Rapid-acquisition myocardial perfusion scintigraphy (MPS) on a novel gamma camera using multipinhole collimation and miniaturized cadmium–zinc–telluride (CZT) detectors: prognostic value and diagnostic accuracy in a ‘real-world’ nuclear cardiology service

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Aims
To study the prognostic value of rapid-acquisition adenosine stress—rest myocardial perfusion scintigraphy (MPS) on a gamma camera using multipinhole collimation and cadmium—zinc—telluride (CZT) detectors. The secondary aim was to assess the diagnostic accuracy of the technique compared with invasive coronary angiography.

Methods and results
Retrospective analysis of 1109 consecutive patients undergoing MPS in a routine clinical setting on a high-efficiency multipinhole gamma camera. MPS acquisition, performed with a standard injection of 550 MBq of ⁹⁹mTc-tetrofosmin, required a mean (±SD) scanning time of 322 ± 51 s. The hard cardiac event rate at a median (inter-quartile range) follow-up of 624 (552–699) days was 0.4% (95% CI 0.1–1.1) in patients with no significant perfusion abnormality versus 6.8% (95% CI 4.3–10.7%, P = 0.001) in those with an abnormal scan. In a sub-group of 165 patients, comparison with obstructive coronary artery disease on X-ray angiography gave a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for rapid-acquisition MPS of 84% (95% CI 74–91), 79% (95% CI 68–87), 82% (95% CI 72–89), 81% (95% CI 70–89), and 82% (95% CI 73–89), respectively.

Conclusions
MPS performed on a CZT solid-state detector camera with multipinhole collimation is an evolutionary development that provides reliable prognostic and diagnostic information, while significantly reducing image acquisition time.

Keywords
myocardial perfusion scintigraphy • high efficiency • cadmium—zinc—telluride • multipinhole collimation • coronary artery disease

Introduction
Myocardial perfusion scintigraphy (MPS) with single-photon emission computed tomography (SPECT) is an established and widely available technique in the assessment of stable patients with suspected or known coronary artery disease (CAD), providing important diagnostic and prognostic information, as acknowledged by current evidence-based imaging algorithms.¹ ² There is a wealth of clinical evidence, accrued over the last 30 years, that has shown that a normal stress—rest MPS confers a < 1% annual probability of a major cardiac event, and it is widely accepted that MPS provides a cost-effective, non-invasive imaging technique in appropriately
selected patients with stable chest pain. However, MPS is often limited by cumbersome imaging protocols, lack of standardization, technical artefacts, and variable diagnostic accuracy. Moreover, recent comparative studies with newer modalities that are not yet universally available in the routine clinical setting, such as cardiac magnetic resonance imaging, have shown the diagnostic superiority of these new techniques over MPS, using angiographically detected CAD as the reference standard. In a quest to reduce imaging time, simplify imaging protocols, and improve image quality, while maintaining the clinical, prognostic, and diagnostic relevance as well as the accuracy of MPS, newer dedicated cardiac gamma cameras have been designed that utilize novel, highly sensitive and efficient semiconductor solid-state detector designs, instead of traditional sodium iodide crystals coupled with photomultiplier tubes.

One such important technical advance is represented by the incorporation of cadmium–zinc–telluride (CZT) solid-state detectors into dedicated cardiac gamma camera designs utilizing multipinhole collimation. The GE Discovery NM 530c (GE Healthcare Ltd., Chalfont St Giles, Buckinghamshire, UK) uses miniaturized solid-state CZT detectors and multipinhole collimators that are serially aligned around the patient and focused on the heart, which creates a highly sensitive and efficient stationary detector ring that has eliminated the need for camera movement around the patient. Several recent studies have shown that it is possible to utilize this technology to substantially reduce imaging time (by a factor of 3–5), and/or reduce the effective radiation dose, while maintaining or improving the diagnostic accuracy of MPS. However, clinical experience with the Discovery NM 530c CZT camera with multipinhole collimation remains limited, with some recently emerging data showing the prognostic value and diagnostic accuracy of MPS obtained using this novel system.

