Coexisting laryngeal tumor in a patient with esophageal carcinoma successfully treated with $^{18}$F FDG PET/CT-based radiation therapy

By Khoa Mai Trong and Phuong Pham Cam
Data courtesy of The Nuclear Medicine and Oncology Center, Bach Mai Hospital, Hanoi, Vietnam

History

A 57-year-old male with history of difficulty in swallowing along with weight loss of more than 5 kg in one month was investigated with upper gastrointestinal endoscopy. Endoscopy revealed a mass in the lower third of the esophagus with irregular thickening of mucosa protruding into the esophageal lumen, causing narrowing such that the endoscope could not pass beyond the esophageal lesion. Histopathology from the mucosal biopsy demonstrated a squamous cell carcinoma.

The patient underwent a CT scan for initial evaluation, as well as CT simulation for radiation therapy. CT showed an irregular thickening of the esophagus at the lower third with protrusion of the mass into the esophageal lumen, causing narrowing. Loco-regional lymph node enlargement was not detected on the CT scan.

CT simulation did not clearly delineate the tumor margins from the normal esophagus and adjacent structures, limiting accurate contouring for radiation therapy. In this context the patient was referred for Fludeoxyglucose $^{18}$F (F18 FDG) PET/CT for delineation of true tumor extent and the presence of local and distant metastases.

An $^{18}$F FDG PET/CT study was performed on a Biograph™ PET/CT system fitted with a flat table top and positioning laser. The scan was...
Fludeoxyglucose F 18 5-10mCi as an IV injection

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 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 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.
- 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.
- Adverse Reactions: Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

Full prescribing information for Fludeoxyglucose F 18 Injection can be found on pages 6-8.

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) of 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.

Fludeoxyglucose F 18 injection is manufactured by Siemens’ PETNET Solutions, 810 Innovation Drive, Knoxville, TN 37932

Diagnosis

As shown in Figure 3, PET/CT sharply delineated hypermetabolic tumor margins in the lower third of esophagus (size 3x4, 6x6 cm; SUV\text{max} 10.4) without evidence of lymph node or distant metastases.

The PET/CT, however, showed focal hypermetabolism in the larynx.

Histopathology of the right pyriform sinus lesion also demonstrated a squamous cell carcinoma suggestive of a second malignancy.

The patient was recommended for radiation therapy with concurrent chemotherapy with the esophageal tumor irradiated initially. Chemotherapy included a Docetaxel and Cisplatin regimen for 3 periods (21-day cycles). The chemotherapy regime included an intravenous administration of Docetaxel 75 mg/m²/day along with Cisplatin 75 mg/m²/day. Radiation therapy planning for the esophageal lesion was performed based on the \(^{18}\text{F FDG PET/CT images with gross tumor volume (GTV) incorporating the FDG-avid tumor zone. A total GTV dose of 50.4 Gy was prescribed to be delivered at the rate of 1.8 Gy/day}.

The patient was reassessed on the completion of 3 chemotherapy cycles combined with radiation therapy. The patient showed a significant improvement in the ability to swallow. A follow up \(^{18}\text{F FDG PET/CT was performed to assess disease status on the completion of chemoradiation therapy. The PET/CT acquisition protocol was similar to the initial staging study. The post chemoradiation PET/CT showed a gross decrease in the esophageal tumor mass with substantial decrease of lesion hypermetabolism and SUV\text{max}. The laryngeal mass showed a slight decrease in size, as well as lesional hypermetabolism and SUV\text{max} following chemotherapy.}

The patient underwent a follow-up gastroscopy to evaluate the esophageal lesion post chemoradiation. The endoscopy confirmed a complete regression of the esophageal tumor.
Clinical Results

Radiation therapy to the laryngeal lesion was subsequently planned based on post chemotherapy PET/CT. GTV was delineated based on the hypermetabolic laryngeal tumor seen on PET/CT and 70 Gy was prescribed to the GTV with 50 Gy delivered to the cervical neck nodes. A standard fractionation regime was used (1.4 Gy/fraction to CTV, including bilateral lymph nodes). The patient developed radiation-related toxicity like oral ulcers, fever and leucopenia, which were adequately managed with antibiotics and parenteral nutrition.

On the completion of laryngeal radiation therapy, the patient underwent a laryngoscopy which showed a disappearance of the laryngeal mass (Figure 8).

A follow-up ¹⁸F FDG PET/CT was performed using similar acquisition parameters as the previous studies. PET/CT showed a disappearance of the laryngeal mass following radiation therapy, confirming the findings of the laryngoscopy.

