Cardiac FDG PET-CT Evaluation

H. Henry Guo, MD, PhD

FDG-PET Cardiac Evaluation: The yin and yang of myocardial imaging

FDG Cardiac PET Clinical Indications
- Cardiac sarcoidosis: Evaluation of cardiac granulomas
  Diagnosis and response to therapy
- Malignant and benign conditions involving the cardiac structures
- Cardiovascular disease: Assessment of viable myocardium
  Ischemia, infarction, hibernation, stunning
- Future Directions

FDG Cardiac PET:
- Theoretical changes in myocardial metabolism highlight distinct pathologic processes
- Basal: 50-75% of energy from oxidation of free fatty acids
- Fasting and low carbohydrate state: Free fatty acid metabolism
- Postprandial state: Aerobic glucose metabolism
- Ischemia: Anoxygenic glucose uptake

FDG Radiotracer Physiology

Inflammation and cardiac sarcoid
- Sarcoisidosis: Multisystem disorder characterized by noncaseating granulomas
- Cardiac involvement estimates range from 5-40%
- Significant cause of morbidity and mortality
  - Ventricular arrhythmias and heart failure
- Rationale for FDG-PET: Inflammatory cells are FDG avid
  - Suppresses cardiac glucose metabolism and drive the heart to metabolize fatty acids exclusively
  - Remaining FDG avid tissue in the myocardium is inflammatory

Blood Glucose: All 3 within normal range!
**Imaging Protocol: sarcoidosis**

Patient preparation: Very low carbohydrate, fat rich meal, >12 hours fast. Can inject 5-10 IU/kg of unfractionated heparin 30 min prior to scan. Can perform perfusion study prior to PET to assess for myocardial scar.

- 1. Tc-99m Tetrofosmin 10 mCi
- 2. FDG 10 mCi

**FDG PET Visualizes Inflammatory Granulomas**

51 year old man with ventricular tachycardia. Sarcoidosis.

**FDG PET monitors response to steroid therapy**

Same patient after steroid therapy.

**FDG-PET can help exclude myocardial inflammation in known sarcoidosis**

**“Patchy” and “Patchy on diffuse” patterns are more specific for cardiac sarcoid**

None

![Patchy](image)

Diffuse

Patchy on diffuse

**MRI and PET-CT in Cardiac Sarcoid**

- Superior spatial resolution and soft tissue characterization
- Contrast sequences allow for wall motion and contractility assessment
- No radiation
- Gadolinium enhancement at site of scar and inflammation
- Likely greater specificity

**FDG PET-CT**

- Imaging of active inflammation, used to assess treatment response
- Guide biopsy
- Patients with cardiac pacemakers/AICD
- Whole body imaging
- Prognosis and risk stratification
- Sensitivity 89%, Specificity 78%
**Causes of increased cardiac FDG uptake**

- Malignancy: primary or metastatic
- Inflammation: sarcoid, amyloid, radiation, surgery
- Infection: endocarditis, myocarditis, pericarditis, Chagas?
- Ischemia, heart failure, pulmonary hypertension
- Brown fat
- Lipomatous hypertrophy of inter-atrial septum
- Physiologic, can be due to inadequate diet preparation

**FDG PET-CT in Malignancy**

Diffuse large B cell lymphoma

**FDG uptake: benign conditions**

12 year old girl with Hodgkin’s lymphoma, with thymic and extensive brown fat uptake

**FDG uptake: benign conditions**

Granulation tissue uptake after trans-apical aortic valve replacement

**Cardiac Viability test utilizes high myocardial glucose metabolism state**

- Free Fatty Acid
- TFA + Glucose
- Glucose loading

**FDG PET viability imaging:**

**Maximize FDG uptake in heart**

*How?*

- Insulin

**FDG**

- Glucose loading: if serum glucose <150. Drink 50g glucose solution
- Eliciting dose insulin
**Summary: Protocols for FDG-PET Cardiac Imaging**

- **Cardiac sarcoidosis**
  - +/- Perfusion study
  - Fatty acid metabolic state whole body FDG PET-CT
- **Malignancy**
  - Whole body FDG PET-CT, consider fatty acid state FDG PET-CT
- **Coronary artery disease**
  - Rest and Stress perfusion study, SPECT or PET
- **Hibernating myocardium**
  - Perfusion study, SPECT or PET
  - Glucose loaded cardiac FDG PET-CT

**Future Directions**

- **FDG applications**
  - Infection: Endocarditis, pericarditis
  - Plaque characterization
- **New tracers**
  - NaF for calcifications, unstable plaque evaluation
  - Perfusion: Rhb2, Nitro, Gd-DTPA, 18-Furindraz
  - Amyloidosis: Amyloid binding agents
- **New modalities**
  - PET-MRI
Patterns of cardiac FDG uptake

None  Diffuse
Pathy  Pathy on diffuse

References:
5. First-pass perfusion cardiac magnetic resonance: (Takeshi Uno, Takemasa Fujino, Takayuki Yamauchi, Shigeru Sone, Sadayuki Ito) JACC Cardiovasc Imaging 2011 Sep;4(9):1375-83.