The primary aim of the present study was to evaluate the prognostic significance of MPS data obtained with a multipinhole CZT cardiac gamma camera using rapid imaging protocols in one of the largest reported cohorts of patients, to date, in a ‘real-world’ nuclear cardiology service utilizing this novel technology. The secondary aim of the study was to evaluate the diagnostic accuracy of the technique in a large sub-group of patients compared with the reference standard of obstructive CAD as identified by X-ray coronary angiography.

**Methods**

**Study population**

The study population was comprised of 1109 consecutive clinical patients referred from the cardiology clinic for adenosine stress–rest MPS for the evaluation of stable suspected or known CAD. Patients were identified retrospectively from the radiology information system (Computerized Radiology Information System, CRIS; Healthcare Software Systems, Mansfield, UK) over a 10-month period (between June 2010 and April 2011). All patients had a minimum of 12-month clinical follow-up to be eligible for inclusion into the study. Follow-up data were obtained by reviewing electronic hospital records, including CRIS and the digital clinical cardiology database (CardioBase, Magnus Software Solutions, Derby, UK). CardioBase is an electronic archiving system for cardiology clinic letters, discharge summaries from inpatient episodes, investigation results and angiogram reports. It is kept constantly updated and provides reliable information on patient episodes. The CRIS system is automatically updated in the event of patient death, so the incidence of patient mortality within the cohort was readily available from this system. Of the total cohort, there was ambiguity in these records as to whether a major cardiac event had occurred or not in 14 cases, where the patient’s general practitioner was contacted to provide further information, and in the event of a death recorded on the CRIS (n = 18), death certificates were obtained from the Coroner’s office to confirm the precise cause of death. Using this methodology, none of the cases of the N = 1109 cohort were lost to follow-up. The Local Research and Ethics Committee (LREC) was approached with details of this study, and a waiver was issued indicating that a formal ethics application was not required for this retrospective evaluation of a standard clinical service.

**MPS technique and image reconstruction**

All MPS studies were performed on a solid-state detector CZT cardiac gamma camera with multipinhole collimation (Discovery NM 530c, GE Healthcare Ltd.). A 2-day imaging protocol was used for stress and rest imaging, with imaging commencing 45–60 min after a standard dose of 550 MBq of $^{99m}$Tc-tetrofosmin (Myoview, GE Healthcare). Based on the manufacturer guidance and an algorithm obtained from the previously described clinical data from the Discovery NM 530c camera at the authors’ institution, a standard dose of 550 MBq and an imaging time of 200–600 s (dependent on patient weight) were used, which ensure good image quality with short scan times for all patients up to 160 kg. The MPS data were acquired using multipinhole collimation and 19 stationary detectors imaging the heart simultaneously, with no detector motion. Each detector contains 32 × 32 pixelated (2.46 × 2.46 mm) CZT crystals. Electrocardiogram gating was performed routinely at both stress and rest to obtain left ventricular ejection fraction (LVEF), end-systolic and end-diastolic volume, and to assess LV wall motion. A 20% energy window at 140 keV was used. SPECT images were reconstructed in short-axis, horizontal long-axis, and vertical long-axis views using a dedicated iterative reconstruction algorithm, comprising maximum-likelihood expectation maximization, and applying a standard Butterworth filter to the reconstructed slices (3D Butterworth filter with a critical frequency of 0.37 and power of 7). The software package Myovation for Alcyone® (GE Healthcare) was used for image reconstruction. CT-based attenuation correction was not available and prone imaging was not used. All stress examinations were performed with intravenous adenosine infusion (140 μg/kg/min), using a standardized 4-min protocol.

