Coronary Artery Disease

Adenosine Stress Cardiovascular Magnetic Resonance With Variable-Density Spiral Pulse Sequences Accurately Detects Coronary Artery Disease

Initial Clinical Evaluation

Michael Salerno, MD, PhD; Angela Taylor, MD; Yang Yang, MS; Sujith Kuruvilla, MD; Michael Ragosta, MD; Craig H. Meyer, PhD; Christopher M. Kramer, MD

Background—Adenosine stress cardiovascular magnetic resonance perfusion imaging can be limited by motion-induced dark-rim artifacts, which may be mistaken for true perfusion abnormalities. A high-resolution variable-density spiral pulse sequence with a novel density compensation strategy has been shown to reduce dark-rim artifacts in first-pass perfusion imaging. We aimed to assess the clinical performance of adenosine stress cardiovascular magnetic resonance using this new perfusion sequence to detect obstructive coronary artery disease.

Methods and Results—Cardiovascular magnetic resonance perfusion imaging was performed during adenosine stress (140 μg/kg per minute) and at rest on a Siemens 1.5-T Avanto scanner in 41 subjects with chest pain scheduled for coronary angiography. Perfusion images were acquired during injection of 0.1 mmol/kg Gadolinium-diethylenetriaminepentaacetic acid at 3 short-axis locations using a saturation recovery interleaved variable-density spiral pulse sequence. Significant stenosis was defined as ≥50% by quantitative coronary angiography. Two blinded reviewers evaluated the perfusion images for the presence of adenosine-induced perfusion abnormalities and assessed image quality using a 5-point scale (1 [poor] to 5 [excellent]). The prevalence of obstructive coronary artery disease by quantitative coronary angiography was 68%. The average sensitivity, specificity, and accuracy were 89%, 85%, and 88%, respectively, with a positive predictive value and negative predictive value of 93% and 79%, respectively. The average image quality score was 4.4±0.7, with only 1 study with more than mild dark-rim artifacts. There was good inter-reader reliability with a κ statistic of 0.67.

Conclusions—Spiral adenosine stress cardiovascular magnetic resonance results in high diagnostic accuracy for the detection of obstructive coronary artery disease with excellent image quality and minimal dark-rim artifacts. (Circ Cardiovasc Imaging. 2014;7:639-646.)

Key Words: coronary artery disease ■ magnetic resonance imaging ■ myocardial perfusion ■ stress tests

It is estimated that 17.6 million Americans have coronary artery disease (CAD) and ≈10.2 million Americans have angina pectoris.1 CAD is a leading cause of morbidity responsible for ≈1 in 6 deaths in the United States.2 Greater than 10 million stress tests are performed annually to evaluate known or suspected CAD, resulting in a significant economic burden to the United States.3 Because recent studies have demonstrated low rates of obstructive CAD of patients undergoing cardiac catheterization, improvement in stress imaging techniques can potentially affect downstream costs of additional noninvasive and invasive evaluation and treatment of CAD.3

Clinical Perspective on p 646

There is a significant body of evidence demonstrating the high diagnostic and prognostic use of adenosine stress cardiovascular magnetic resonance (CMR) imaging.4,5 Recent head-to-head comparisons between stress CMR and single-photon emission computed tomography have demonstrated equivalent or superior accuracy of CMR.6,7 Despite these advantages, CMR perfusion imaging is still limited by artifacts that may be mistaken for perfusion abnormalities and has limited spatial and temporal resolution.8,9 Recent studies have extended the capabilities of CMR, improving spatial coverage or spatial resolution using k-t acceleration, but these techniques have limitations in the setting of inadequate breath-holding.10-12 Clinically available CMR pulse sequences for perfusion imaging use Cartesian trajectories that are robust but are not efficient in collecting the data and are particularly susceptible to ringing artifacts in the phase-encoding direction of the
image.13 Non-Cartesian pulse sequences such as spiral imaging collect the required data in a spiral trajectory, which is more efficient and may be less susceptible to motion-induced dark-rim artifacts (DRA).14,15 Non-Cartesian techniques can also be combined with parallel imaging techniques and hold potential for large gains in spatial–temporal resolution.16 To date, there have been relatively few studies evaluating these techniques.17 We have previously demonstrated that spiral pulse sequences with short readout durations and optimized sequence parameters can efficiently produce perfusion images with high spatial resolution, signal-to-noise ratio (SNR), and minimal artifacts.18 By extending this technique to the use of variable-density spiral (VDS) trajectories with a novel density compensation strategy, high-resolution perfusion images with reduced imaging artifacts could be produced with a further increase in efficiency compared with standard spiral techniques.19 However, these techniques need to be tested in a realistic clinical setting for the evaluation of known or suspected CAD compared with a reference standard.

