**18**F FDG PET/CT delineation of diffuse large B-cell lymphoma involving lower spinal cord and spinal nerve roots

By Partha Ghosh, MD, Siemens Healthineers, Hoffman Estates, IL, USA

Data and images courtesy of Osaka City University Hospital, Osaka, Japan

**History**

A 50-year-old female with progressive weakness in both legs underwent PET/CT imaging to evaluate a spinal pathology. The study was conducted on a Biograph Vision™ 450 scanner using Fludeoxyglucose F 18 (18F FDG) Injection.[a]

Approximately 51 minutes following the intravenous (IV) injection of 4.6 mCi (173 MBq) of 18F FDG and completion of the initial low-dose CT, a dynamic whole-body PET acquisition was performed with FlowMotion™ continuous-bed-motion technology. A total of 6 consecutive whole-body passes were acquired at 3 minutes and 19 seconds per pass and subsequently summed into a single PET dataset. The individual dynamic whole-body PET acquisitions, as well as the summed PET data, were evaluated on a syngo®.via workstation.

![Whole-body PET MIP images of 6 sequential whole-body PET FlowMotion acquisitions, acquired at 3 minutes and 19 seconds per pass (20-minute total scan time), along with the summed PET image.](image)

[a] Please see Indications and Important Safety Information for Fludeoxyglucose F 18 (18F FDG) Injection on page 2. For full Prescribing Information, please see pages 8-10.
Findings

The visual evaluation of the sequential dynamic whole-body PET acquisitions, as well as the summed PET image comprised of data acquired over 20 minutes, shows intense $^{18}$F FDG uptake in the lower spinal cord, lumbar spinal nerve roots, and cauda equina. In addition, a linear mass in the region of right psoas muscle, which includes the sacral spinal nerve roots within the pelvis is evident.

As depicted in Figures 4-9, the $^{18}$F FDG PET/CT shows hypermetabolic and enlarged lower spinal cord and spinal nerve roots in bilateral L1 and L2, L4 and L5, and S1 and S2. The large right psoas mass appears to be an enlarged extension of the hypermetabolic right L2 nerve root. The right sacral nerve roots also show an extension of hypermetabolism along the neural sheath.

The pattern of such hypermetabolism—including the involvement of the spinal cord with continuous extension into spinal nerve roots seen in the lower spinal cord and L1 and L2 spinal nerve roots, as well as discontinuous involvement of right L4-L5 and S1 and S2 nerve roots with extension along nerve tracts—suggests a primary spinal cord lesion with diffuse extension along nerve sheaths, which indicates the possibility of a primary spinal cord lymphoma or leukemia.

The patient underwent resection of the psoas lesion and a biopsy was performed on a surgical specimen of the involved nerve roots. The histopathology report revealed diffuse large B-cell lymphoma (DLBCL), and the patient was diagnosed with primary central nervous system DLBCL derived from the lumbar spinal cord.
A MIP of summed whole-body PET/CT image shows intense $^{18}$F FDG uptake in the spinal cord at the T12-L4 vertebral bodies (arrow), as well as at the spinal nerve roots of L1 and L2 vertebrae bilaterally (arrow). Intense uptake in the right L2 spinal nerve root expands into a large hypermetabolic mass within the right psoas muscle (arrow). Right lumbosacral trunk (L4 and L5 spinal nerve roots) as well as right S1 and S2 nerve roots are also enlarged and show hypermetabolic activity.

The coronal thin MIP of the summed PET image (left to right, posterior to anterior) visualizes an enlarged and hypermetabolic lower spinal cord from T12-L4 (arrow) along with bilaterally enlarged and hypermetabolic L1 (arrow) and L2 spinal nerve roots. An enlarged hypermetabolic psoas mass (arrow) is shown arising from the right L2 spinal nerve root. The enlarged hypermetabolic lumbosacral trunk (L4 and L5 spinal nerve roots) and S1 spinal nerve roots show hypermetabolism (arrows). The S1 spinal nerve depicts hypermetabolism along the entire nerve fiber.
Clinical Results

Coronal views of CT, PET, and fused images demonstrate spinal cord and spinal nerve enlargement and hypermetabolism. The hypermetabolic psoas mass arising from the right L2 spinal nerve root measures 9 cm x 3.3 cm and appears to be a lymphomatous expansion of the spinal nerve passing along the psoas muscle.