**Analysis and categorization of MPS findings**

All MPS studies were analysed visually in multiple standard planes and semi-quantitatively using the commercially available software (Cedars Quantitative Perfusion SPECT (QPS) and Quantitative Gated SPECT (QGS), Cedars-Sinai Medical Centre, Los Angeles, CA, USA). Clinical reports were issued using a standard clinical template by one of four experienced nuclear cardiology reporters. Cases were categorized qualitatively as ‘normal’, ‘no significant perfusion defect’ (i.e. fixed or reversible perfusion defects constituting <10% of the LV myocardium, with normal left ventricular function, LVEF, and no wall motion abnormality), or ‘abnormal’ (i.e. fixed- or stress-induced reversible perfusion defects constituting >10% of the LV myocardium or wall motion abnormality impaired LVEF) based on standard clinical reporting templates at the authors’ institution. The size, extent, and location of perfusion defects were categorized according to standard LV myocardial segmentation using a 20-segment myocardial model, with a moderate defect accounting for 10–20% of the LV myocardium and a large defect accounting for >20%. Attenuation artefact was defined as fixed (i.e. non-reversible) areas of reduced count density in a typical distribution in males (inferior
Primary and secondary outcome measures

For the primary outcome measure, a ‘hard’ cardiac event was defined as non-fatal myocardial infarction (MI) or cardiac death. Comparison was made between the normal and no significant perfusion group combined versus the abnormal MPS group using the categorization based on quantitative assessment from the initial clinical read-out, as perfusion defects (either reversible or fixed) affecting <10% of the LV myocardium were considered clinically not significant. Further comparison was made using quantitative data and SSS categorization between the hard cardiac event-positive and -negative groups. For the secondary outcome measure, cases were included in the analysis if X-ray coronary angiography had been performed within 8 weeks following the MPS. Secondary outcome analysis was ‘ischaemia-driven’, both in order to reflect clinical decision-making and also to evaluate the accuracy of the initial clinical read-out (which was performed qualitatively using a 10% threshold), so an abnormal MPS for this purpose was defined as showing stress-induced reversible perfusion abnormality affecting >10% of the LV myocardium (i.e. >2 myocardial segments in a standard 20-segment model). Obstructive CAD was defined as ≥70% stenosis of an epicardial or branch coronary artery or ≥50% stenosis of the left main stem on X-ray angiography.

Statistical analysis

All subjects were included in the analysis using the intent-to-treat principle. Comparisons of baseline characteristics between treatment groups were made with the use of Student’s t-test for continuous variables and the χ² test for categorical variables. A binary logistic regression model was constructed using predictor variables shown to be significantly associated with the independent variables on an initial univariate analysis or those deemed of importance a priori from the literature or on the basis of biological plausibility. These included age, gender, cardiovascular risk factors (hypertension, hypercholesterolaemia, diabetes, smoking, prior ischaemic heart disease, and a family history of coronary disease), resting ejection fraction, and extent of reversible or fixed perfusion abnormalities. A block entry method was used. On the initial univariate analysis, age, ischaemic heart disease, resting ejection fraction, MPS results and severity of perfusion defects were deemed significant. Assumptions for running a logistic regression were tested by analysing model summary statistics and coefficients. Residuals were tested for normality to ensure assumptions for the models had been met. Further post hoc testing for linearity of the logit and the absence of significant multicollinearity in the model were performed by checking for interaction terms and performing collinearity diagnostics. Odds ratios computed through logistic regression were also converted to risk ratios using the formula RR = OR × [(1 − P₀) + (P₀ × OR)], as previously described by Zhang and Yu. Time-to-event-free survival was calculated using the Kaplan–Meier method, and patients in the normal and abnormal groups were compared using the log-rank (Mantel–Cox) test. QPS data were analysed as scale data using parametric tests after visual analysis of the data and constructing Q–Q plots. Analyses between those with a hard cardiac event and those without such events were conducted using a Student’s t-test. Time-to-event-free survival was calculated and curve comparisons performed as for the qualitative MPS data. All statistical analyses were performed using SPSS version 17.0 (Chicago, IL, USA). Two-tailed P-values of < 0.05 or 95% confidence intervals (95% CI) that did not include 1.0 were considered to be statistically significant.

