Physiological Basis of Myocardial Perfusion
SPECT and PET

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(Nuclear Medicine) and Medicine (Cardiology)
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Director, Biomedical Imaging Institute

Relation of Degree of Stenosis to Coronary Blood Flow

Flow = pressure/resistance

Factors Determining Regional Myocardial Uptake of Radioactivity

Regional myocardial blood flow
X
Extraction fraction
Relationship Between Tracer Uptake and Myocardial Blood Flow

Myocardial Tracer Uptake

Myocardial Blood Flow (ml/min/g)

Teboroxime
TI-201
Tc-99m Sestamibi
Tc-99m Tetrofosmin

Defect intensity = 2.3/2.9 = 0.79
(21% below normal)
Relationship Between Tracer Uptake and Myocardial Blood Flow

Defect intensity = $\frac{1.5}{1.7} = 0.88$
(12% below normal)

![Graph showing the relationship between myocardial tracer uptake and blood flow.](image)

Protocol for Tc-99m Labeled Perfusion Imaging
Same Day Rest-Stress

![Protocol diagram showing the procedure and time intervals.](image)

Total time: 5 hrs
Protocol for Tc-99m Labeled Perfusion Imaging
Same Day Rest-Stress

- Tc-99m
- 6.3 mCi

Rest image
Stress
Stress image

0 45 60
1/2 hr
minutes
Total time: 2.5 hrs

Protocol for Tc-99m Labeled Perfusion Imaging
Same Day Stress-Rest

- Tc-99m
- 6.3 mCi

Stress
Stress image
Rest image

30 45 60
1/2 hr
minutes
Total time: 2.5 hrs
Methods to Diagnose/Reduce/Eliminate Soft Tissue Attenuation

- Gated acquisition to assess regional wall motion
- Prone imaging
- Upright imaging
- Attenuation correction

Identification of Attenuation artifact by Gated Imaging to Assess Regional Wall Motion

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### Identification of Attenuation artifact by Gated Imaging to Assess Regional Wall Motion

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<td><em>Artifact</em></td>
<td><em>Shifting artifact or ischemia</em></td>
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<td><em>Scar</em></td>
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Methods to Diagnose/Reduce/Eliminate Soft Tissue Attenuation

- Gated acquisition to assess regional wall motion
- Prone imaging
- Upright imaging
- Attenuation correction
Semi-recumbent imaging

Stress
Rest
Stress
Rest
Stress
Rest
Stress
Rest

Upright imaging

Stress
Rest
Stress
Rest
Stress
Rest
Stress
Rest
SPECT Based Transmission Imaging

- Scanning Line Source
  - Gd-153
- Scanning Point Source
  - Ba-133
- Line Source/Fan Beam
- Line Source Array

J. Cullom, Ph.D., MAHI
SPECT-CT Imaging (No Attenuation Correction)

SPECT-CT Imaging (After Attenuation Correction)
**X-ACT Attenuation Correction System**

Fluorescence X-rays

Fanbeam collimators

Solid-State Detectors Operating In High Counting Rate Mode (>5 x 10^6 cps per 20 cm x 15 cm detector area)

*X-Ray Line Source Generator*

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* Maddahi J, et al. ICNC 2009*
P015 after AC

P026 no AC
Multi-Center Validation of AC for Upright SPECT MPI

Confidence of interpretation

Maddahi et al, JNC Submitted
Multi-Center Validation of AC for Upright SPECT MPI

Overall Detection of CAD

Maddahi et al, JNC Submitted

Multi-Center Validation of AC for Upright SPECT MPI

LAD

LCX

RCA

Maddahi et al, JNC Submitted
### Possibility of Short Protocol with Same-Day Stress-Rest Imaging

<table>
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<td>No</td>
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### Possibility of Short Protocol with Same-Day Stress-Rest Imaging

<table>
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<th>Stress</th>
<th>Stress + AC</th>
<th>Rest</th>
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<td>Definite normal</td>
<td>Normal</td>
<td>No</td>
</tr>
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<td>Defect</td>
<td>Yes</td>
</tr>
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<td>Definite defect</td>
<td>Normal</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Defect</td>
<td>Yes</td>
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Stress

Stress-Rest AC
Rest-Stress Protocols

Rapid Imaging
Benefits of Rapid SPECT Imaging

- Patient convenience
- Decreased patient motion and associated artifact
- Increased patient throughput
- Decrease radiation dose to patients
- Potential for dynamic imaging and absolute quantitation of myocardial blood flow

2-Minute Gated Acquisition with D-SPECT
nSPEED Rest-Stress Upright Imaging (5.3 and 2.9 min, Dual Head)

Blinded Visual Assessment of Image Quality

\( n\text{SPEED vs. Standard (}\text{n=448}\)\)

- nSPEED = Standard
- nSPEED better than Standard
- nSPEED worse than Standard

<table>
<thead>
<tr>
<th>Stress Images</th>
<th>Rest Images</th>
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<tbody>
<tr>
<td>79.5%</td>
<td>78.6%</td>
</tr>
<tr>
<td>19.2%</td>
<td>19.4%</td>
</tr>
<tr>
<td>1.3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Maddahi et al, JNC 2009; 16(3): 351-7
Measurement of LVEF (%) from Gated Stress SPECT
nSPEED vs. Standard

\[ y = 1.005x \]

\[ R^2 = 0.957 \]

