SPECT CT
Current Status and Future Direction
Nuclear Cardiology

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No conflict of interest
Contents

• Coronary artery disease
• CT for AC (attenuation correction)
• CT for CAC (Coronary artery calcification)
• CT for CTCA (CT coronary angiography)
• The future?
Spectrum of Coronary Artery Disease

Stary Classification of Atherosclerotic Plaques

<table>
<thead>
<tr>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Va,b,c</th>
<th>VIa,b,c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Early</td>
<td>Lipid rich</td>
<td>Internal rupture</td>
<td>Calcified shell</td>
<td>Calcified plaque</td>
</tr>
<tr>
<td>Fatty streaks</td>
<td>White blood cells</td>
<td>Red blood cells</td>
<td>Lipid rich plaque</td>
<td>Scar</td>
<td>White blood cells</td>
</tr>
<tr>
<td>Inflammation and calcification</td>
<td>Platelets and fibrin</td>
<td>Scar development with calcification</td>
<td>Vulnerable Rupture</td>
<td>Thrombus</td>
<td>Myocardial Obstructive infarction</td>
</tr>
</tbody>
</table>

MDCT

MPS/DSE
Where can Nuclear Cardiology help?

- Perfusion
- Function
- Metabolism
- Cellular Injury
- Interstitial dysfunction
- Neurohormonal receptor function
Attenuation correction

• None
• Line source
• CT
AC with CT

- Reliable
- Accurate
- Quality

- Good resolution
  - Any isotope
  - Any protocol
Coronary artery calcification (CAC)

- CAC surrogate for atherosclerosis
- CAC represents approx 1/5 overall atheroma burden
- CT best technique for detecting CAC
What does CAC do for you?

- Amount of CAC correlates with amount of atheroma
- CAC >400 usually indicates significant disease
- Distribution of CAC does not correlate with angiographic severity of disease
- Most useful in intermediate risk patients
CAC and Framingham in asymptomatic patients


Predicted 7-Year Event Rates from Cox Regression Model for CHD Death or Nonfatal Myocardial Infarction for Categories of FRS or CACS

The receiver operating characteristic curves illustrate FRS alone or plus coronary artery calcium score (CACS). Areas under the curves are 0.63 for FRS alone, 0.68 for FRS plus CACS. \textit{P.001 for the comparison between} the 2 areas.
CAC and prognosis

Budoff et al. JACC 2007; 49:1860-70
Limitations of CAC

• Overall low event rates in asymptomatic
• No pharmacological therapy to reduce CAC
• Potential harm from false-positive tests
• Radiation risks in asymptomatic population
• CAC result does not motivate the patient
• Soft plaque not detected
• Stability of plaque not characterised
CT for CAC

- Well established
- Independent prognostic value
- Easy to do
- Early detection of atherosclerosis

- Combined with SPECT?
MPS and CAC

- Normal SPECT with abnormal CAC
  - Can predict MVD
- More useful in patients with higher prevalence of CAD
  - DM, elderly
- Increasing CAC = increasing ischaemia
  - CAC >400; 20% likelihood of ischaemia
  - CAC >100 important in DM, strong FH IHD
SPECT & CAC in pre-op non cardiac surgery

Ghadri et al. JNM 2012; 53:1081–1086
Lung ca. PET/CT incidental finding

Image courtesy of Prof Fergus Gleeson, Oxford
SPECT/CT and PET/CT
CTCA and ischaemia

- CTCA stenosis <50% ≈ normal MPS (NPV >90%)
- CTCA stenosis ≥50% ≠ abnormal MPS (PPV <50%)
  (Nicol et al. JNC 2008;15:311-8)

- Anatomy and ischaemia are complementary

- Refined plaque scoring techniques likely to be superior in predicting positive MPS
  - Location, distribution, composition etc
CTA and prognosis

Min et al. JACC 2007; 50: 1161-70
### CTA plaque characteristics with potential prognostic value

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis severity</td>
<td>&gt;50% or &gt;70% intraluminal stenosis</td>
</tr>
<tr>
<td>Location</td>
<td>Left main, LAD</td>
</tr>
<tr>
<td>Composition</td>
<td>&quot;Mixed&quot; composition; low attenuation density (&lt;30 Hounsfield units)</td>
</tr>
<tr>
<td>Remodeling</td>
<td>Positive remodelling</td>
</tr>
<tr>
<td>Overall plaque burden</td>
<td>Cumulative measure of plaque extent and severity</td>
</tr>
<tr>
<td>Distribution</td>
<td>Cumulative measure of plaque diffusivity</td>
</tr>
</tbody>
</table>
Cardiac hybrid imaging in a patient with a single coronary artery originating from the right sinus of Valsalva

