Relevant Financial Disclosure(s)
Thomas A. Holly, MD

• I have nothing to disclose
Outline

• New technology
• Not new but not common technology (PET)
• New approaches with old technology
• New uses
  – Cardiac amyloidosis
  – Cardiac sarcoidosis
• Combined pharmacologic stress and exercise
  – because that’s what I like to talk about
• ImageGuide
New Technology

• New cameras and algorithms
  – D-SPECT
  – Discovery
  – CardiArc
  – Cardius X-ACT
  – Wide Beam Reconstruction
  – Flash 3D
Why New Technology?

• To make prettier pictures
• To reduce imaging time
• To reduce radiation exposure
• To reduce radiation exposure
• To reduce radiation exposure
Effective Dose Estimates

<table>
<thead>
<tr>
<th>Perfusion agent</th>
<th>mSv</th>
</tr>
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<tbody>
<tr>
<td>Tc-99m sestamibi rest/stress</td>
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<td>26.5</td>
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<tr>
<td>Rb-82</td>
<td>4.1</td>
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</tbody>
</table>

From: RADAR Medical Procedure Radiation Dose Calculator and Consent Language Generator
Reduced isotope dose and imaging time with a high-efficiency CZT SPECT camera

W. Lane Duvall, MD, a Lori B. Croft, MD, a Eric S. Ginsberg, MD, b Andrew J. Einstein, MD, PhD, c Krista A. Guma, CNMT, a Titus George, CNMT, a and Milena J. Henzlova, MD a

- 5 mCi rest and 15 mCi stress doses
- Rest images: 5- and 8-minute acquisition times (CZT)
- Stress images: 3- and 5-minute acquisition times (CZT)
- Stress images: 15-minute acquisition time (standard SPECT)
- No difference in image quality between the different CZT acquisition times
- When compared to standard SPECT, no difference in perfusion defects or calculated LVEF on CZT camera
Excellent Image Quality with CZT Cameras

Absolute Myocardial Blood Flow: Comparison with N-13 Ammonia PET

- Top rows: SPECT
- Bottom rows: PET

Unadjusted Annual Event Rates by CZT SPECT Findings

Cardiac Events Based on SPECT Imaging Results (n=5,183)

- Open bars = MI
- Solid bars = cardiac death

Event Rate (%)

- Normal: 0.3%
- Mildly Abnormal: 0.8%
- Moderately Abnormal: 2.7%
- Severely Abnormal: 4.2%

Prognosis: CZT vs. Standard SPECT Camera

- Yellow: CZT SPECT normal scans
- Blue: Standard SPECT normal scans
- Green: Standard SPECT abnormal scans
- Purple: CZT SPECT abnormal scans

Days Cumulative Survival

How Else Can We Reduce Radiation Exposure?

- Different perfusion agents/techniques
Effective Dose Estimates

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From: RADAR Medical Procedure Radiation Dose Calculator and Consent Language Generator
Rb-82 PET imaging

- Rb-82 is a potassium analog (like Tl)
- Half-life of 75 seconds
- 40-60 mCi injected for rest and stress images
- Only pharmacologic stress testing
- Always utilizes attenuation correction
- Possibility for quantification of blood flow (ml/min/g)
- Ability to assess LV function at rest and peak stress
  - May be helpful for detecting patients with 3 vessel disease and balanced ischemia
Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT

Timothy M. Bateman, MD,abc Gary V. Heller, MD, PhD,cd A. Iain McGhie, MD,ac John D. Friedman, MD,e James A. Case, PhD,bc Jan R. Bryngelson, BN,b Ginger K. Hertenstein, CNMT,b Kelly L. Moutray, MEd,c Kimberly Reid, MS,c and S. James Cullom, PhDbc

• 112 SPECT Tc-99m studies compared with 112 PET Rb-82 studies
• No attenuation correction for the SPECT studies
• 4 readers – 2 with no PET experience
• 76% in each group underwent coronary angiography
SPECT vs. PET

Scan Quality

• 81% of SPECT scans were interpreted as definitely normal or abnormal vs 96% with PET
• PET was superior at localizing disease

• Graph shows sens, spec and accuracy for detecting 50% and 70% stenosis

• For BMI >30, accuracy 87% vs 67% (PET vs SPECT)
Event Free Survival as a Function of Percent Myocardium Abnormal

Event Rates in Patients with Normal and Abnormal LVEF Reserve

- **Cardiac Events**
  - LVEF Reserve ≥0: 2.1 (N=801)
  - LVEF Reserve <0: 5.3† (N=184)

