Measurement of Absolute Myocardial Perfusion in Patients with CAD Using 3.0 Tesla CMR: Validation against PET

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Background
Cardiovascular Magnetic Resonance (CMR) has established itself as a technique for the assessment of myocardial perfusion in patients with coronary artery disease (CAD). Assessment of myocardial perfusion with CMR at 3.0 Tesla (3T) may provide improved diagnostic accuracy over 1.5T CMR due to improved signal-to-noise ratio (SNR) and contrast to noise ratio (CNR). Quantitative measurements of myocardial blood flow (MBF) using CMR perfusion combined with model independent deconvolution have been validated against radioactive microspheres in animals. Recently, signal quality has been shown to be superior using higher field strengths which may offer an advantage for estimating MBF in areas of ischemia. No study to date has evaluated the accuracy and reproducibility of absolute MBF quantification using 3T CMR in humans compared to the gold standard positron emission tomography (PET) measurement.

Aim
To validate absolute measurement of MBF in humans with 3T CMR using PET as the gold standard and assess their respective sensitivities and specificities for the detection of significant stenosis.

Methods
Nineteen patients with CAD [at least 1 stenosis > 50% on quantitative coronary angiography (QCA)] and 10 age and gender matched healthy subjects (HS) underwent 3T CMR and PET using oxygen 15-labelled water on two different days. MBF was assessed at rest and during adenosine stress with both techniques. The diagnostic x-ray angiogram served as the reference standard in defining the degree of coronary stenosis. Diameter of reference and stenotic coronary arteries were measured by Quantcor Coronary Analyis software (Siemens Medical Solutions).

CMR Protocol:
- Subjects were scanned at 3T (Trio, Siemens, Medical Solutions). Three short-axis images acquired at every heartbeat using a T2-weighted saturation recovery fast-gradient echo sequence.

- Gadolinium (Gadodiamide) was administered at a dose of 0.04 mmol/kg bodyweight (IV injection rate 6 ml/s), followed by a 15 ml saline flush at the same rate during the sixth minute of stress. The same sequence was repeated 20 minutes after stress to acquire baseline (rest) perfusion.

- Endocardial and epicardial contours were traced using QMass software (version 6.2.3, Medis, Netherlands) and corrected manually for displacements (Figure 1). The ventricle was divided into 16 segments. Segmental MBF was determined by deconvolution of the signal intensity (SI) curves with an arterial input function measured in the left ventricular blood pool. Blood pool signal was corrected for saturation using calibration curves.

PET Protocol:
- Subjects underwent PET scanning with PET 962 (HR) scanner (Siemens, Knoxville, Tennessee) using oxygen 15-labeled water (H215O).

- Myocardial images were directly generated from the dynamic H215O study. Regions of interest (ROIs) were drawn within the left ventricular myocardium, right ventricular cavity and left atrium and projected onto the dynamic H215O images to obtain tissue activity curves (TACs) (Figure 1). Myocardial and blood TACs were then generated from the dynamic image and fitted to a single-tissue compartment tracer kinetic model to give values of MBF (ml/min/g).

- PET and CMR images were co-registered using anatomical landmarks in a 16 segment model.

- Receiver-operator characteristic (ROC) analyses for all 16 segments were employed to determine the diagnostic performance of each imaging modality for the detection of CAD.

- Data are mean ±SD

Results
Study Population
The baseline characteristics of the population are outlined in Table 1. Single-vessel disease was found in 68% of patients whilst 2-vessel disease was found in 32%. The LAD was the most commonly affected vessel (43%), followed by the CX (30%) and the RCA (26%).

In patients, resting MBF was 0.94 ± 0.03 ml/min/g by PET and 0.64 ± 0.17 ml/min/g by CMR. Hyperemic MBF was 1.95 ± 0.84 ml/min/g by PET and 1.86 ± 0.64 ml/min/g by CMR (Figure 2).

Conclusions
• There is an excellent agreement between PET and 3T CMR for the measurement of resting MBF both in patients and HS.
• The limits of agreement are broader under stress conditions mainly in HS.

• In comparison with PET and QCA, the ROC analyses indicate a reasonable diagnostic performance of 3T CMR.

• Myocardial contrast enhancement saturation with a 0.04 mmol/kg dosage of contrast may result in an underestimate of MBF which is more noticeable during stress.

Table 1: Baseline Characteristics of Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>Age (years)</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>10/9</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28 ± 4</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>130 ± 15</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80 ± 10</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>70 ± 15</td>
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</table>

Figure 3: Blinded-Armon Plot of Resting and Hyperemic MBF in Healthy Subjects

In HS, resting MBF was 1.01 ± 0.25 ml/min/g by PET and 0.78 ± 0.22 ml/min/g by CMR. Hyperemic MBF was 3.24 ± 0.86 ml/min/g by PET and 2.9 ± 0.86 ml/min/g by CMR. (Figure 3).

Sensitivity and specificity for detecting stenosis ≥50% were 83% and 82% for PET (threshold 1.85) and 61% and 78% for CMR (threshold 1.73). Sensitivity and specificity for detecting stenosis ≥70% were 87% and 77% for PET (threshold 1.69) and 60% and 73% for CMR (threshold 1.73) (Figure 4).