Cardiac FDG Patterns Seen In Oncologic PET Studies: What’s Normal and What’s Not?

Alan H. Maurer, M.D.
Director of Nuclear Medicine
Temple University Hospital
And School of Medicine
Philadelphia, PA
Objectives

• Review PET myocardial metabolism
  – Role of fatty acids, glucose, oxidative metabolism
  – Fasting vs glucose loaded conditions
  – Classic patterns
    » Acute ischemia
    » Chronic stunning/hibernation

• Review differential diagnosis of abnormal cardiac FDG uptake seen in fasted oncologic patients

• Explore range of normal patterns of cardiac FDG uptake seen in oncologic PET studies
  – Personal observations
  – Literature
Cardiac PET Agents

• Blood flow
  – NH-13 (cyclotron)
  – Rubidium -82 (generator)

• Viability
  – F18 FDG

• Other
  – Oxygen utilization
    » O-15
  – Fatty Acids
    » C-11 Palmitate
  – Acetate
    » C-11 Acetate
  – Apoptosis
    » F-18 annexin V
“Normal” Distribution of FDG

- Brain: high uptake in the gray matter
- Head/Neck: Salivary and lymphoid tissues variable
- Myocardium: very variable uptake
- Lungs: very low/no uptake
- Mediastinum: low uptake (nodes vessels)
- Liver: low uptake
- Spleen: no/very low uptake
- GI tract: variable activity (esophagus, stomach, colon)
- Urinary tract: excretes FDG
- Ovarian/uterine: variable with menstrual cycle
- Testicular: variable
- Muscular system: low uptake at rest
- Musculoskeletal
  - Promininet periarticular muscle, joints
“Normal” Distribution of FDG

- Brain: high uptake in the gray matter
- Head/Neck: Salivary and lymphoid tissues variable
- **Myocardium**: very variable uptake
- Lungs: very low/no uptake
- Mediastinum: low uptake (nodes vessels)
- Liver: low uptake
- Spleen: no/very low uptake
- GI tract: variable activity (esophagus, stomach, colon)
- Urinary tract: excretes FDG
- Ovarian/uterine: variable with menstrual cycle
- Testicular: variable
- Muscular system: low uptake at rest
- Musculoskeletal
  - Prominent periarticular muscle, joints
What is Normal Cardiac Appearance on Oncologic FDG PET?

- Answer?

- Depends!
Normal Myocardial Metabolism

- Complex interplay between:
  - Myocardial blood flow
  - Energy demand/work load
  - Substrate availability
    » Fasted
    » Fed state
  - Hormonal control
Simplified Cardiac Metabolism

Glucose
  ↓ Glycolysis
  ↓ Pyruvate

Fatty Acids
  ↓ β Oxidation

Acetyl CoA
  ↓ Krebs cycle

ATP
  → Contraction
Myocardial Substrait Metabolism Plasticity

• Normal Conditions
  – 50-70% energy from oxidation of fatty acids
  – 50-30% energy from carbohydrate (glucose & lactate)

• Fasting
  – > 90% from Fatty Acids
    » Increased lipolysis in peripheral adipose tissue... increases plasma fatty acids
    » Decrease in transport of glucose into myocyte
PET Tracers
Myocardial Metabolism

Factors Which Can Change Myocardial Metabolism

FDG Fasted/Non Fasting Patient Preparation

- **Myocardial Viability Studies**
  - Oral glucose loading (one hour before injection)
  - Euglycemic-hyperinsulinemic clamp
  - Niacin (nicotinic acid derivative)

- **Oncologic Studies (Glucose < 200)**
  - NPO after midnight
  - Minimum 4-6 hr fast
  - Diabetics (no recent insulin)
Dietary Effect  Myocardial Uptake

“Fasting”/Regular Diet  Low Carbohydrate/High Protein Diet
What is Normal Cardiac Appearance on Oncologic FDG PET?

• Depends - Patient Prep!

• & Depends
  – Technique
    » Window/Leveling
    » Gating
Window/Levels for Cardiac Detail
Window/Levels - Cardiac Heterogeneity
Normal Patterns 01-03
Normal Cardiac Appearance
Fasted vs Glucose Loading
First Report - Increased Posterolateral Cardiac FDG (1990)


<table>
<thead>
<tr>
<th></th>
<th>Fasting</th>
<th>Fed</th>
<th>C11-acetate</th>
<th>FDG</th>
<th>C11-acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septum</td>
<td>0.65</td>
<td>0.88</td>
<td>0.98</td>
<td></td>
<td>1.1</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.68</td>
<td>0.90</td>
<td>0.94</td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.87</td>
<td>1.00</td>
<td>1.02</td>
<td></td>
<td>1.01</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.80</td>
<td>1.07</td>
<td>1.01</td>
<td></td>
<td>1.08</td>
</tr>
</tbody>
</table>

Slides are not to be reproduced without permission of author.
Regional myocardial blood flow and glucose utilization during fasting and physiological hyperinsulinemia in humans

