Hybrid imaging of the heart

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Hibrid imaging of the heart

- ECG
- systole
- diastole
- perfusion
- innervation
- metabolism

GATED SPECT/CT or GATED PET/CT

SPECT/CT or PET/CT

O$_2$

time
Cardiac Image Fusion from Stand-Alone SPECT and CT: Clinical Experience

Oliver Gaemperli\textsuperscript{1}, Tiziano Schepis\textsuperscript{1}, Ines Valenta\textsuperscript{1}, Lars Husmann\textsuperscript{2}, Hans Scheffel\textsuperscript{2}, Victor Duerst\textsuperscript{1}, Franz R. Eberli\textsuperscript{1}, Thomas F. Luscher\textsuperscript{1}, Hatem Alkadhi\textsuperscript{2}, and Philipp A. Kaufmann\textsuperscript{1,3}

\textbf{FIGURE 2.} (A) Stress and rest perfusion polar maps of SPECT-MPI study show mixed basal anterolateral defect and reversible interapical perfusion defect (arrowheads). (B and D) Fused SPECT/CT images reveal total occlusion of LAD and subtotal occlusion of first diagonal branch (DA1), which are confirmed by conventional CA (C). Anterolateral perfusion defect is caused by lesion of partially calcified small intermediary branch (IM); however, this vessel is not well visualized by CA.
• **PET vs SPECT in Cardiology**
  – Better spatial resolution
  – Higher contrast resolution
  – Higher diagnostic accuracy
  – Cuantification of molecular imagen
    Cuantification of flow (mL/min/g)
  – Assessment of LV function
    • Stress and Rest
  – Higher efficiency (short half-life RF)
• **PET/CT Indications in Cardiology**
  - Coronary artery disease
    • Perfusion
    • Viability
    • Atherosclerosis
  - Cardiac Insufficiency
    • Cardiac Innervation
Perfusion: $^{82}\text{Rubidium PET}$

"Cardiac positron emission tomography and the role of adenosine pharmacologic stress"

Rubidium-82:
- A generator product
- Potassium analogous
- Similar kinetic to TI-201 (lower hepatic and bowel uptake)
- T1/2: 76 sc
- Infusion in 30 sc
- Pharmacologic stress

Bateman TM et al, Am J Cardiol. 2004
<table>
<thead>
<tr>
<th>Coronary Territory</th>
<th>Rest MBF (mL/min/g)</th>
<th>Stress MBF (mL/min/g)</th>
<th>CFR (Stress/Rest MBF)</th>
<th>Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>0.83</td>
<td>0.89</td>
<td>1.47</td>
<td>75%</td>
</tr>
<tr>
<td>LCX</td>
<td>0.86</td>
<td>1.01</td>
<td>1.17</td>
<td>100%</td>
</tr>
<tr>
<td>RCA</td>
<td>0.64</td>
<td>0.66</td>
<td>1.03</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Di Carli S et al, 2009*
Perfusion: $^{82}$Rubidium PET

“Value of vasodilator left ventricular ejection fraction reserve in evaluating the magnitude of myocardium at risk and the extent of angiographic coronary artery disease: a $^{82}$Rb PET/CT study.”

- PET stress-rest: normal
- Gated PET: LVEF decreases in stress
- CT: calcified lesion in the left main stem → Bypass

Dorbala S et al, J N Med. 2007
Cardiac PET / CT

”PET/CT is greater than the sum of its parts”

**PET Value:**
- Perfusion
- Myocardial Flow Quantification
- Coronary Reserve
- Endotelial Disfunction
- Viability
- Function (LVEF)

**CT Value:**
- Patient positioning
- Attenuation correction
- Calcium score
- CT coronary angiography
- Left ventriculography

*Di Carli et al, J N Cardiol 2008*
*Dorbala S et al, J N Med. 2007*
Cardiac PET / CT

Di Carli et al, J Nuc Med 2007
Perfusion: $^{82}$Rubidium and $^{13}$N-Ammonia

“Reproducibility and Accuracy of Quantitative Myocardial Blood Flow Assessment with $^{82}$Rb PET: Comparison with $^{13}$N-Ammonia PET.”