Results

Study population

The mean (range) age of the study population was 63 (23–89) years; 52% were male. Cardiovascular risk factors were present in 61% (681 of 1109), with diabetes mellitus in 16% (176 of 1109) of patients and known ischaemic heart disease in 33% (368 of 1109). Clinical indication for MPS was typical anginal pain in 45% (497 of 1109), atypical chest pain in 36% (396 of 1109), and other indications (including pre-surgical risk assessment, functional evaluation of residual coronary artery stenosis, and investigation of unexplained LV dysfunction) in 19% (216 of 1109). The median (inter-quartile range, IQR) follow-up was 624 (552–699) days in the entire cohort, 628 (555–701) days in the normal group and 620 (547–687) days in those with an abnormal MPS result; the difference between groups was not significant. The baseline characteristics of the study population are summarized in Table 1, with comparison between the patients with a normal MPS and those with an abnormal test result.

MPS results

The mean (range) scanning time was 322 (200–420) s. Using qualitative analysis, the MPS was normal in 24% (263 of 1109). There was no significant perfusion deficit in 51% (567 of 1109), of whom 22% (127 of 567) were classified as showing typical attenuation artefacts. Abnormal scans (i.e. >10% of the LV myocardium showing scar or ischaemia ± wall motion abnormality ± abnormal LVEF) were seen in 25% (279 of 1109). Quantitative analysis using QPS data was possible in 1043 of 1109 (94%). This showed that the mean (± SD) scores for all patients who had QPS data available were as follows: SSS 5.4 (± 6.5), SRS 2.2 (± 4.6), SDS 3.1 (± 3.5), defect extent (stress) 7.7 (± 10.0), and defect extent (rest) 5.0 (± 7.9). The distribution of reversible and fixed perfusion defects, based on qualitative assessment, in the patients with abnormal MPS is shown in Figure 1.
non-fatal MIs in this group. Kaplan–Meier event-free survival curves based on qualitative interpretation are demonstrated in Figure 2.

There were highly significant differences in the QPS-generated summed scores between the event-positive and -negative groups with a mean difference (95% CI) of 10.1 (7.3–12.9) for SSS, 6.6 (4.7–8.6) for SRS, 2.8 (1.3–4.3) for SDS, 14.6 (10.4–18.9) for defect extent (stress), and 9.6 (4.5–14.8) for defect extent (rest) (Figures 3 and 4). During the follow-up period, seven patients died of non-cardiac causes, which included fractured neck of femur, pneumonia, pancreatitis, renal failure, and metastatic cancer. Multivariate analysis of prognostic factors derived from rapid-acquisition MPS showed that impaired resting LVEF and the presence of significant inducible perfusion defects (>10% of the LV myocardium) were independent predictors of poor outcome (Table 2).

Secondary outcomes

The sub-group of patients who underwent X-ray coronary angiography within 8 weeks following the MPS included 15% of subjects (165 of 1109), of whom 58% (95 of 165) had an abnormal MPS (i.e. >10% of the LV myocardium showing inducible ischaemia), and significant obstructive CAD was found in 53% (88 of 165) (Figure 5). The

