Imaging for Ischaemia
*Insights from Gated Scintigraphy* in the era of Cardiac CT

Dr Felix Keng
MBBS, FRCP (Edin, Lond), FAMS,
Dip CBNC, MMed (Int Med), FAPSC
Director, Nuclear Cardiology
National Heart Centre
Singapore
Adjunct Asst Professor
YLL School of Medicine
National University of Singapore

How To Convince Physicians to Use MPI instead of CTA

Dr Felix Keng
MBBS, FRCP (Edin, Lond), FAMS,
Dip CBNC, MMed (Int Med), FAPSC
Director, Nuclear Cardiology
National Heart Centre
Singapore
Adjunct Asst Professor
YLL School of Medicine
National University of Singapore

Stress Myocardial Perfusion Imaging (Nuclear SPECT) NHC 1984-2008

- Cardiac PET
- Cardiac MRI
- 16 MDCT
- 64 MDCT
- 320 MDCT

In the beginning…….
First pass radionuclide ventriculography

- Cardiac transit time using intravenous radionuclide injection
  - Blumgart et al, 1926, Beth Israel Hospital

Survival based on first pass exercise LVEF

- < 30
- 30-39
- 40-49
- < 60
Equilibrium Blood Pool Radionuclide Ventriculography

One year mortality post MI based on pre-discharge LVEF by NIH (Multicenter Postinfarction Research Group) N Eng J Med 1983;309:331

Equilibrium blood pool imaging with ECG-gating
Green et al, 1970s, NIH

Post MI patients

Equilibrium Blood Pool Radionuclide Ventriculography

Perfusion Imaging: Use of Flow Tracers

Uptake of tracer proportional to flow

Linear Relationship Between the Distribution of Thallium-201 and Blood Flow in Ischemic and Non-ischemic Myocardium During Exercise Nielsen AP, et al Circ 1980;61:797

Ischaemic Cascade


Coronary Flow Reserve

From Gould et al Physiologic basis for assessing critical stenosis Am J Cardiol 35:91,1974
Myocardial Perfusion Imaging

Planar thallium imaging - Pohost, Strauss, 1977

Exercise stress → Gamma camera → Myocardial images

Tracer

Stress ECG Peak Exercise

Rest ECG

Case Example

Pohost, Strauss, 1977

Planar thallium imaging - Pohost, Strauss, 1977

Stress ECG Peak Exercise

Rest ECG

Case Example

Pohost, Strauss, 1977

Accuracy of Exercise ECG vs SPECT for Detection of CAD

- 10,627 patients with no prior MI or revascularization who underwent exercise or adenosine MPI and were followed up (90.6% complete; mean: 1.9±0.6 years).
- Patients classified as undergoing revascularisation (671) within 60 days or medical therapy (9956)
- Cardiac death
  - 1.4% overall
  - 2.8% in revascularization group
  - 1.3% in medical therapy group (P=0.0004)


Stress Imaging identifies patients who will benefit from Intervention

- Sensitivity
- Specificity
- Accuracy

p=0.0004
Perfusion Imaging predicts risk of Infarction & Cardiac Death

- 2,686 patients undergoing rest thallium/stress MIBI gated SPECT for evaluation of CAD
- Most powerful predictor of cardiac death was post-stress gated SPECT LV Ejection Fraction
- Best predictor of MI was amount of ischemia (summed difference score, SDS)

Prediction of MI by Stress Induced Ischemia (SDS)

Prediction of Cardiac Death by Gated Perfusion SPECT

Cardiac Death rate (% per year) as function of amount of ischemia and EF

Patients with EF >50% or EF 30% - 50%

Patients with EF < 30%

Post-stress EF

EF > 50%
EF = 30-50%
Low risk (<1%)
Intermediate risk (2-3%)
Medical therapy
Revascularisation
High Risk (>4%)

Gold standard: > 50% stenosis on angiography
Test detects ischaemia, not atherosclerosis
Which is more important?
Why not go direct to coronary angiography?

Limitations of Stress Testing

Sensitivity 85 to 90% : 10-15% of patients “missed”

Adapted from O'Rourke RA et al ACC/AHA expert committee on EBCT. Circ 2000;102:126
Progression of Atherosclerosis
Glagov Phenomenon

- Normal artery
  - No plaque
  - No stenosis

- Compensatory expansion
  - Lumen constant, no stenosis

- Expansion limit
  - Onset of stenosis

Adapted from Berman ASNC 2004

Multi-Detector CT for calcium scoring and CT angiography of the coronary arteries

64 slice:
- Sensitivity: 70-98%
- Specificity: 85-95%
- PPV ??
- NPV 95-99%

Myocardial Perfusion Imaging
for the detection of myocardial ischemia (which may kill you in the long run)

- Sensitivity: 80-85%
- Specificity: 75-80%

Amount of ischemia correlates well with likelihood of myocardial infarction (Sharir 2001)

Well-established
Stress test detects obstructive CAD

But does not detect early non flow-limiting disease, which can still progress and cause infarction

Potential role for techniques that can detect early atherosclerosis for prevention of disease?