$^{82}$Rubidium

$^{13}$N-Ammonia

El Fakhri G et al, JNM 2009
PET: $^{13}$N-Ammonia

43-year-old man, type 1 Diabetes Mellitus, CAD (DA and Cx) → Stent Stress ECG (+) and Echocardiography: diffuse hypokinesia.
Perfusion: Radiotracers

Rubidium-82:
- A generator product
- Potassium analogous
- Similar kinetic to Tl-201 (lower hepatic and bowel uptake)
- T1/2: 76 sc
- Infusion in 30 sc
- Pharmacologic stress

15O-Water:
- A cyclotron product
- T1/2: 2 min
- RF diffusible (C15O Inhalation)

Rubidium-82:
- A generator product
- Potassium analogous
- Similar kinetic to Tl-201 (lower hepatic and bowel uptake)
- T1/2: 76 sc
- Infusion in 30 sc
- Pharmacologic stress

13N-Ammonia:
- A cyclotron product
- T1/2: 9.96 min
- Active myocardial extraction (hepatic and bowel uptake)
- “Bolus” injection
- Pharmacologic stress

15O-Water:
- A cyclotron product
- T1/2: 2 min
- RF diffusible (C15O Inhalation)
Kinetic Modeling of $^{15}$O-water

Improved accuracy & precision by including LV/RV spillover

$$R(t) = PTF \cdot MBF \cdot C_a(t) \otimes e^{MBF \cdot t} + V_a \cdot C_a(t)$$

$$R(t) = PTF \cdot MBF \cdot C_a(t) \otimes e^{MBF \cdot t} + V_a \cdot C_a(t) - V_{RV} \cdot RV(t)$$

Appropriate modeling enables accurate quantitation of MBF, which can be standardized among institutions.

- lida et al., Circulation 78: 104-115; 1988
- lida et al JNM 33: 1669-1677; 1992
- Harms HJ et al., EJNMI 38: 930–939, 2011
Myocardial Perfusion: $^{18}$F-BMS

Evaluation of the Novel Myocardial Perfusion Positron-Emission Tomography Tracer $^{18}$F-BMS-747158-02 ($^{18}$F-Flurpiridaz)

Higher availability ($^{18}$F)
Better image quality
Higher contrast resolution
High first pass extraction fraction
Good correlation with flow

First-pass uptake in isolated rabbit hearts
BMS747158 vs $^{201}$TI and $^{99m}$Tc-sestamibi

- BMS747158 (n=4)
- $^{201}$TI (n=3)
- $^{99m}$Tc-sestamibi (n=3)

* Indicates $p<0.05$

Phase II Safety and Clinical Comparison With Single-Photon Emission Computed Tomography Myocardial Perfusion Imaging for Detection of Coronary Artery Disease

Flurpiridaz F 18 Positron Emission Tomography
Daniel S. Berman, MD,* Jamshid Maddahi, MD,† B. K. Tamarappoo, PhD, MD,* Johannes Czernin, MD,† Raymond Taillefer, MD,‡ James E. Udelson, MD,§ C. Michael Gibson, MD,¶ Marybeth Devine, BS,‖ Joel Lazewatsky, PhD,‖ Gajanan Bhat, PhD,‖ Dana Washburn, MD‖
Los Angeles, California; Montréal, Quebec, Canada; and Boston and North Billerica, Massachusetts
PET: CAD diagnosis


Inclusion Criteria:
• PET as a diagnostic test for CAD
• Coronariography (≥50% diameter stenosis)

- 19 studies (1985 - 2007)
- 1442 patients
- prevalence 77%

Analysis by patient:
S = 0.92 (95% CI: 0.90 - 0.94)
Sp = 0.85 (95% CI: 0.79 - 0.90)
LR+ = 6.2 (95% CI: 3.3 - 11.8)
LR- = 0.11 (95% CI: 0.08 - 0.14).

- MPI-PET is cost-effective in CAD diagnosis
- MPI-PET provides prognostic value (severe cardiac events)

Nandalur KR et al, Acad Radiol 2008
PET perfusion: indications

- Pharmacologic stress
- Obese Patients (BMI > 30)
- Women
  - AC and spatial resolution
- Patients with Diabetes Mellitus
  - Multivessel coronary disease
<table>
<thead>
<tr>
<th>Myocardial Viability</th>
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</thead>
<tbody>
<tr>
<td><strong>Function</strong></td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Disfunction</td>
</tr>
<tr>
<td>Reversible</td>
</tr>
<tr>
<td>Reversible (Surgery)</td>
</tr>
<tr>
<td>Irreversible</td>
</tr>
<tr>
<td><strong>Perfusion</strong></td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

- Normal: N
- Stunned: Disfunction (Reversible)
- Mismatch: Disfunction (Reversible (Surgery))
- Necrosis: Disfunction (Irreversible)

Mismatch Disfunction Reversible (Surgery)
“PET is the gold standard to determine the viability of heart tissue for revascularization. PET can determine whether bypass surgery or transplant is the appropriate treatment.”

https://www.crump.ucla.edu
Myocardial Viability Testing and Impact of Revascularization on Prognosis in Patients With Coronary Artery Disease and Left Ventricular Dysfunction: A Meta-Analysis

- 24 studies
- 3088 patients
- EF = 32% ± 8%
- Follow-up 25 months

There was no measurable performance difference for predicting revascularization benefit between the three testing techniques.