Sagittal views of CT, PET, and fused images show an enlarged hypermetabolic lower spinal cord from T1-L4, which reveals involvement of spinal nerve roots, enlarged psoas mass, and sacral nerve roots.
Axial views of CT, PET, and fused images from the level at lower end of the T12 vertebra to the L2 vertebrae show a hypermetabolic spinal cord (arrow) with enlarged hypermetabolic bilateral L1 and L2 spinal nerve roots (arrows).

Axial views of CT, PET, and fused images from L2-L4 show hypermetabolic spinal cord and spinal nerve roots in addition to a hypermetabolic mass in the region of the right psoas muscle (arrows) measuring 3.9 cm x 3.83 cm maximum dimension in the axial section.
Axial views of CT, PET, and fused images from L4-S1 show an enlarged hypermetabolic psoas mass (arrow), which bifurcates further into the pelvic nerve roots (arrow). A hypermetabolic right lumbosacral nerve root (L4 and L5 spinal nerve root combined) exiting from the right L5-S1 spinal canal is also visualized (arrow).

Axial views of CT, PET, and fused images through the sacrum and pelvis demonstrate a hypermetabolic enlarged sacral nerve roots on the right side (arrows), specifically the lumbosacral S1 and S2 nerve roots.
**Discussion**

Primary central nervous system B-cell lymphoma accounts for 4-6% of all malignant lymphomas.\(^1\) There is increased incidence in immunocompromised individuals, including acquired immunodeficiency syndrome and transplant recipients. Direct infiltration of the cauda equina is rare and is usually in the form of a primary localized or disseminated form of central nervous system (CNS) lymphoma. Most common presentations are muscular weakness, paraparesis or paraplegia, and radiculopathy. Magnetic resonance imaging (MRI) findings include swelling of the involved spinal cord and nerve roots, which is either hypo- or iso-intense to the normal spinal cord in both T1 and T2 with enhancement following contrast. \(^1\)\(^8\)F FDG PET/CT shows increased tracer accumulation in the involved areas with the SUV being lower than that of general DLBCL. In a case report of lower spinal cord and cauda equina DLCBL, the calculated SUV\(_{\text{max}}\) in two lesions at 9.6 and 4.9 were deemed lower than those reported for non-neurological DLBCL.\(^1\)

In this particular case, the SUV\(_{\text{max}}\) were much higher, although consideration should be given to the Biograph Vision 450 PET/CT system and its 214 picosecond time-of-flight (ToF) performance with high-resolution PET acquisition, which results in higher SUV\(_{\text{max}}\) levels.

Intense accumulation of \(^1\)\(^8\)F FDG in the lower spinal cord from T12-L4, as well as the spinal nerve roots seen in the present case are typical of spinal cord DLBCL. The enlargement of the involved nerve roots seen on both CT and PET correlates with typical MRI findings in similar clinical situations. The large, intensely hypermetabolic mass in the right psoas region, which arises from the involved right L2 spinal nerve root may be an affected paravertebral ganglion. In the absence of any non-nervous system involvement, the right psoas mass was evaluated as the primary neurological origin, and the biopsy revealed it to be a primary CNS large B-cell lymphoma.

**Conclusion**

This case illustrates how a comprehensive PET/CT evaluation of nervous system lymphoma helps delineate the extent of disease infiltration. The high resolution of the Biograph Vision 450 system paired with the high contrast-to-background ratio achieved due to high ToF performance helps achieve sharp definition with high contrast within nerve tract lesions, as seen in the involved pelvic nerves arising from the S1 and S2 nerve roots that are clearly defined on PET/CT.

---

**Examination protocol**

Scanner: Biograph Vision 450

<table>
<thead>
<tr>
<th>PET</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injected dose</td>
<td>4.6 mCi (173 MBq)</td>
</tr>
<tr>
<td>Post-injection delay</td>
<td>51 minutes</td>
</tr>
<tr>
<td>Acquisition</td>
<td>6 whole-body passes acquired with FlowMotion technology</td>
</tr>
<tr>
<td>Scan time</td>
<td>Total scan time of 20 minutes: 3 minutes and 19 seconds per pass</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The outcomes achieved by the Siemens Healthineers customer 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**

HIGHLIGHTS OF PRESCRIBING INFORMATION
The Highlights do not include all the information needed to use Fludeoxyglucose F 18 Injection safely and effectively. See full prescribing information for Fludeoxyglucose F 18 Injection.