Table 1  Baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N = 1109)</th>
<th>MPS—normal or no significant defect (N = 830)</th>
<th>MPS—abnormal (N = 279)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years—mean (range)</td>
<td>63 (23–89)</td>
<td>63 (23–89)</td>
<td>63 (34–87)</td>
<td>0.62</td>
</tr>
<tr>
<td>Sex, males—n (%)</td>
<td>572 (52)</td>
<td>386 (46)</td>
<td>186 (67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)—mean (SD)</td>
<td>82.0 (17.3)</td>
<td>81.1 (17.5)</td>
<td>84.4 (16.4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Cardiovascular risk factors—total n (%)b</td>
<td>681 (61)</td>
<td>512 (62)</td>
<td>169 (61)</td>
<td>0.72</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>176 (16)</td>
<td>126 (15)</td>
<td>50 (18)</td>
<td>0.28</td>
</tr>
<tr>
<td>Prior ischaemic heart disease</td>
<td>368 (33)</td>
<td>208 (25)</td>
<td>160 (57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Indication for scan—n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anginal chest pain</td>
<td>497 (45)</td>
<td>350 (42)</td>
<td>147 (53)</td>
<td>0.002</td>
</tr>
<tr>
<td>Atypical chest pain</td>
<td>396 (36)</td>
<td>329 (40)</td>
<td>67 (24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Others</td>
<td>216 (19)</td>
<td>151 (18)</td>
<td>65 (23)</td>
<td>0.74</td>
</tr>
<tr>
<td>Stress acquisition time, s—mean (SD)</td>
<td>321.6 (50.9)</td>
<td>321.0 (50.1)</td>
<td>323.4 (53.3)</td>
<td>0.53</td>
</tr>
<tr>
<td>X-ray angiography—n (%)</td>
<td>165 (15)</td>
<td>70 (8)</td>
<td>95 (34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*% figures in parentheses are given for within-group denominators.
*Cardiovascular risk factors evaluated included hypertension, hypercholesterolaemia, diabetes, smoking, prior ischaemic heart disease, and a family history of coronary disease.
*P-values are derived from a Student’s t-test for scale variables and χ² test for categorical variables.
Post-test cardiac catheterization rate was 34% (95 of 279) in the abnormal MPS group and 8% (70 of 830) in the no significant defect group (P < 0.001). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of rapid-acquisition MPS were 84% (95% CI 74–91), 79% (95% CI 68–87), 82% (95% CI 72–89), 81% (95% CI 70–89), and 82% (95% CI 73–89), respectively. There were 14 false-negative cases and 16 false-positives based on the initial MPS clinical read-out. All of these cases were retrospectively reviewed by consensus by the expert panel, blinded to the result of the coronary angiogram, which found that one of the false-negative cases was incorrectly reported by the original reporter, while 13 of 14 cases did not demonstrate any significant perfusion defect. At X-ray coronary angiography in this group, there were three patients with three-vessel CAD, two with two-vessel CAD, one with a critical left main stem stenosis, with the remaining patients demonstrating single-vessel disease with no predilection for any particular vessel. Of the false-positive cases, again only one was incorrectly reported by the original reporter, whereas diffuse heterogeneity in tracer uptake at stress due to unexplained technical factors (37.5%), movement artefact (31%), and incorrect patient positioning (12.5%) were felt by the expert panel to be the underlying cause of false-positive findings in 13 of 16 cases (Figure 6). It should be emphasized that the retrospective expert panel review was for educational and feedback purposes only and did not alter the secondary outcome evaluation, which was based on the original clinical read-out.

**Discussion**

MPS with SPECT is a powerful tool for the prediction of major adverse cardiac events, as the technique provides an assessment of some of the key prognostic indicators for cardiovascular disease, including the degree of LV dysfunction, the volume of infarcted myocardial tissue, and the extent of jeopardized myocardium, as represented by stress-induced reversible perfusion abnormality. Despite the proven strengths of the technique, MPS can be adversely affected by cumbersome protocols, technical artefacts, and variable accuracy for the detection of CAD.9,23 The recent advent of novel cardiac gamma cameras utilizing multipinhole collimation and solid-state detectors heralds an evolutionary technological advance that promises significantly faster acquisition of MPS data, improving patient convenience due to shorter scanning times, while maintaining diagnostic accuracy.13–16,24,25

The present study confirms the ability to perform clinical MPS with a rapid-acquisition time on a gamma camera with multipinhole collimation, with an average (± SD) acquisition time of 322 ± 51 s. This effectively represents a 3-4-fold reduction in scanning time compared with conventional myocardial SPECT and offers greater patient convenience while increasing scanner efficiency. To achieve an optimum balance between scan time, injected activity, image quality, and patient scheduling, the present study used a standard injected activity of 550 MBq of 99mTc-tetrofosmin and varied the acquisition time between 200 and 600 s depending on patient weight, based on previously described methodology.17 Other workers have demonstrated that even shorter acquisition times are possible using this technology (so-called ‘ultrafast’ imaging with 3-min stress and 2-min rest studies), and it may also facilitate lower-dose imaging.13–16

Although there have been several studies evaluating imaging protocols, strategies to reduce effective radiation dose and diagnostic accuracy of the multipinhole CZT camera, there are little emerging
data on the prognostic strength of MPS acquired using this technology. In the largest cohort of patients, to date, with clinical follow-up after rapid-acquisition MPS, Nakazato et al.26 showed in a series of 1613 patients with 79 deaths that a total perfusion deficit of 10% was an independent predictor of all-cause mortality.

