Experience with Rubidium-82 PET Myocardial Perfusion Scintigraphy in Clinical Routine and Research

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Myocardial Perfusion Imaging
Myocardial Perfusion Imaging

**MRI**

**SPECT**

- Thallium
- Tc-99m Sestamibi, Tetrafosmin

**PET**

- O-15 Water, N-13 Ammonia
- **Rb-82 Chloride**
Why perform Rubidium MPI?

• The patient
  – Stress and Rest Imaging in less than 30 minutes
  – Reduced Radiation Burden

• The technologist

• The scientist
  – Potential for Quantitative Flow Measurements

• The clinician
  – Quick and complete picture of gross and detailed flow
  – Potential to combine with simultaneous CT investigations
  – Rapid Access

• The accountant
  – Cost effective for high throughput centres
Rubidium Chloride

- Monovalent potassium analog
- *Partially* extracted by myocardial cells via Na/K adenosine triphosphatase pump
- Extraction is inversely and non-linearly proportional to perfusion
Production of Rubidium-82

• Rubidium-82 produced from Strontium-82 generator
  – Rb-82 T$_{1/2}$ 75 Seconds
  – Sr-82 T$_{1/2}$ 25.55 Days

• Rubidium given as an i.v. infusion
  – 60 mCi maximum (2D Mode)
  – 35 seconds maximum
  – Approximately 30 mls
  – 3D Mode give 40mCi

• Generator lifetime 4 weeks
Production of Rubidium-82
Production of Rubidium-82
Production of Rubidium-82

• QC of product
  – Column Wash
  – Breakthrough Test (Sr82/Sr85)
  – Infusion System Calibration
Production of Rubidium-82

Interference with PET QA
Rubidium Imaging
Basic Imaging Protocol

Scout (Topogram)

Rest CTAC

Rest PET

Adenosine Stress

Stress PET

Stress CTAC
Rubidium PETCT Protocol - CT

- Scout
  - AP view
  - 120 kVp, 10 mA
- CT
  - 140 kVp, 50 mA, 0.8s Pitch 1.75
  - Assessment of calcification and AC
- Often need two CT’s for attenuation correction
  - Can capture heart end-systole
The need for Attenuation Correction
The mis-registration problem
Misregistration of Emission and CTAC

Software related reduction techniques
Misregistration of Emission and CTAC

Protocol related reduction techniques

- Cine CT (Pan et al, Med Phys 2006)
  - Series of CTs performed over 6 seconds
  - Low mA - CT AC use only (5mGy)
Rubidium PETCT Protocol - PET

- Rb82 infusion - 60 mCi (or no more than 35 seconds)
- Data acquired 2D in list mode (BGO)
- Acquisition
  - Delay before imaging (2:30 stress, 2:40 rest)
  - 5 minute (8 bin) gated data for both stress and rest
  - Additionally dynamic data for flow estimation
- Reconstruction OSEM
- Display GE Myometrix
  - QGS difficulties with base
Rubidium PETCT Protocol - PET

- Rb82 infusion - 60 mCi (or no more than 35 seconds)
- At end of generator, delivery of 60mCi results in too much decay of delivered tracer

- Delay before imaging (2:30 stress, 2:40 rest)
- To start earlier adds more bloodpool counts than myocardial counts
Processing Rb-82 data

• Base plane difficult to define
• Standard QGS, ECToolbox, 4D-MSPECT make assumptions on data reconstruction
• Better solutions
  – QPET
  – GE CardIQPhysio (Adw)
  – GE Myometrix (Xel)
ECG Gating

- ECG Gated Bins
  - SPECT (16 bins)
  - PET (8 bins)
- Better temporal resolution  → More accurate LVEFs

- Rubidium data – noisy
- To calculate LVEF  → Segment Myocardium

<table>
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<tr>
<th>ECG Bins</th>
<th>Segmentation Failure (%)</th>
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<td>6</td>
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<td>8</td>
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<td>16</td>
<td>45</td>
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Rubidium PETCT Protocol
Adenosine Stress Test