Fludeoxyglucose F 18 Injection, USP
For intravenous use
Init. U.S. Approval: 2005

INDICATIONS AND USAGE
Fludeoxyglucose F 18 Injection 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 function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- Neurology: For the identification of regional abnormalities of glucose metabolism associated with foci of epileptic seizures.

Dosage And Administration
Fludeoxyglucose F 18 Injection emits radiation. Use procedures to minimize radiation exposure. See Screen for blood glucose abnormalities.

- In the oncology and neurology settings, instruct patients to fast for 4 to 6 hours prior to the drug's injection. Consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to the drug's administration.
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 100 grams) prior to the drug's injection facilitates localization of cardiac ischemia (2.3).

The recommended dose:
- for adults: 5 to 10 mCi (185 to 370 MBq)
- for pediatric patients: 2.6 mCi in the neurology setting (2.2)

- Radiation risks: use smallest dose necessary for imaging (5.1).

- Blood glucose abnormalities: may cause suboptimal imaging (5.2).

ADVERSE REACTIONS
Hypersensitivity reactions have occurred; have emergency resuscitation equipment and personnel immediately available.

To report SUSPECTED ADVERSE REACTIONS, contact PETNET Solutions, Inc. at 877-456-6368 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS
- Lactation: Temporarily discontinue breast-feeding. A lactating woman should pump and discard breast milk for 9 hours after Fludeoxyglucose F 18 Injection (8.2).

- Pediatric Use: Safety and effectiveness in pediatric patients have not been established in the oncology and cardiology settings.

See 17 FOR PATIENT COUNSELING INFORMATION

Revised: 10/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
1.1 Oncology
1.2 Cardiology
1.3 Neurology

2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dose for Adults
2.2 Recommended Dose for Pediatric Patients
2.3 Patient Preparation
2.4 Radiation Dosimetry
2.5 Radiation Safety – Drug Handling
2.6 Drug Preparation and Administration
2.7 Imagery Guidelines

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINdicATIONS

5 WARNINGS AND PRECAUTIONS
5.1 Radiation Risks
5.2 Blood Glucose Abnormalities
5.3 Radiation Exposure

6 ADVERSE REACTIONS

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

FULL PRESCRIBING INFORMATION

Fludeoxyglucose F 18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

1.1 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.

1.2 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.

1.3 Neurology

- For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

2 DOSAGE AND ADMINISTRATION

Fludeoxyglucose F 18 Injection emits radiation. Use procedures to minimize radiation exposure. 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).

2.1 Recommended Dose for Adults

- Within the oncology, cardiology and neurology settings, the recommended dose for adults is 5 to 10 mCi (185 to 370 MBq) as an intravenous injection.

2.2 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 (see Use in Special Populations (8.4)).

2.3 Patient Preparation

- To minimize the radiation absorbed dose to the bladder, encourage adequate hydration.

- Encourage the patient to drink water or other fluids (as tolerated) in the 4 hours before their PET study.

- Screen patients for clinically significant blood glucose abnormalities by obtaining a history and/or laboratory tests (see Warnings and Precautions (5.2)). Prior to Fludeoxyglucose F 18 PET imaging in the oncology and neurology settings, instruct patient to fast for 4 to 6 hours prior to the drug's injection.

- 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.