The present study of 1109 consecutive patients represents one of the largest cohorts with follow-up to evaluate clinical outcome after rapid-acquisition MPS performed on a multipinhole collimator CZT camera. This study demonstrates that, over a median (IQR) follow-up of 624 (552–699) days, the hard cardiac event rate was 0.4% (95% CI 0.1–1.1) in patients with no significant perfusion abnormality versus 6.8% (95% CI 4.3–10.7) in those with an abnormal scan (P < 0.001). Using multivariate logistic regression, impaired resting LVEF and the presence of inducible ischaemia affecting 10% of the LV myocardium were identified as independent predictors of poor outcome in terms of the hard cardiac event rate. Indeed, the odds of having a hard cardiac event (95% CI) were 6:1 (2–20) with a moderate perfusion defect, and 14:1 (4–45) with a large perfusion defect. Given the low background prevalence of a hard cardiac event in our patient population (<2% of our population), the calculated risk ratios were similar to the odds ratios. For example, patients with a moderate sized reversible perfusion defect were six times as likely to develop a hard cardiac event and 11 times as likely in subjects with large reversible perfusion defects using the calculation described in the Methods section. Similarly, an impaired resting LVEF predicted significantly greater odds of having a hard cardiac event, albeit to a lesser magnitude. Further analysis of quantified data also shows significant differences in QPS-generated scores between ‘event-positive’ and ‘event-negative’ patients. The present study, therefore, provides strong clinical validation of the prognostic relevance of MPS acquired using rapid-acquisition protocols and confirms that, similar to conventional SPECT,6 MPS data obtained using this new technology have the ability to identify subsets of low- and high-risk patients among those presenting with stable chest pain.

Table 2  Multivariate regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE)</th>
<th>Odds ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>−2.93 (1.94)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>0.06 (0.02)</td>
<td>1.06</td>
<td>1.01</td>
<td>1.11</td>
<td>0.02</td>
</tr>
<tr>
<td>Risk factors (N)</td>
<td>0 (0.5)</td>
<td>1.00</td>
<td>0.38</td>
<td>2.63</td>
<td>0.99</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>−0.07 (0.02)</td>
<td>0.93</td>
<td>0.89</td>
<td>0.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate reversible perfusion defect</td>
<td>1.85 (0.58)</td>
<td>6.35</td>
<td>2.04</td>
<td>19.81</td>
<td>0.001</td>
</tr>
<tr>
<td>Large reversible perfusion defect</td>
<td>2.64 (0.60)</td>
<td>14.03</td>
<td>4.34</td>
<td>45.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Small fixed defect</td>
<td>−0.06 (0.76)</td>
<td>0.943</td>
<td>0.21</td>
<td>4.17</td>
<td>0.938</td>
</tr>
<tr>
<td>Moderate fixed defect</td>
<td>1.04 (0.68)</td>
<td>2.83</td>
<td>0.74</td>
<td>10.80</td>
<td>0.129</td>
</tr>
<tr>
<td>Large fixed defect</td>
<td>−0.10 (0.96)</td>
<td>0.90</td>
<td>0.14</td>
<td>5.99</td>
<td>0.917</td>
</tr>
</tbody>
</table>

