PET Radiopharmaceuticals

OVERVIEW

After reviewing this tutorial, participants should be able to:

- define the term PET and explain the basic principle of coincidence detection
- explain how PET is different than other modalities
- explain how PET radiopharmaceuticals display organ function rather than anatomy
- state the risks, benefits and clinical value of PET
- name the PET radiopharmaceuticals available and their physical characteristics
- relate the safety of these drugs
- compare the radiation dose of F-18 FDG to that of other commonly used radiopharmaceuticals
- recognize the chemical structures of FDG and glucose
- discuss reimbursement issues and approved indications for F-18 FDG
- discuss use of this drug in oncology, neurology, and cardiology.

Topics to be covered

- What is PET?
- What is the Value of PET
- What are PET Radiopharmaceuticals
- Underlying Principle of Utilizing PET Radiopharmaceuticals
- Importance of F-18 -FDG
- Preparation of F-18 -FDG
- Comparison: Structures of FDG and Glucose
- PET Radiopharmaceuticals: Other Compounds
- PET Radiopharmaceuticals: C-11 Compounds
- PET Radiopharmaceuticals: N-13, O-15 Compounds
- PET Radiopharmaceuticals: F-18 Compounds
- PET Pharmaceuticals: Clinical Utility
- PET Reimbursement Issues
- General Tumor Imaging with FDG
- PET in Cardiology
- PET in Neurology

- Conclusions:

What is PET?

- "PET" stands for Positron Emission Tomography. This technique allows us to measure organ function while the patient is comfortable, conscious and alert. A better name would be ART as we really are performing Annihilation Radiation Tomography, and not positron emission tomography.
- PET represents a step forward in evaluating function of internal organs and in diagnosing malignant tumors. Unlike X-rays or a CT scan, which show only structural details within the body, PET excels at determining organ function.
- We are very interested in organ function because functional change, such as tissue metabolism or altered physiologic function physiologic function, often predates structural change in tissues. In oncology, PET is the only modality that can accurately image many organs of the body with a single pass to allow determination of malignancy.
- PET helps determine whether a primary cancer has metastasized to other parts of the body.

What is the Value of PET

- PET has significantly impacted patient care and has proven to be a very cost-effective way to diagnose and stage diseases, especially in oncology
- Medicare and other insurers are approving an increasing number of indications every year. F-18 FDG has replaced most other tumor imaging agents.
- Permits cost effective, whole-body metastatic surveys
- Avoids biopsies for low grade tumors
- Permits non-invasive differentiation of tumors from radiation necrosis
- Permits early change in course of ineffective chemotherapy
- Avoids unnecessary diagnostic and therapeutic surgeries.

Patient Management Outcomes showed that

- PET can change staging of CA in 43% of cases*
- PET leads to major changes in management decisions in 39%*
- PET increases diagnostic understanding in 59%**
- PET influenced therapy choice in 36%**

*(seltzer et al: abstract #408 snm 6/99; **(comens et al: abstract #427 snm 6/99-

What are PET RADIOPHARMACEUTICALS?

- PET radiopharmaceuticals commonly incorporate short-lived radionuclides of elements encountered in nature, e.g.,
- O-15 ($t_{1/2}$ = 2 min), N-13 ($t_{1/2}$ = 10 min),
- C-11 ($t_{1/2}$ = 20 min), F-18 ($t_{1/2}$ = 110 min).
- Produce no physiological or pharmacological effects; inherently have a high degree of safety.
- No documented adverse reactions of clinical significance after hundreds of thousands of studies performed in humans worldwide.
- Radiation exposure from a PET imaging procedure is comparable to that of other Nuclear Medicine diagnostic procedures using gamma-emitting radiopharmaceuticals, many of which have been in use for decades.
- The radioactive substance used to evaluate the metabolic or physiologic process must not alter the process it is attempting to measure.
- Therefore, most substances used in PET are chemically equivalent or close analogs to naturally occurring compounds.
- Many PET Radiopharmaceuticals are radiolabeled version of substances commonly present in the body, e.g., N-13-ammonia, O-15-water, C-11-acetate, C-11-methionine, and F-18 FDG
- F-18 FDG is the most common radiopharmaceutical used in PET worldwide.

Underlying Principle of Utilizing PET Radiopharmaceuticals

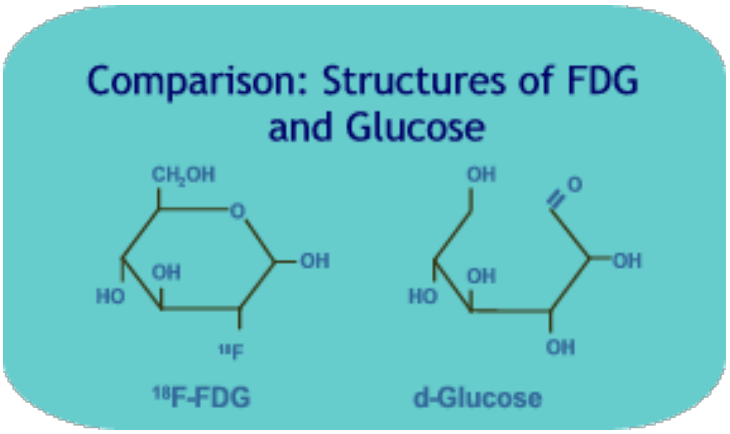
- Compounds are generally chemically equivalent or close analogs to naturally occurring compounds.
- They provide functional images of the human body.
- Many PET radiopharmaceuticals are radiolabeled versions of substances commonly present in the body, e.g., N-13 ammonia, O-15 water, C-11-acetate, C-11 methionine, F-18 fluoride.