- **All Cause Death**
  - LVEF Reserve ≥0: 4.3 (N=801)
  - LVEF Reserve <0: 9.2† (N=184)

Myocardial Blood Flow with Rb-82 PET

A 56-year-old woman with a history of obesity, hypertension, hyperlipidemia, and type 2 diabetes complicated of retinopathy and renal failure
Making N-13 Ammonia More Available?
What if You Don’t Have a Fancy New Camera?
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What if You Don’t Have a Fancy New Camera?
Effective Dose Estimates

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From: RADAR Medical Procedure Radiation Dose Calculator and Consent Language Generator
Tc-99m sestamibi/tetrofosmin

*Same Day, Rest-Stress Protocol*

- 8-10 mCi Tc-99m sestamibi/tetrofosmin
- 25-30 mCi Tc-99m sestamibi/tetrofosmin

**Imaging**

**Stress**

**Imaging**

- Time between injections ≥ 2 hours
- Dose ratio of second to first injection = ~3:1
- Delay post-stress depends on the type of stress and the particular imaging agent
Tc-99m sestamibi/tetrofosmin

Same Day, Stress-Rest Protocol

- 8-10 mCi Tc-99m sestamibi/tetrofosmin
- Time between injections ≥ 2 hours
- Dose ratio of second to first injection = ~3:1
- Delay post-stress depends on the type of stress and the particular imaging agent

- 25-30 mCi Tc-99m sestamibi/tetrofosmin
- 15-60 min
- 45-60 min
Tc-99m sestamibi/tetrofosmin

*Same Day, Stress-Only Protocol*

- 8-10 mCi Tc-99m sestamibi/tetrofosmin
- Imaging
- Delay post-stress depends on the type of stress and the particular imaging agent
- 25-30 mCi Tc-99m sestamibi/tetrofosmin
- Imaging
- Time between injections ≥ 2 hours
- Dose ratio of second to first injection = ~3:1
Prognosis with Stress-Only Imaging

A model for the prediction of a successful stress-first Tc-99m SPECT MPI

W. Lane Duvall, MD, Usman Baber, MD, Elliot J. Levine, MD, Lori B. Croft, MD, and Milena J. Henzlova

<table>
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<tr>
<th>Clinical variables</th>
<th>OR (95% CI)</th>
<th>Score value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency</td>
<td>0.61 (0.43-0.86)</td>
<td>-2</td>
</tr>
<tr>
<td>Department</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td>1.32 (1.01-1.67)</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.55 (1.21-1.98)</td>
<td>2</td>
</tr>
<tr>
<td>Typical chest pain</td>
<td>1.79 (1.30-2.45)</td>
<td>2</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.20 (1.41-3.41)</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>2.78 (2.20-3.51)</td>
<td>4</td>
</tr>
<tr>
<td>Male gender</td>
<td>3.53 (2.78-4.50)</td>
<td>4(5)*</td>
</tr>
<tr>
<td>Documented CAD</td>
<td>3.90 (3.04-4.99)</td>
<td>5</td>
</tr>
</tbody>
</table>
Stress-Only Imaging

How to Select Patients

Triage of patients for attenuation-corrected stress-first Tc-99m SPECT MPI using a simplified clinical pre-test scoring model

Shreyas Gowdar, MD, a Waseem Chaudhry, MD, b Alan W. Ahlberg, MA, a Milena J. Henzlova, MD, c and W. Lane Duvall, MD a

Ultra-Low-Dose Stress-First Myocardial Perfusion Imaging

- High efficiency camera (Discovery NM 530c)
- 5 mCi Tc-99m tetrofosmin at stress
- 15-minute acquisitions, supine and prone
- Rest imaging done if needed (31/100)

Stress supine and prone images

Stress supine and prone images

Effectiveness dose (mSv)

Frequency

0.25 0.50 0.75 1.00 1.25

Stress-only

0.25 0.50 0.75 1.00 1.25

Stress-rest

Effectiveness dose (mSv)

Stress-only

Frequency

0.25 0.50 0.75 1.00 1.25

Stress-rest

0.93 mSv

Ultra-Low-Dose Stress-First Myocardial Perfusion Imaging

Septal ischemia
3.34 mSv

LAD stenosis

Stress-Only Imaging
How to Select Patients

• Ways to get the ball rolling...
  – 2-day studies because of patient weight
Tc-99m Sestamibi/Tetrofosmin