Model $\chi^2 (1) = 62.45, P < 0.001.$

Figure 5  Patient presenting with atypical chest pain. (A) Stress–rest myocardial perfusion SPECT with mid-ventricular short-axis, vertical long-axis, and horizontal long-axis views, and (B) stress and rest polar maps show profound inducible perfusion defects affecting the apex, adjacent apical segments, and anterior and lateral walls. There was also ventricular cavity dilatation at stress along with stress-induced LV dysfunction. Subsequent X-ray coronary angiogram (C) showed severe three-vessel CAD. There were no suitable targets for percutaneous intervention, and the patient was treated successfully with maximal medical management.
Coronary angiography was performed within 8 weeks following the MPS in 15% (165 of 1109), with significant obstructive CAD found in 53% of these patients (88 of 165). Invasive imaging was undertaken in 34% (95 of 279) of patients with an abnormal MPS and in only 8% (70 of 830) of patients who had a normal study or showed no significant perfusion defect (P < 0.001). The observed intervention rate is slightly higher than that quoted in other comparative studies, which may be explained by the prevalent clinical cardiology practice at the tertiary referral centre where this study was conducted, the types of patients referred, the inclusion of complex patients in the study with known CAD, and also the effects of the recommendations of recent national guidelines in patients with stable chest pain. In fact, the intervention rate is not out of keeping with data from other similarly large patient cohorts evaluated with non-invasive imaging. For instance, the recent multicenter SPARC study showed in a prospective registry of 1703 patients that cardiac catheterization was performed following non-invasive cardiac imaging in 9.6% at 90 days, with obstructive CAD identified in 63% at angiography. It is also recognized that up to 60% of patients with abnormal non-invasive imaging (including MPS and coronary CT) do not, in fact, go on to post-test X-ray coronary angiography, even in those with the most severe test results.

The assessment of diagnostic accuracy of rapid-acquisition MPS, in the present cohort, compared with obstructive CAD on X-ray coronary angiography, relying on qualitative assessment from the initial clinical read-out, showed sensitivity, specificity, PPV, NPV, and accuracy of 84, 79, 82, 81, and 82%, respectively. These compare favourably with data from conventional SPECT, as well as recent data from other cohorts of patients studied using this novel gamma camera technology. For traditional SPECT, using adenosine stress, sensitivity and specificity have been shown to be variable ranging between 75–96 and 38–100%, respectively, with a large meta-analysis of vasodilator stress MPS showing figures of 89% (95% CI 84–93) and 65% (95% CI 54–74), respectively. There are now several series which have compared the accuracy of rapid-acquisition MPS with the ‘gold standard’ of X-ray coronary angiography. In a series of 66 patients, Fiechter et al. showed sensitivity, specificity, PPV, NPV, and accuracy of 87, 67, 92, 53 and 83%, respectively. Duvall et al., in a similar study of 71 patients, showed sensitivity, specificity, and accuracy of 89, 66 and 78%, respectively. Further recent correlation studies include a 309 patient cohort, which showed an accuracy of 82% in women and 88% in men, and a study of 230 patients which showed a high sensitivity of 95%, but a low accuracy of 69%. In recent study by Duvall et al. on the GE Discovery NM 530c where supine and prone imaging were used in a series of 160 patients, the accuracy was found to be similar for both visual and quantified analyses at 69–74%. Interestingly, this is lower than the accuracy demonstrated in this study of 82%, where accuracy analysis was performed solely based on a clinical read-out by an experienced reporter using a 10% reversible defect extent as the threshold for a ‘positive’ MPS. Using the anatomical ‘gold standard’ of obstructive CAD on X-ray coronary angiography is generally considered a flawed reference standard for a functional test like MPS. This is especially relevant as the majority of coronary lesions with 50–70% narrowing has been shown to have no haemodynamic relevance, and even in lesions with 70–90% narrowing only 40% demonstrate haemodynamic significance on fractional flow reserve measurements. However, comparison with angiographic CAD remains relevant in a ‘real-world’ study such as the present one, as the role of MPS in clinical practice is often a dual one, i.e. in providing prognostic as well as diagnostic data with regard to both the risk and probability of underlying obstructive CAD.