The patient was subsequently clinically followed up and showed progressive improvement with increase in body weight, absence of swallowing difficulties and freedom from any respiratory distress.
Clinical Results

**Comments**

This case demonstrates the value of 18F FDG high-resolution PET/CT in initial staging and radiation therapy planning for both esophageal and laryngeal cancer and also illustrates an uncommon condition of a second primary cancer (laryngeal squamous cell carcinoma) associated with a primary esophageal carcinoma. 18F FDG PET/CT enabled an accurate delineation of tumor extent for precise radiation therapy planning, allowing adequate tumor dose to be delivered to a hypermetabolic viable tumor while sparing surrounding normal tissue and thereby, reducing radiation-induced toxicity. Sequential 18F FDG PET/CT helped to ascertain tumor response and to plan subsequent therapy. As evident from the sequential images, the esophageal tumor showed a complete regression following initial chemotherapy and radiation to the esophageal GTV. However, the laryngeal tumor showed a minor response to initial chemotherapy, and second-phase radiation to the laryngeal tumor was planned on the post-chemotherapy PET/CT, enabling precise GTV delineation. This enabled a dose of 70 Gy to be delivered to the tumor with only mild toxicity (oral ulcers), which were easily managed.

6 Follow-up gastroscopy shows a complete regression of the esophageal tumor.

7 Radiation dose plan for laryngeal tumor and adjacent tissue including bilateral neck nodes with simultaneous boost to FDG-avid tumor volume.

8 Post-radiation laryngoscopy shows a disappearance of the laryngeal tumor following therapy.
Clinical Results

Conclusion

$^{18}$F FDG PET/CT enables detection of second primary tumor in the larynx in a patient with esophageal carcinoma. Chemoradiation therapy with accurate targeting of metabolically active tumor volume demonstrated on PET/CT was instrumental in achieving tumor free status.

Examination Protocol

Scanner: Biograph mCT

<table>
<thead>
<tr>
<th>Component</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PET</strong></td>
<td></td>
</tr>
<tr>
<td>Injected Dose</td>
<td>Fludeoxyglucose F 18 Injection ($^{18}$F FDG) 370 MBq</td>
</tr>
<tr>
<td>Scan Delay</td>
<td>90 min</td>
</tr>
<tr>
<td>Acquisition</td>
<td>3 min</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td></td>
</tr>
<tr>
<td>Tube Voltage</td>
<td>130 kV</td>
</tr>
<tr>
<td>Tube current</td>
<td>94 mAs</td>
</tr>
<tr>
<td>Slice collimation</td>
<td>2 mm</td>
</tr>
</tbody>
</table>

The statements by Siemens customers described herein are based on results that 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 other customers will achieve the same results.

For indications and usage information for Fludeoxyglucose F 18 Injection ($^{18}$F FDG) see page 2. For full prescribing information see pages 6-8.

Sequential CT and fused PET/CT images at the level of the esophageal tumor show a gross decrease in tumor size and uptake following initial chemoradiation therapy with further decrease in the subsequent follow-up study. Initial esophageal tumor SUV$_{max}$ was 10.4, which decreased to 2.6 following chemoradiation with further decrease to background level on the subsequent follow-up study.

Sequential CT and fused PET/CT images at the level of the laryngeal tumor showing a slight decrease in size and degree of hypermetabolism of the laryngeal mass following initial chemotherapy for 3 cycles. Following subsequent radiation therapy (70 Gy to the laryngeal tumor GTV, including hypermetabolic tumor), there was a complete regression of the tumor as seen in the follow-up PET/CT scan.
Fludeoxyglucose F 18 Injection, USP

HIGHLIGHTS OF PRESCRIBING INFORMATION
These 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

Initial U.S. Approval: 2005

1. INDICATIONS AND USAGE

1.1 Oncology

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

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 and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.

2. DOSAGE AND ADMINISTRATION

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

- Oncology: For assessment of abnormal glucose metabolism 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 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.
- Neurology: For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

3. DOSAGE FORMS AND STRENGTHS

Fludeoxyglucose F 18 Injection is a sterile, pyrogen-free liquid intended for intravenous injection. Use procedures to minimize radiation exposure. Screen for blood glucose abnormalities.

- For intravenous administration, administer Fludeoxyglucose F 18 Injection as an intravenous injection. The optimal dose adjustment on the basis of body size or weight has not been determined [see Use in Specific Populations (8.4)].

4. ADVERSE REACTIONS

- Hypersensitivity reactions have occurred, transient elevations of liver enzymes, and eosinophilia.

5.1 Radiation Risks

Hypersensitivity reactions have occurred; may cause fever and rash.

5.2 Imaging Guidelines

Use procedures to minimize radiation exposure. Screen for blood glucose abnormalities.

- In the oncology, cardiology, and neurology settings, 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 Specific Populations (8.4)].

