Time-of-Flight Paves the Way to Faster Scans and Lower Radiation Dose

Researchers at Central Manchester University Hospital in the United Kingdom conducted a study to optimize their Time-of-Flight-equipped PET/CT scanner. As a result, the institution adopted a new protocol that has led to reduced radiation exposure to patients and staff, and has provided the flexibility to perform more PET/CT scans per year.

By John C. Hayes

The growing demand for PET/CT in oncology poses a challenge for Central Manchester University Hospital, with a projected 14 percent annual increase on scanning numbers. Its use of F 18 Fludeoxyglucose (18F FDG) in oncology produced reliable results, but there was a clear need to increase efficiency to accommodate this increasing demand.

Additionally, the departmental physicists are always looking for ways to reduce radiation exposures while maintaining the same high quality results. Both staff and patients, some of them relatively young, were being exposed to relatively high levels of ionizing radiation during PET/CT scans.

New technology offered a possible solution.

Central Manchester researchers found their solution in a Siemens Biograph™ mCT PET/CT scanner, equipped with TrueV and Time-of-Flight (ToF) technology. By measuring the actual time difference between the detection of each coincidence photon, ToF can localize the event within a small range along each line of response. This increases signal-to-noise ratio (SNR), enabling faster scans, lower injected dose and improved image quality.1,2

Though studies have shown that ToF improves both SNR and definition of small lesions, Manchester researchers had
a more involved question: Could ToF help them develop a protocol that could reduce radiation exposure, while increasing flexibility in scheduling to handle the approximately 3,300 annual patient scans. Of that 3,300, about half of the annual scans are \(^{18}\text{F FDG}\) related, the other being for Rubidium-82 cardiac PET.

Therefore, the Manchester team conducted two studies, examining different times for bed positions and doses. The team used a strategy of trimming photon counts with ToF reconstructions to simulate shorter bed times and less \(^{18}\text{F FDG}\) administration. Today, they use a protocol based on the weight of the patient that has reduced bed times and \(^{18}\text{F FDG}\) administration. They estimate that the changes have reduced radiation exposure for both patients and staff by up to 30 percent and have increased annual throughput by 100 scans.\(^{3,4}\)

Before, most UK institutions had been using a protocol from a government advisory committee (ARSAC, the Administration of Radioactive Substances Advisory Committee) with two prescribed \(^{18}\text{F FDG}\) dose levels (350 MBq and 400 MBq, based on weight), and a bed position segment time (2.5 minutes) that failed to reflect advances in PET detector technology and reconstruction algorithms. Central Manchester University Hospital was among those using the ARSAC guidelines.

“We followed the standard practice, and I always said, given our state-of-the-art equipment, surely we can do better,” said Ian S. Armstrong, principal physicist at the department, who spearheaded the research and was lead author on a publication of results.

To explore the possibilities of ToF, the Manchester team developed a strategy: Run patients through the scanner, and reconstruct the data without ToF. After that, the researchers used list-
“Time-of-Flight is a win-win. You can’t go wrong with it. Image quality is improved, being more consistent across our patient population, and quantification is preserved.”

Ian S. Armstrong, Principal Physicist, Nuclear Medicine, Central Manchester University Hospital, Manchester, United Kingdom

mode data to reduce photon counts and reconstruct the data again using ToF. Scan quality was evaluated by measuring SNR in the liver, standard uptake values (SUV) and a qualitative assessment of the images.

The purpose of reducing counts was to simulate a reduction in bed times and also as a surrogate for reduced radiation exposure. To simulate reduced doses of $^{18}$F FDG, the researchers used a phantom to quantify the equivalence of reduced dose and reduced acquisition time.

In the published study, the researchers presented data from 58 patients. Of these, 49 weighed less than 100 kg (220.5 lb); nine weighed more. The members of the lighter cohort were administered 350 MBq of $^{18}$F FDG. Those who weighed more were administered 400 MBq. To test the effect of ToF, the researchers trimmed counts for the lighter cohort by 20 and 40 percent and, for the heavier cohort, by 16 and 30 percent.

The results supported their hypothesis that ToF could be used to substantially reduce dose and/or bed times. Among the 49 patients weighing less than 100 kg, all images with a 20 percent count reduction were considered adequate.

