Computed Tomography Myocardial Perfusion Imaging with 320-Row Detector CT Accurately Detects Myocardial Ischemia in Patients with Obstructive Coronary Artery Disease

George et al: 320 CT Perfusion Imaging

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Abstract

Background—Computed tomography coronary angiography (CTA) has been shown to be accurate in detecting anatomic coronary arterial obstruction, but is limited for the detection of myocardial ischemia. The primary aim of this study was to assess the accuracy of 320-row CT perfusion imaging (CTP) to detect atherosclerosis causing myocardial ischemia.

Methods and Results—Fifty symptomatic patients with recent single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) underwent a comprehensive cardiac CT protocol that included 320-CTA followed by adenosine stress CTP. CTP images were analyzed quantitatively for the presence of subendocardial perfusion deficits. All analyses were blinded to imaging and clinical results. CTA alone was a limited predictor of myocardial ischemia compared with SPECT with a sensitivity, specificity, positive (PPV) and negative predictive value (NPV) of 56%, 75%, 56%, 75%, and the AUC was 0.65 (95%CI: 0.51-0.78, p=0.07). CTP was a better predictor of myocardial ischemia with a sensitivity, specificity, PPV, and NPV of 72%, 91%, 81%, 85%, with an AUC of 0.81 (95%CI: 0.68-0.91, p<0.001) and was an excellent predictor of myocardial ischemia on SPECT-MPI in the presence of stenosis (>50% on CTA) with a sensitivity, specificity, PPV, and NPV of 100%, 81%, 50%, 100%, with an AUC of 0.92 (95%CI: 0.80-0.97, p<0.001). The radiation dose for the comprehensive cardiac CT protocol and SPECT were 13.8±2.9 and 13.1±1.7; respectively (p=0.15).

Conclusions—CTP imaging with rest and adenosine stress 320-row CT is accurate in detecting obstructive atherosclerosis causing myocardial ischemia.

Key Words: imaging, atherosclerosis, ischemia, perfusion, myocardial blood flow
Coronary computed tomography angiography (CTA) provides high sensitivity and negative predictive value for the detection of obstructive coronary artery disease (CAD)\textsuperscript{1-3}. Its primary strengths are the ability to quantify atherosclerosis and accurately exclude the presence of obstructive CAD\textsuperscript{1-5}. However, the degree of coronary obstruction measured by CTA or conventional angiography remains a poor predictor of reversible ischemia caused by atherosclerosis.\textsuperscript{6-8}

Rest and stress single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has become the most common diagnostic test for evaluating patients with symptoms suggestive of obstructive CAD. Studies in diverse populations have established the diagnostic and prognostic value of SPECT-MPI\textsuperscript{9,10} as an effective tool in therapeutic decision making for patients with suspected CAD\textsuperscript{11}. Recent advances in cardiac computed tomography (CT) technology have enabled the assessment of the physiologic significance of coronary stenoses using myocardial CT perfusion imaging (CTP)\textsuperscript{12-15}. This promising technology, when combined with coronary CTA has the capability of evaluating CAD in comprehensive fashion\textsuperscript{16-18} and is likely to be most useful in the evaluation of lesions detected by CT angiography.

The primary objective of this study was to determine if adenosine stress 320-row CTP imaging can detect atherosclerosis causing myocardial ischemia in symptomatic patients with suspected CAD.
Methods

Patient Selection

The study protocol was approved by the Johns Hopkins University Institutional Review Board. Patients were enrolled from December 2007 to January 2010 and all participants signed written informed consent. The study included men and non-pregnant women who underwent a clinically indicated SPECT-MPI within the past 60 days (mean: 18.6±12.4 days) with an intermediate to high pretest probability of CAD or prior history of CAD. Exclusion criteria included: history of renal insufficiency, contraindications to iodinated contrast, atrial fibrillation, bronchospastic lung disease, 2nd or 3rd degree heart block, NYHA Class III or IV congestive heart failure, inability to lie flat, history of organ transplant, recent illicit drug use, excessive X-ray CT, fluoroscopy in the past 30 days, or any interim event between studies that would potentially change results (i.e. myocardial infarction, bypass surgery, coronary stenting, etc).

