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1 **Quantitative myocardial perfusion imaging versus visual analysis in diagnosing myocardial**
2 **ischaemia: a CE-MARC sub-study**

3
4 **John D Biglands – BSc., MSc., PhD.**

5 *j.biglands@nhs.net*

6 Address: John Biglands, Room 8.6, Division of Medical Physics, Worsley Building, University
7 of Leeds, LS2 9JT

8 Division of Biomedical Imaging, Leeds Institute of Cardiovascular and Metabolic Medicine,
9 University of Leeds, Leeds, United Kingdom.

10 Department of Medical Physics and Engineering, Leeds Teaching Hospitals NHS Trust, Leeds,
11 United Kingdom.

12 No relationship with Industry

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14 **Montasir Ibraheem – MSc.**

15 *montasiribraheem@nhs.net*

16 Division of Biomedical Imaging, Leeds Institute of Cardiovascular and Metabolic Medicine,
17 University of Leeds, Leeds, United Kingdom.

18 No relationship with Industry

19 **Derek R Magee – BSc., PhD.**

20 *D.R.Magee@leeds.ac.uk*

21 School of Computing, University of Leeds, Leeds, United Kingdom.

22 No relationship with Industry

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24 Wellcome Trust and EPSRC, under grant number WT 088908/Z/09/Z

25 **Aleksandra Radjenovic – BSc. MSc. PhD.**

26 *aleksandra.radjenovic@glasgow.ac.uk*

27 Institute of Cardiovascular and Medical Sciences, College of Medical, Veterinary and Life
28 Sciences, University of Glasgow, Glasgow, UK

29 No relationship with Industry

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31 Wellcome Trust and EPSRC, under grant number WT 088908/Z/09/Z.

32 **Sven Plein – MD, PhD**

33 *s.plein@leeds.ac.uk*

34 Division of Biomedical Imaging, Leeds Institute of Cardiovascular and Metabolic Medicine,
35 University of Leeds, Leeds, United Kingdom.

36 No relationship with Industry

37 Funded by a British Heart Foundation fellowship (FS/10/62/28409)

38 **John P Greenwood – MBChB, PhD**

39 *j.greenwood@leeds.ac.uk*

40 Division of Biomedical Imaging, Leeds Institute of Cardiovascular and Metabolic Medicine,
41 University of Leeds, Leeds, United Kingdom.

42 No relationship with Industry

43
44 Address for correspondence

45 John Biglands, Room 8.6, Division of Medical Physics, Worsley Building, University of Leeds,
46 LS2 9JT

1 tel: 0113 34 38322
2 email: *j.biglands@nhs.net*

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14

1 **Abstract**

2 **Objectives:** To compare the diagnostic accuracy of visual and quantitative analyses of
3 myocardial perfusion cardiovascular magnetic resonance (CMR) against a reference standard of
4 quantitative coronary angiography.

5 **Background:** Visual analysis of perfusion CMR studies for assessing myocardial perfusion has
6 been shown to have high diagnostic accuracy for coronary artery disease. However, only a few
7 small studies have assessed the diagnostic accuracy of quantitative myocardial perfusion.

8 **Methods:** This retrospective study included 128 patients randomly selected from the CE-MARC
9 population such that the distribution of risk factors and disease status was proportionate to the
10 full population. Visual analysis results of CMR perfusion images, by consensus of two expert
11 readers, were taken from the original study reports. Quantitative myocardial blood flow (MBF)
12 estimates were obtained using Fermi-constrained deconvolution. The reference standard for
13 myocardial ischaemia was a quantitative coronary X-ray angiogram (QCA) stenosis severity of
14 $\geq 70\%$ diameter in any coronary artery of $> 2\text{mm}$ diameter, or $\geq 50\%$ in the left main stem.
15 Diagnostic performance was calculated using receiver operator characteristic (ROC) curve
16 analysis.

17 **Results:** The AUC for visual analysis was 0.88 (95% confidence interval: 0.81, 0.95) with a
18 sensitivity of 81.0% (95% confidence interval: 69.1%, 92.8%) and specificity of 86.0% (95%
19 confidence interval: 78.7%, 93.4%). For quantitative stress MBF the AUC was 0.89 (95%
20 confidence interval: 0.83, 0.96) with a sensitivity of 87.5% (95% confidence interval: 77.3%,
21 97.7%) and specificity of 84.5% (95% confidence interval: 76.8%, 92.3%). There was no
22 statistically significant difference between the diagnostic performance of quantitative and visual
23 analyses ($p=0.72$). Incorporating rest MBF values to generate an MPR did not significantly
24 increase the quantitative analysis AUC ($p=0.79$).

