Myocardial Perfusion SPECT
In Ischemic Heart Disease

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I have no conflict of interest to declare
Physiologically assessing coronary stenosis


12 dogs, diatrizoate, LCx occlusion

$^{99m}$Tc-macroaggregates

Dynamic exercise
Vasodilators
Dobutamine
Myocardial SPECT imaging in diagnosis


➢ Values derived from “unselected” populations
Diagnostic performance of functional tests

- Exerc ECG
  - Sensitivity: 66
  - Specificity: 89
  - 147 st
  - 24074 pts

- Stress echo
  - Sensitivity: 81
  - Specificity: 77
  - 46 st
  - 5615 pts

- SPECT
  - Sensitivity: 77
  - Specificity: 80
  - 51 st
  - 9954 pts
Myocardial SPECT in risk stratification

Russell RR, Zaret BL. Curr Probl Cardiol 2006;31:557-629

Annual event rate (%)
Myocardial SPECT in clinical decision making


10,627 pts
1.9 yrs f-u
Suspected CAD
Cardiac death
Economic outcomes in suspected CAD (SPARC)

Hlatky MA, et al. JACC 2014;63:1002-1008

2-year downstream costs

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cost</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>$6,647</td>
<td>5.5%</td>
</tr>
<tr>
<td>CCTA</td>
<td>$4,909</td>
<td>0.7%</td>
</tr>
<tr>
<td>SPECT</td>
<td>$3,965</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

SPECT had the lowest cost and better cost-effectiveness ratio

1,703 pts
41 centers
# Multimodality Appropriate Use Criteria


## Symptomatic

<table>
<thead>
<tr>
<th>Pretest Probability</th>
<th>Exercise ECG</th>
<th>SPECT MPI</th>
<th>Stress echo</th>
<th>Stress CMR</th>
<th>Calcium scoring</th>
<th>CCTA</th>
<th>Invasive Angiogr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Low</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>M</td>
<td>R</td>
<td>M</td>
<td>R</td>
</tr>
<tr>
<td>Intermediate</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>M</td>
<td>R</td>
<td>M</td>
<td>R</td>
</tr>
<tr>
<td>Intermediate</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>High</td>
<td>M</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>A</td>
</tr>
<tr>
<td>High</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>R</td>
<td>M</td>
<td>A</td>
</tr>
</tbody>
</table>

Low pretest probability of CAD
ECG interpretable AND able to exercise

Low pretest probability of CAD
ECG uninterpretable OR unable to exercise

Intermediate pretest probability of CAD
ECG interpretable AND able to exercise

Intermediate pretest probability of CAD
ECG uninterpretable OR unable to exercise

High pretest probability of CAD
ECG interpretable AND able to exercise

High pretest probability of CAD
ECG uninterpretable OR unable to exercise
Multivessel disease pattern?


<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>(%)</td>
<td>58%</td>
<td>95%</td>
</tr>
</tbody>
</table>
Low risk patient? Vessel identification-patency?

LIMA-LAD patent
LAD 80% prox, 100% mid
LCx 100% prox
RCA 100% prox
SVG-PDA 100%
Myocardial perfusion SPECT in prognosis


Hard event rates (%)

- Normal: 2%
- Mild: 8%
- Mod/Severe: 12%

Frequency of hard events (%)

- Normal-Mild: 48%
- Moderate-Severe: 52%
Myocardial SPECT imaging in all-cause death


11,880 pts
8.7 yrs f-u
Suspected -known CAD
MI <10%
All cause death
Myocardial SPECT in clinical decision making

## Comparative definition of significant ischemia


<table>
<thead>
<tr>
<th>Test Type</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Event rate (Death, MI)</strong> 5%/year</td>
<td></td>
</tr>
<tr>
<td><strong>Nuclear testing</strong></td>
<td>≥ 10% ischemic myocardium</td>
</tr>
<tr>
<td><strong>Echo stress</strong></td>
<td>≥ 19% (3/16 segments) dysfunctional myocardium</td>
</tr>
<tr>
<td><strong>CMR</strong></td>
<td>≥ 13% (4/32 segments) with perfusion deficit</td>
</tr>
<tr>
<td></td>
<td>≥ 19% (3/16 segments) dysfunctional myocardium</td>
</tr>
</tbody>
</table>
Software packages in quantification


![Diagram showing software packages in quantification with percentages:](image)
Extent of ischemia measurements

Intra-observer trainee

Intra-observer experienced
### Extent of ischemia intra-observer reproducibility

<table>
<thead>
<tr>
<th>Observation 1</th>
<th>no</th>
<th>small</th>
<th>moderate</th>
<th>large</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>small</td>
<td>0</td>
<td>17</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>moderate</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>large</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

* kappa = 0.906 (p<0.001)  
  absolute agreement 94%
Optimal medical therapy ± PCI in SIHD

In the COURAGE nuclear substudies, SPECT ischemia did not predict adverse events and did not alter treatment effectiveness.
Fractional Flow Reserve guided PCI

Tonino PM, et al. NEJM 2009;360:213-224


20 sites, 1005 pts, 1 yr f-u
Death, MI, repeat revascularization

28 sites, 1220 pts, stopped <1 yr
Death, MI, urgent revascularization
SPECT ischemia in suspected CAD 1991-2009


39,515 diagnostic tests
Angiographic CAD by time

ETT vs MPI in low-intermediate risk women

SPECT in suspected CAD in women

- Higher risk SPECT: 1.9%
- Low probability: 2.7%
- Intermediate probability: 0%
➢ Offer 64-slice (or above) CT coronary angiography if:
• clinical assessment indicates typical or atypical angina
• clinical assessment indicates non-anginal chest pain but there are ST-T changes or Q waves.