Baseline characteristics are listed in Table 1. All patients underwent the research CT examination and 19 patients underwent a clinically indicated invasive coronary angiogram.

CT Image Acquisition and Reconstruction

Prior to arrival, patients were asked to refrain from caffeine for 12 hours and hold morning blood pressure medications except for beta-blockers. Baseline blood pressure (BP), heart rate (HR), and ECG were acquired prior to CT. Oral and/or intravenous metoprolol was given if the resting HR was greater than 65 beats per minute. IV access was obtained in the right and left antecubital veins for the administration of iodinated contrast and adenosine, respectively and blood was sampled for serum creatinine measurement. Patients were hydrated with 250 – 500 ml normal saline prior to CT imaging.
320-Row Detector CT Acquisition and Reconstruction

A timeline for the comprehensive CT protocol is shown in Figure 1 and the CT imaging acquisition parameters are summarized in Table 2. In summary, patients were placed supine in a 320-row CT (320-CT) scanner (Aquilion One, Toshiba Medical Systems, Nasu, Japan) and attached to a rhythm and automated BP monitor. Four sequential imaging series were performed: 1) Coronary Artery Calcium Scoring (CACS) as previously described, 2) Rest CTA/CTP Imaging during the infusion of 60 cc of iopamidol (Isovue, 370 mg iodine/ml, Bracco Diagnostics)\textsuperscript{18}, 3) Stress CTP Imaging was performed ten minutes following rest CTA/CTP imaging during the intravenous infusion of adenosine (0.14 mg/kg/min) during continuous ECG monitoring. Four minutes into the adenosine infusion, 60 cc of iopamidol was infused and stress CTP Imaging was performed, and 4) Delayed Enhanced CT (DECT) imaging was performed 5 minutes later.

Image reconstruction parameters are summarized in Table 2. All contrast enhanced images were reconstructed using beam hardening correction and the phase with least coronary and myocardial motion\textsuperscript{15}.

Myocardial CTP Image Analysis

Rest and stress CTP axial images were transferred to an analysis workstation (Myoperfusion, Toshiba Medical Systems, Nasu, Japan). Using multi-planar reformations, rest and stress perfusion images were arranged in the cardiac short axis with a 3 mm slice thickness and the images were analyzed quantitatively as previously described\textsuperscript{18}. In summary, the software automatically and equally divided the myocardium into three myocardial layers – the
subendocardium, mid-myocardium, and subepicardium; using a 16-segment model (apex was excluded). A radiology technologist blinded to all other data made manual adjustments if needed. The software calculated the mean attenuation of each myocardial layer within each segment; and the transmural perfusion ratio (TPR) was calculated as the ratio of the segment specific subendocardial attenuation and the entire subepicardial attenuation at the basal, mid and distal left ventricle. TPR was considered abnormal when it was <0.99 as previously described. Due to lower attenuation in the basal lateral segments, the basal anterolateral and basal inferolateral walls were only considered abnormal if the adjacent mid anterolateral or mid inferolateral wall was also abnormal.

A participant was defined positive for myocardial ischemia when the TPR was < 0.99 on stress CTP that worsened compared to the rest CTP in greater than one myocardial segment. Fixed myocardial infarction was visually determined by the presence of hyperenhancement on DECT by a single experienced blinded observer (R.G.).