25 **Conclusions:** Quantitative perfusion has a high diagnostic accuracy for detecting coronary artery
26 disease, but is not superior to visual analysis. The incorporation of rest perfusion imaging does
27 not improve diagnostic accuracy in quantitative perfusion analysis.

28
29 **Key words:** cardiovascular magnetic resonance, myocardial ischaemia, quantitative myocardial
30 perfusion, diagnostic accuracy

31
32 **Abbreviations**

33 AHA = American heart association
34 AIF = arterial input function
35 AUC = area under the curve
36 CAD = coronary artery disease
37 CMR = cardiovascular magnetic resonance
38 LGE = late gadolinium enhancement
39 LMS = left main stem
40 MBF = myocardial blood flow
41 MPR = myocardial perfusion reserve
42 QCA = quantitative coronary angiography
43 ROC = receiver operator characteristic
44 SR-TFE = saturation recovery turbo field echo
45

1 **Introduction**

2 Cardiovascular Magnetic Resonance (CMR) is a well-established technique for the assessment of
3 patients with coronary artery disease (CAD), being diagnostically superior (1,2), cost effective
4 (3,4) and a better predictor of cardiovascular events (5) than myocardial perfusion scintigraphy
5 by single-photon emission computed tomography (SPECT). CMR compares favourably with
6 positron emission tomography (PET) (6), has higher image resolution, is more widely available,
7 does not use ionizing radiation; and can evaluate function, perfusion and viability in the same
8 investigation. Perfusion CMR requires the passage of a contrast agent bolus through the heart to
9 be visualised over time. Typically a saturation prepared single-shot readout sequence is used to
10 achieve adequate coverage and spatial and temporal resolution (7,8). Post-processing of CMR
11 perfusion images can generate estimates of absolute myocardial blood flow (MBF). Absolute
12 MBFs provide an objective measure of perfusion which does not require a healthy region of
13 myocardium for visual comparison. They have been used to show diffuse perfusion changes due
14 to smoking (9) and type 2 diabetes mellitus (10) and there is evidence to suggest that these
15 measurements may bring improvements in diagnostic performance (11). However assessments of
16 the diagnostic accuracy of MBF estimates have been limited to small studies (typically <50
17 patients) (11–15). Perfusion is often expressed as myocardial perfusion reserve ($MPR = \text{stress}$
18 $MBF / \text{rest MBF}$). However, it is unknown whether the use of MPR values improves diagnostic
19 performance over stress perfusion measurements alone. If not, the time consuming rest perfusion
20 scan could potentially be removed from the acquisition protocol without reducing the
21 performance of the test (16,17).

22 The primary objective of this study was to compare the sensitivity, specificity and diagnostic
23 accuracy of expert visual analysis and MBF estimates against a reference standard of quantitative

1 coronary angiography (QCA). This was done using a large representative subsample of the CE-
2 MARC (clinical evaluation of magnetic resonance imaging in coronary heart disease) study (2).
3 We hypothesised that quantitative CMR would have a higher diagnostic accuracy than visual
4 analysis for identifying significant coronary artery stenosis. A secondary objective was to
5 compare the diagnostic accuracy of MPR measurements, which use both rest and stress MBF
6 data, with stress MBF measurements only.

7 **Methods**

8 **Patients:** The study protocol was approved by the national research ethics service. CE-MARC
9 recruited patients with suspected angina pectoris, of which 676 had assessable CMR and
10 angiography (2,18). For this sub-study 128 cases were randomly selected by an independent
11 statistician from the CE-MARC population, such that the distribution of risk factors
12 (hypertension, diabetes, smoking, age) and disease status (normal, single, double or triple vessel
13 disease) was proportionate to those in the full population. This sub-sample contained 50 patients
14 that have been included in a previous study (16).

15 **Image acquisition:** Myocardial perfusion CMR and QCA data were acquired from each patient
16 as previously described (2,18). All patients underwent invasive quantitative coronary
17 angiography (QCA) within 32 days of their CMR examination. Adenosine (140 µg/kg/min)
18 induced stress imaging was performed at least 15 minutes before rest imaging. Myocardial
19 perfusion CMR was performed using a bolus intravenous injection of 0.05 mmol/kg
20 dimeglumine gadopentetate (Magnevist®, Schering AG, West Sussex, UK) through an arm vein
21 at an injection rate of 5ml/s. CMR imaging was carried out on 1.5T Philips Intera (Best, The
22 Netherlands) equipped with 'Master' gradients (30 mT/m peak gradients and 150 mT/m/ms slew
23 rate) using a 5-element cardiac phased-array coil and triggering performed by the

