_6\text{H}_{11}^{18}\text{FO}_5$ with a molecular weight of 181.26, and has the following chemical structure:



Fludeoxyglucose F 18 Injection, USP is provided as a ready to use sterile, pyrogen free, clear, colorless solution. Each mL contains between 0.740 to 7.40 GBq (20.0 to 200 mCi) of 2-deoxy-2- ^{18}F fluoro-D-glucose at the EOS, 4.5 mg of sodium chloride and 0.1 to 0.5% w/w ethanol as a stabilizer. The pH of the solution is between 4.5 and 7.5. The solution is packaged in a multiple-dose glass vial and does not contain any preservative.

11.2 Physical Characteristics

Fluorine F 18 has a physical half-life of 109.7 minutes and decays to Oxygen O 16 (stable) by positron decay. The principal photons useful for imaging are the dual 511 keV “annihilation” gamma photons, that are produced and emitted simultaneously in opposite direction when the positron interacts with an electron (Table 2).

Table 2. Principal Radiation Emission Data for Fluorine F 18		
Radiation/Emission	% Per Disintegration	Mean Energy
Positron(β^+)	96.73	249.8 keV
Gamma($\pm$)*	193.46	511.0 keV

*Produced by positron annihilation

From: Kocher, D.C. Radioactive Decay Tables DOE/TIC-I 1026, 89 (1981)

The specific gamma ray constant (point source air kerma coefficient) for fluorine F 18 is 5.7 R/hr/mCi (1.35×10^{-6} Gy/hr/kBq) at 1 cm. The half-value layer (HVL) for the 511 keV photons is 4 mm lead (Pb). The range of attenuation coefficients for this radionuclide as a function of lead shield thickness is shown in Table 3. For example, the interposition of an 8 mm thickness of Pb, with a coefficient of attenuation of 0.25, will decrease the external radiation by 75%.

Table 3. Radiation Attenuation of 511 keV Photons by lead (Pb) shielding	
Shield thickness (Pb) mm	Coefficient of attenuation
0	0.00
4	0.50
8	0.25
13	0.10
26	0.01
39	0.001
52	0.0001

For use in correcting for physical decay of this radionuclide, the fractions remaining at selected intervals after calibration are shown in Table 4.

Table 4. Physical Decay Chart for Fluorine F 18

Minutes	Fraction Remaining
0*	1.000
15	0.909
30	0.826
60	0.683
110	0.500
220	0.250

*calibration time

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fludeoxyglucose F 18 is a glucose analog that concentrates in cells that rely upon glucose as an energy source, or in cells whose dependence on glucose increases under pathophysiological conditions. Fludeoxyglucose F 18 is transported through the cell membrane by facilitative glucose transporter proteins and is phosphorylated within the cell to [^{18}F]-FDG-6-phosphate by the enzyme hexokinase. Once phosphorylated it cannot exit until it is dephosphorylated by glucose-6-phosphatase. Therefore, within a given tissue or pathophysiological process, the retention and clearance of Fludeoxyglucose F 18 reflect a balance involving glucose transporter, hexokinase and glucose-6-phosphatase activities. Fludeoxyglucose F 18 is used to assess glucose metabolism.

In comparison to background activity of the specific organ or tissue type, regions of decreased or absent uptake of Fludeoxyglucose F 18 reflect the decrease or absence of glucose metabolism. Regions of increased uptake of Fludeoxyglucose F 18 reflect greater than normal rates of glucose metabolism.

12.2 Pharmacodynamics

Fludeoxyglucose F 18 Injection is rapidly distributed to all organs of the body after intravenous administration. After background clearance of Fludeoxyglucose F 18 Injection, optimal PET imaging is generally achieved between 30 to 40 minutes after administration.

In cancer, the cells are generally characterized by enhanced glucose metabolism partially due to (1) an increase in activity of glucose transporters, (2) an increased rate of phosphorylation activity, (3) a reduction of phosphatase activity or, (4) a dynamic alteration in the balance among all these processes. However, glucose metabolism of cancer as reflected by Fludeoxyglucose F 18 accumulation shows considerable variability. Depending on tumor type, stage, and location, Fludeoxyglucose F 18 accumulation may be increased, normal, or decreased. Also, inflammatory cells can have the same variability of uptake of Fludeoxyglucose F 18.

In the heart, under normal aerobic conditions, the myocardium meets the bulk of its energy requirements by oxidizing free fatty acids. Most of the exogenous glucose taken up by the myocyte is converted into glycogen. However, under ischemic conditions, the oxidation of free fatty acids decreases, exogenous glucose becomes the preferred myocardial substrate, glycolysis is stimulated, and glucose taken up by the myocyte is metabolized immediately instead of being converted into glycogen. Under these conditions, phosphorylated Fludeoxyglucose F 18 accumulates in the myocyte and can be detected with PET imaging.