Importance of $^{F-18}$-FDG

- The most widely used PET radiopharmaceutical $^{F-18}$-FDG is similar in structure to glucose, this compound is used in PET due to the ubiquitous use of glucose by the human body.

F-18 FDG: Mechanism of Uptake

- Called metabolic trapping
- Tumors have higher metabolic rate than normal tissue.
- Structures of FDG and glucose are similar enough for there to be uptake, but different enough that metabolism cannot take place



Preparation of F-18 FDG

- FDG is labeled with F-18, a cyclotron produced radioisotope with a half-life of approximately 110 minutes.
  1. Synthesis is based on the nucleophilic substitution with F-18 -, promoted by a phase transfer catalyst.
  2. The process includes the separation of the O-18 from the F-18, labeling reaction, hydrolysis and finally formulation as an injectable solution.
  3. Process time is < 30 min.
  4. The radiochemical yield is 50 to 60 % depending on purity of starting material
  5. The specific activity is >10 Ci/μmol (370 GBq/μmol)
  6. The radiochemical purity is > 98.5 %.

Other PET Radiopharmaceuticals: C-11 Compounds

● CO ● Raclopride ● N-methylspiroperidol ● hydroxyephedrine ● acetate	● L-deprenyl ● L-methionine ● thymidine ● flumazenil

Other PET Radiopharmaceuticals: N-13, O-15 Compounds

- 13 N-ammonia
- 15 O-water
- 15 O-butanol

Other PET Radiopharmaceuticals: F-18 Compounds

- fluoride
- FDG
- 6-fluoroDOPA
- fluoromethane
- N-methylspiroperidol
- 6-fluoronorepinephrine
- 14-fluoro-6-thiaheptadecanoate
- 16-fluoro-17b-estradiol
- fluoroethyl-oubain
- fluoromisonidazole

Other PET Radiopharmaceuticals: Other Radioisotopes

- Rb-82 Rb+ ion
- Ga-68 EDTA
- Cu-62 PTSM
- Br-76 bromolisuride
- I-124 monoclonal antibody

PET Reimbursement Issues

- FDA and Medicare approval of the radiopharmaceuticals used in PET has always been a prerequisite for public-sector reimbursement.
- Medicare will pay for unapproved indications for PET if:

1. The patient is enrolled in a study of PET efficacy
2. If institutions are part of a "PET Registry"

Insurance Coverage

- Most major insurers cover PET
- Coverage varies by carrier
- Pre-certification usually required
- Carriers may limit facilities at which PET is covered.

PET Pharmaceuticals: Clinical Utility

Patient Management Outcomes showed that:

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2. PET leads to major changes in management decisions in 39%*
3. PET increases diagnostic understanding in 59%**
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General Tumor Imaging with FDG

- Most commonly used in oncology to detect and evaluate tumors
- FDG-PET is effective in the diagnosis and staging of the following cancers: brain tumor, breast cancer, colorectal cancer, head and neck cancer, lung cancer, lymphoma, melanoma, musculoskeletal tumors, ovarian cancer, pancreatic cancer, and thyroid cancer.

Approved indications for whole-body F-18 -FDG PET scans:

- solitary pulmonary nodule
- completion of staging and restaging NSCLC (non-small cell lung cancer)
- staging and restaging- esophageal ca, colon cancer, melanoma, lymphoma, head & neck ca
- restaging and monitoring advanced breast ca
- follicular thyroid ca post Rx
- initial staging cervical ca

Awaiting Medicare Approval for whole-body F-18 FDG PET scans:

- pancreatic ca
- hepatoma
- ovarian ca
- testicular ca
- thyroid ca
- brain tumor
- bladder ca
- sarcoma

F-18 FDG PET in Cardiology: Useful in assessment of myocardial viability.

Approved Indications for Cardiac PET scans:

- screen for coronary artery disease
- assess flow rates and flow reserve
- distinguish viable from nonviable myocardium for bypass and transplant candidates.

CPT CODE Indication

- 78459 Cardiac metabolism
- 78499 Cardiac perfusion
- 78990 Radiopharmaceutical

PET in Neurology: useful for diagnosis of a variety of neurological conditions

Approved indications for cerebral F-18 -FDG PET scans:

- PET enables assessment of Alzheimer's and other dementias, Parkinson's, and Huntington's
- Localizes epileptic foci for qualifying and identifying the site for surgical intervention
- Permits characterization, grading, and assessment of possible brain tumor recurrence

CPT CODE Indication

- 78608 Brain metabolism
- 78609 Brain perfusion
- 78990 Radiopharmaceutical

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