Two-Day Protocols

- High dose Tc-99m for both injections
- Order of stress/rest doesn’t matter
  - although stress first could be stress only

Day 1

30-40 mCi Tc-99m sestamibi or tetrofosmin

Stress

15-60 min

Imaging

Day 2

30-40 mCi Tc-99m sestamibi or tetrofosmin

Imaging

45-60 min
Tc-99m Sestamibi/Tetrofosmin

Two-Day Protocols

Day 1

30-40 mCi Tc-99m sestamibi or tetrofosmin

Stress

15-60 min

Imaging

Day 2

30-40 mCi Tc-99m sestamibi or tetrofosmin

Imaging

45-60 min

• High dose Tc-99m for both injections
• Order of stress/rest doesn’t matter
  – although stress first could be stress only
MM – 52 yo man, 76 in, 327 lbs, with HTN, DM, preoperative evaluation for kidney transplant
MM – 52 yo man, 76 in, 327 lbs, with HTN, DM, preoperative evaluation for kidney transplant
BC – 54 yo man, 78 in, 350 lbs, h/o heart failure, preoperative evaluation
BC – 54 yo man, 78 in, 350 lbs, h/o heart failure, preoperative evaluation
BC – 54 yo man, 78 in, 350 lbs, h/o heart failure, preoperative evaluation
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Stress prone images
BC – 54 yo man, 78 in, 350 lbs, h/o heart failure, preoperative evaluation

Stress supine and prone images
Ways to get the ball rolling...

- 2-day studies because of patient weight
- The late afternoon request
EV – 71 yo woman with HTN and chest pain admitted to the observation unit
EV – 71 yo woman with HTN and chest pain admitted to the observation unit
EV – 71 yo woman with HTN and chest pain admitted to the observation unit

Stress supine and prone images
EV – 71 yo woman with HTN and chest pain admitted to the observation unit
Heart Failure with Preserved Ejection Fraction

• More than 50% of HF patients have HFP EF

• No specific therapy shown to be effective in HFP EF

• Identifying subgroups of patients with HFP EF is important because the mechanism of disease, prognosis and treatment may differ

• Transthyretin (TTR) cardiac amyloidosis is being more commonly recognized as a cause of HFP EF

Diagnosis of TTR Amyloid

• Diagnosis is difficult on clinical grounds
• Echo findings can be suggestive
• CMR very sensitive but not specific
• Gold standard is an endomyocardial biopsy

Tc-99m Pyrophosphate Scanning for Amyloidosis

- Not suggestive: Score of 0 or H/CL ratio < 1
- Strongly suggestive: Score of 2 or 3 or H/CL ratio > 1.5
- Equivocal: Score of 1 or H/CL 1-1.5

<table>
<thead>
<tr>
<th>Grade</th>
<th>Myocardial $^{99m}$Tc-PYP Uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>no uptake and normal bone uptake</td>
</tr>
<tr>
<td>Grade 1</td>
<td>uptake less than rib uptake</td>
</tr>
<tr>
<td>Grade 2</td>
<td>uptake equal to rib uptake</td>
</tr>
<tr>
<td>Grade 3</td>
<td>uptake greater than rib uptake with mild/absent rib uptake</td>
</tr>
</tbody>
</table>
Tc-99m PYP for ATTR Amyloidosis

- 3 academic centers
- 121 patients with ATTR cardiac amyloid
- 50 patients with non-ATTR cardiac amyloid (34 with AL amyloid and 16 with nonamyloid HFpEF)
- 91% sensitivity and 92% specificity for detecting ATTR cardiac amyloid
- H/CL ratio of $\geq 1.6$ predicted worse survival

Tc-99m PYP Predicts Survival in Patients with ATTR Amyloidosis

Feel Free to Send Us Your Amyloid Patients!

- For patients with TTR cardiac amyloid: there are currently no RCTs that are currently enrolling.