1 vectorcardiographic method. Three short axes images were acquired using a T1-weighted
2 saturation recovery turbo field echo (SR-TFE) imaging sequence. A shared (non-slice selective)
3 saturation pulse was used giving pre-pulse delay times to the centre of k-space of 126ms, 272ms
4 and 418ms for the basal, middle and apical slices respectively. The image acquisition parameters
5 were: TE 1.0 ms, TR 2.7 ms, flip angle 15°, SENSE factor 2, matrix 144 × 144, field of view
6 320–460 mm, pixel size 2.2-3.2mm, slice thickness 10 mm and partial Fourier 0.67 giving a
7 readout window of 130.2ms per slice. Imaging continued until the first pass had been observed to
8 pass through the myocardium. The average number of frames in the perfusion series was 56
9 (range 26, 78).

10 Late gadolinium enhanced CMR was performed between 10-15 minutes after the rest perfusion
11 study with a T1-weighted, segmented inversion-recovery gradient echo sequence; pulse sequence
12 parameters: TE 1.9 ms, TR 4.9 ms, flip angle 15°, 10–12 short axis slices, single slice per breath-
13 hold, matrix 240 × 240, field of view 320–460 mm as per patient size. The optimal inversion
14 time to null signal from normal myocardium was determined prior to the scan using a Look-
15 Locker approach (19).

16 **Image Analysis:** Quantitative CMR analysis was performed blinded to the results of all other
17 investigations. Contours describing the myocardium and a region within the left ventricular
18 blood pool, avoiding papillary muscles, were drawn using dedicated cardiac image analysis
19 software (Mass 7.0, Medis, Leiden University, Leiden, The Netherlands). Contours were copied
20 to all time frames and manually adjusted for motion. Adjustments were limited to rigid
21 translations only. Manual contouring took around one hour per patient. The myocardium was
22 subdivided into 6 circumferentially equidistant regions in the basal and mid slices and 4 in the
23 apical slice according to the AHA standard (20). Individual perfusion data sets exhibiting

1 excessive (more than one frame) through plane motion (typically due to ECG gating failure)
2 were visually identified and excluded prior to MBF quantitation. Signal versus time curves from
3 the myocardium and blood pool were converted to contrast agent concentration curves assuming
4 a linear signal response to contrast agent as described previously (16). All pre-contrast signal
5 estimates were taken from the stress study. Values of 1435ms and $4.3 \text{ s}^{-1} \cdot \text{mM}^{-1}$ were used for the
6 blood T1 and contrast agent relaxivity respectively. To avoid remnant contrast agent from the
7 stress perfusion scan affecting the rest perfusion analysis the pre-contrast signal intensity was
8 subtracted from the rest perfusion curves prior to analysis. Myocardial blood flow (MBF) values
9 were estimated using Fermi-constrained deconvolution (16,21). The arterial input function was
10 taken from the basal slice. The pre-contrast baseline signal, end of first pass time point and the
11 bolus arrival time delay between the blood pool and myocardial curves were calculated using
12 previously described automated methods (16,22)

13 Visual CMR perfusion images were jointly reported by two cardiologists (JPG, SP) with >6
14 years' experience in CMR at the time, and who were blind to the results of all other
15 investigations. This was a perfusion only assessment that did not take into account cine, LGE or
16 angiography images sets. Scores for hypoperfusion (ischaemia) of 0 (normal), 1 (equivocal), 2
17 (subendocardial ischaemia), or 3 (transmural ischaemia) were given by visual comparison of
18 stress and rest CMR perfusion scans (16 segments of the 17 segment AHA model, excluding the
19 apical cap segment). To generate the receiver operator characteristic (ROC) curve the summed
20 scores over all AHA segments were used. Diagnostic performance was ascertained from the
21 ROC curve as the area under the curve (AUC) value. The cut-off value that generated the
22 optimal sensitivity and specificity for the test was determined by maximising the Youden index

1 (23). A separate assessment of LGE was performed with a score of 0 (none), 1 (1–25%), 2 (26–
2 50%), 3 (51–75%) or 4 (>75%) allocated to each segment of the AHA model.

3 All x-ray angiograms were performed after CMR. Quantitative coronary angiography (QCA)
4 analysis was performed off-line by a cardiologist blinded to the CMR results using QCAPlus
5 software (Sanders Data Systems, Palo Alto, California, USA). Significant CAD was defined as
6 $\geq 70\%$ diameter stenosis of a first order coronary artery measuring $\geq 2\text{mm}$ in diameter, or left
7 main stem stenosis $\geq 50\%$. Single, double and triple vessel disease was defined as significant
8 stenosis affecting one, two or three vessels respectively. Both visual CMR perfusion and QCA
9 scores were taken from the original CE-MARC reports and were not reanalysed for this sub-
10 study.