**Coronary CTA Analysis**

CT angiographic images were transferred to a dedicated workstation (Vitrea v. 5.0, Vital Images, Minnetonka, Minnesota) for analysis by a level III certified CT angiographer (A.A) blinded to all other data. All segments ≥ 1.5 mm were analyzed using a 19-segment model. Each coronary segment was visually assessed for the percent luminal stenosis and a vessel supplying a territory was considered obstructive if there was at least one segment of a vessel with a ≥ 50% luminal diameter stenosis. In addition, a luminal diameter stenosis threshold of ≥70% was used in secondary analyses. Uninterpretable segments were excluded from the analysis.
SPECT Imaging and Analysis

In all patients, stress-rest SPECT-MPI (using technetium-99m sestamibi) was performed with symptom limited treadmill exercise or pharmacologic (dipyridamole or adenosine) stress according to protocols endorsed by the American Society of Nuclear Cardiology and transferred to an independent nuclear core laboratory for analysis. Using a 16-segment model (apex was excluded), a single experienced blinded observer (Board Certified in Nuclear Medicine) (F.B.) scored myocardial segments using a semi-quantitative visual assessment (0 = normal, 1 = mild reduction in radioisotope, 2 = moderate reduction, 3 = severe reduction) and reversibility was determined. The summed rest score (SRS) and summed stress score (SSS) was calculated as the sum of scores on the rest and stress images, respectively.23

Invasive Coronary Angiography Acquisition and Quantitative Coronary Analysis

Invasive coronary angiography (ICA) was performed in a subset of patients using standard orthogonal views and was clinically driven. Quantitative coronary angiography (QCA) was performed by an independent angiographic core laboratory on all coronary segments >1.5mm in diameter (CAAS II QCA Research version 2.0.1 software, PIE Medical Imaging, Maastricht, the Netherlands) on the most significant stenosis ≥ 30% severity within each coronary segment using the same 19 segment coronary model. A vessel supplying a territory was considered obstructive if at least one segment of a vessel contained a ≥ 50% luminal stenosis.

Hybridization of Multimodality Imaging

Perfusion deficits noted on CTP and SPECT-MPI were assigned a coronary artery territory according to well established criteria. In cases where variation of the coronary arterial
anatomy varied from standard practice, the CTA was used to reassign myocardial segments to the appropriate vessel territory for both SPECT and CTP as previously\textsuperscript{18}.

**Reference Standard**

The reference standard in the study was defined as reversible ischemia on SPECT-MPI. In addition, we studied the overall accuracy of CTP to diagnose reversible ischemia on SPECT-MPI in the presence of an obstructive lesion (≥50\%) on CTA with a reference of CTA stenosis ≥ 50\% and a reversible SPECT perfusion deficit. For any of the combined variables, a patient or a vessel/territory were positive only if the stenosis and perfusion deficit were in the same vascular distribution.

**Radiation Dose Calculations** - CT radiation doses were estimated using the dose length product reported on the scanner and converted to effective dose by multiplying by the constant (k=0.014 mSv/mGy/cm) according to standard methodology outlined in the European Guidelines on Quality Criteria for Computed Tomography\textsuperscript{25}. Estimates of effective radiation dose from SPECT were calculated by converting millicurie to millisievert.\textsuperscript{26}

**Statistical Analysis**

Means were expressed ± standard deviation and compared using paired t-test. Accuracy was determined by calculating the sensitivity, specificity, positive predictive value, and negative predictive value, and 95\% confidence intervals were calculated according to the efficient-score method\textsuperscript{27}. The area under the receiver operating characteristic (ROC) was calculated and reported with 95\% confidence intervals with a p-value to compare the significance of the ROC
Results

Patient Population - Fifty-three consecutive patients (68% male and mean age 58.3±10 years) were enrolled in the study and fifty patients completed the protocol. Three patients did not complete the full CT protocol secondary to: renal dysfunction on baseline testing (1), allergic reaction to iopamidol (1), and the development of atrial fibrillation during the adenosine infusion (1). Baseline characteristics are shown in Table 1.