Nuclear Medicine Myocardial Evaluations

- Perfusion Cardiac PET (N-13 NH, Rb-82)
  - Evaluation of stress-induced ischemia or infarction: SPECT
  - Thallium
  - Tetrofamom / Sestamibi

- Viability Cardiac PET (FDG)
  - Evaluation of hibernating (viable) myocardium
  - Thallium (24-48 hr delay)
  - FDG PET
  - Tetrofamom / Sestamibi

- Cardiac sarcoidosis
  - Evaluation of myocardial granulomas

- FDG PET/CT

Tissue characteristics

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Perfusion</th>
<th>FDG Uptake</th>
<th>CeMRI</th>
</tr>
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<tbody>
<tr>
<td>Normal</td>
<td>+</td>
<td>− / + poor prep</td>
<td>−</td>
</tr>
<tr>
<td>Active Inflammation</td>
<td>+</td>
<td>+</td>
<td>− / +</td>
</tr>
<tr>
<td>Scar</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>Viable tissue</td>
<td>−</td>
<td>− Low carb</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ Hi carb</td>
<td>−</td>
</tr>
</tbody>
</table>
**Cardiac Anatomy and PET Images**

- **Anatomy**
  - Vertical Long Axis
  - Horizontal Long Axis
  - Short Axis

- **PET Images**
  - Apex
  - Dist
  - Mid
  - Prox

**Nuclear Medicine Protocols for FDG-PET Cardiac Imaging**

- “I want to evaluate for coronary artery disease”
  - Rest and stress perfusion study either with PET (NH_3/Rb 82) or SPECT (Tetrofosmin/SeSTMI/Thallium)

- “I want to evaluate for hibernating myocardium”
  - Perfusion study first to determine if there is a suspected infarct. If there is a suspected infarct, then FDG PET or Thallium SPECT

- “I want to evaluate for cardiac sarcoidosis”
  - Myocardial fatty acid metabolic state FDG PET-CT

- “I want to evaluate for malignancy”
  - Whole body FDG PET-CT, consider glucose uptake suppression

**FDG Viability PET Pre-injection Protocol**

- **Non-diabetic patients**
  - 6 hour fast (optional)

- **Patient scheduled to arrive 2 hours prior to scan time**

- **Check glucose:**< 130. Drink 50g glucose containing solution

- **Recheck glucose in 20 minutes and administer insulin according to a sliding scale:**
  - 130-140 mg/dL: 1 Unit regular insulin IV
  - 140-160 mg/dL: 2 Units regular insulin IV
  - 160-180 mg/dL: 3 Units regular insulin IV
  - 180-200 mg/dL: 5 Units regular insulin IV

- **Recheck glucose every 20 minutes until glucose is less than 140 mg/dL and then inject 10 mCi FDG.

**Brown fat FDG uptake is suppressed by warming and benzodiazepine**

**Myocardial Viability or Potentially Reversible Contractile Dysfunction**

**CONCEPTS**

- **Myocardial Hibernation**
  - Perfusion and thus supply declines, contractile function decreases to reduce demand, new supply-demand balance

- **Myocardial Stunning (Repetitive)**
  - Transient ischemic episode, prompt normalization of perfusion but delayed recovery of contractile function

**Nuclear Medicine Protocols for Cardiac Imaging**

- “I want to evaluate for coronary artery disease”
  - Rest and stress perfusion study either with PET (NH_3/Rb 82) or SPECT (Tetrofosmin/SeSTMI/Thallium)

- “I want to evaluate for hibernating myocardium”
  - Must do a perfusion study first to determine if there is a suspected infarct. If there is a suspected infarct, then FDG PET or Thallium SPECT

- “I want to evaluate for cardiac sarcoidosis”
  - Myocardial fatty acid metabolic state FDG PET
Thank you

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Sarcoidosis and cardiac involvement