Stress test detects obstructive CAD

But early atherosclerosis is undetected

CASE EXAMPLE

Options:
1. Strict risk factor control
   Proven to reduce events
2. Stress testing +/- imaging
   Is there ischaemia?
   If so, consider intervention
   If not, medical therapy
3. Coronary angiography
   Consider cath/intervention
   “All lesions can rupture & cause MI”
   “Don’t take any risk!”

Does the degree of stenosis predict the likelihood of plaque rupture and infarction?

Data from serial angiographic studies

Because less-severe plaques by far outnumber severely obstructive plaques, most infarctions are from rupture of less severe plaques (29 vs 10) Nobuyoshi et al.

Myocardial Infarction often occurs in lesions that are not severely stenotic

Data from serial angiographic studies.

Myocardial infarction evolves most frequently from plaques that are only mildly to moderately obstructive months to years before infarction.
Does ischaemia matter? Can it help us decide which lesions to treat? Or should we treat all lesions?

Conventional approach:
• PTCA only >70% lesions with demonstrated flow-limitation or ischaemia on stress testing.

"Plaque sealing" - "Pre-emptive" PCI to prevent rupture
Requirements:
• Identifying which plaque will rupture (or treat all)
• Proving that PCI can reduce event rate

Identifying which plaque will rupture

Not easy
Treat all lesions?
"Plaque sealing"?

Can pre-emptive intervention prevent events?
Ideally it should be evidence-based.

In preventive action:
Primum Non Nocere
(First Do No Harm)

Is flow limitation/ischaemia important?
Fractional flow reserve (FFR) derived from coronary pressure measurement is an indicator of the hemodynamic effect of a stenosis. FFR < 0.75 indicates hemodynamic significance.

FFR < 0.75 indicates flow limitation/ischaemia
DEFER study
325 patients planned for PTCA

**FFR > 0.75**
- No ischaemia
- PTCA deferred (91)

**FFR < 0.75**
- Ischaemia
- PTCA performed (144)

**FFR < 0.75**
- PTCA performed (90)

Is there benefit from PCI in the absence of ischaemia? Can plaque rupture be prevented?

**Event rate at 2 years:**
- 11% in the defer group
- 17% in the perform group (P=NS)
- 23% in the reference group (FFR<0.75, PTCA performed)

After 2 years of follow-up, symptomatic improvement was greater in the defer group than the perform group (P<0.02).

In patients with FFR >0.75, no benefit of PTCA was present, either in terms of adverse events or in functional class.

Pre-emptive “plaque sealing” does not appear to prevent events.

**Considerable overlap in stenosis severity despite differing FFR value:**

**Difficult to predict haemodynamic effect from degree of stenosis**

**Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis. A Randomized Trial.**
Bech et al. Circ 2001;103

**Go direct to angiography or use stress imaging to select patients for intervention?**
**Economics of Non-Invasive Diagnosis Study (ENDS)**

- Observational study comparing 2 diagnostic strategies:
  - 5,423 patients referred for Direct Cardiac Catheterization
  - 5,826 patients referred for Myocardial Perfusion Imaging with Selective cardiac catheterization.

- 2 groups matched for pretest likelihood of CAD
- Comparisons of clinical outcome and costs
- 7 hospitals (Cedars-Sinai, Cleveland Clinic, Duke University, Hartford Hospital, Roger Williams Medical Centre, St Louis VA and St Louis University Health Sciences Center)
- Shaw et al. JACC 1999;33:661-9
Go direct to angiography or use stress imaging to select patients for intervention? Economics of Non-Invasive Diagnosis Study (ENDS)

Comparison of 2 diagnostic strategies

Direct Cardiac Catheterization
5,423 patients

Myocardial Perfusion Imaging with Selective cardiac catheterization
5,826 patients

Long term Clinical Outcome & Costs

Includes long term event rate, costs of misdiagnoses

Long term Clinical Outcome & Costs

Compared to direct cath, myocardial perfusion imaging followed by selective cath associated with 30-40% lower revasc rate and equivalent death or Ml rate.

Case Example: Disease Progression
Intervention is useful, but has its limitations

M/66/Politician

• 1978 - Heart attack #1 (age 37)
• 1984 - Heart attack #2
• 1988 - Heart attack #3
• 1988 - Coronary bypass surgery
• 2000 - Heart attack #4
• 2000 - Coronary stent placed
• 2000 - Impaired heart function
• 2001 - Unstable angina
• 2001 - Coronary angioplasty
• 2001 - Cardiac defibrillator implanted

Compared to direct cath, myocardial perfusion imaging followed by selective cath associated with 30-40% lower cost, equivalent clinical outcome.
Changing the Diagnostic Paradigm

Stress imaging detects severe disease
But early atherosclerosis is undetected
Role of CT angiography or calcium score?