The goal of this study was to assess the clinical performance of VDS perfusion pulse sequences for adenosine stress CMR to detect obstructive CAD disease compared with quantitative coronary angiography (QCA).

Methods

Study Population
Forty-three patients who were scheduled for CA for evaluation of chest pain with known or suspected CAD were prospectively recruited to undergo a research adenosine stress study between March 2010 and June 2013. Patients with a known history of prior CAD, myocardial infarction, or prior percutaneous coronary intervention were eligible for the study; however, patients with prior coronary artery bypass surgery were excluded because adenosine stress CMR has been shown to have different test characteristics in this population.20-22 Exclusion criteria included known ejection fraction <45%; evaluation for workup of cardiomyopathy, significant valvular pathology, pulmonary hypertension, or transplant vasculopathy; glomerular filtration rate <45 mL/min per 1.73 m²; contraindications to MRI including implantable cardiac devices; contraindications to adenosine infusion (asthma or severe chronic obstructive pulmonary disease); or a history of prior gadolinium contrast reaction. All patients had their renal function assessed within 30 days before the CMR study. All CMR imaging studies were performed on the morning of the scheduled cardiac catheterization. A detailed history and physical examination was performed by a physician before the CMR study. The research was performed under an institutional review board–approved protocol.

Stress CMR Protocol
All stress CMR studies were performed on a 1.5-T scanner (Avanto, Siemens Medical Systems) using the standard spine and body phased-array coils. An ECG was obtained before the CMR study, and resting heart rate and blood pressure were recorded. CMR protocol included anatomic imaging using a single-shot steady-state free precession pulse sequence, ventricular function imaging using a cine steady-state free precession pulse sequence, and late gadolinium enhancement (LGE) using a phase-sensitive inversion recovery pulse sequences following standard published methodology.25 For the vasodilator stress imaging, adenosine (Astellas Pharmaceuticals) was infused at 140 μg/kg per minute through a peripheral IV for 3 minutes. A bolus of 0.1 mmol/kg of gadolinium contrast (Magnevist, Bayer Pharmaceuticals) was injected via power injector (Medrad Continuum, Warrendale, PA) through a second IV in the other arm at 4 mL/s. Three short-axis slice locations were imaged per heart beat over a 50 heart beat acquisition using a saturation recovery VDS perfusion pulse sequence. The technical details of the pulse sequence have been described previously.14 Pulse sequence parameters included the following: saturation recovery time of 80 ms (to first radiofrequency pulse of the readout); echo time, 1 ms; repetition time, 9 ms; slice thickness, 10 mm; flip angle, 30°; field of view, 320 mm; 8 spiral interleaves; 6.1 s readout duration per spiral; and nominal spatial resolution of 2 mm². Low-resolution field maps were obtained using 2 single-shot spiral images for off-resonance correction with each perfusion image. The time to acquire each image was 176 ms. Images were reconstructed with a fast conjugate-phase semiautomated reconstruction with Chebyshev approximation of the off-resonance phase term.26 Images were reconstructed with a novel density compensation function that improves signal-to-noise and reduces ringing (DRA) as previously described.14 After a 10-minute washout delay subsequent to the stress perfusion acquisition, resting perfusion imaging was performed during a second injection of 0.1 mmol/kg of Magnevist using the same imaging protocol as described above. Steady-state free precession functional imaging was performed between the perfusion acquisitions, and LGE imaging was performed 5 minutes after resting perfusion imaging using standard methodology.19 The protocol took on average 35 to 45 minutes.

Image Analysis

Two reviewers blinded to the CA data evaluated the CMR images to assess the presence of perfusion abnormalities consistent with myocardial ischemia on a per-patient basis. Image quality was graded on a 5-point scale (1 [poor] to 5 [excellent]). Images were also assessed for the presence and severity of DRA (0, none; 1, mild; 2, moderate; 3, severe). The perfusion images were read off-line in Image J (http://rsweb.nih.gov/ij/) after conversion of the images to animated gifs. In cases of perfusion abnormalities, LGE images were assessed to determine whether the region of perfusion abnormality was larger than the area of scar. A positive study was considered one with evidence of a perfusion abnormality exceeding the area of scar on LGE, indicating evidence of ischemia.

