Agenda

• Perfusion PET
• Metabolic PET (Viability)
• Hybrid Imaging (PET/CTA)
Progression of Atherosclerosis

Why PET Perfusion?

- Better spatial & temporal resolution: Small hearts, large patients.
- Improved diagnostic accuracy, lower false positive.
- Identification of multivessel ischemia.
- Accurate depth-independent attenuation correction.
- Faster protocols.
- Lower radiation burden.
- Quantification capabilities.
<table>
<thead>
<tr>
<th>SPECT</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy: 78-140 KeV</td>
<td>511 KeV</td>
</tr>
<tr>
<td>Attenuation correction: sometimes</td>
<td>Attenuation correction: always</td>
</tr>
<tr>
<td>Stress: exercise, pharmacologic</td>
<td>Stress: pharmacologic, exercise in future (F-18)</td>
</tr>
<tr>
<td>Protocol, start to finish: 2–2/12 hours</td>
<td>Protocol, start to finish: 30–45 minutes</td>
</tr>
<tr>
<td>Ventricular function: post-stress, rest</td>
<td>Ventricular function: stress, rest</td>
</tr>
</tbody>
</table>
Radiation Exposure (mSv)

**PET vs SPECT**
Myocardial Blood Flow and Radiotracer Uptake
## PET Cardiac Radiotracers

<table>
<thead>
<tr>
<th></th>
<th>N-13</th>
<th>Rb-82</th>
<th>F-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half life</td>
<td>9.96 min</td>
<td>75 sec</td>
<td>110 min</td>
</tr>
<tr>
<td>Patient Dose</td>
<td>10-20 mCi</td>
<td>40-60 mCi</td>
<td>5-15 mCi</td>
</tr>
<tr>
<td>Emax</td>
<td>1.20 MeV</td>
<td>3.15 MeV</td>
<td>0.635 MeV</td>
</tr>
<tr>
<td>Positron range</td>
<td>.7 mm</td>
<td>2.8 mm</td>
<td>.3 mm</td>
</tr>
</tbody>
</table>
# PET Perfusion for Detecting CAD

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th># Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gould</td>
<td>95%</td>
<td>100%</td>
<td>50</td>
</tr>
<tr>
<td>Demer</td>
<td>94%</td>
<td>95%</td>
<td>193</td>
</tr>
<tr>
<td>Go</td>
<td>93%</td>
<td>78%</td>
<td>202</td>
</tr>
<tr>
<td>Schelbert</td>
<td>97%</td>
<td>100%</td>
<td>45</td>
</tr>
<tr>
<td>Yonekura</td>
<td>93%</td>
<td>100%</td>
<td>49</td>
</tr>
<tr>
<td>Williams</td>
<td>98%</td>
<td>93%</td>
<td>146</td>
</tr>
<tr>
<td>Stewart</td>
<td>84%</td>
<td>88%</td>
<td>319</td>
</tr>
<tr>
<td>Weighted Avg.</td>
<td>93% +/- 8</td>
<td>92% +/- 5</td>
<td>766</td>
</tr>
</tbody>
</table>
Freedom From Any Cardiac Events Following Rb-82 Myocardial Perfusion PET

Characteristics of a Normal Myocardial Perfusion PET Study

- Uniform distribution of tracer, independent of gender
- LV cavity at peak stress equal to/smaller than at rest
- Uniform and normal wall thickness and thickening
- Uniform and normal regional wall motion
- Peak stress LVEF > rest LVEF
N13-Ammonia PET Images
Characteristics of an Abnormal Myocardial Perfusion PET Study

- Decrease in regional tracer uptake at peak stress
- LV cavity at peak stress larger than at rest
- Frequent regional contraction abnormality (stunning) at peak stress
- Peak stress LVEF $\leq$ rest LVEF
Abnormal N-13 perfusion study

72 year old man with peripheral vascular disease.

Coronary arteriography:
- LAD: 60% ostial and 80% mid vessel stenoses
- LCX: 90% proximal stenosis and occluded OM
- RCA: 90% ostial stenosis
Abnormal N-13 perfusion study
Multivessel Disease

Ischemia + Transient Dilatation
PET Perfusion/Metabolic Imaging Protocols

- **Transm.**
- **Rest**
- **Exercise Pharm.**
- **Stress**
- **Metabolic Imaging**

- **13N-ammonia**
- **82Rb**

- **Dipyridamole**
- **Adenosine**
- **Dobutamine**

- **18F-FDG**
Progression of Atherosclerosis

PET Perfusion
Quantification of Myocardial Blood Flow

LAO

Rest

Stress

RAO
Control of Coronary Blood Flow

Conductance Vessel

Resistance Vessels

Vascular Smooth Muscle Cell

Shear Stress

Endothelial Cell
Normal Response
about 10-20% diameter increase

Resistance to Flow

- Length of Vessel (L)
- Flow Velocity (V)
- Diameter of Vessel (D; $4^{th}$ power)
Conductance Vessel