Intervention reduces events in high risk group
Intervention not proven to reduce events
Aggressive medical therapy reduces risk

CASE EXAMPLE

Patient: JB
M/52/Caucasian
Lipids: LDL 3.3 mmol/L
Asymptomatic but went for health screening and CT angiography elsewhere:
"Moderate plaque in left anterior descending artery"
"Doctor, what should I do?"

Options:
1. Strict risk factor control
   Proven to reduce events
2. Stress testing +/- imaging
   Is there ischaemia?
   If so, consider intervention
   If not, medical therapy
3. Coronary angiography
   All lesions can rupture & cause MI
   Consider cath/intervention
   "Don’t take any risk!"

CASE EXAMPLE

Patient: CCH
M/48/Chinese
Symptomatic heart failure, LVEF 25%
Suspected coronary artery disease

Options:
1. Medical +/- device therapy
   Proven to reduce events
2. Viability testing
   Is there viability?
   If so, cath & revascularise
   If not, medical or transplant
3. Coronary angiography
   “He is young, revascularise regardless of viability”
   “Don’t take any risk”

Options:
1. CABG
2. PTCA
3. CABG

Heart Failure: Predicting who will benefit from intervention

Use viability testing or revascularise all patients?

24 studies involving 3,088 patients with viability testing and mortality outcomes.

Use Viability Testing or Revascularise all patients?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Viable</th>
<th>Revasc</th>
<th>Non-Viable</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viable</td>
<td>12</td>
<td>14</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Mortality (%/year)</td>
<td>15</td>
<td>16</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>X2=1.43</td>
<td></td>
<td></td>
<td>+23.0%</td>
<td>P&lt;0.23</td>
</tr>
</tbody>
</table>

Mortality (%/year)

-79.6% p<0.0001

Insights from Stress Scintigraphy: Anatomy & Physiology

Information needed for CAD management:

- Is there coronary artery disease?
  - If so, there is a risk of plaque rupture and infarction.
  - Advise diagnosis, start antiplatelet, lipid lowering
- What is the severity of disease?
  - Is there ischemia and/or viability?
  - If so, symptoms and/or prognosis may be improved by PCI or CABG

Imaging for IHD: Current Options

Future trends

- Minimal
- Moderate
- Severe

Progression of CAD
**Diagnostic Options for Detection of CAD**

- **Low Likelihood of CAD**
  - Asymptomatic, no risks
  - Asymptomatic, but abnormal result or multiple risks

- **Moderate Likelihood of CAD**
  - Atypical symptoms
  - Risk factors ++
  - ECG/Trop -ve

- **High Likelihood of CAD**
  - Typical Symptoms
  - ECG/Trop +ve

**Stress ECG**
- Stress Echo
- Stress SPECT
- MDCT

**Coronary Angiogram**
- Normal
- Moderate
- Severe

**Control**
- Risk factor
- Control

**Diagnostic Options for Detection of CAD**

- **High Risk**
  - Typical Symptoms
  - ECG/Trop +ve

- **Moderate Risk**
  - Atypical symptoms
  - Risk factors ++
  - ECG/Trop -ve

- **Low Risk**
  - Asymptomatic
  - no risks

**Asymptomatic**
- but abnormal result or multiple risks

**Typical Symptoms**
- ECG/Trop +ve

**Atypical Symptoms**
- Risk factors ++
- ECG/Trop -ve

**Stress ECG**
- Stress Echo
- Stress SPECT
- MDCT

**CT**
- Nuclear

**Echo**
- CT
- Nuclear

**CTA vs Nuclear**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CTA</th>
<th>Nuclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation Dose</td>
<td>Higher?</td>
<td>Lower?</td>
</tr>
<tr>
<td>Function</td>
<td>Anatomy</td>
<td>Physiology</td>
</tr>
<tr>
<td>Sub-clinical Disease</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Price</td>
<td>↑Expensive</td>
<td>↓Expensive</td>
</tr>
<tr>
<td>Contrast</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>LV function/wall motion</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Calcium</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Stress Data</td>
<td>Contrast Allergy</td>
<td>Stress Complications</td>
</tr>
<tr>
<td>Complications</td>
<td>Renal Complications</td>
<td>Dipyridamole Effects</td>
</tr>
<tr>
<td></td>
<td>Extravasation</td>
<td>↑Imaging Problems</td>
</tr>
<tr>
<td></td>
<td>↑Imaging Problems</td>
<td>↓Imaging Problems</td>
</tr>
</tbody>
</table>

**Remember to be an advocate:**
- Not for the test....
- Not for the treatment.....
- Not for the technology.....
- But for the patient.

**Multiple Imaging Options in Cardiology**

- **Echo**
- **CT**
- **Cath***
- **Nuclear***
- **MRI***

**How has Cardiac CTA Impacted Nuclear Cardiology?**

- **Predict the future?**
  - Yes
  - No

- **Or image it with confidence?**
  - Yes
  - No

**Nuclear Cardiology**

- **The whole landscape**

- **Where does Nuclear Cardiology stand in Present Day Cardiology?**