SPECT-MPI Findings – On SPECT-MPI, 20/50(40%) patients and 36/150(24%) vascular territories had perfusion abnormalities. Eighteen patients (90%) had reversible ischemia and 2 patients had fixed perfusion deficits. Of the 36 vascular territories with perfusion abnormalities, 26(72%) were reversible, 7/36(19%) were partially reversible, and 4/36(11%) were fixed. The mean (range) SSS and SRS was 4.3±6.6 (0-34) and 1.3±5.2 (0-34), respectively. Eighteen patients had a SSS=0 and 38 patients had a SRS=0.

CACS Findings – The mean Agatston score was 170±281 with a median of 18 and a range of 0-1148.

CTA Findings – CTA imaging demonstrated 18/50(36%) of patients and 26/150(17%) of vessels had stenoses graded at ≥50% severity and 10/50(20%) of patients had stenoses graded at
\[ \geq 70\% \text{ severity.} \text{ Of patients with } \geq 50\% \text{ stenosis severity, 12 patients had 1-vessel, 4 patients had} \]
\[ \text{2-vessel, and 2 patients had 3-vessel disease. Overall, 5.1\% of coronary segments were deemed}\]
\[ \text{uninterpretable. CTA alone was a limited predictor of myocardial ischemia compared with}\]
\[ \text{SPECT using a } \geq 50\% \text{ and } \geq 70\% \text{ threshold, see Table 3.}\]

**CTP Findings** - CTP imaging revealed 18/50 (36\%) of patients and 32/150 (21\%) of vascular territories had perfusion abnormalities. Of the 31 vascular territories with perfusion abnormalities, 24/31 (77\%) were reversible and 7/31 (23\%) were partially reversible. There were two patients with delayed enhancement on DECT consistent with chronic myocardial infarction and these matched the two patients with fixed perfusion deficits on SPECT. Quantitative analysis of CTP imaging and a representative patient is shown in Figure 2.

*Diagnostic Accuracy of CTP* - Overall, the diagnostic accuracy of CTP to detect myocardial ischemia by SPECT was better than CTA, see Table 3. In addition, the overall sensitivity and specificity of CTP to detect obstructive atherosclerosis causing myocardial ischemia compared with the reference standard of CTA+SPECT was excellent, see Table 4.

In addition, we restricted an analysis to those patients or vascular territories with stenoses \[ \geq 50\% \text{ identified by CTA (N=18) in need of determining the physiologic significance of the}\]
\[ \text{stenosis. The accuracy of CTP detecting myocardial ischemia in patients with stenoses } \geq 50\% \]
\[ \text{compared with SPECT demonstrated a sensitivity and specificity of 90\% and 75\%, and the AUC}\]
\[ \text{was 0.83 (95\%CI: 0.58-0.96, p=0.001) in the per-patient analysis and 100\% and 78\%, and the}\]
\[ \text{AUC was 0.89 (95\%CI: 0.70-0.98, p<0.001) in the per-vessel/territory analysis; respectively. In}\]
\[ \text{these patients with CTA stenoses } \geq 50\%, \text{ ROC analysis demonstrated an optimal TPR decrease}\]
\[ \text{below the threshold of 0.99 for detecting significant myocardial ischemia (SSS } \geq 4) \text{ to be 0.10}\]
with a sensitivity of 100% and a specificity of 73%, AUC=0.87 (95%CI: 0.74-0.95, p<0.001).

There was a strong correlation between the global TPR decrease below the threshold of 0.99 and the SSS in territories with obstructive CAD and ischemia, Figure 3.

**CTP Sub-analysis Compared with QCA** – In the subset of patients (N=19) with invasive angiography available, we compared the accuracy of CTP in combination with CTA - Because CTP will be used to compliment CTA, we analyzed the accuracy of CTA alone and the combination of CTA and CTP to predict the combination of QCA and SPECT. In the per-patient analysis, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and AUC of CTA alone was 100%, 60%, 69%, 100 %, 0.80 and for CTA + CTP was 89%, 90%, 89%, 90%, and 0.89; respectively demonstrating an improvement specificity and positive predictive value with small reductions in sensitivity and NPV. Furthermore, of the 19 patients that underwent invasive angiography 12 patients underwent revascularization (coronary bypass: 12 and percutaneous coronary intervention: 7) and 7 did not. CTP was 83% sensitive and 86% specific (AUC: 0.845) and CTA/CTP was 83% sensitive and 100% specific (AUC: 0.917) for revascularization.