- If you have a patient with genetic (hereditary) TTR (which we can test for at Northwestern), there is a compassionate use extension study that allows us to provide the RNA interference therapeutic (i.e., the real drug, not placebo) to these patients if they also have neuropathy (Dr. Senda Driss, our amyloid neurologist, checks for this)

- Sanjiv Shah says to send us your patients with cardiac amyloidosis because Northwestern does the most stem cell transplants for AL amyloid and we’re the only ones who have this treatment for TTR amyloid.
FDG PET for Cardiac Sarcoidosis

• Low carbohydrate, high fat diet the day before the study
# FDG PET Findings in Cardiac Sarcoidosis

## Spectrum of disease by PET/CT to evaluate rest perfusion and metabolism

<table>
<thead>
<tr>
<th>Spectrum of disease</th>
<th>Normal perfusion and metabolism</th>
<th>Abnormal metabolism</th>
<th>Abnormal perfusion and/or metabolism</th>
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</thead>
<tbody>
<tr>
<td><strong>Perfusion</strong></td>
<td><img src="image1" alt="Normal" /></td>
<td><img src="image2" alt="Abnormal" /></td>
<td><img src="image3" alt="Abnormal" /></td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Abnormal</td>
<td>Abnormal</td>
</tr>
<tr>
<td><strong>FDG</strong></td>
<td><img src="image1" alt="Normal" /></td>
<td><img src="image2" alt="Abnormal" /></td>
<td><img src="image3" alt="Abnormal" /></td>
</tr>
<tr>
<td></td>
<td>Normal (Negative)</td>
<td>Focal increase</td>
<td>Focal increase (different areas)</td>
</tr>
<tr>
<td></td>
<td>Diffuse (non-specific)</td>
<td></td>
<td>Normal (Negative)</td>
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<tr>
<td><strong>Interpretation</strong></td>
<td>Normal</td>
<td>Non-specific</td>
<td>Early Disease</td>
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<tr>
<td></td>
<td>Mismatch Pattern</td>
<td>Scar and Inflammation</td>
<td>Scar</td>
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FDG PET to Assess Response to Therapy

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<th>Examples of response to therapy</th>
<th>Baseline</th>
<th>After treatment</th>
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<tr>
<td>Whole Body FDG</td>
<td></td>
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<tr>
<td>Myocardial Perfusion</td>
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<tr>
<td>Inflammation (FDG)</td>
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<tr>
<td>No Response</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short axis</td>
<td>Horizontal Long axis</td>
</tr>
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<td></td>
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<td>Horizontal Long axis</td>
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<td>Marked Response</td>
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CMR Findings in Cardiac Sarcoidosis

Spectrum of Late Gadolinium Enhancement

- Normal
- Focal
- Multi Focal
- Extensive LGE

Suggested Algorithm for Using Imaging to Diagnose Cardiac Sarcoidosis

Suspected Cardiac Sarcoidosis

- If contraindication to CMR
  - CMR
    - Negative
    - Positive / inconclusive
      - PET (Cardiac and whole-body)
      * If high clinical suspicion persists
FDG PET Findings Predict Outcomes

What Other Stress Testing Issues Do We Face?

- Exercise vs. pharmacologic stress
Active 65 yo man with h/o HTN on metoprolol and amlodipine with occasional exertional chest pain; HR 64 at rest

• No way he’ll reach target HR, just order pharm stress
• Stop his meds and have him do an exercise stress test
• Try exercise stress and convert to pharm stress if needed
  – If needed, how?
Benefits of Adding Exercise to Pharmacologic Stress

• Decrease side effects

• Decrease splanchnic uptake of tracer
  – Improved heart:background ratios
  – Allows imaging sooner after tracer injection

• Obtain functional capacity (BEAST/BERST)
Adenosine Stress Testing

**Adjunctive Exercise**

**6 MINUTE ADENOSINE (STANDARD)**

**6 MINUTE ADENOSINE + EXERCISE**
Effect of Walking During Adenosine

*Improved Heart:Liver Ratios*

\[ p = 0.0003 \]

Elliott et al, JNC 2000

Regadenoson With Exercise

- Start exercise just before regadenoson is injected
- Inject tracer when you normally would after regadenoson
- Exercise for 4+ min total

![Graph showing the timeline for regadenoson injection and exercise]
Combined Exercise and Pharmacologic Stress

• What about maximal exercise?
Adenosine During Maximal Exercise

*The BEAST Trial*

EXERCISE (STANDARD)