➢ Offer non-invasive functional testing
• for people with known CAD, when there is uncertainty if chest pain is caused by myocardial ischaemia.
Cardiac CT as first line test for CAD


<table>
<thead>
<tr>
<th>SCOT-HEART and PROMISE trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td><strong>Randomisation</strong></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td><strong>Control</strong></td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
</tr>
<tr>
<td><strong>CAD, &gt;50% stenosis (n)</strong></td>
</tr>
<tr>
<td>42% (752)</td>
</tr>
<tr>
<td>All-cause death/non-fatal MI(^a) (n)</td>
</tr>
<tr>
<td>Cardiac death/non-fatal MI(^b) (n)</td>
</tr>
<tr>
<td>Non-fatal MI(^a) (n)</td>
</tr>
<tr>
<td>Revascularisation (n)</td>
</tr>
<tr>
<td>Cardiac death/non-fatal MI in revascularisation group (n)</td>
</tr>
</tbody>
</table>
Hybrid cardiac SPECT/CT


- 53% ischemia with CAC \( \geq 400 \)
- 25% ischemia with CAC < 400
Revascularization outcomes

- Healthier population - More effective drugs

- Imaging issues
  - Relative perfusion
  - Regional abnormalities and coronary anatomy?
  - Balanced ischemia
  - From populations to individuals

- Does “reversibility” equal “ischemia”?
- Can there be “ischemia” without reversibility?
- Is there a better way to quantify ischemia than the SSS?
- Is there a benefit in revascularization of territories with “normal” perfusion and high-grade disease on angiography?
Novel SPECT Technologies and Approaches

- New SPECT Systems
- Low-Dose Imaging Protocols
- Attenuation Correction
- Two-Position Imaging
- Motion Correction
- Developments in Automation Processing
- Quantification of Ischemic Change
- Simultaneous Dual-Isotope Imaging
- Stress-Only Imaging
- Hybrid CT Angiography - SPECT
- Dynamic Flow with SPECT
- Early EF Assessment
- Machine Learning
<table>
<thead>
<tr>
<th>First author</th>
<th>Tracer</th>
<th>Year</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taki J</td>
<td>Sestamibi</td>
<td>2001</td>
<td>For CFR values &lt;2.5, increase in tracer retention and CFR showed a good linear correlation</td>
</tr>
<tr>
<td>Sugihara H</td>
<td>Tetrofosmin</td>
<td>2001</td>
<td>CFR values of 1.47 in healthy subjects, 1.08 in infarcted regions and 1.11 in ischemic regions</td>
</tr>
<tr>
<td>Ito Y</td>
<td>Sestamibi</td>
<td>2003</td>
<td>CFR estimated by dynamic acquisition correlated well with the values measured by PET</td>
</tr>
<tr>
<td>Storto G</td>
<td>Sestamibi</td>
<td>2004</td>
<td>Good correlation between sestamibi CFR values and those measured by intravascular Doppler ultrasound in patients undergoing PCI</td>
</tr>
<tr>
<td>Ben-Haim S</td>
<td>Sestamibi</td>
<td>2013</td>
<td>the MPR index is lower in patients with perfusion defects and in regions supplied by obstructed coronary arteries</td>
</tr>
<tr>
<td>Apostolopoulos J</td>
<td>Tetrofosmin</td>
<td>2015</td>
<td>sMBFi managed to discriminate certain CAD subgroups (normal MPI/ischemia/scar/scar and ischemia) more efficiently than CFR</td>
</tr>
</tbody>
</table>
Myocardial Perfusion Reserve (CZT cameras)


Angiography: LAD prox occlusion, RCA severe atherosclerosis
Coronary Flow Reserve in risk assessment


Annual mortality (%)
CFR and FFR in CAD

FFR and CFR in risk stratification


No. at risk:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Time (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR &gt; 0.80 / CFVR ≥ 2.0</td>
<td>78 75 71 66 57 48</td>
</tr>
<tr>
<td>FFR &gt; 0.80 / CFVR &lt; 2.0</td>
<td>10 3 3 2 2 2</td>
</tr>
<tr>
<td>FFR ≤ 0.80 / CFVR ≥ 2.0</td>
<td>48 44 40 35 31 24</td>
</tr>
</tbody>
</table>
Benefit of revascularization with a low PET CFR


*Adjusted for pretest clinical score, LV ejection fraction, LV ischemia, and coronary artery disease prognostic index.

1 CFR denotes coronary flow reserve: high (≥1.6), low (<1.6).

2 Early revascularization strategy denotes revascularization with percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), or neither (No Revasc), within 90 days of noninvasive imaging.
Nuclear Cardiology and Ischemia at crossroads

➢ era of low event rates
➢ updated models of risk
➢ CAD beyond the paradigm of obstructive epicardial disease
➢ translate group CRT data to individual patient management