**Adverse Events** – There was one serious adverse event that involved a single participant going into atrial fibrillation during adenosine infusion. The adenosine infusion was discontinued and imaging aborted resulting in normal sinus rhythm without any further intervention.

**Radiation Dose** – The effective radiation doses are shown in Figure 4.
Discussion

This study demonstrates that myocardial perfusion assessment by computed tomography can detect myocardial ischemia compared with the reference standard SPECT-MPI and CTP is highly accurate in determining the presence or absence of myocardial ischemia in patients with obstructive CAD in need of physiologic assessment when compared with CTA and SPECT-MPI. When combined with coronary CTA, this test can provide anatomic visualization of the coronary arteries, thus providing a comprehensive evaluation of atherosclerosis and its direct influence on myocardial perfusion.

The development of methods based on the injection of radioactive isotopes, first thallium-201\textsuperscript{29} and then technetium-99m based tracers\textsuperscript{10,30,31}, to index myocardial perfusion revolutionized the clinical assessment of patients with suspected CAD in the last three decades\textsuperscript{32} and have become one of the most frequently utilized diagnostic tests in American cardiology. Perfusion abnormalities detected at rest and/or during exercise or pharmacologic induced stress are excellent markers of flow limiting coronary stenoses and relate directly to prognosis in patients with suspected CAD. However, despite their established clinical utility, these tests have well known limitations, the most important of which is the inability to measure the type, location and severity of coronary atherosclerosis non-invasively. Moreover, these methods do not permit the quantification of sub-clinical atherosclerosis currently used for risk factor modification and preventive purposes. Such limitations are in part responsible for referral for angiography of a large number of patients who do not have obstructive CAD\textsuperscript{33} costing patients unnecessary invasive procedures and the nation increased health care associated costs. The development of other tests based on functional contractile alterations detected by ultrasound or ECG changes during traditional stress testing have not impacted the utilization of SPECT tests significantly.
because they do not index myocardial perfusion, the most direct consequence of chronic coronary obstruction. The measurement of myocardial perfusion by positron emission tomography or magnetic resonance imaging, although as or more efficacious than SPECT imaging, are expensive and require larger investments in terms of personnel and equipment by health care providers and organizations\textsuperscript{34,35}. The advent of computed tomography has challenged this paradigm, at least for patients with low or intermediate probability of having obstructive CAD.