11 All perfusion results were compared to QCA on a per-patient basis. MPR values were calculated
12 as the stress MBF estimate divided by the resting MBF estimate. To generate the ROC curve the
13 AHA segment with the lowest perfusion measure (MPR or stress MBF) was used as the
14 quantitative measure.

15 Diagnostic performance was evaluated using ROC curve analysis taking the QCA diagnosis as
16 the reference standard. Diagnostic performance was first assessed in terms of the ability of the
17 perfusion index to detect disease in any coronary artery. A separate assessment of the diagnostic
18 performance for detecting disease in each individual coronary artery was performed using the
19 AHA segmentation recommendations to map myocardial segments to individual coronary
20 arteries. The number of detected perfusion defects that correctly corresponded to disease in the
21 coronary artery specified by the AHA mapping was then assessed.

22 **Statistical Analysis:** Categorical variables are expressed as numbers and percentages.
23 Continuous variables are expressed as mean \pm standard deviations unless otherwise stated. With

1 a sample size of 128 and using a correlation between the scores of $r=0.45$, the study was powered
2 to detect a difference of 0.15 in the AUC values between ROC curves with a power of 80% at the
3 5% significance level (24). ROC curves were generated using Analyse-it (Analyse-it Software
4 Ltd. UK). All other statistical analysis was carried out using SPSS (version 21.0, Chicago, IL).
5 Comparison of ROC curves was performed using the DeLong method (25). There was no
6 correction for multiple comparisons of AUC curves. Normally distributed data were compared
7 using Student's t-test.

8 **Results**

9 Baseline patient characteristics are summarised in Table 1. The study consisted of 128 patients
10 (mean age 61 years; age range 37-77 years). 77 (60%) were male (mean age 61 years; age range,
11 45-76 years) and 51 were female (mean age, 60 years; age range, 37-77 years). There was no
12 significant age difference between male and female groups ($p=0.33$). 42 patients had significant
13 coronary artery disease as assessed by QCA and 86 did not. Four whole patient perfusion data
14 sets (3%) were excluded from the study because of severe through plane motion caused by
15 electrocardiographic (ECG) triggering failures (3 stress scans and 1 rest scan). These consisted
16 of one patient with single vessel disease, one with double vessel disease and two healthy patients
17 as assessed by QCA. Post-exclusion, 40 patients with significant coronary heart disease and 84
18 without remained for analysis. Analysis of late gadolinium enhancement images showed 33
19 patients had evidence of myocardial scarring (infarct pattern).

20 Mean global (i.e. mean MBF per slice averaged over all three slices) myocardial blood flow
21 values over all three slices are shown in Table 2. Mean MBFs from healthy patients for each
22 slice are shown in Table 3. Perfusion was significantly lower in ischaemic patients than in
23 normal; Stress MBF 2.16 (0.70) ml/min/g vs. 3.00 (0.81) ml/min/g, ($p<0.001$) and MPR 1.86

1 (0.57) vs 2.31 (0.67), ($p < 0.001$). Receiver operator characteristic curves for visual and
2 quantitative perfusion analysis are shown in
3 Figure 1. The sensitivity, specificity, area under the curve (AUC) and optimal cut-off values are
4 shown in Table 4 and Table 5 shows the respective contingency tables The highest diagnostic
5 accuracy was achieved using MPR measurements. There was no statistically significant
6 difference in diagnostic performance between visual (AUC 0.88, cut-off 2.0) and quantitative
7 analysis for MPR (AUC 0.89, cut-off 1.11; $p = 0.72$) or stress MBF (AUC 0.87, cut-off 1.27
8 ml/min/g; $p = 0.54$). There was no significant difference in diagnostic accuracy between MPR and
9 stress MBF quantitative ROC curves ($p = 0.79$).

10 Separate assessments for single, double and multi (double or triple) vessel disease patients are
11 shown in Table 6. There was no significant difference between the diagnostic accuracy of visual
12 and quantitative analysis in single, double or multi vessel disease groups. In 28 (70%) out of 40
13 cases the minimum quantitative perfusion score mapped correctly to a coronary artery territory
14 that contained a significant stenosis according to the AHA segmentation model. 8 out of 9 (89%)
15 defects correctly corresponded to a stenosis in the LCX, 12 out of 19 (63%) correctly
16 corresponded to a stenosis in the LAD and 8 out of 12 (70%) correctly corresponded to a stenosis
17 in the RCA. Separate assessments for the individual coronary arteries are shown in Table 7.
18 Quantitative measures (stress MBF or MPR) did not perform significantly better than visual
19 analysis for any of the coronary arteries.