Coronary Angiography

Immediately after the CMR examination, the patients were brought to the cardiac catheterization laboratory for their clinically indicated CA. Angiograms were performed using standard techniques. The severity of stenosis was performed by an independent blinded reviewer using QCA. QCA was performed using automatic edge-detection software at an end-diastolic frame based on the demonstration of the most severe stenosis with minimal foreshortening or branch overlap. The minimal lumen diameter was recorded in each coronary branch with a reference diameter >2 mm. A QCA percent diameter stenosis >50% was used as the reference standard.

Statistical Analysis

Continuous data are expressed as mean±SD, and categorical data are expressed as percentages. The mean sensitivity, specificity, and accuracy of visual analysis of the CMR stress images to detect obstructive CAD as defined by a >50% stenosis by QCA were determined for each of the reviewers. The inter-reader variability was assessed by determining the κ statistic. Statistical analysis was performed using SPSS 19 (IBM, Armonk, NY). Ninety-five percent confidence intervals (CIs) were determined using an exact binomial method based on the F-distribution.21

Results

Patient Characteristics

Forty-one of the 43 patients successfully completed the CMR study and were included in the final analysis. One subject could not tolerate the CMR procedure because of claustrophobia and the other subject developed a long run of nonsustained ventricular tachycardia immediately before initiation of adenosine
stress, and the stress study was not completed. This patient was subsequently found to have a 99% proximal stenosis of his left anterior descending (LAD) artery during CA. In 40 of the 41 subjects, CA was performed immediately after the CMR stress protocol. One subject was found to have thrombocytopenia, and his catheterization was not performed on the same day, but the patient underwent CA 7 months later. Table 1 summarizes the patient characteristics of the subjects included in the study.

Table 2 summarizes the hemodynamic data from the stress CMR studies. With adenosine the average heart rate increased by 10 bpm without a change in systolic blood pressure. All patients successfully underwent both adenosine stress and rest imaging without any complications. The average left ventricular ejection fraction as determined from cine-CMR was 61±7, and the lowest ejection fraction was 49%. Fourteen patients (34%) had evidence of LGE in a CAD pattern, and 2 patients had evidence of midwall fibrosis.

Table 3 shows the results of QCA. CA demonstrated significant coronary artery stenoses (>50% luminal diameter reduction in vessels with >2 mm diameter) in 28 patients (68%). Eight patients (20%) had single-vessel disease, 6 (15%) had 2-vessel disease, and 14 (34%) had 3-vessel disease. Two (5%) patients had left main disease (as well as 3-vessel disease). In the patients with single-vessel disease, 6 were in the LAD territory and 2 in the right coronary artery (RCA) territory.

**Diagnostic Performance and Image Quality**

All CMR perfusion imaging studies were of diagnostic quality. Figure 1A and 1B shows stress and rest spiral perfusion images from a subject who had normal left ventricular function and no LGE. There is a reversible perfusion abnormality in the anterior wall and anteroseptum (arrows). CA demonstrated 85% stenosis of his LAD at cardiac catheterization (Figure 1C). Figure 2A and 2B shows stress and rest perfusion images respectively from another subject with a normal left ventricular function and no LGE. There is a subendocardial perfusion abnormality in the anterior and lateral walls (arrow). CA showed an 80% stenosis in the LAD, an 80% stenosis in the left circumflex artery, and a 70% stenosis in a nondominant RCA (Figure 2C). Figure 3A and 3B shows stress and rest perfusion images respectively from a third subject with normal left ventricular function and no LGE demonstrating a large perfusion abnormality in the inferior wall. An exercise nuclear single-photon emission computed tomographic study (Figure 3C) did not identify any quantitative evidence of myocardial ischemia. CA demonstrated a 90% stenosis in an RCA. These CMR images demonstrate high SNR, minimal blurring, and no DRA (Figure 3D). Figure 4A demonstrates an adenosine stress perfusion abnormality in the LAD and RCA territories and a milder defect in the left circumflex artery territory in the setting of a prior inferior myocardial infarction. Evidence of enhancement in the inferior wall (Figure 4B) early in the resting perfusion image series and a lack of a (Figure 4C) resting perfusion defect are expected because stress imaging is performed before rest imaging and the infarct is already demonstrating LGE from the first contrast bolus. The LGE images confirm an inferior myocardial infarction but no infarction in the other coronary territories (Figure 4D). The coronary angiogram demonstrated 80% mid LAD, 50% left circumflex artery, and 99% RCA stenosis (Figure 4E).