Patricia Iozzo, Panithaya Chareonthaitawee, Marco Di Terlizzi, D. John Betteridge, Ele Ferrannini and Paolo C. Camici

doi:10.1152/ajpendo.00386.2001

![Image](image_url)
Intra-individual Variability - 2005

- **Is fasted FDG cardiac activity consistent on serial studies?**
  - *Answer = YES*

- **Visual grading of low (less than lung) or high (greater than lung) cardiac FDG activity**

- **47 patients with 218 scans**
  - Good reproducibility
  - Diabetics less likely to have high cardiac activity
  - Pts with lymphoma more likely to have high uptake
  - No association with age, sex or weight

*Khandani et al - Intra-individual variability of cardiac uptake on serial whole-body 18F-FDG PET. Nuc Med Com 26(9):787-91, 2005*
PET FDG - Viability

Potentially Reversible Cardiac Dysfunction Concepts

- **Non viable** tissue = infarction with no recovery of function
- **Hibernation** = Perfusion and contractile function decreases to reduce demand, new supply-demand balance
- **Repetitive stunning** = Transient ischemic episode, prompt normalization of perfusion but delayed recovery of contractile function
Classic Ischemia

Rest MBF

Stress MBF

FDG
Perfusion
$^{13}\text{NH}_3$

Metabolism
$^{18}\text{FDG}$

Perfusion-Metabolism Mismatch
Reversible Contractile Dysfunction

H. Schelbert, UCLA - PLC

Slides are not to be reproduced without permission of author.
Perfusion

$^{13}\text{NH}_3$

Metabolism

$^{18}\text{FDG}$

Perfusion-Metabolism Match

Irreversible Contractile Dysfunction
Abnormal Cardiac FDG Activity
Differential Diagnoses

• Diffuse
  – LVH, RVH
  – Atrial Fibrillation
  – Post Cardiac Transplantation
  – Myocarditis
    » Radiation induced

• Focal
  – Ischemia/Hibernation
  – Fat
  – Sarcoidosis
  – Pericardial disease (mets)
  – Valve infection
    » Native and prosthetic
  – Muscular Dystrophy
  – Technical
    » Misalignment artifact (attenuation correction)
Diffuse Chamber Enlargement

- LV
  - Hypertension
  - Other myopathies

- RV
  - COPD
  - Shunts

- Atria
  - A Fib
    - LA, RA, Bi-atrial
  - Normal Variant
    - Right
4 Chamber Enlargement
Atrial Enlargement

Generalized cardiac enlargement: chronic atrial fibrillation

Slides are not to be reproduced without permission of author.
LA Enlargement (Atrial Fibrillation)
Case: 54 yo male, lymphoma (No Cardiac History)
Increased R Atrial Activity
? Common Finding

Increased FDG uptake in the wall of the right atrium in people who participated in a cancer screening program with whole-body PET

Hirofumi Fujii,*,** Michiru Ide,* Seici Yasuda,* Wakoh Takahashi,* Akira Shohtsu* and Atsushi Kubo**

*HIMEDIC Imaging Center at Lake Yanagawa
**Department of Radiology, Keio University School of Medicine

Table 1 Cardiac disease and medication

<table>
<thead>
<tr>
<th>No.</th>
<th>age, sex</th>
<th>cardiac disease</th>
<th>cardiac medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64 M</td>
<td>Af (chronic)</td>
<td>verapamil, pilscainide</td>
</tr>
<tr>
<td>2</td>
<td>59 M</td>
<td>HF, TR, MR, complete AV block</td>
<td>nifedipine</td>
</tr>
<tr>
<td>3</td>
<td>57 M</td>
<td>Af (chronic)</td>
<td>metildigoxin, disopyramide</td>
</tr>
<tr>
<td>4</td>
<td>68 M</td>
<td>Af (chronic)</td>
<td>carvedilol</td>
</tr>
<tr>
<td>5</td>
<td>50 M</td>
<td>Af (paroxymal)</td>
<td>pilscainide, disopyramide</td>
</tr>
<tr>
<td>6</td>
<td>48 F</td>
<td>Af (chronic)</td>
<td>metildigoxin, disopyramide</td>
</tr>
<tr>
<td>7</td>
<td>75 M</td>
<td>ASD</td>
<td>metildigoxin, nifedipine</td>
</tr>
<tr>
<td>8</td>
<td>72 M</td>
<td>MSR, Af (chronic)</td>
<td>nifedipine</td>
</tr>
<tr>
<td>9</td>
<td>70 M</td>
<td>Af (chronic)</td>
<td>none</td>
</tr>
<tr>
<td>10</td>
<td>66 M</td>
<td>OMI (A-S), Af (chronic)</td>
<td>atenolol</td>
</tr>
</tbody>
</table>

No! - Observed in 10 patients of 2,367 screenings

Slides are not to be reproduced without permission of author.
RA Uptake vs LA in A Fib
(RA > LA inc glucose utilization?)