Maddahi et al, JNC 2009; 16(3): 351-7

Dedicated PET

- Germanium rod sources for AC
- Minimal radiation exposure
- Relatively inexpensive

Hybrid PET/CT

- CT used for transmission map
- More radiation
- Expensive (but anatomic data & CTA)

Adapted from E Garcia, Emory Univ
PET Myocardial Perfusion Tracers

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Ext. Fraction</th>
<th>T1/2</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-15 Water</td>
<td>100%</td>
<td>2.09 min</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>N-13 Ammonia</td>
<td>85%</td>
<td>9.96 min</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Rubidium-82</td>
<td>65%</td>
<td>76 sec</td>
<td>Generator</td>
</tr>
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Advantages of PET vs. SPECT

- Fast protocols
- Improved image quality in obese patients
- Improved specificity (less attenuation artifacts)
- Improved sensitivity for detection of CAD
  - Better tracers with higher extraction fraction
  - Higher system resolution
  - Imaging at peak stress
PET Perfusion Imaging Protocol
N-13 Ammonia

N-13 ammonia
30 mCi

Rest Perfusion

Adenosine
Stress Perfusion

0 5 20 30 36 41 56
minutes
Total time: <1 hr

Rapid PET Rb-82 ECG-Gated Rest/Peak Stress Acquisition Protocol

Rb-82
40 mCi

10 s

Emission Scan, (150 secs), 3D with gating, starting 2.5 mins after Rb-82

Tx Scan

Emission Scan, (150 secs), 3D with gating, starting 2.5 mins after Rb-82

Total time: <20 mins

Bateman t, Mid America Heart Institute
Left Ventricular Ejection Fraction Reserve Improves Identification of Multivessel CAD

**MPI Alone**

- 1-vessel CAD: 72%
- 2-vessel CAD: 56%
- Left main/3-vessel CAD: 43%

**MPI + EF Reserve**

- 1-vessel CAD: 67%
- 2-vessel CAD: 33%
- Left main/3-vessel CAD: 21%

BMS747158 (Flurpiridaz): Chemical Structure

(characteristic image)

2-tert-Butyl-4-chloro-5-[4-(2-(18F)fluoro-ethoxymethyl)-benzyloxy]-2H-pyridazin-3-one

Characteristics of the Ideal PET Perfusion Tracer

- **F-18 label**
  - Available as unit dose from a regional cyclotron
  - Ideal PET resolution (positron range)
  - Possibility of rest-exercise imaging

- **High extraction fraction**
  - Better perfusion defect detection
  - Reliable absolute quantitation
Sequential Whole Body Images of $^{18}$F flurpiridaz

Conclusions of Phase 1 Flurpiridaz F 18 Study

- No tracer related adverse events were noted.
- Dosimetry was within the clinically acceptable range, using up to 14 mCi combined rest-stress dose.
- Stress imaging was feasible with both treadmill exercise and pharmacologic vasodilation.
- Myocardium was clearly visualized for several hours after rest and stress injection with good myocardial to background ratio.
- Five minute gated acquisition - starting 2 minutes after injection - yielded high quality images.


Objectives

• To assess clinical safety

• To compare flurpiridaz F 18 PET and Tc-99m labeled SPECT MPI with respect to:
  – Image quality
  – Certainty of interpretation
  – Detection of CAD


Study Population (N = 143)

• 21 US centers
• 107 males and 36 females
• Age range: 29-88 yrs (mean = 62.4 yrs)
• 108 White, 3 Asian, 16 African American, 16 Others
• Height (cm): 134-191 (mean = 171.1)
• Weight (kg): 49-132 (mean = 82.9)
• BMI: 17.4 – 41.9 (mean = 28.3)

BMS747158-201
Flurpiridaz F 18 Injection Phase 2 Study

Image Quality (N=86)
(% rated excellent or good)

<table>
<thead>
<tr>
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<th>SPECT</th>
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<tbody>
<tr>
<td>Rest</td>
<td>95.3</td>
<td>69.8</td>
</tr>
<tr>
<td>Stress</td>
<td>98.8</td>
<td>84.9</td>
</tr>
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P<0.01


BMS747158-201
Flurpiridaz F 18 Injection Phase 2 Study

Certainty of Interpretation (N=86)
(% definitely normal or abnormal)

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<td>Overall CAD Diagnosis</td>
<td>90.7</td>
<td>75.6</td>
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P<0.01

In this Phase 2 clinical trial, flurpiridaz F 18 injection:

- Had a favorable safety profile and was well tolerated.
- Was an improvement compared to Tc-99m SPECT MPI with respect to:
  - Rest and stress image quality
  - Certainty of image interpretation
  - Sensitivity for detection of CAD

Quantitation of Myocardial Blood Flow

- **Absolute** = ml/min/g
- **Flow Reserve** = Peak hyperemic/resting flow
- **Relative** = Normalized to best perfused region
Advantages of PET vs. SPECT

**Absolute Quantitation of Blood Flow**

- Better identification of MVD
- Assessment of microvascular disease
- Evaluation of endothelial dysfunction and response to Rx
Absolute Quantitation of Myocardial Blood Flow with $^{18}$F Flurpiridaz PET

Maddahi J, Huang SC, et al, ASNC 2011  * p<0.002 vs. Normal