**Table 1. Demographic Data and Patient Characteristics**

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>43 (41 Analyzed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical variables</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>62±9</td>
</tr>
<tr>
<td>Male sex</td>
<td>68%</td>
</tr>
<tr>
<td>Weight, lbs</td>
<td>201±44</td>
</tr>
<tr>
<td>Height, inches</td>
<td>67±5</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>31±6</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>78%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>95%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>46%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>17%</td>
</tr>
<tr>
<td>Prior smoker</td>
<td>34%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>85%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>42%</td>
</tr>
<tr>
<td>History of CAD</td>
<td>39%</td>
</tr>
<tr>
<td>Prior PTCA</td>
<td>22%</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>27%</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>71%</td>
</tr>
<tr>
<td>Plavix</td>
<td>22%</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>56%</td>
</tr>
<tr>
<td>ACE Inhibitor/ARB</td>
<td>68%</td>
</tr>
<tr>
<td>Statin</td>
<td>71%</td>
</tr>
<tr>
<td>Other cholesterol medication(s)</td>
<td>24%</td>
</tr>
<tr>
<td>Oral hyperglycemic agent</td>
<td>34%</td>
</tr>
<tr>
<td>Insulin therapy</td>
<td>15%</td>
</tr>
</tbody>
</table>

**Table 2. Hemodynamic Data**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>66±11</td>
<td>76±15</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>138±13</td>
<td>139±19</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>76±11</td>
<td>65±11</td>
</tr>
<tr>
<td>Rate pressure product (HR*SBP)</td>
<td>9101±1395</td>
<td>10548±2614</td>
</tr>
</tbody>
</table>

HR indicates heart rate; and SBP, systolic blood pressure.

**Table 3. Quantitative Angiography Findings**

<table>
<thead>
<tr>
<th>Angiography Findings</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No coronary disease</td>
<td>3</td>
</tr>
<tr>
<td>Significance criteria</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Any significant disease</td>
<td>28 (68%)</td>
</tr>
<tr>
<td>Single-vessel</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Three-vessel</td>
<td>14 (34%)</td>
</tr>
<tr>
<td>Left main</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CAD, coronary artery disease; and, PTCA, percutaneous transluminal coronary angioplasty.
The diagnostic accuracy for adenosine stress perfusion by patient and by coronary territory is presented in Table 4. For the detection of a 50% stenosis by CA, the average sensitivities, specificities, and accuracies and their 95% CIs of the 2 readers were 89% (CI, 71%–98%), 85% (CI, 55%–98%), and 88% (CI, 74%–96%), respectively, on a per-patient basis. The positive predictive value was 93% (CI, 75%–99%), and the negative predictive value was 79% (CI, 49%–95%). There was good inter-reader reliability with a $\kappa$ statistic of 0.67. For detection of a 70% stenosis, the average sensitivities, specificities, accuracies, positive predictive value, and negative predictive value were 91%, 67%, 80%, 78%, and 86% respectively. In the 1 case that was read as a false-positive by both readers, there was a perfusion abnormality and LGE, but the patient had a patent stent in the RCA and history of a prior ST-segment–elevation myocardial infarction in this territory. In the 1 case that was read as a false-negative by both readers, there was a 54% stenosis in the LAD territory by quantitative QCA.

In 5 cardiac catheterizations, fractional flow reserve (FFR) was performed at the discretion of the operator (12.5% of cases). Of these 5 cases, 3 had an FFR <0.75 and 2 had an FFR >0.75. CMR agreed with FFR in 4 of the 5 cases (80%). The 1 discordant case was a patient with known CAD, prior RCA ST-segment–elevation myocardial infarction with LGE, and diffusely diseased coronary arteries with a 60% LAD lesion by QCA who had an FFR >0.75 but an abnormal CMR perfusion study.

**Image Quality**

The mean image quality score was 4.4±0.7, with only 1 study demonstrating more than minimal DRA, yielding a DRA score of 0.37. Diagnostic quality images were obtained and could be interpreted in all subjects.

**Discussion**

Our study is the first to clinically evaluate spiral pulse sequences for adenosine stress CMR. We demonstrate that these sequences produce high-quality images with minimal DRA and demonstrate high diagnostic accuracy for assessment of CAD. There are several advantages to spiral pulse sequences, including high efficiency, high SNR efficiency, robustness to motion, and isotropic spatial resolution. The novel density compensation strategy used in this study further reduces ringing artifacts and improves SNR by underweighting the high spatial frequencies. Although most clinically used pulse sequences use

---

![Figure 1](http://circimaging.ahajournals.org/)

**Figure 1.** Stress (A) and rest spiral perfusion (B) images from a subject who had normal left ventricular function and no late gadolinium enhancement demonstrate a reversible perfusion abnormality in the anterior wall and anteroseptum. Coronary angiogram (C) shows an 85% stenosis of his left anterior descending artery.