- 6 minute stress test
- Second iv access for Adenosine
- Rubidium infusion starts two minutes into Adenosine

- We don’t use Dobutamine with Rubidium imaging
The result

- Scout (Topogram)
- Rest CTAC
- Rest PET
- Adenosine Stress
- Stress PET
- Stress CTAC
Advanced Imaging Protocols

Ca Score + MPI

- Rest Ca Score (CTAC)
- Rest PET
- Adenosine Stress
- Stress PET
- Stress CTAC

MPI + CT CA

- Scout (Topogram)
- Stress CTAC
- Adenosine Stress
- Stress PET
- Rest PET
- Rest CTAC

Ca Score + MPI + CT CA

- Scout (Topogram)
- Stress CTAC
- Rest PET
- Rest CTAC
- Rest Ca Score (CTAC)
Rubidium MPI + CT CA

- Scout (Topogram)
- Stress CTAC
- Adenosine Stress
- Stress PET
- Rest PET
- Rest CTAC
- Rest CT CA
Radiation Protection Issues

• Patient Dose
  – PET – 5.5 mSv (2 x 60 mCi)
    • TI-201 – 14 mSv (80 MBq)
    • Tc-99m Tetrafosmin – 12 mSv (2 x 800 MBq)
    • Tc-99m Sestamibi – 16 mSv (2 x 800 MBq)
  – CT CA - 6-12 mSv
    • Newer technology allowing lower (sub 5mSv) doses

• Staff Dose
  – Less than that seen with Tc-99m MPI
  – Patient managed remotely from control room
Quantitative myocardial perfusion imaging (Q MPI)
What do we mean by Q MPI
Why perform Quantitative MPI?

• Triple vessel disease
  – Standard imaging compares relative flow
  – Balanced disease may appear normal

• Microcirculatory disease
  – Can’t visualise microcirculation
  – Use Myocardial Blood Flow (MBF) or Coronary Flow Reserve (CFR) as an indicator

\[ CFR = \frac{\text{Stress MBF}}{\text{Rest MBF}} \]
Why perform Quantitative MPI?

• Detection of early disease
• Disease progression
  – Treatment, or lifestyle changes e.g. Smoking, diet
• Evaluation of endothelial function
  – Regulatory mechanism for changes in flow
Quantitative analysis of coronary endothelial function with generator-produced $^{82}$Rb PET: comparison with $^{15}$O-labelled water PET

Keiichiro Yoshinaga • Osamu Manabe • Chietsugu Katoh • Li Chen • Ran Klein • Masanao Naya • Robert A. deKemp • Kathryn Williams • Rob S. B. Beanlands • Nagara Tamaki
Endothelial Dysfunction in Systemic Lupus Erythematosus: Evaluation with $^{13}$N-Ammonia PET

Erick Alexánderson$^{1,2}$, Juan M. Ochoa$^2$, Rodrigo Calleja$^2$, Juan G. Juárez-Rojas$^3$, John O. Prior$^4$, Rodrigo Jácome$^2$, Edgar Romero$^2$, Aloha Meave$^{1,2}$, and Carlos Posadas-Romero$^3$

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**TABLE 4**

Endothelial Function Indices

<table>
<thead>
<tr>
<th>Index</th>
<th>SLE</th>
<th>Healthy control</th>
<th>$P$</th>
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<tbody>
<tr>
<td>Endothelium-dependent</td>
<td>1.18 ± 0.55</td>
<td>1.63 ± 0.65</td>
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<td>vasodilatation index</td>
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<tr>
<td>MFR</td>
<td>2.41 ± 0.59</td>
<td>2.73 ± 0.77</td>
<td>0.20</td>
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<tr>
<td>Corrected</td>
<td>3.37 ± 0.64</td>
<td>4.11 ± 1.02</td>
<td>0.02</td>
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<tr>
<td>Uncorrected</td>
<td>18 ± 55</td>
<td>63 ± 65</td>
<td>0.04</td>
</tr>
<tr>
<td>%ΔMBF</td>
<td>0.37 ± 0.35</td>
<td>0.71 ± 0.63</td>
<td>0.06</td>
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</tbody>
</table>
Models
Rubidium Chloride