It is not surprising, given the superior efficiency and sensitivity of solid-state detector rings with multipinhole collimation, that rapid-acquisition MPS provides improved image quality compared with conventional SPECT. However, analysis of the false-negative

**Figure 6** Patient presenting with anginal chest pain. (A) Stress—rest myocardial perfusion SPECT with mid-ventricular short-axis, vertical long-axis, and horizontal long-axis views, and (B) stress and rest polar maps show apparent inducible perfusion defects in the inferoseptal wall and apex. Subsequent X-ray coronary angiogram (C) did not show any obstructive CAD. On review, the false-positive findings on the stress images were felt to be artifactual secondary to a combination of soft tissue attenuation and suboptimal patient positioning.
and false-positive findings in the sub-group with coronary angiographic correlation in this study shows that even the latest MPS technology continues to suffer from limitations. Underestimation of CAD compared with angiography is well recognized with MPS using vasodilator stress, in particular, with only 25% of patients with three-vessel disease showing significant perfusion defects in some series. Berman et al. found that, among 101 patients with significant left main stem disease, 40% had radionuclide scans showing no significant perfusion defect. Rapid-acquisition MPS also cannot resolve ‘balanced ischaemia’ whereby low myocardial extraction of technetium-labelled MPS tracers relative to hyperaemic flow can lead to underestimation of the degree of underlying CAD. Although recent work has been conducted into dynamic SPECT imaging that allows flow quantification and estimation of flow reserve, which has the potential to address this issue, this has not translated into clinical practice.

Some of the technical artefacts leading to false-positive interpretation in this study (e.g. attenuation and patient movement) are, in fact, more difficult to recognize on rapid-acquisition MPS than conventional SPECT. This results from certain inherent characteristics of MPS on the Discovery NM 530c CZT camera, notably multipinhole collimation, a narrow field of view focused on the heart, unavailability of full raw data review, and sophisticated reconstruction algorithms that are subject to unpredictable artefacts that may be inadequately understood by reporting clinicians who have limited experience of this new technology. Some of these limitations could potentially be ameliorated with increasing familiarity with this new camera, use of supine and prone imaging, and also with judicious use of hybrid imaging technology with SPECT/CT (where available), as this allows CT-based attenuation correction, calcium scoring, and CT coronary angiography in selected patients, providing complementary anatomical information that increases the utility of the technique, as demonstrated in recent studies.

There were some limitations in the present study, which should be mentioned. Quantification with summed stress, rest, and difference scores was not utilized in secondary outcome evaluation (i.e. assessment of diagnostic accuracy of rapid-acquisition MPS compared with coronary angiography). Although this is recognized to reduce inter-observer variability in the interpretation of MPS, its role in improving accuracy is unknown, and as this was a study into a ‘real-world’ clinical nuclear cardiology practice, it was felt that a threshold of >10% of the LV myocardium based on the original clinical read-out would serve as a more relevant parameter that reflects practical experience at the authors’ centre and also guides clinical decision-making. The patient cohort was heterogeneous, containing patients with suspected as well as known CAD, but this merely represents the diverse clinical practice that is experienced in most nuclear cardiology departments. The retrospective nature of data collection meant that accurate pre-test risk stratification could not be performed in patients who were not known to have CAD, and only the hard cardiac event rate could be analysed reliably, rather than all major adverse cardiac events. Finally, exclusive pharmacological stress testing with adenosine, the lack of CT-based attenuation correction, and a ‘post-test’ referral bias will undoubtedly have an impact on the accuracy of MPS compared with X-ray coronary angiography that was observed in this study, but again this was felt to be an accepted part of routine clinical experience with MPS.

Conclusions

Rapid-acquisition adenosine stress–rest studies performed on a solid-state detector CZT camera with multipinhole collimation are an evolutionary development in MPS that provide valuable prognostic and diagnostic information in stable patients with suspected or known CAD, while significantly reducing image acquisition time. Although the technique continues to suffer from some of the known limitations of conventional SPECT, it shows a diagnostic accuracy in a ‘real-world’ clinical service that is well within the range of conventional radionuclide perfusion imaging. Incorporation of hybrid imaging technology in the form of SPECT/CT is increasingly being recognized as a method for further improving diagnostic accuracy to maximize the utility of rapid-acquisition MPS in the non-invasive imaging of CAD.

Conflict of interest: None declared.

References