In the brain, cells normally rely on aerobic metabolism. In epilepsy, the glucose metabolism varies. Generally, during a seizure, glucose metabolism increases. Interictally, the seizure focus tends to be hypometabolic.

12.3 Pharmacokinetics

Distribution: In four healthy male volunteers, receiving an intravenous administration of 30 seconds in duration, the arterial blood level profile for Fludeoxyglucose F 18 decayed triexponentially. The effective half-life ranges of the three phases were 0.2 to 0.3 minutes, 10 to 13 minutes with a mean and standard deviation (STD) of 11.6 ($\pm$) 1.1 min, and 80 to 95 minutes with a mean and STD of 88 ($\pm$) 4 min.

Plasma protein binding of Fludeoxyglucose F 18 has not been studied.

Metabolism: Fludeoxyglucose F 18 is transported into cells and phosphorylated to [^{18}F]-FDG-6-phosphate at a rate proportional to the rate of glucose utilization within that tissue. [^{18}F]-FDG-6-phosphate presumably is metabolized to 2-deoxy-2- [^{18}F]fluoro-6-phospho-D-mannose([^{18}F]FDM-6-phosphate).

Fludeoxyglucose F 18 Injection may contain several impurities (e.g., 2-deoxy-2-chloro-D-glucose (CIDG)). Biodistribution and metabolism of CIDG are presumed to be similar to Fludeoxyglucose F 18 and would be expected to result in intracellular formation of 2-deoxy-2-chloro-6-phospho-D-glucose (CIDG-6-phosphate) and 2-deoxy-2-chloro-6-phospho-D-mannose (CIDM-6-phosphate). The phosphorylated deoxyglucose compounds are dephosphorylated and the resulting compounds (FDG, FDM, CIDG, and CIDM) presumably leave cells by passive diffusion. Fludeoxyglucose F 18 and related compounds are cleared from non-cardiac tissues within 3 to 24 hours after administration. Clearance from the cardiac tissue may require more than 96 hours. Fludeoxyglucose F 18 that is not involved in glucose metabolism in any tissue is then excreted in the urine.

Elimination: Fludeoxyglucose F 18 is cleared from most tissues within 24 hours and can be eliminated from the body unchanged in the urine. Within 33 minutes, a mean of 3.9% of the administered radioactive dose was measured in the urine. The amount of radiation exposure of the urinary bladder at two hours post-administration suggests that 20.6% (mean) of the radioactive dose was present in the bladder.

Special Populations:

The pharmacokinetics of Fludeoxyglucose F 18 Injection have not been studied in renally-impaired, hepatically impaired or pediatric patients. Fludeoxyglucose F 18 is eliminated through the renal system. Avoid excessive radiation exposure to this organ system and adjacent tissues.

The effects of fasting, varying blood sugar levels, conditions of glucose intolerance, and diabetes mellitus on Fludeoxyglucose F 18 distribution in humans have not been ascertained [see [Warnings and Precautions \(5.2\)](#)].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been performed to evaluate the Fludeoxyglucose F 18 Injection carcinogenic potential, mutagenic potential or effects on fertility.

14 CLINICAL STUDIES

14.1 Oncology

The efficacy of Fludeoxyglucose F 18 Injection in positron emission tomography cancer imaging was demonstrated in 16 independent studies. These studies prospectively evaluated the use of Fludeoxyglucose F 18 in patients with suspected or known malignancies, including non-small cell lung cancer, colo-rectal, pancreatic, breast, thyroid, melanoma, Hodgkin's and non-Hodgkin's lymphoma, and various types of metastatic cancers to lung, liver, bone, and axillary nodes. All these studies had at least 50 patients and used pathology as a standard of truth. The Fludeoxyglucose F 18 Injection doses in the studies ranged from 200 MBq to 740 MBq with a median and mean dose of 370 MBq.

In the studies, the diagnostic performance of Fludeoxyglucose F 18 Injection varied with the type of cancer, size of cancer, and other clinical conditions. False negative and false positive scans were observed. Negative Fludeoxyglucose F 18 Injection PET scans do not exclude the diagnosis of cancer. Positive Fludeoxyglucose F 18 Injection PET scans can not replace pathology to establish a diagnosis of cancer. Non-malignant conditions such as fungal infections, inflammatory processes and benign tumors have patterns of increased glucose metabolism that may give rise to false-positive scans. The efficacy of Fludeoxyglucose F 18 Injection PET imaging in cancer screening was not studied.