Multisystem disorder characterized by inflammatory cells are glucose (FDG) avid
- Suppress cardiac glucose metabolism and drive it to fatty acid metabolism
- Any remaining FDG avid tissue in the myocardium is inflammatory

Advantage: Can follow metabolic response to therapy, similar to cancer patients

Cardiac PET Tracers (Approved for Clinical Use)

1. $^{18}$F-FDG: Glucose transporter
2. $^{11}$C-Met: Amino acid transporter

Cardiac PET Versus Conventional Cardiac SPECT

Advantage:
- Improved image quality
- PET scanning better than SPECT
- Attenuation correction from CT
- Slightly improved sensitivity and specificity

Disadvantage:
- Cost
- No gated (wall motion) data available yet

Theoretical Advantage of PET vs. SPECT

Higher resolution of PET increases sensitivity for
- Less severe coronary stenoses
- Multivessel coronary disease

Attenuation correction with PET increases specificity for
- LAD disease in women
- RCA disease in men

PET vs SPECT

Josef Machac, Mount Sinai, New York

Stress-rest Tc-99m sestamibi study in a 52-year-old woman showing a small reversible defect in the anterior wall.
PET vs SPECT
Josef Machac, Mount Sinai, New York

Normal stress-rest Rb-82 PET study in the same patient

Perfusion Radiotracer Physiology

\[ ^{13}\text{NH}_3 \text{ Physiology} \]

Coronary Vasculature

\[
^{13}\text{NH}_3 \rightarrow ^{15}\text{NH}_4 \rightarrow ^{14}\text{NH}_4
\]

Myocyte

\[
\text{glutamate dehydrogenase}
\]

1. glutamate dehydrogenase
2. glutamine synthetase

Cardiac PET Perfusion Tracers

\[
^{13}\text{NH}_3 \rightarrow ^{15}\text{NH}_4 \rightarrow ^{14}\text{NH}_4
\]

Coronary Vasculature

MYOCYTE

Cardiac PET Perfusion Tracers

<table>
<thead>
<tr>
<th>Agent</th>
<th>Half-Life</th>
<th>Source</th>
<th>Cardiac Extraction Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{82}\text{Rb}$</td>
<td>10 minutes</td>
<td>Cyclotron</td>
<td>50% to 60%</td>
</tr>
<tr>
<td>$^{82}\text{Rb}$</td>
<td>76 seconds</td>
<td>Gamma</td>
<td>50% to 60%</td>
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<tr>
<td>$^{81}\text{Rb}$</td>
<td>24 hours</td>
<td>Cyclotron</td>
<td>85%</td>
</tr>
<tr>
<td>$^{81}\text{Rb}$</td>
<td>6 hours</td>
<td>Gamma</td>
<td>50% to 60%</td>
</tr>
</tbody>
</table>

Imaging Protocols: PET perfusion

Input scan stress input scan

$^{82}\text{Rb}$ 60 mCi

Input scan stress input scan

$^{13}\text{N}$-ammonia 30 mCi
**Rb-82 Infusion System**

**Viability Radiotracer Physiology**

**Cardiac Sarcoidosis Preparation Protocol**
- Ensure myocardial uptake is driven to fatty acid metabolism
- No carbohydrate, high protein and fat meal for dinner night before
- Avoid vigorous exercise for at least 24 hours

**FDG Uptake in Glucose avid Cells**

- GLUT 1
- Glucose
- Hexokinase
- Glc-6-P
- Enolase
- Pycnate
- Oxidation
- F6P
- F1,6B

**Normal NH3 perfusion study**

**Cardiac PET Read-Out**
Abnormal NH3 perfusion study

71 year old man with 3 vessel CABG and angina

Cardiac Sarcoidosis: effect of no-carbohydrate diet

Cardiac Sarcoidosis: FDG-PET and pathology correlation

Cardiac Sarcoidosis: pre- and post-treatment

Nuclear Medicine Protocols for Cardiac Imaging

- "I want to evaluate for coronary artery disease":
  Rest and stress perfusion study either with PET (NH3/Rb 82) or SPECT (Tetrofosmin/Sestamibi/Thallium)

- "I want to evaluate for hibernating myocardium":
  Must do a perfusion study first to determine if there is a suspected infarct.
  If there is a suspected infarct, then FDG PET or Thallium SPECT

- "I want to evaluate for cardiac sarcoidosis":
  +/- Rest perfusion study either with PET or SPECT
  Myocardial fatty acid metabolic state FDG PET

Viability Radiotracer Physiology

Blood Glucose: All 3 within normal range