There are several strengths of the current study and the comprehensive cardiac CT protocol implemented that should be highlighted. Compared with prior studies of vasodilator stress CTP imaging the current study utilizes a 320 row detector scanner using a protocol with the rest scan performed first, followed by stress scanning in an intermediate to high risk population with abnormal patients having primarily myocardial ischemia. Prior studies from our institution and others have primarily utilized 64 detector CT scanning systems for CTP imaging, performing stress imaging followed by rest imaging, in populations with a very high prevalence of disease\textsuperscript{16,18,36}. For instance, in the study from our institution, the prevalence of SPECT myocardial perfusion deficits was 90% and the prevalence of obstructive atherosclerosis was 59%. Similarly, the study by Blankstein, et al demonstrated a prevalence of disease - 76% by SPECT and 74% by angiography and the study by Cury et al. demonstrated a prevalence of 100% by SPECT and 69% by angiography. In comparison, the current study demonstrated a prevalence of 40% by SPECT and 36% by CT angiography allowing for a fairer assessment of diagnostic accuracy. However, this study, similar to other single center studies of myocardial CTP, is limited in size and conclusions drawn from these results should be taken with caution. While these studies have firmly established the feasibility of 64-CT myocardial perfusion
imaging, cardiac imaging over portions of 1 or 2 heart beats using a 320-CT system allows for several advantages including targeting a specific portion of the contrast bolus, temporal uniformity of image acquisition, and reductions in radiation and contrast dose. We consider a rest/stress protocol to have several advantages compared to a stress/rest protocol. First, the clinical use of CTA/CTP will take advantage of the high sensitivity and negative predictive value of CTA. A protocol structured with CTA first provides the ability to exclude disease in patients with high negative predictive value and detect subclinical atherosclerosis in patients at risk of future cardiac events. Patients with normal or mildly abnormal studies do not require CTP imaging and can avoid additional testing and the additional radiation exposure. In our study, on average, these patients would receive an effective radiation dose of 4.5 mSv. For those patients with potentially obstructive CAD (stenoses ≥ 50%), adenosine stress CTP imaging can be performed to determine the physiologic significance of these stenoses and determine if a medical versus invasive approach to treatment should be pursued. Only those patients with disease would require exposure to a total effective radiation dose that is comparable to SPECT-MPI alone. There are, of course, disadvantages to this approach. An approach with CTA first requires the administration of beta blockers prior to the CTA, potentially masking the presence of myocardial ischemia. In addition, there is a theoretical risk that contrast could contaminate the stress CT image. However, despite these theoretical risks, these factors did not appear to significantly affect diagnostic accuracy in this study. Rest/Stress CTP imaging with beta blockade will be further tested in the large multicenter, international study - the CORE320 study.37

There are several limitations of the current study that are important to point out. First, the per-vessel sensitivity of CTP compared to SPECT was limited. It is unclear why this occurred
and these false negative results could be the result of false positive SPECT studies. The excellent sensitivity of CTP in detecting obstructive atherosclerosis and myocardial ischemia by CTA+SPECT on a per-patient and per-vessel basis argues in favor of this. This study used a semi-quantitative analysis, TPR. Quantitative CTP analyses can be limited by imaging artifacts such as motion, beam hardening, and reconstruction artifacts and in the setting of global transmural ischemia may underestimate the presence of ischemia. In addition, CTP is limited in patients at risk of contrast induced nephropathy and adenosine is contraindicated in patients with high grade AV block and bronchospastic lung disease.

In conclusion, this study in patients at intermediate to high risk of CAD demonstrates that CTP imaging, when combined with coronary CTA has the potential to transform the management of patients with suspected obstructive CAD.
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References


**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Age - years</td>
<td>58.3±10.0</td>
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<tr>
<td>Body Mass Index – kg/m²</td>
<td>29.5±4.8</td>
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<tr>
<td>Male</td>
<td>36 (68)</td>
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<tr>
<td>Female</td>
<td>14 (32)</td>
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<tr>
<td>Intermediate Risk</td>
<td>41 (77)</td>
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<tr>
<td>High Risk</td>
<td>12 (23)</td>
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<tr>
<td>Tobacco Use (Current or Prior)</td>
<td>33 (62)</td>
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<td>Family History of Premature CAD</td>
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<td>Diabetes Mellitus</td>
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<td>Prior CAD</td>
<td>6 (11)</td>
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<td>Hyperlipidemia</td>
<td>41 (77)</td>
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<td>Hypertension</td>
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<td>Chronic Beta-blocker Use</td>
<td>19 (35)</td>
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<td><strong>Acquisition Parameters</strong></td>
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<tr>
<td>Slice thickness – (mm)</td>
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</table>

Abbreviations: CACS; coronary artery calcium scoring, CTA; computed tomography angiography, CTP; computed tomography myocardial perfusion imaging, DECT; delayed enhanced computed tomography imaging
imaging

* For the rest CTA and stress CTP imaging, single heart beat prospective ECG-triggered acquisition was used for heart rates \( \leq 65 \) and 2-beat prospective ECG-triggered multi-segment acquisition was used for heart rates \( >65 \).
Table 3. Diagnostic accuracy of myocardial CTP and coronary CTA (using ≥ 50% and ≥70% diameter stenosis thresholds) to diagnose reversible ischemia compared to the reference standard SPECT myocardial perfusion imaging.