20 **Discussion**

21 The primary finding of this study is that quantitative myocardial perfusion analysis has a high
22 diagnostic accuracy but does not out-perform expert visual analysis. In addition, diagnostic
23 performance of quantitative perfusion was not significantly improved by including rest perfusion

1 measurements. This suggests that the rest perfusion acquisition may not be necessary for
2 quantitative analysis, potentially saving time, expense (less contrast) and patient inconvenience.
3 To the author's knowledge this is the largest investigation into the diagnostic performance of
4 quantitative CMR perfusion to date, around twice as large as the previous largest study with
5 n=67 (11).

6 The presence of myocardial infarction can make visual diagnosis of superimposed ischaemia
7 challenging. In this study quantitation achieved a high diagnostic accuracy even though a
8 significant number (thirty three) of cases in the study had myocardial infarction as assessed by
9 LGE imaging. Therefore the quantitative diagnostic accuracy reported in this study supports the
10 robustness of this technique in 'real-world' clinical cases.

11 Our data showed comparable diagnostic accuracy in single and multi-vessel disease with visual
12 or quantitative analysis implying that there was no advantage in quantitative analysis in patients
13 with different extents of CAD. Furthermore, we found similar diagnostic accuracies for the
14 ability of visual or quantitative analysis to detect perfusion defects in the three coronary arteries
15 (LCX, LAD and RCA). Although MPR appears to perform slightly better than visual or stress
16 MBF analysis, especially at sensitivities above 80% (Figure 1), these differences were not
17 statistically significant. The high diagnostic accuracy observed using stress MBF alone agrees
18 well with previous studies that analysed stress only images using semi-quantitative, (6,26,27)
19 visual (28,29) and quantitative analyses. These observations demonstrate that stress data alone
20 can yield excellent diagnostic performance and a rest perfusion study may not be necessary in a
21 standard protocol to detect or exclude CAD. MPR is a measure of the potential flow increase the
22 myocardium has in reserve before maximal vasodilation occurs. Whereas stress perfusion is
23 uncoupled from oxygen demand resting perfusion is not (6), so factors influencing resting

1 myocardial oxygen demand cannot be controlled for in a clinical setting. This uncontrolled
2 aspect of the rest perfusion measurement may account for the fact that dividing by the rest MBF
3 measurement did not improve diagnostic accuracy in our quantitative data.

4 Our finding that the diagnostic performance of quantitative perfusion is comparable to, but not
5 significantly better than, visual analysis is consistent with previous, smaller studies (13,15).
6 However, Mordini et al. (11) did report a diagnostic advantage using quantitation. This may be
7 due in part to the fact that Mordini measured the ratio between the endocardial segment and the
8 median epicardial value and required at least two segments to fall below the threshold before a
9 patient was classed as ischaemic, whereas our study used the minimum segmental MBF score.

10 Our study did not replicate this transmural subdivision strategy due to concerns over increasing
11 the noise in the signal versus time curves.

12 MBF values in patients without ischaemia were comparable with those published in studies of
13 healthy volunteers (30,31). At 1.23ml/min/g the resting MBF is somewhat higher than most
14 studies, due to non-linearity effects in the AIF, but still well within the range of MBF values
15 quoted in the literature. The total exclusion rate was 3% (4/128). This compares favourably with
16 other quantitative studies.; for instance, Patel et al (9) excluded 23% of patients and Costa et al
17 (6) excluded 16%.

18 The optimal threshold for abnormal perfusion from the ROC analysis was set at an MPR of 1.11
19 and a stress MBF of 1.27 ml/min/g. The MPR threshold is somewhat lower than other studies
20 (Huber et al. 1.54 (17), Patel et al 1.55, (13)) possibly due to the high rest MBF measurements in
21 our study. The stress MBF threshold of 1.27 ml/min/g was somewhat lower than that of Mordini
22 et al. at 1.58 ml/min/g (11), possibly because their model required two AHA segments below the
23 cut-off threshold whereas our model only required one.