Table 2  FDG uptake in the walls of the cardiac chamber

<table>
<thead>
<tr>
<th>No.</th>
<th>RA</th>
<th>LA</th>
<th>RV</th>
<th>LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>±</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>±</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>±</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle, −: no FDG uptake, ±: slight FDG uptake, +: FDG uptake
Focal FDG Abnormalities

- Ischemia/Hibernation (short term and chronic)
- Fat
- Sarcoidosis
- Pericardial disease (mets)
- Endocarditis
  » Native and prosthetic valve infection
- Muscular Dystrophy
- Technical
  » Misalignment artifact (attenuation correction)
Papillary Muscle Ischemia - Case Report

Perfusion

Metabolism

Stress
$^{13}\text{NH}_3$

Rest
$^{13}\text{NH}_3$

$^{18}\text{FDG}$

Slides are not to be reproduced without permission of author.
Case: 71 yo male, s/p resection LUL NSCLC (Prominent Fat AV Groove)
LHIS

Lipomatous Hypertrophy of the Interatrial Septum*

Prevalence and Features on Fusion 18F Fluorodeoxyglucose Positron Emission Tomography/CT

Landon B. Kuester; Alan J. Fischman, MD, PhD; Chieh-Min Fan, MD; Elkan F. Halpern, PhD; and Suzanne L. Aquino, MD

(Chest 2005; 128:3888-3893)
Cardiac Sarcoidosis

- Cardiac involvement 20-80% patients
- Bundle branch or AV block 25%
- Cardiac death up to 75%
FDG Sarcoid Detection

Usefulness of Fasting $^{18}$F-FDG PET in Identification of Cardiac Sarcoidosis

Wataru Okumura, MD$^1$; Tsutomu Iwasaki, MD$^1$; Takuji Toyama, MD$^1$; Tatsuya Iso, MD$^1$; Masashi Arai, MD$^1$; Noboru Oriuchi, MD$^2$; Keigo Endo, MD$^2$; Tomoyuki Yokoyama, MD$^2$; Tadashi Suzuki, MD$^4$; and Masahiko Kurabayashi, MD$^1$

Metastatic Disease
Infection

74 yo female with history of melanoma, breast ca and new pulmonary nodule

Diagnosis: Infected mitral valve prosthetic ring
Personal Observations on Normal Oncologic FDG Cardiac Patterns

- Predominant anterolateral and inferolateral wall FDG activity
- Basal ring FDG activity
  - Variants: partial and full
- Combinations of A and B
- Uniform FDG pattern
- Physiologic variants
  - Prominent papillary muscle
  - Fat:
    » Epicardial, pericardial, interatrial septum
  - RVH, LVH
  - Atrial variants
    » Normal junction with SVC
    » Atrial fibrillation
  - Myocardial heterogeneity
Normal Diffuse - Min Cardiac
43 yo female, cervical cancer (not “blood pool”)

Slides are not to be reproduced without permission of author.
NI Ant-Lat, Posterior with Basal Ring
Normal - Basal Ring Patterns
Normal - Half Base
Focal Base + Pap Muscle
FDG Uptake Vascular Inflammation/Atherosclerosis

- FDG activity commonly seen in atherosclerotic areas in vessels on CT
- Animal studies correlate FDG activity with Macrophage rich experimental atherosclerotic lesions
- Macrophage activity is increased in:
  - Acute coronary syndrome
  - Ruptured plaques
Aortitis
FDG Correlation with Macrophages

- Inflamed Plaque
- Fibrous Plaque

Graphs showing correlation:
- SUV vs. Inflammation
- SUV vs. Smooth Muscle Cell Staining
- SUV vs. Vessel Thickness
- SUV vs. Plaque Thickness

Statistical analysis:
- SUV vs. Inflammation: P<0.0001, r=0.93
- SUV vs. Smooth Muscle Cell Staining: P=NS
- SUV vs. Vessel Thickness: P=NS
- SUV vs. Plaque Thickness: P=NS
FDG Uptake in Symptomatic Plaque

Lipid core
Fibrous cap

CS - AORTIC FINDINGS
Normal AO/ Abn Node
vs
Calc AO and Pre Carinal Node
FDG + Calcified AO Plaque vs FDG + Neg Plaque
Conclusions

• Cardiac FDG patterns are very heterogeneous in the fasted state and any interpretations should be cautious without clinical history or other evidence of significance

• Both diffuse and focal patterns however can have clinical relevance and should be reported when appropriate

• Focal FDG activity in atherosclerotic plaque may also have clinical significance and can be confused with nodal pathology
Question

Under fasting conditions regional myocardial glucose activity is normally highest in which of the following left ventricular myocardial segments?

A. Septum and anterior walls
B. Septum and posterior walls
C. Lateral and posterior walls
D. Lateral and anterior walls
Answers

- A is incorrect - *
- B is incorrect - *
- C is correct. While regional glucose activity is very heterogeneous in the fasted state several articles document higher uptake in the lateral and posterior LV walls.*
- D is incorrect - *

Case: 38 yo male with LUL nodule