<table>
<thead>
<tr>
<th></th>
<th>CTP vs. SPECT</th>
<th>CTA Stenosis ≥ 50% vs. SPECT</th>
<th>CTA Stenosis ≥ 70% vs. SPECT</th>
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<tbody>
<tr>
<td><strong>Per-Patient Analysis vs. SPECT</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>72 (46-89) 13/18</td>
<td>56 (31-78) 10/18</td>
<td>39 (18-64) 7/18</td>
</tr>
<tr>
<td>Specificity</td>
<td>91 (74-98) 29/32</td>
<td>75 (56-88) 24/32</td>
<td>91 (74-98) 29/32,</td>
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<tr>
<td>PPV</td>
<td>81 (54-95) 13/16</td>
<td>56 (31-78) 10/18</td>
<td>70 (35-92) 7/10</td>
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<tr>
<td>NPV</td>
<td>85 (68-94) 29/34</td>
<td>75 (56-88) 24/32</td>
<td>73 (56-85) 29/40</td>
</tr>
<tr>
<td>AUC</td>
<td>0.81 (0.68-0.91) p&lt;0.001</td>
<td>0.65 (0.51-0.78) p=0.07</td>
<td>0.65 (0.50-0.78) p=0.08</td>
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<tr>
<td><strong>Per-Vessel Analysis vs. SPECT</strong></td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>50 (32-68) 16/32,</td>
<td>25 (12-44) 8/32</td>
<td>22 (10-40) 7/32</td>
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<tr>
<td>Specificity</td>
<td>89 (82-94) 105/118</td>
<td>85 (77-90) 100/118</td>
<td>96 (90-98) 113/118</td>
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<tr>
<td>PPV</td>
<td>55 (35-73) 16/29</td>
<td>31 (15-52) 8/26</td>
<td>58 (29-84) 7/12</td>
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<td>NPV</td>
<td>87 (79-92) 105/121</td>
<td>81 (72-87) 100/124</td>
<td>82 (74-88) 113/138</td>
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<tr>
<td>AUC</td>
<td>0.70 (0.62-0.77) p&lt;0.001</td>
<td>0.55 (0.47-0.63) p=0.40</td>
<td>0.59 (0.51-0.67) p=0.13</td>
</tr>
</tbody>
</table>

CTP: Computed tomography myocardial perfusion imaging, SPECT: single photon emission computed tomography, CTA: Computed tomography coronary angiography, PPV: Positive predictive value, NPV: negative predictive value, AUC: Area under the receiver operator characteristic curve.
Table 4. Diagnostic accuracy of myocardial CTP to diagnose reversible ischemia in the presence of obstructive atherosclerosis (using ≥ 50% and ≥70% diameter stenosis thresholds).

<table>
<thead>
<tr>
<th></th>
<th>Per-Patient Analysis vs. CTA/SPECT</th>
<th>Per-Vessel Analysis vs. CTA/SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CTP vs. CTA Stenosis ≥50% + SPECT</td>
<td>CTP vs. CTA Stenosis ≥70% + SPECT</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100 (60-100) 8/8</td>
<td>100 (56-100) 7/7</td>
</tr>
<tr>
<td>Specificity</td>
<td>81 (65-91) 34/42</td>
<td>79 (64-89) 34/43</td>
</tr>
<tr>
<td>PPV</td>
<td>50 (26-74) 8/16</td>
<td>44 (21-69) 7/16</td>
</tr>
<tr>
<td>NPV</td>
<td>100 (87-100) 34/34</td>
<td>100 (87-100) 34/34</td>
</tr>
<tr>
<td>AUC</td>
<td>0.91 (0.79-0.97) p&lt;0.001</td>
<td>0.90 (0.78-0.96) p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>CTP vs. CTA Stenosis ≥50% + SPECT</td>
<td>CTP vs. CTA Stenosis ≥70% + SPECT</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100 (60-100) 8/8</td>
<td>100 (56-100) 7/7</td>
</tr>
<tr>
<td>Specificity</td>
<td>85 (78-90) 121/142</td>
<td>85 (77-90) 120/142</td>
</tr>
<tr>
<td>PPV</td>
<td>28 (13-47) 8/29</td>
<td>25 (11-44) 7/28</td>
</tr>
<tr>
<td>NPV</td>
<td>100 (96-100) 121/121</td>
<td>100 (96-100) 121/121</td>
</tr>
<tr>
<td>AUC</td>
<td>0.93 (0.87-0.96) p&lt;0.001</td>
<td>0.92 (0.87-0.96) p&lt;0.001</td>
</tr>
</tbody>
</table>