Thirty-nine patients with a 40 percent count reduction were considered adequate. Among the nine patients weighing more than 100 kg, all images with a 16 percent count reduction were considered adequate. Five with a 30 percent count reduction were considered adequate.

In the next phase of the study, a new protocol optimized for ToF incorporated the findings of the first phase. Beginning in September 2014, the Manchester team switched from the 350 and 400 MBq doses of $^{18}$F FDG in favor of a 280 MBq dose administered to all patients, a reduction of 20 percent for the lighter cohort and 30 percent for the heavier cohort. In addition, the researchers adjusted scan times per bed positions based on weight or body mass index (BMI).

Reducing the scan times per bed position to two minutes cut the total time for a six-position scan from 15 to 12 minutes and the time for a seven-position scan from 17.5 to 14 minutes.

The overall result was a significant reduction in radiation exposure to both patients and staff working with PET/CT, the researchers concluded. This is particularly important for patients with certain types of cancer, such as lymphoma. These patients may be relatively young, respond well to treatment, and are likely to undergo multiple PET/CT scans to monitor therapy response (the youngest patient in the study was 25 years old).

Under the reduced dose protocol, there was a marked improvement in the flexibility of scanner scheduling with additional scans such as local views or separate head and neck scans having less of an impact on workflow for the session, according to the researchers.

They also observed fairly uniform gains in image quality (SNR) with ToF across the entire patient group, he said. This was not anticipated.

“Based on Time-of-Flight theory, I was expecting small or negligible gains in the smaller patients, but for our data,
that wasn’t the case,” Armstrong said. “This meant that we could focus further on the smaller patients to develop a weight-based protocol, reducing radiation dose further. Without this information we would have needed to be more conservative.”

That finding led to an even more refined ToF 18F FDG protocol for patients weighing less than 80 kg (176.4 lb). The protocols were tested using 48 routine oncology patients who were given 280 MBq of 18F FDG (these data have not yet been published). Simulations using reduced counts were employed, as they were in the published study, for patients based on 4.0 or 3.5 MBq per kg (2.205 lb) of weight with measures of image signal to noise used to assess the consistency of image quality over the population. Having concluded that 3.5 MBq per kg was the more effective scheme, they compared SUV max and found the fixed 280 MBq protocol and the 3.5 MBq per kg weight-based protocol produced essentially equivalent quantification. The protocol was adopted in December 2014, establishing the top 18F FDG administration level at 280 MBq. Bed times are two minutes per segment, but may be increased for larger patients. The weight-based protocol is also used in pediatric cases.

The Manchester team manually administers 18F FDG with either 3 ml or 5 ml syringes, without the use of an automatic injector. Compliance with the protocol at Central Manchester University Hospital has been very good. “The volumes that are dispensed can be quite small in some cases. The seamless adoption of the weight-based scheme with manual dispensing is a credit to the skills of our technical staff,” Armstrong commented.

A look at administration levels for 136 patients following the weight-based protocol found clear reductions in 18F FDG administration, with smaller patients benefitting considerably. The median 18F FDG administration was 255.2 MBq, down from 280 MBq under the published protocol.

“There were no real obstacles,” Armstrong said. “Time-of-Flight is a win-win. You can’t go wrong with it. Image quality is improved, being more consistent across our patient population, and quantification is preserved.”

References:

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 5. The full prescribing information can be found on page 6-8.

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.
Fludeoxyglucose F18 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 39732
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.

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

- Oncology: For the identification of cardiac ischemia (2.3).
- Cardiology: For the identification of left ventricular myocardium with residual glucose metabolism in patients with an existing diagnosis of cancer.
- Neurology: For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures (1).

Patient Preparation
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to the drug's injection facilitates localization of cardiac ischemia (2.3). Aseptically withdraw Fludeoxyglucose F 18 Injection from its container and administer by intravenous injection (2).

INFORMATION NEEDED TO USE FLUDEOXYGLUCOSE F 18 INJECTION
Use procedures to minimize radiation exposure. Screen for blood glucose abnormalities. In the oncology and neurology settings, instruct patient 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 (2.2). In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to the drug's injection facilitates localization of cardiac ischemia (2.3). The radiosensitive organs (in descending order) across all age groups evaluated are the urinary bladder, small intestine, and bladder (3.3).

Full prescribing information is not listed.