14.2 Cardiology

The efficacy of Fludeoxyglucose F 18 Injection for cardiac use was demonstrated in ten independent, prospective studies of patients with coronary artery disease and chronic left ventricular systolic dysfunction who were scheduled to undergo coronary revascularization. Before revascularization, patients underwent PET imaging with Fludeoxyglucose F 18 Injection (74 to 370 MBq, 2 to 10 mCi) and perfusion imaging with other diagnostic radiopharmaceuticals. Doses of Fludeoxyglucose F 18 Injection ranged from 74 to 370 MBq (2 to 10 mCi). Segmental, left ventricular, wall-motion assessments of asynergic areas made before revascularization were compared in a

blinded manner to assessments made after successful revascularization to identify myocardial segments with functional recovery.

Left ventricular myocardial segments were predicted to have reversible loss of systolic function if they showed Fludeoxyglucose F 18 accumulation and reduced perfusion (i.e., flow-metabolism mismatch). Conversely, myocardial segments were predicted to have irreversible loss of systolic function if they showed reductions in both Fludeoxyglucose F 18 accumulation and perfusion (i.e., matched defects).

Findings of flow-metabolism mismatch in a myocardial segment may suggest that successful revascularization will restore myocardial function in that segment. However, false-positive tests occur regularly, and the decision to have a patient undergo revascularization should not be based on PET findings alone. Similarly, findings of a matched defect in a myocardial segment may suggest that myocardial function will not recover in that segment, even if it is successfully revascularized. However, false-negative tests occur regularly, and the decision to recommend against coronary revascularization, or to recommend a cardiac transplant, should not be based on PET findings alone. The reversibility of segmental dysfunction as predicted with Fludeoxyglucose F 18 PET imaging depends on successful coronary revascularization. Therefore, in patients with a low likelihood of successful revascularization, the diagnostic usefulness of PET imaging with Fludeoxyglucose F 18 Injection is more limited.

14.3 Neurology

In a prospective, open label trial, Fludeoxyglucose F 18 Injection was evaluated in 86 patients with epilepsy. Each patient received a dose of Fludeoxyglucose F 18 Injection in the range of 185 to 370 MBq (5 to 10 mCi). The mean age was 16.4 years (range: 4 months to 58 years; of these, 42 patients were less than 12 years and 16 patients were less than 2 years old). Patients had a known diagnosis of complex partial epilepsy and were under evaluation for surgical treatment of their seizure disorder. Seizure foci had been previously identified on ictal EEGs and sphenoidal EEGs. Fludeoxyglucose F 18 Injection PET imaging confirmed previous diagnostic findings in 16% (14/87) of the patients; in 34% (30/87) of the patients, Fludeoxyglucose F 18 Injection PET images provided new findings. In 32% (27/87), imaging with Fludeoxyglucose F 18 Injection was inconclusive. The impact of these imaging findings on clinical outcomes is not known.

Several other studies comparing imaging with Fludeoxyglucose F 18 Injection results to subsphenoidal EEG, MRI and/or surgical findings supported the concept that the degree of hypometabolism corresponds to areas of confirmed epileptogenic foci. The safety and effectiveness of Fludeoxyglucose F 18 Injection to distinguish idiopathic epileptogenic foci from tumors or other brain lesions that may cause seizures have not been established.

16 HOW SUPPLIED/STORAGE AND DRUG HANDLING

Fludeoxyglucose F 18 Injection, USP is supplied in a multi-dose, capped 50 mL and 100 mL

glass vial containing between 0.740 to 7.40 GBq/mL (20 to 200 mCi/mL), of no carrier added 2-deoxy-2-[¹⁸F]-fluoro-D-glucose, at end of synthesis, in approximately 15 to 100 mL. The contents of each vial are sterile, pyrogen-free and preservative-free.

NDC 40028-511-50; 40028-511-99

Receipt, transfer, handling, possession, or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

Store the Fludeoxyglucose F 18 Injection, USP vial upright in a lead shielded container at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Store and dispose of Fludeoxyglucose F 18 Injection, USP in accordance with the regulations and a general license, or its equivalent, of an Agreement State or a Licensing State.

The expiration date and time are provided on the container label. Use Fludeoxyglucose F 18 Injection, USP within 12 hours from the EOS time.

17 PATIENT COUNSELING INFORMATION

Instruct patients in procedures that increase renal clearance of radioactivity.

Encourage patients to:

- drink water or other fluids (as tolerated) in the 4 hours before their PET study.
- void as soon as the imaging study is completed and as often as possible thereafter for at least one hour.

Pregnancy: Advise pregnant women of the risk of fetal exposure to radiation with Fludeoxyglucose F 18 Injection [see [Use in Specific Populations \(8.1\)](#)].

Lactation: Advise lactating women that exposure to Fludeoxyglucose F 18 Injection through breast milk can be minimized by pumping and discarding breast milk and avoiding close (breast) contact with the infant for 9 hours after Fludeoxyglucose F 18 Injection [see [Use in Specific Populations \(8.2\)](#)].

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