Ghadri et al. EHJ. doi:10.1093/eurheartj/ehr273
Incremental diagnostic accuracy of hybrid SPECT/CT coronary angiography in a population with an intermediate to high pre-test likelihood of CAD (n=98)

Schapp et al. EHJ. doi:10.1093/ehjci/jes303
Rapid cardiac hybrid imaging with minimized radiation dose for accurate non-invasive assessment of ischemic coronary artery disease

Herzog et al. IJC 2011; 153: 10–13
Impact of cardiac hybrid SPECT/CT imaging on choice of treatment strategy in coronary artery disease (n=318)

Pazhenkottil et al. EHJ. doi:10.1093/eurheartj/ehr232
Prognostic value of cardiac hybrid imaging integrating SPECT with CCTA (n=355)

Pazhenkottil et al. EHJ. doi:10.1093/eurheartj/ehr047
MPS – Inferior ischaemia

Stress

Rest
Added value of fusion imaging
The Future?
18F – NaF PET and valve disease

- 18F – NaF – novel biomarker of disease activity
- Inflammation and calcification both increased in aortic valve stenosis compared to controls and with increasing disease severity
- ? target therapies towards calcification

Dweck et al. Circ 2012;125:76-86
Myocardial metabolism

Normal myocardial metabolism
  Free fatty acids provide up to 90% ATP
  Glycolysis provides the rest
During periods of ischaemia
  Myocardial metabolism switches to glucose
Final common pathway
  TCA ("Krebs") cycle
All pathways can be imaged with nuclear techniques
Glucose metabolism

$^{18}$F FDG PET
- Glucose analogue
- Phosphorylated and trapped intracellularly

Preservation of FDG uptake defines hibernation within hypoperfused myocardium
- Patients with advanced CAD impaired LV function
FFA/TCA metabolism

**FFA**

\[ ^{123}\text{I}-\text{BMIPP SPECT} \]

-Decreased uptake = ischaemic myocardium
-“Ischaemic memory” of remote resolved ischaemia

\[ ^{11}\text{C}-\text{palmitate PET} \]

**TCA**

\[ ^{11}\text{C}-\text{acetate PET} \]
**Cellular injury**

$^{99m}\text{Tc}$-annexin V
- Binds to phosphatidylserine (apoptotic cells)
- Ongoing research in cardiac transplantation
- Uptake associated with ↓LVEF/NYHA in HF patients

$^{111}\text{In}$-antimyosin
- Uptake with loss of sarcolemmal integrity
- Allograft rejection, DCM, myocarditis
- 92% NPV for myocarditis
Noninvasive detection of apoptosis in acute myocardial infarction using Annexin V
Interstitial dysregulation

Limited potential in myocardial fibrosis
Murine model of $^{99m}$Tc tracer for MMPs

Angiogenesis more promising
  Initiated by VEGF
  Modulated by $\alpha_v\beta_3$ integrin (RGD)
  PET/SPECT agents for VEGF / $\alpha_v\beta_3$ integrin
SPECT and angiogenesis

Late Gd – CMR

Tc99m-tetrofosmin

Tc99m-RGD
Neurohormonal receptor dysfunction

- Autonomic dysfunction ↑ cardiac death
- Increased sympathetic tone is directly linked to disease progression, prognosis, and risk of sudden cardiac death (SCD).
- Myocardium that is viable but sympathetically denervated has a greater propensity for arrhythmogenesis
- PET
  - $^{11}\text{C}$-hydroxyephedrine ($^{11}\text{C}$-HED)
  - $^{11}\text{C}$-epinephrine
Cardiac $m$IBG

- $^{123}$I-$m$IBG – images sympathetic nerves
  - Norepinephrine analogue
- Planar imaging
  - Heart/mediastinum ratio calculated
- Lower cardiac uptake = poorer outcome
- Abnormal H/M <1.6

![Images showing normal innervation and NYHA II, NYHA IV]

Normal innervation
H/M 2.2

NYHA II
H/M 1.7

NYHA IV
H/M 1.1
Myocardial Blood Flow (MBF)

- SPECT – CT
- CZT detectors
- Measure MBF/CFR
  - “absolute flow”
  - No more “balanced ischaemia”
  - Reduced uncertainty
  - Reduce the need for PET-CT
Summary

• Overview of cardiac SPECT CT
• Evidence
• Diagnosis/Prognosis
• Technological developments
Working together for the patient?

Fraser et al. EHJ 2006: 27: 1750-1753
“Medicine is a science of uncertainty and art of probability”

Sir William Osler
Annual Scientific Meeting
Monday 2nd December 2013
NHLI
London

www.bnecs.org.uk