1 **Limitations**

2 Perfusion CMR assesses myocardial ischaemia, whereas QCA is a measure of coronary artery
3 stenosis, which is itself an imperfect reference standard. Thus, false-negative results could occur
4 if lesions not causing ischaemia (as assessed by CMR) were judged clinically significant on the
5 basis of angiographic stenosis severity. Invasive measurement of fractional flow reserve is now
6 the reference standard for the measurement of haemodynamic significance of a coronary artery
7 stenosis, but was not routinely performed at the time of recruitment to the CE-MARC study.
8 The combination of a 0.05mmol/kg contrast dose and a pre-pulse delay of 126ms yields a non-
9 linear signal response to contrast agent concentration in the AIF, resulting in an over-estimate of
10 MBF. The lack of a linear AIF measurement constitutes a limitation to this retrospective dataset.
11 This could potentially diminish the range of MBF estimates and reduce the performance of
12 quantitative perfusion, including the benefits of rest perfusion. However, our analyses achieved a
13 high sensitivity and specificity in agreement with other studies employing dual-bolus techniques
14 implying that non-linearity errors have not profoundly affected the results. This agrees with
15 previous work directly comparing dual and single bolus strategies and finding no significant
16 difference in diagnostic performance (32).

17 The use of a shared pre-pulse to acquire all three perfusion slices results in different T1 contrast
18 between the three image slices. This has been addressed by using the basal AIF for all three
19 slices and by applying a linear correction to the myocardial curves. This approach may be subject
20 to errors if the myocardial signal to concentration relationship is sufficiently non-linear, although
21 there were no significant differences in MBF between the three slices in the study population
22 (Table 3).

1 Manual correction for breathing motion introduces an extra source of error into the
2 measurements as the signal curves can be contaminated by high signal blood pixels in the LV or
3 other surrounding tissues deteriorating the results of MBF quantitation. Although care was taken
4 to avoid these errors an automated, non-rigid registration might have improved our quantitative
5 results. The use of quantitative perfusion analysis in clinical practice requires a known
6 healthy/diseased threshold value. Currently this value may vary between studies because of
7 variations in MBFs due to differing methodologies. Before MBF measurements can be used
8 widely standardisation of these methods and multi-centre studies are necessary to show that a
9 single cut-off across different sites and CMR vendors is suitable and can still achieve the high
10 diagnostic accuracies reported in this study. This is even more relevant if the rest perfusion
11 measurement is to be discarded because expressing perfusion as a ratio can normalise systematic
12 shifts in MBF, due to differences in methodology, that remain if a stress only perfusion
13 measurement is used. It also noteworthy that quantitative perfusion can impose limits on the
14 acquisition such as lower contrast dose and reduced image T1-weighting that can force a
15 reduction in image quality and or heart coverage, which may adversely affect visual assessment.

16 **Conclusions**

17 Quantitative myocardial perfusion has a high diagnostic accuracy for detecting coronary artery
18 disease, but is not superior to expert visual analysis, even in multi-vessel disease. Rest perfusion
19 data acquisition does not increase the diagnostic accuracy of quantitative myocardial perfusion
20 and could be eliminated from the imaging protocol.

1 **Perspectives**

2 **Competency in Medical Knowledge**

3 This work has shown that quantitative myocardial perfusion estimates obtained from CMR have
4 a high diagnostic accuracy equivalent to, but not better than, that of expert visual analysis. In
5 addition, the use of a rest perfusion measurement did not improve diagnostic performance above
6 stress perfusion quantitation alone. The clinical implications are that these observations support
7 removal of rest perfusion imaging from the acquisition protocol.

8

9 **Translational Outlook**

10 For quantitative perfusion estimates to be accepted as a standard clinical tool a number of
11 obstacles need to be overcome. Firstly, the time consuming analysis needs to be streamlined so
12 that quantitative estimates are easily available to a non-expert user within a reasonable time
13 frame. Secondly, diagnosis using quantitative measurement requires a known healthy/diseased
14 cut-off value. These cut-off points vary between studies because of the variation in quantitative
15 values due to the wide range of methods used. These include differences in contrast dose
16 administered, CMR acquisition sequence, methods for correcting non-linearity between contrast
17 agent concentration and signal intensity, motion correction and modelling methods used to
18 generate the final flow value. If these measurements are to be used widely standardisation of
19 these methods is required in order to reduce these variations. Multi-centre studies would then be
20 necessary to show that a single cut-off across different sites and CMR vendors is suitable and can
21 still achieve the high diagnostic accuracies reported in this study.