Abnormal Response
no change or decrease in diameter

Resistance to Flow

• Length of Vessel (L)
• Flow Velocity (V)
• Diameter of Vessel (D; 4\textsuperscript{th} power)
Control of Coronary Blood Flow

Resistance Vessels

< 400µm

Adenosine
Dipyridamole
Papaverine

Vascular Smooth Muscle Cell

Coronary Blood Flow

Shear Stress

Endothelial Cell
As Atherosclerosis Progresses, the Artery Usually Compensates by Dilating

Compensatory Expansion Maintains Constant Lumen

Expansion Overcome: Lumen Narrows

Conductance and Resistance Vessel Interaction

Zeiher et al., Circulation 1991; 84:1984-92
Arterial Tracer Input Function and Changes in Myocardial Tracer Concentration

Activity Concentration (cts / pixel / sec)

Time (sec)

Myocardium

Arterial Blood
**Clinical Value Long Term Known**

**MBF in Kawasaki Disease**

Myocardial Blood Flow (ml/100g/min)

- **Control**
  - Rest
  - Adenosine
  - n = 10

- **Kawasaki**
  - Rest
  - Adenosine
  - n = 10

*p = 0.01*

Clinical Value Long Term Known Therapy MBF Changes in Insulin Resistance

RPP

MBF

NS

P <0.05

Percent Increase

Baseline On Treat Off Treat

Percent Increase

Baseline On Treat Off Treat

Long Term Prognostic Value PET Perfusion
Added Value of Coronary Flow Reserve

Herzog et al. JACC 2009;54:150-156.
Quantitative PET

• Serial PET imaging is validated, reproducible approach to quantify non-invasively myocardial blood flow at rest and during stress in healthy individuals and patients with heart disease

• The effects of pharmacological interventions, drug effects, noxious stimuli or lifestyle modification programs on myocardial blood flow and flow reserve can be measured

• The effects of physiologic processes such as aging can be evaluated in humans

• The hemodynamic significance of coronary artery disease can be estimated
Why Is PET More Suitable to Follow Pro/Regression of CAD

- Coronary blood flow is a function of the arterial radius raised to the fourth power.

- Small changes in diameter not measurable by anatomic imaging are magnified into much larger changes in blood flow readily quantifiable by PET.

- Changes in PET perfusion can be seen in 40–90 days after intense risk factor treatment is begun.

Agenda

• Perfusion PET
• Metabolic PET (Viability)
• Hybrid Imaging (PET/CTA)
Duke Database
Medical therapy vs. CABG

Circulation 1992
Viability PET Study

Chronic LVEF Dysfunction

• Traditionally the gold standard
• Two sets of resting images to detect viable and hibernating myocardium:
  • Perfusion image (usually with N-13 ammonia or rubidium-82) Cellular membrane integrity
  • Glucose metabolic image (with F-18 fluorodeoxyglucose = FDG) Glucose metabolism
Myocyte FDG Uptake

Normal Myocyte

Ischemic Myocyte

Glucose 6-phosphatase

Hexokinase

G6P

FDG

D-Glucose

FFA

Glycolytic Pathway
PET Myocardial Viability

**NH$_3$**  
- **Stress**  
- **Rest**

**FDG**  
- Match
- Mismatch

- Fixed
- Partially Reversible
- Partially Reversible

**FDG**  
- Match
- Mismatch

**FDG**  
- Match
- Mismatch

**FDG**  
- Match
- Mismatch
PET viability protocols

Traditional semi-quantitative flow/metabolism match-mismatch following oral glucose load

Quantitative measurement (HH) of FDG uptake during glucose clamp

Circulation 1996; 93: 737-744
J Clin Invest 1996; 98: 2094-2099
PET Viability

Improved symptoms of CHF

r = 0.87, SEE = 10.8, P < 0.001

Multivessel CAD
Mean LVEF = 28 ± 6%

F-18-Fluorodeoxyglucose Positron Emission Tomography Imaging-Assisted Management of Patients With Severe Left Ventricular Dysfunction and Suspected Coronary Disease

A Randomized, Controlled Trial (PARR-2)

Rob S. B. Beanlands, MD, FRCPC, FACC,* Graham Nichol, MD, FRCPC,††
Ella Huszti, MSc,¶ Dennis Humen, MD, FRCPC, FACP, FACC,† Normand Racine, MD, FRCPC,#
Michael Freeman, MD, FACC, FRCPC,‡ Karen Y. Gulenchyn, MD, FRCPC,¶
Linda Garrard, BSc, RN,* Robert deKemp, PhD,* Ann Guo, MEng,*
Terrence D. Ruddy, MD, FRCPC, FACC,* François Benard, MD, FRCPC,**
André Lamy, MD, MHSc,∥ Robert M. Iwanochko, MD, FRCPC, FACC,§ and the PARR-2 Investigators‡‡

