New Opportunities For Nuclear Cardiology in Heart Failure

Prem Soman, MD, PhD
Division of Cardiology
University of Pittsburgh Medical Center
Pittsburgh, PA
Disclosures

Consultant Fees/Honoraria
Astellas; GE Healthcare
“For the assessment of myocardial sympathetic innervation in the evaluation of patients with NYHA class II-III heart failure and an ejection fraction < 35%”
What is I-123 MIBG?

- I-123 Metaiodobenzylguanidine
- Analogue of guanethidine (structurally similar to norepinephrine)
- Thus, kinetics at the sympathetic nerve terminal mimic norepinephrine
Sympathetic Neuron Synapse

PRESYNAPSE (Axon) →

Tyrosine → Dopa → Dopamine → Norepinephrine

SYNAPTIC CLEFT

NE, NE, NE

VESICLES

NE → NE → NE

POSTSYNAPSE

α₁ β₁ β₂

Post-synaptic receptors

Myocyte

Cocaine, tricyclics, phenylephrine, phenothiazines, labetolol, Ca –blockers, glycosides, chocolate, blue cheese

Uptake 1 (Na-dependent)

Uptake 2 (Passive diffusion)

To plasma (>20%)

NE, norepinephrine; NET, norepinephrine transporter

Travin ML. J Nucl Cardiol 2012
**Myocardial MIBG Uptake: Planar**

**Normal**

- HM ratio: 2.3

**Heart Failure**

- HM ratio: 1.1

- Early (15 min):
- Late (4-hr):
- Washout rate:
HM Ratio

<table>
<thead>
<tr>
<th></th>
<th>Counts</th>
<th>Pixels</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>188855</td>
<td>601</td>
<td>314.2</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>10715</td>
<td>49</td>
<td>218.7</td>
</tr>
<tr>
<td>HMR</td>
<td>1.44</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Counts</th>
<th>Pixels</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>EARLY</td>
<td>100370</td>
<td>548</td>
<td>183.2</td>
</tr>
<tr>
<td>LATE</td>
<td>7630</td>
<td>49</td>
<td>155.7</td>
</tr>
</tbody>
</table>

Normal = 1.9 to 2.8 (2.2±0.3)
Washout Rate

Early counts – late counts corrected for decay × 100

Early counts

(normal = < 10%)
**MIBG Parameters**

Late HM: uptake+ storage+ release

Early HM

Washout (symp. Drive): Not specific to HF

Uptake 1

Post-synaptic receptors

Myocyte

α₁  β₁  β₂
Practical Considerations

• Thyroid blockade probably not necessary with I-123

• Dose: 10 mCi for planar + SPECT (~5 mSv)

• Energy window 159 keV ± 20%

• Collimator considerations: Lead septal penetration by high energy photons (3%)
Imaging Myocardial Innervation: \(^{123}\)I-mIBG

**H/M: 2.3**
- Normal

**H/M: 1.7**
- NYHA II

**H/M: 1.1**
- NYHA IV
ADMIRE-HF: Primary Efficacy Analysis

n=961 pts w NYHA II/III, EF < 35%; F/U 17m

H/M ≥ 1.60: 2-year event-free survival 85%

H/M < 1.60: 2-year event-free survival 63%

*p<0.0001 vs H/M ≥ 1.60

Event-free Survival Probability

Time (days)

n: Low H/M: 760
    High H/M: 201

762 658 562 462 356 265 149
195 179 157 136 109 79 52

HF progression
Cardiac death
Arrhythmic event
ADMIRE-HF: Arrhythmic Events

Event-free Survival Probability

- Episode of sustained ventricular tachyarrhythmia
- Appropriate ICD discharge
- Aborted cardiac arrest

Time (days)

n=961 pts w NYHA II/III, EF < 35%; F/U 17m

H/M≥1.60: 2-year event-free survival 96%

H/M<1.60: 2-year event-free survival 85%*

*p=0.002 vs H/M ≥1.60

Jacobson AF. JACC 2010
mIBG Cases:
Three patients with NYHA II HF and Low EF

Case 1
65 y/o M
NYHA 2
LVEF=25%
H/M=0.96
Died at 8 mo
HF Progression

Case 2
51 y/o M
NYHA 2
LVEF=33%
H/M=1.38
Died at 8 mo, SCD
(No ICD)

Case 3
64 y/o M
NYHA 2
LVEF=30%
H/M=1.67
No event

Based upon the H/M ratios, 2-year cardiac mortality risk for patient 1 is 10 times that of patient 3.

Jacobson A
mIBG: Potential Clinical Applications

- Patient selection for ICD
Incidence of Appropriate Device Therapy in HF Patients

Weeke et al. Europace, 2013
mIBG Case
mlBG: Potential Clinical Applications

- Patient selection for ICD
- Objective assessment of response to Rx
mIBG Case: Before and After LVAD

Before LVAD

After LVAD

Dracos SG JACC 2010; 3: 64
mIBG:
Potential Clinical Applications

- Patient selection for ICD
- Objective assessment of response to Rx
- Guidance for EP procedures
MIBG-Guided Afib Ablation

Courtesy S. Ben-Haim/ S. Ernst
mIBG: Potential Clinical Applications

- Patient selection for ICD
- Objective assessment of response to Rx
- Guidance for EP procedures
- Explore pathogenetic mechanisms
Regional Sympathetic Denervation in Takotsubo’s CM

10/24/2013

Tc-99m

MIBG

12/14/2013

MIBG

Harris D/ Soman P. JNC 2015 (in press)
Billing and Reimbursement

- Emerging Technology (T) Code: Category 3 code
  - 0331 T (Planar)
  - 0332 T (SPECT)

- List price: $3900
- Negotiated price: $2200-$2900

- Reimbursement:
  - MFPS: 95% of the average wholesale cost
  - HOPPS: $1153.62
Radionuclide Imaging of Infiltrative Cardiomyopathies
18F-FDG PET For Inflammation

- Vulnerable plaque
- Device infections
- Sarcoidosis
F-FDG Imaging of Inflammation: Rationale

- Macrophage dense areas

- High metabolic rate makes them reliant on external glucose for fuel
18 F-FDG Cardiac Imaging

**Inflammation**
- Suppress (normal) myocardial uptake
- high fat diet, overnight fast

**Ischemia**
- Facilitate myocardial uptake
- glucose loading + insulin
- Acipimox (suppress free-fatty acid)
Radionuclide Imaging In HF: Infiltrative Cardiomyopathies

Sarcoidosis: PET

FDG uptake in areas of active inflammation

Youssef/ Beanlands. JMN 2012

Change in LV Ejection Fraction Per Scan According to Inflammation Response

Osborne M/Blankstein R. JNC 2014
Cardiac Amyloidosis

- Cardiac amyloid light chain (AL)
  - Plasma cell dyscrasia

- Transthyretin-related amyloidosis (ATTR)
  - Familial (AD mutation)
  - Wild type - senile cardiac amyloidosis
Radionuclide Imaging of Amyloidosis

SPECT
- Tc-99m DPD
- Tc-99m PYP

PET
- C-11 PIB
- F-18 Florbetapir (Amyvid)
Radionuclide Imaging of Amyloidosis

- Amyloidosis: Primary (AL), TTR (mutant, familial)
  - SPECT (Tc-99m PYP)- TTR
  - PET: C-11 PIB and F-18 Florbetapir - Primary and TTR

Al-Jaroudi. JNC 2014