3 DOSAGE FORMS AND STRENGTHS

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

<table>
<thead>
<tr>
<th>Organ</th>
<th>Newborn (3.4 kg)</th>
<th>1-year old (9.8 kg)</th>
<th>5-year old (19 kg)</th>
<th>10-year old (32 kg)</th>
<th>15-year old (57 kg)</th>
<th>Adult (70 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder wall</td>
<td>4.3</td>
<td>1.7</td>
<td>0.93</td>
<td>0.60</td>
<td>0.32</td>
<td>0.26</td>
</tr>
<tr>
<td>Heart wall</td>
<td>2.4</td>
<td>1.2</td>
<td>0.70</td>
<td>0.44</td>
<td>0.29</td>
<td>0.22</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2.1</td>
<td>0.68</td>
<td>0.33</td>
<td>0.25</td>
<td>0.13</td>
<td>0.08</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.2</td>
<td>0.84</td>
<td>0.46</td>
<td>0.29</td>
<td>0.19</td>
<td>0.14</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.96</td>
<td>0.38</td>
<td>0.20</td>
<td>0.13</td>
<td>0.092</td>
<td>0.064</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.81</td>
<td>0.34</td>
<td>0.19</td>
<td>0.13</td>
<td>0.089</td>
<td>0.074</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.80</td>
<td>0.08</td>
<td>0.19</td>
<td>0.11</td>
<td>0.058</td>
<td>0.053</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.79</td>
<td>0.35</td>
<td>0.19</td>
<td>0.12</td>
<td>0.076</td>
<td>0.062</td>
</tr>
<tr>
<td>LLi wall *</td>
<td>0.69</td>
<td>0.28</td>
<td>0.15</td>
<td>0.097</td>
<td>0.060</td>
<td>0.051</td>
</tr>
<tr>
<td>Liver</td>
<td>0.69</td>
<td>0.31</td>
<td>0.17</td>
<td>0.11</td>
<td>0.076</td>
<td>0.058</td>
</tr>
<tr>
<td>Gallbladder wall</td>
<td>0.69</td>
<td>0.26</td>
<td>0.14</td>
<td>0.093</td>
<td>0.059</td>
<td>0.049</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.68</td>
<td>0.29</td>
<td>0.15</td>
<td>0.096</td>
<td>0.060</td>
<td>0.047</td>
</tr>
<tr>
<td>ULI wall **</td>
<td>0.67</td>
<td>0.27</td>
<td>0.15</td>
<td>0.090</td>
<td>0.057</td>
<td>0.046</td>
</tr>
<tr>
<td>Stomach wall</td>
<td>0.65</td>
<td>0.27</td>
<td>0.14</td>
<td>0.089</td>
<td>0.057</td>
<td>0.047</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.65</td>
<td>0.28</td>
<td>0.15</td>
<td>0.095</td>
<td>0.061</td>
<td>0.048</td>
</tr>
<tr>
<td>Testes</td>
<td>0.64</td>
<td>0.27</td>
<td>0.15</td>
<td>0.085</td>
<td>0.053</td>
<td>0.045</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.62</td>
<td>0.26</td>
<td>0.14</td>
<td>0.089</td>
<td>0.057</td>
<td>0.047</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.61</td>
<td>0.26</td>
<td>0.14</td>
<td>0.086</td>
<td>0.056</td>
<td>0.044</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.61</td>
<td>0.26</td>
<td>0.13</td>
<td>0.080</td>
<td>0.049</td>
<td>0.039</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.58</td>
<td>0.25</td>
<td>0.13</td>
<td>0.078</td>
<td>0.049</td>
<td>0.039</td>
</tr>
<tr>
<td>Bone surface</td>
<td>0.57</td>
<td>0.24</td>
<td>0.12</td>
<td>0.079</td>
<td>0.052</td>
<td>0.041</td>
</tr>
<tr>
<td>Breast</td>
<td>0.54</td>
<td>0.22</td>
<td>0.11</td>
<td>0.068</td>
<td>0.043</td>
<td>0.034</td>
</tr>
<tr>
<td>Skin</td>
<td>0.49</td>
<td>0.20</td>
<td>0.10</td>
<td>0.060</td>
<td>0.037</td>
<td>0.030</td>
</tr>
<tr>
<td>Brain</td>
<td>0.29</td>
<td>0.13</td>
<td>0.09</td>
<td>0.078</td>
<td>0.072</td>
<td>0.070</td>
</tr>
<tr>
<td>Other tissues</td>
<td>0.59</td>
<td>0.25</td>
<td>0.13</td>
<td>0.083</td>
<td>0.052</td>
<td>0.042</td>
</tr>
</tbody>
</table>

* MRDOS 2 software was used to calculate the radiation absorbed dose.

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

Clinical Results

PET/CT Case Study · siemens-healthineers.com/micc

8

8
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 discontinue use if administration is uncertain.
- 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 30 mL and 50 mL glass vials containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 Injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/v ethanol as a stabilizer (approximately 15 to 50 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 placental barrier 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 fetal or maternal 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 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. Exposing 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 is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. The radioactive species 

\[
{}^{18}F\text{-FDG}
\]

is produced by positron annihilation, which is a process where a free electron and a free positron come together and annihilate each other, producing two gamma photons. These photons are detected by a PET scanner to create an image of the body. The photons are detected with a high level of spatial and temporal resolution, allowing for accurate imaging of the body's metabolic activity.