Ottawa, London, Toronto, and Hamilton, Ontario, Canada; Montréal, Sherbrooke, and Québec City, Quebec, Canada; and Seattle, Washington
PARR-2
PET-guided Therapy vs Standard Care

Event-free survival

ADHERE arm

Standard arm

p = 0.019

Agenda

• Perfusion PET
• Metabolic PET (Viability)
• Hybrid Imaging (PET/CTA)
Hybrid PET/CTA: Myocardial Perfusion and Function

Cardiac Perfusion

Concurrent Rest & Peak Stress Function

Coronary Calcium Assessment

CTA
Progression of Atherosclerosis

SPECT Underestimates Disease Burden: **Stable CAD**

Calcium score: 890
Relationship of Stress-Induced Ischemia and Atherosclerosis (CAC)

<table>
<thead>
<tr>
<th>Distribution of the normal MPS studies (N=1,119)</th>
<th>CAC score</th>
</tr>
</thead>
<tbody>
<tr>
<td>22%</td>
<td>0</td>
</tr>
<tr>
<td>18%</td>
<td>1-9</td>
</tr>
<tr>
<td>25%</td>
<td>10-99</td>
</tr>
<tr>
<td>20%</td>
<td>100-399</td>
</tr>
<tr>
<td>11%</td>
<td>≥1000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distribution of the ischemic MPS studies (N=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
</tr>
<tr>
<td>0%</td>
</tr>
<tr>
<td>7%</td>
</tr>
<tr>
<td>20%</td>
</tr>
<tr>
<td>29%</td>
</tr>
<tr>
<td>39%</td>
</tr>
</tbody>
</table>

Why use PET/CTA?

• Non invasive.
• Offer high diagnostic accuracy.
• Monitor the course of disease.
• Allow quantification of myocardial blood flow and coronary reserve.
• Detect early functional abnormalities.
• Monitor consequences of lifestyle modifications.
# Effective Radiation Dose for Cardiac PET/CT Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Effective Radiation (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PET</strong></td>
<td></td>
</tr>
<tr>
<td>F-18 FDG (370 MBq)</td>
<td>7.0</td>
</tr>
<tr>
<td>N-13 NH3 rest/stress (2X 550 MBq)</td>
<td>2.2</td>
</tr>
<tr>
<td>Rb82 rest/stress (2 x 740 MBq)</td>
<td>3.6</td>
</tr>
<tr>
<td>H2O-15 rest/stress (2 x 740 MBq)</td>
<td>1.4</td>
</tr>
<tr>
<td>Transmission Ge-68 rod source</td>
<td>0.08-0.13</td>
</tr>
<tr>
<td><strong>MSCT</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium Scoring</td>
<td>0.7-6.2</td>
</tr>
<tr>
<td>CT angiography</td>
<td>3.7-13.0</td>
</tr>
<tr>
<td>CT based PET attenuation correction</td>
<td>0.23-5.66</td>
</tr>
</tbody>
</table>
Prognosis of Cardiac Events by PET-CT
Added Value of CAC

Hybrid PET/CTA: Myocardial Perfusion and Function

Kajander, S. et al. Circulation 2010;122:603-613
PET and CTA Complement Each Other

- Calcium (blooming)
- Stents
- Limited spatial resolution, <1.5-mm vessels
- Overestimation of stenosis
- Positive predictive value MDCT ~50%
- Clinical outcomes data
- Preclinical disease

Abnormal CT Angiography: Limited Positive Predictive Value
Discordance Between Noninvasively Determined Anatomic and Functional Measures of Atherosclerosis

- Percent stenosis a moderate descriptor of coronary resistance
  - Stenosis difficult to estimate with soft plaque
- Coronary vasodilator reserve integrates coronary epicardial and microvascular function
- Noncoronary causes of myocardial damage
<table>
<thead>
<tr>
<th>PET</th>
<th>CTA</th>
<th>Diagnosis</th>
<th>Potential Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>No CAD</td>
<td>Discharge</td>
</tr>
<tr>
<td>Normal</td>
<td>Abnormal</td>
<td>Non-significant CAD</td>
<td>Medical Tx &amp; Follow-up</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Abnormal</td>
<td>Significant CAD</td>
<td>Medical Tx &amp; Consider Cath</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Normal</td>
<td>Coronary microvascular dysfunction</td>
<td>Risk Profile Modification &amp; Consider Antianginal Tx</td>
</tr>
</tbody>
</table>
Infarct size measurement
The Next Thing is….  
Tracking of Genetically Labeled Progenitor Cells by PET
Changes Coming With Hybrid Imaging

Nuclear Cardiology Evolution

• PET-CT:
  Comprehensive evaluation of CAD Perfusion Function Viability Vulnerable Plaque Assessment (FDG ?)
Take Home Message

• Excellent sensitivity and prognosticator, CAD, severe LV dysfunction.
• Integrates function and morphology, PET/CTA.
• Unsurpassed ability to calculate MBF in preclinical and during therapy.
• Unlimited molecular imaging capabilities to target specific pathophysiology questions.