- Stage 1
- Stage 2
- Stage 3
- Stage 4

EXERCISE + ADENOSINE

- Stage 1
- ADENOSINE
- Stage 2
- Stage 3
- Stage 4

## BEAST Study

### Symptoms

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<th>Symptom</th>
<th>Adenosine Only</th>
<th>Adenosine + Exercise</th>
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<tr>
<td>Flushing</td>
<td>11 (58%)</td>
<td>6 (32%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>11 (58%)</td>
<td>4 (21%) *</td>
</tr>
<tr>
<td>Headache</td>
<td>8 (42%)</td>
<td>2 (11%) *</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>5 (26%)</td>
<td>4 (21%)</td>
</tr>
<tr>
<td>Lightheaded</td>
<td>5 (26%)</td>
<td>4 (21%)</td>
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<td>Arm discomfort</td>
<td>4 (21%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Abd. discomfort</td>
<td>3 (16%)</td>
<td>2 (11%)</td>
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<tr>
<td>Throat discomfort</td>
<td>4 (16%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (5%)</td>
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*Significant difference*

Elliott et al, JNC 2000

BEAST Study
Effect on Perfusion Scores

Patients ordered for pharm stress offered chance to undergo exercise stress test

Patients who didn’t reach THR with exercise randomized to:
- 1) regadenoson at peak exercise
- 2) exercise stopped and regadenoson given at rest

Patients who reached target were injected with sestamibi
BERST Results

- 125 of 200 patients were able to achieve THR
- All stress protocols were well tolerated without significant adverse events
- No differences in the extent of perfusion abnormalities, image quality, rate of referral to cath
- Beta blocker use and diabetes were predictors of failure to reach THR

Regadenoson pharmacologic stress for myocardial perfusion imaging: A three-way comparison between regadenoson administered at peak exercise, during walk recovery, or no-exercise

Randall C. Thompson, MD, Harshal Patil, MD, Elaine C. Thompson, BA, Gregory S. Thomas, MD, MPH, Mohammed Al-Amoodi, MD, Kevin F. Kennedy, MS, Kevin A. Bybee, MD, A. Iain McGhie, MD, James H. O’Keefe Jr., MD, Lisa Oakes, BSN, and Timothy M. Bateman, MD

• 531 patients randomized to:
  – regadenoson at peak exercise (ExPeak-Reg)
  – regadenoson during walking/recovery (ExRec-Reg)
  – regadenoson at rest (Rest-Reg)
Regadenoson 3-way Comparison

• Greater BP changes in the ExPeak-Reg group than the other groups
• Chest discomfort, nausea, dizziness and interfering abdominal tracer activity were less common in both exercise groups
• Conclusion: No advantage of administering regadenoson at peak exercise rather than during walk recovery
Active 65 yo man with h/o HTN on metoprolol and amlodipine with occasional exertional chest pain; HR 64 at rest

• I would BERST him!
What is ImageGuide?

The ImageGuide Registry is the first cardiovascular registry of its kind, focusing on SPECT and PET imaging studies.

The primary purpose of the registry is quality improvement, and it provides a platform to collect data in nuclear imaging labs to measure quality, safety, and efficiency.
ImageGuide provides the framework to support a community of practices committed to patient centered imaging, practice transformation, and innovation through ongoing data collection and quality improvement.
The Future of Health care

“No outcomes, no income.”

David Nash, MD, founding dean of Thomas Jefferson University’s School of Population Health in Philadelphia
Why Participate in a Registry?

In the current evolving healthcare environment, in which reimbursement is increasingly tied to performance, it is essential that medical professionals partake in quality improvement initiatives to:

- Advance clinical practice
- Enhance patient care
- Justify services to payers and policymakers
### How Does ImageGuide Differ From Other Registries?

<table>
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<th><strong>ImageGuide</strong></th>
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<td>is an effective solution for imaging physicians</td>
</tr>
<tr>
<td>ImageGuide does not duplicate any existing system</td>
</tr>
<tr>
<td>Data collection is focused on SPECT and PET studies</td>
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#### Efficient Quality Improvement

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<thead>
<tr>
<th><strong>Other office based registries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>require data submission for every patient encounter</td>
</tr>
<tr>
<td>ImageGuide requires data collection only on nuclear imaging tests</td>
</tr>
</tbody>
</table>

#### Representation of Nuclear Cardiology

<table>
<thead>
<tr>
<th><strong>Other hospital-based registries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>may not apply to physicians not performing invasive procedures</td>
</tr>
<tr>
<td>ImageGuide captures a greater level of granularity on nuclear imaging studies</td>
</tr>
</tbody>
</table>
Summary

• There is new imaging technology that can benefit patients
• Hopefully PET can become more widely adopted
• There are approaches that can be taken to improve the patient experience without expensive new technology
• We actually have new uses for nuclear imaging!
• Combine pharmacologic stress with exercise
  – You’ll like it
  – Your patients will certainly like it
Thank You!