22

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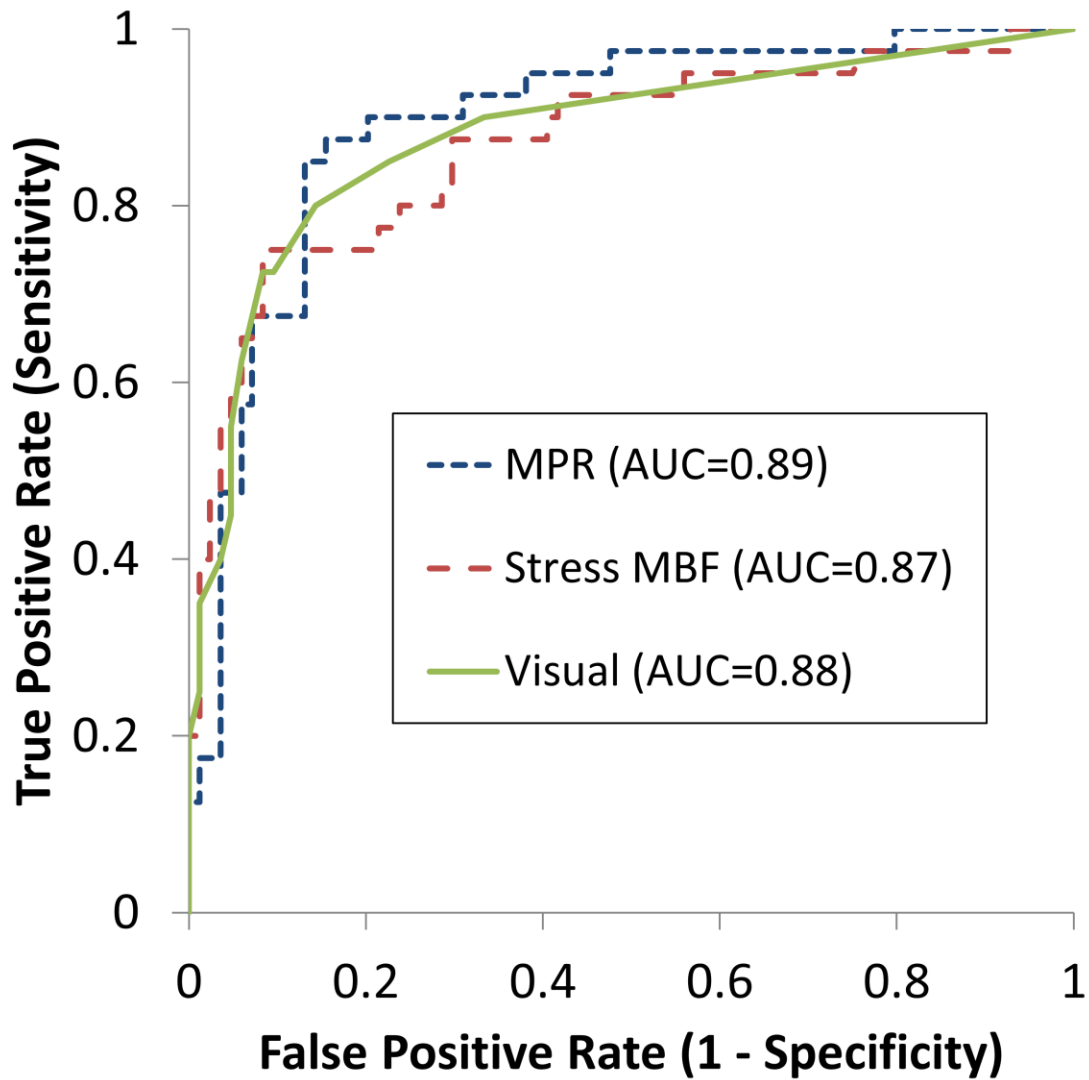
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7

1 **Figure 1 ROC curves for quantitative and visual analyses.** ROC curves for visual analysis,
2 myocardial perfusion reserve (MPR) and stress myocardial blood flow (MBF) showing
3 diagnostic accuracy for detecting significant stenosis as assessed by QCA. There was no
4 statistically significant difference in diagnostic performance between visual and MPR ($p=0.72$)
5 or stress MBF ($p=0.54$).
6



7
8

1 **Table 1-** Patient Characteristics

Age [years]	61 ± 9
Female	51 (40)
Hypertension	65 (51)
Diabetes	17 (13)
Smoking	16 (13)
1 vessel disease	23 (18) (1 excluded)
2 vessel disease	15 (12) (1 excluded)
3 vessel disease	4 (3) (0 excluded)
Total patients with CAD	42 (33) (2 excluded)

2

3 Data are mean ± SD or number of cases (%)

4

5

1 **Table 2:** Quantitative perfusion results for ischaemic and non-ischaemic groups