• Monovalent potassium analog
• *Partially* extracted by myocardial cells via Na/K adenosine triphosphatase pump
• Extraction is inversely and non-linearly proportional to perfusion
Three Compartment Model

Physiological Model (almost)
[heterogeneous flow rates, variable capillary level, axial diffusion]

$PS_{\text{cap}}$ – Permeability surface products of capillaries
$PS_{\text{cell}}$ – Permeability surface product of cell walls
$V_i$ – Fractional volumes of compartments
$F$ – specific volume blood flow
Two Compartment Model

Plasma and capillary compartments are lumped

Assumption: They both equilibrate rapidly
One Compartment Model

Uptake and washout parameters only
Which Compartmental Model?

- Rubidium PET data is noisy
- Three and two compartment models difficult to implement
  - Wavelet based noise reduction can help
  - Needs \textit{a priori} values of some model parameters
- One compartment model
  - Good reproducibility at rest and stress
  - Better fit than two compartment model
- Two and one compartment model
  - \( K_1 \) dependent on both blood flow and extraction
  - Requires non-linear extraction correction
Non-linear extraction model

Lortie M 2007: EJNMMI
Alternatives

**Factor Analysis (GFADS)**
(El-Fakhiri et al 2005)

- GFADS used to estimate LV and RV TACs
  - Estimate k1 and k2
- Accounts spillover from LV and RV blood
- More robust to noise

**Retention Model**
(Herrero et al 1990)

- Division of stable uptake in myocardium by integrated blood input gives k1
- Derive flow from k1
- Assumes tracer doesn’t leave myocardium during acquisition
Technical Issues
High Count Rates

• Randoms, Deadtime & Decay Correction
  – Very high count rates (>3 Mcps) at start of dynamic acquisition
  – Short half-life with relatively long frames can cause decay correction problems
Spillover and partial volume effects

- **Rb-82**
  - Positron energy 3.4 MeV
  - Average Range 5.9 mm
- **Myocardial Wall**
  - 8-12 mm thickness
Software
Imagen Q (CVIT, Kansas: Bateman et al)
Carimas (Turku PET Centre, Knuuti et al)
Dynamic Quantitative MPI

Results Display

Stress/Rest = CFR

Coronary Flow Reserve!

Innovation is in our genes.
Molecular Imaging
Case Studies
Indications

• 2 previous PCIs to Cx and LAD.
• New onset chest pain ?cause.
• Not exertional but previous episodes have been atypical.
PET findings

- There is no inducible ischaemia during adenosine vasodilatation.
- There has been good revascularization.
- The proximal LAD disease is not flow limiting.
CT Findings
CT findings

- **LEFT MAIN STEM**: Normal origin and course. The LMS is plaque free.
- **LEFT ANTERIOR DESCENDING**: There is diffuse heterogenous plaque of the proximal LAD, causing mild to moderate (up to 50%) stenosis. The mid-LAD stent is patent. The distal LAD is plaque free, albeit small calibre. The 1st & 2nd DIAGONALs are plaque free.
- **LEFT CIRCUMFLEX**: The proximal LCx is plaque free. The stent in the AV segment is patent, and takes an OBTUSE MARGINAL course. The distal OM is plaque free. The distal LCx is plaque free, albeit small calibre.
- **RIGHT CORONARY**: Normal origin and course. There is a small eccentric calcified plaque in mid-RCA, not causing any stenosis. The RCA is dominant, supplying the PDA which is plaque free.
Flow Findings
Summary

• MPI with Rubidium PET/CT:
  – is fast and effective (Stress and Rest < 30 min)
  – allows simple add-ons for CT CA, or Ca Score
  – Can provide true quantitative data to assess balanced disease, early disease, and/or compromised micro-circulature and endothelial function
Acknowledgements

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