Fludeoxyglucose F 18 Injection 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\text{fluoro-D-glucose} at the EOS, 4.5 mg of sodium chloride and 0.1 to 0.5% w/v 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 primary 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

<table>
<thead>
<tr>
<th>Radiation/Emission</th>
<th>% Per Disintegration</th>
<th>Mean Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positron (β+)</td>
<td>96.73</td>
<td>249.8 keV</td>
</tr>
</tbody>
</table>

| Gamma (γ)          | 3.27                 | 511.0 keV   |

*Produced by positron annihilation*

From: Kocher, D.C. Radioactive Decay Tables DOE/TIC-11026, 89 (1981)

The specific gamma ray constant (point source air kerma coefficient) for fluorine F 18 is 5.7 mR/hr/μCi (1.35 x 10^{-4} Gy/hr/μCi) 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

<table>
<thead>
<tr>
<th>Shield thickness (Pb) mm</th>
<th>Coefficient of attenuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>4</td>
<td>0.50</td>
</tr>
<tr>
<td>8</td>
<td>0.25</td>
</tr>
<tr>
<td>13</td>
<td>0.10</td>
</tr>
<tr>
<td>26</td>
<td>0.01</td>
</tr>
<tr>
<td>39</td>
<td>0.001</td>
</tr>
<tr>
<td>52</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Fraction Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>15</td>
<td>0.9096</td>
</tr>
<tr>
<td>30</td>
<td>0.826</td>
</tr>
<tr>
<td>60</td>
<td>0.683</td>
</tr>
<tr>
<td>110</td>
<td>0.500</td>
</tr>
<tr>
<td>220</td>
<td>0.250</td>
</tr>
</tbody>
</table>

*calibration time*

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fludeoxyglucose F 18 injection is a glucose analog that concentrates in cells that rely upon glucose as a source of energy, or cells that depend on glucose increases under pathophysiological conditions. Fludeoxyglucose F 18 is transported through the cell membrane by a facilitated glucose transporter proteins and is phosphorylated within the cell to \[{}^{[1]^{18}}\text{FDG}\] which enters the hexokinase and is phosphorylated 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. F 18 is used to assess 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 utilizing 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, glycogen 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. Intercitially, the seizure focus tends to be hypometabolic.

12.3 Pharmacokinetics Distribution: In four healthy male volunteers, receiving an intravenous administration of 30 seconds induction, 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 (±) 1.1 min, and 80 to 95 minutes with a mean STD of 88 (±) 4 min.

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

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

Fludeoxyglucose F 18 injection may contain several impurities (e.g., 2-deoxy-2-chloro-D-glucose (CDG)), biodegradation and metabolism of CDG 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 (CDG-6-phosphate) and 2-deoxy-2-chloro-6-phospho-D-mannose (CDG-6-mannose). The phosphorylated deoxyglucose compounds are dephosphorylated and the resulting compounds (FDG, FDM, CDG, 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. 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 naïve, non-epileptic or pediatric patients. Fludeoxyglucose F 18 injection 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 seen [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 position 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, colorectal, pancreatic, breast, thyroid, melanoma, Hodgkin’s and non-Hodgkin’s lymphoma, and various types of metastatic cancers to lung, liver, bone, and abdominal lymph nodes. All these studies had at least 50 patients and used published 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 increased uptake 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 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 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 performed other diagnostically radioisotopes. Doses of Fludeoxyglucose F 18 Injection ranged from 74 to 370 MBq (2 to 10 mCi). Segmental, left ventricular, wall-motion assessments of asymmetric 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., mismatch). Findings of flow-metabolism mismatch in a myocardial segment may suggest that successful revascularization will restore myocardial function in that segment. However, false-negative 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 the degree of myocardial vascularity. Therefore, in patients with a low likelihood of successful revascularization, the diagnostic usefulness of PET imaging with Fludeoxyglucose F 18 Injection is more limited.
Legal information: On account of certain regional limitations of sales rights and service availability, we cannot guarantee that all products included in this publication are available through the Siemens Healthineers sales organization worldwide. Availability and packaging may vary by country and is subject to change without prior notice. Some/all of the features and products described herein may not be available in the United States.

The information in this document contains general technical descriptions of specifications and options as well as standard and optional features, which do not always have to be present in individual cases.

Please contact your local Siemens Healthineers sales representative for the most current information.

Note: Any technical data contained in this document may vary within defined tolerances. Original images always lose a certain amount of detail when reproduced.

"Siemens Healthineers" is considered a brand name. Its use is not intended to represent the legal entity to which this product is registered. Please contact your local Siemens organization for further details.