5.3 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 human data and using the data published by the International Commission on Radiological Protection for Fludeoxyglucose F 18 F. 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

<table>
<thead>
<tr>
<th>Organ</th>
<th>1-year old</th>
<th>5-year old</th>
<th>10-year old</th>
<th>15-year old</th>
<th>Adult</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>0.40</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>
</tr>
<tr>
<td>Pancreas</td>
<td>2.2</td>
<td>0.68</td>
<td>0.33</td>
<td>0.25</td>
<td>0.13</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.6</td>
<td>0.84</td>
<td>0.46</td>
<td>0.29</td>
<td>0.19</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>
</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>
</tr>
<tr>
<td>Ovaries</td>
<td>0.80</td>
<td>0.80</td>
<td>0.19</td>
<td>0.11</td>
<td>0.058</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>
</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>
</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>
</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>
</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>
</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>
</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>
</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>
</tr>
<tr>
<td>Testes</td>
<td>0.64</td>
<td>0.27</td>
<td>0.14</td>
<td>0.085</td>
<td>0.052</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>
</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>
</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>
</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>
</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>
</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>
</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>
</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>
</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>
</tr>
</tbody>
</table>

* MRI was used to calculate the radiation absorbed dose. Assumptions on the biodistribution based on data from Gallagher et al. and Jones et al.

** The dynamic bladder model with a uniform voiding frequency of 1.5 hours was used. *LLI = lower large intestine, **ULI = upper large intestine.

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Fludeoxyglucose F 18 Injection, USP

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 30 mL and 50 mL glass vial 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 possibility of 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

Pregnancy Category C

Animal reproduction studies have not been conducted with Fludeoxyglucose F 18 Injection. It is also not known whether Fludeoxyglucose F 18 Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Consider alternative diagnostic tests in a pregnant woman; administer Fludeoxyglucose F 18 Injection only if clearly needed.

8.3 Nursing Mothers

It is not known whether Fludeoxyglucose F 18 Injection is excreted in human milk. Consider alternative diagnostic tests in women who are breast-feeding. Use alternatives to breastfeeding (e.g., stored breast milk or infant formula) for at least 10 half-lives of radiopharmaceuticals. If the mother chooses to continue breastfeeding, advise her to closely monitor the infant for any signs of adverse reactions.

8.4 Pediatric Use

The safety and effectiveness of Fludeoxyglucose F 18 Injection in pediatrics with epilepsy, or 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 eluting radiopharmaceutical that is used for diagnostic purposes in conjunction with a nuclear medicine PET imaging. The active ingredient 2-deoxy-2-[18F]fluoro-D-glucose has the molecular formula of C$_6$H$_{10}$FO$_5$ with a molecular weight of 181.26, and has the following chemical structure.

Fludeoxyglucose F 18 Injection is provided as a ready to use sterile, pyrogen free, clear, colorless solution. Each mL contains between 0.740 to 7.400Bq (20.0 to 200.0 mCi) of 2-deoxy-2-[18F]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

Fludeoxyglucose F 18 decays by emitting positron to Oxygen O 16 (stable) and has a physical half-life of 109.7 minutes. The principal photons useful for imaging are the dual 511 keV 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>Position (d)</td>
<td>Gamma (±)</td>
<td></td>
</tr>
<tr>
<td>96.73</td>
<td>193.46</td>
<td>511.0 keV</td>
</tr>
</tbody>
</table>


The specific gamma ray constant (point source air kerma coefficient) for Fluorine F 18 is 5.7 R/h/mCi (1.35 x 10^4 Gy/h/mCi) 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 thickness is shown in Table 3. For example, the intersection 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>1.000</td>
</tr>
<tr>
<td>4</td>
<td>2.50</td>
</tr>
<tr>
<td>8</td>
<td>1.00</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>1.000</td>
</tr>
<tr>
<td>15</td>
<td>0.909</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 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 [18F] 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. When allowance is made for the kinetic differences between glucose and Fludeoxyglucose F 18 transport and phosphorylation (expressed as the ['lumped constant'] ratio), 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 myocardium 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 myocardium is metabolized immediately instead of being converted into glycogen. Under these condi-
Fludeoxyglucose F 18 Injection, USP

14.1 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 structural imaging. 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 imaging 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 subclinical 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 epilepto-
genetic foci from tumors or other brain lesions that may cause seizures have not been established.

15 REFERENCES


16  HOW SUPPLIED/STORAGE AND DRUG HANDLING

Fludeoxyglucose F 18 Injection is supplied in a multi-dose, capped 30 mL and 50 mL glass vial containing between 0.740 to 7.400 MBq/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 50 mL. The contents of each vial are sterile, pyrogen-free and preservative-free.

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