	Number of cases	Stress MBF [ml/min/g]	Rest MBF [ml/min/g]	MPR
Ischaemic	40	2.16 ± 0.70	1.23 ± 0.41	1.86 ± 0.57
Non Ischaemic	84	3.00 ± 0.81	1.37 ± 0.39	2.31 ± 0.67
All	124	2.73 ± 0.87	1.32 ± 0.40	2.17 ± 0.67

2

3 Data are mean ± SD.

4 MBF = myocardial blood flow, MPR = myocardial perfusion reserve

5

6

1 **Table 3:** Quantitative perfusion values by slice in healthy cases

Slice	Stress MBF [ml/min/g]	Rest MBF [ml/min/g]	MPR
1	2.81 ± 0.75	1.29 ± 0.27	2.25 ± 0.73
2	3.15 ± 0.65	1.41 ± 0.38	2.34 ± 0.55
3	3.04 ± 0.98	1.40 ± 0.48	2.33 ± 0.74

2

3 Data are mean ± SD.

4 MBF = myocardial blood flow, MPR = myocardial perfusion reserve

5

6

1 **Table 4:** Diagnostic performance of quantitative and visual methods to detect stenosis as
 2 measured by QCA. Scores need to be greater than the optimal cut-off value to classify the patient
 3 as ischaemic.

	AUC	Sensitivity (%)	Specificity (%)	Optimal cut-off
Stress MBF [ml/min/g]	0.87 (0.80, 0.94)	75.0 (61.6, 88.4)	91.7 (85.8, 97.6)	1.27
MPR	0.89 (0.83, 0.96)	87.5 (77.3, 97.7)	84.5 (76.8, 92.3)	1.11
Visual	0.88 (0.81, 0.95)	81.0 (69.1, 92.8)	86.0 (78.7, 93.4)	2.00

4 Data are value (95% confidence interval)

5 AUC = area under the curve, MBF = myocardial blood flow, MPR = myocardial perfusion

6 reserve

1 **Table 5:** Contingency tables for Stress MBF, MPR and visual analysis

2 a)

CAD as assessed by:		X-ray (QCA)	
		+	-
MRI (MPR)	+	35; 0.67 (0.21)	13; 0.75 (0.18)
	-	5; 1.39 (0.24)	71; 1.61 (0.39)

3 b)

CAD as assessed by:		X-ray (QCA)	
		+	-
MRI (stress MBF)	+	30; 0.76 (0.29)	7; 0.94 (0.23)
	-	10; 1.99 (0.54)	77; 2.17 (0.62)

4 c)

CAD as assessed by:		X-ray (QCA)	
		+	-
visual	+	34; 11.71 (6.59)	12; 6.58 (4.10)
	-	8; 0.75 (0.89)	74; 0.31 (0.64)

5

6 Contingency tables showing number of cases, mean value and standard deviation of the values

7 for a) MPR, b) stress MBF and c) visual analysis.

8 Data values are: number of cases; mean (standard deviation). Symbols '+' and '-' correspond to
9 positive and negative assessments for coronary artery disease respectively.

10

11

1 **Table 6:** Area under the curve (AUC) values for single, double and multiple vessel disease.

	Single vessel disease	Double vessel disease	Multiple vessel disease
Stress MBF	0.93 (0.85, 1.0)	0.81 (0.67, 0.95)	0.83 (0.71, 0.95)
MPR	0.88 (0.78, 0.98)	0.94 (0.84, 1.00)	0.91 (0.82, 1.00)
Visual	0.89 (0.80 , 0.98)	0.85 (0.72, 0.98)	0.87 (0.76, 0.98)
No. of cases	22	14	18

2 Data are values (95% confidence interval)

3 MBF = myocardial blood flow, MPR = myocardial perfusion reserve.

4 Multiple vessel disease is defined as a patient with either double or triple vessel disease.

5

1 **Table 7:** Area under the curve (AUC) values for quantitative perfusion for individual coronary
2 arteries

	LCX	LAD	RCA
Stress MBF	0.75 (0.62, 0.89)	0.76 (0.64, 0.89)	0.83 (0.69, 0.97)
MPR	0.74 (0.60, 0.87)	0.77 (0.65, 0.89)	0.73 (0.56, 0.89)
Visual	0.69 (0.56, 0.83)	0.77 (0.64, 0.88)	0.73 (0.57, 0.89)

3
4 Data are value (95% confidence interval)
5 LCX = left circumflex, LAD = left anterior descending, RCA = right coronary artery, MBF =
6 myocardial blood flow, MPR = myocardial perfusion reserve.