CTP: Computed tomography myocardial perfusion imaging, SPECT: single photon emission computed tomography, CTA: Computed tomography coronary angiography, PPV: Positive predictive value, NPV: negative predictive value, AUC: Area under the receiver operator characteristic curve,
Figure Legends

Figure 1. Timeline of a comprehensive cardiac CT protocol that includes coronary artery calcium scoring (CACS), rest CT angiography and perfusion (CTA), stress CT perfusion (CTP), and delayed enhanced CT (DE-CT).

Figure 2. 55 year old with exertional chest pressure. Panel A displays short axis, horizontal, and vertical long axis myocardial perfusion images from single photon emission computed tomography demonstrating a reversible perfusion deficit in the basal to mid inferolateral wall consistent with myocardial ischemia (white arrows). Panel B and C show an intermediate severity stenosis (50-69%) in the mid left anterior descending artery and a severe stenoses in the left circumflex (70-99%) and obtuse marginal branch (70-99%) (White arrows). Panel D displays the quantitative analysis of rest CT perfusion (CTP) using a 16 segment polar plot with blue representing normal perfusion (transmural perfusion ratio (TPR) ≥ 0.99). Panel E demonstrates adenosine stress CTP. The 16 segment polar plot and images demonstrate abnormal perfusion in the inferolateral and distal anterior wall (white arrow). Abnormal TPR (<0.99) is displayed in yellow, orange and red.

Figure 3. CT Perfusion derived Transmural Perfusion Ratio (TPR) compared with the Summed Stress Score (SSS) measured on SPECT in patients with stenoses ≥ 50%. Panel A demonstrates the receiver operator characteristic curve describing the diagnostic performance for the TPR to detect a SSS ≥ 4 in patients with stenoses ≥ 50% (n=18). The area under the curve (AUC) was 0.87 (95% CI: 0.74-0.95), p<0.001. Panel B demonstrates the correlation between
the reduction in TPR and the SSS in patients with both a stenosis \( \geq 50\% \) and myocardial ischemia on SPECT-MPI (n=9).

**Figure 4.** Radiation doses in millisievert (mSv) for coronary artery calcium scoring (CACS), rest CT angiography and perfusion, stress CT perfusion, delayed enhanced CT, rest single photon emission computed tomography (SPECT), and stress SPECT.
CACS
Rest CTA
5 min
5 min
Stress CTP
5 min
DE-CT

Iopamidol 370
5 ml/sec x 60 ml
Adenosine
140 µg/kg/min
Iopamidol 370
5 ml/sec x 60 ml
Adenosine OFF
A

B

Reduction in TPR

$y = 0.0145 - 0.0409x$

$R^2 = 0.84, p = 0.001$
Computed Tomography Myocardial Perfusion Imaging with 320-Row Detector CT Accurately Detects Myocardial Ischemia in Patients with Obstructive Coronary Artery Disease
Richard T. George, Armin Arbab-Zadeh, Julie M. Miller, Andrea L. Vavere, Frank M. Bengel, Albert C. Lardo and João A.C. Lima

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