REFERENCES

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

<table>
<thead>
<tr>
<th>Organ</th>
<th>Newborn</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>
<td>0.32</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>
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<tr>
<td>Pancreas</td>
<td>2.2</td>
<td>0.68</td>
<td>0.33</td>
<td>0.25</td>
<td>0.13</td>
<td>0.096</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>
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<tr>
<td>Ovaries</td>
<td>0.80</td>
<td>0.8</td>
<td>0.19</td>
<td>0.11</td>
<td>0.058</td>
<td>0.053</td>
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<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>
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<tr>
<td>Gallbladder wall</td>
<td>0.69</td>
<td>0.26</td>
<td>0.15</td>
<td>0.093</td>
<td>0.059</td>
<td>0.049</td>
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<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>LLI 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>
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<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>
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<tr>
<td>Testes</td>
<td>0.64</td>
<td>0.27</td>
<td>0.14</td>
<td>0.085</td>
<td>0.052</td>
<td>0.041</td>
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<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>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>

* MIRDOS 2 software was used to calculate the radiation absorbed dose. Assumptions on the biodistribution based on data from Gallagher et al and Jones et al.1

** LLI = lower large intestine

The dynamic bladder model with a uniform voiding frequency of 1.5 hours was used. *LLI = lower large intestine.
Fludeoxyglucose F 18 Injection, USP

2.5 Radiation Safety – Drug Handling

- Use appropriate personal protective equipment, including radiation shielding.
- Adhere to safe handling practices as per institutional guidelines.
- Following handling, treat all radiation-emitting waste, including syringes, as radioactive waste.

2.6 Drug Preparation and Administration

- Do not administer the drug if it contains particulate matter or discoloration.
- Store Fludeoxyglucose F 18 Injection in a closed, dry container at 15° to 30°C.

3 DOSAGE FORMS AND STRENGTHS

Fludeoxyglucose F 18 Injection is a colorless solution containing a sterile formulation of 2-deoxy-2-18F-fluoro-D-glucose. Each mL contains between 0.740 to 7.40 GBq (20.0 to 200 mCi) of 18F-fluoride 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.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Radiation Risks

- Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk of cancer, especially in pediatric patients.
- It is not known whether Fludeoxyglucose F 18 Injection is excreted in human milk. Consider use in breastfeeding only if clearly needed.

5.2 Blood Glucose Abnormalities

- In the oncology or cardiology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels.

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

8.3 Nursing Mothers

- It is not known whether Fludeoxyglucose F 18 Injection is excreted in human milk.

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.

11 CLINICAL PHARMACOLOGY

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 active ingredient 2-deoxy-2-18F-fluoro-D-glucose has the chemical formula of C8H12F3O6 with a molecular weight of 181.26.

<table>
<thead>
<tr>
<th>Table 2. Principal Radiation Emission Data for Fluorine F18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation/Emission</td>
</tr>
<tr>
<td>Positron (b+* )</td>
</tr>
<tr>
<td>Gamma (* )</td>
</tr>
</tbody>
</table>

*Produced by positron annihilation

<table>
<thead>
<tr>
<th>Table 3. Radiation Attenuation of 511 keV Photons by lead (Pb) shielding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shield thickness (Pb) mm</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>13</td>
</tr>
<tr>
<td>26</td>
</tr>
<tr>
<td>59</td>
</tr>
<tr>
<td>119</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 on 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 ‘jumped 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 Pharmokinetics

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 energetic 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 conditions, Fludeoxyglucose F 18 is a useful probe for imaging myocardial oxidative stress, as it accumulates to a greater extent in ischemic regions compared to normal myocardium.
14.2 Cardiology
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 Injection in patients with suspected or known malignancies, including non-small cell lung cancer, colon, rectal, 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 all 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.

14.2.1 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 radio-pharmaceuticals. 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 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 subphrenoidal 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 epilep-

tic foci from tumors or other brain lesions that may cause seizures have not been established.

15 REFERENCES

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

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 GBq/mL (20 to 200 mCi/mL), of no carrier added 2-deoxy-2-[F 18] fluoro-d-glucose, at end of synthesis, in approximately 15 to 50 mL of the contents of each vial are sterile, pyrogen-free and preservative-free.

NDC 40028-511-30; 40028-511-50
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 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 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 within 12 hours from the E0S time. The expiration date and time are provided on the container label.

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.

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