Allman KC et al, JACC 2002
Cardiac Inervation

Langer O, EJNM 2002
## Cardiac Inervation

<table>
<thead>
<tr>
<th>PROCESS</th>
<th>RADIOTRACER</th>
<th>PARAMETERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport and storage into axoplasmic vesicles</td>
<td>$^{18}$F-fluorodopamine</td>
<td>Peak myocardial concentration</td>
</tr>
<tr>
<td>Presynaptic uptake-1 and storage</td>
<td>$^{11}$C-HED (hydroxyephedrine)</td>
<td>Retention fraction Volume distribution</td>
</tr>
<tr>
<td>Presynaptic uptake-1 and storage and metabolism</td>
<td>$^{11}$C-EPI (epinephrine)</td>
<td>Retention fraction Volume distribution</td>
</tr>
<tr>
<td>Postsynaptic adrenoceptor density</td>
<td>$^{11}$C-CGP (4-(3-t-butylamino-2-hydroxypropoxy)-benzimidazol-1)</td>
<td>Cardiac Bmax</td>
</tr>
<tr>
<td>Postsynaptic adrenoceptor density</td>
<td>$^{18}$F-fluorocarazolol</td>
<td>Cardiac Bmax</td>
</tr>
<tr>
<td>Postsynaptic muscarinic receptor density</td>
<td>$^{11}$C-MQNB (methylquinuclidinyl benzylate)</td>
<td>Cardiac Bmax</td>
</tr>
<tr>
<td>Presynaptic uptake-1 and storage</td>
<td>$^{123}$I-MIBG</td>
<td>Retention fraction</td>
</tr>
</tbody>
</table>

Carrió I, JNM 2001
Cardiac Transplant. Reinnervation

"Evaluation of sympathetic nerve terminals with $^{11}$C-epinephrine and $^{11}$C-hydroxiephedrine and positron emission tomography"

Munch G et al, Circulation 2000
"Reduced myocardial carbon-11 hydroxyephedrine retention is associated with poor prognosis in chronic heart failure"

Cardiac Sympathetic Nervous System Imaging
LMI 1195 (F-18)

Short axis

Long axis

Non-human primates

Yu/Robinson
Prognostic Value

EAC crónica-Disfunción ventricular

Viabilidad miocárdica

Recuperación de la función

Evolución del paciente
Mejoría de los síntomas de IC

PERSPECTIVAS DE FUTURO

Investigación  Radiofármacos  Instrumentación
Dual Gated Cardiac PET

Minipig

Patient

"Imaging techniques for the assessment of myocardial hibernation"

European Society of Cardiology

Eur Heart J 2004
Underwood SR
Bax JJ
vom Dahl J
Henein MY
Rossum AC
Schwarz ER
Vanoverschelde JL
van der Wall EE
Wijns W
“PET/MRI hybrid imaging: devices and initial results.”

“Assessment of the metabolism of cardiac tissue with the tracer 18F-FDG allows the identification of viable myocardium.

Simultaneous acquisition of wall motion and myocardial anatomy can be performed using MRI.

The combination allows the exact attribution of functional aspects to underlying regional metabolic conditions/viability.”

“Integrated Whole Body MR/PET Imaging. First Examples of Clinical Application”
A. Drzezga; A.J. Beer; S. Furst; S. Ziegler; S.G. Nekolla; M. Schwaiger
Technische Universität München, Klinik und Poliklinik für Nuklearmedizin, Klinikum rechts der Isar, Munich, Germany
Noninvasive procedure that allows to study perfusion, function, metabolism and myocardial innervation.

<table>
<thead>
<tr>
<th>PET images reflected, depending on the RF used:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Coronary blood flow</td>
</tr>
<tr>
<td>• Myocardial metabolism of glucose, fatty acids, etc.</td>
</tr>
<tr>
<td>• The myocardial oxygen consumption</td>
</tr>
<tr>
<td>• Neuroreceptor status</td>
</tr>
<tr>
<td>• Inflammatory activity of atherosclerotic plaques</td>
</tr>
</tbody>
</table>

The approved clinical indication is the detection of myocardial viability in patients with chronic coronary artery disease and poor ventricular function.