![Figure 2](http://circimaging.ahajournals.org/)

**Figure 2.** Stress (A) and rest perfusion (B) images from a second subject with a normal left ventricular function and no late gadolinium enhancement demonstrate a subendocardial perfusion abnormality in the anterior and lateral walls. Coronary angiogram (C) shows multivessel coronary artery disease with an 80% stenosis in the left anterior descending artery, an 80% stenosis in the left circumflex artery, and a 70% stenosis in a nondominant right coronary artery.
parallel imaging techniques to achieve high temporal and spatial resolution, the VDS technique described in this article has 2.2 mm isotropic spatial resolution (after apodization) and high temporal resolution with data collected over an 80-ms acquisition window without the use of any parallel imaging techniques. Although this study began before we started using parallel imaging techniques for spiral perfusion imaging, the choice not to add parallel imaging techniques had multiple advantages for this study in that all images were reconstructed in real time on the scanner console using noniterative techniques, and it allowed us to evaluate the clinical performance of spiral pulse sequences without any additional artifacts that could result from parallel imaging. However, when VDS trajectories are combined with parallel imaging techniques, complete ventricular coverage with high spatial resolution is achievable. The clinical evaluation of such techniques is currently underway.

The diagnostic performance of the spiral technique described in this article compares favorably with the data reported from a large meta-analysis of stress CMR perfusion imaging. Nandalur et al reported a sensitivity of 91% and a specificity of 81% from a total of 24 published studies of vasodilator stress CMR imaging studies with variation in the definition of a positive study. The largest prospective evaluation of adenosine stress CMR imaging, the Cardiovascular Magnetic Resonance and Single-Photon Emission Computed Tomography For Diagnosis of Coronary Heart Disease (CE-MARC) trial, demonstrated a sensitivity of 82% and a specificity of 79%, with a positive study defined by a multicomponent composite that included any regional wall motion abnormality, hypoperfusion, or presence of LGE. The Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial: Perfusion-Cardiac Magnetic Resonance vs. Single-Photon Emission Computed Tomography For the Detection of Coronary Artery Disease: A Comparative Multicentre, Multivendor trial (MR IMPACT II) study demonstrated a more modest performance of stress CMR with a sensitivity of 72% and a specificity of 59%. Notably, 6% of the studies were deemed unevaluable. The specificity for the MR-IMPACT II study may be lower because of the fact that only perfusion images were used to define a positive study. Klem et al demonstrated that using the perfusion images only to define a positive study resulted in a sensitivity of 82% but with a specificity of only 63%; however, adding LGE to the interpretation algorithm increased the specificity to 88%. A major contributor to the lower specificity of CMR perfusion imaging has been the presence of DRA and other motion-induced artifacts on the perfusion imaging and may contribute to the discrepancy in specificity between CE-MARC and MR-IMPACT II. The important implication is
that better CMR perfusion imaging techniques could further improve the specificity of adenosine stress CMR particularly when the goal of the evaluation is to assess the presence of a flow-limiting stenosis rather than establishing the diagnosis of CAD. In this setting, the presence of LGE does not help define whether the vessel is causing ischemia in myocardium, which could benefit from revascularization.

Non-Cartesian techniques such as spiral and radial trajectories have the potential to reduce DRA by multiple mechanisms. We have previously demonstrated that non-Cartesian trajectories inherently have reduced cardiac motion–induced DRA compared with conventional Cartesian acquisition strategies. In addition, the acquisition efficiency and benign aliasing artifacts enable acquisition of higher resolution images for a given acquisition time. Some of this increased spatial resolution can be traded for reduction in ringing artifacts (both Gibbs and cardiac motion–induced) using apodization or windowing of the raw data.

Apodization is a well-established technique for reducing Gibbs ringing. Di Bella et al demonstrated the use of windowing data in the phase-encoding direction to reduce Gibbs ringing in Cartesian perfusion imaging, but this results in a significant loss of spatial resolution in the phase-encoding direction, which can only be compensated for by increasing the time to acquire each perfusion image. We previously described the use of a density-weighted acquisition and apodizing density compensation function for VDS perfusion imaging to both increase SNR and reduce DRA. By using a VDS trajectory, a

### Table 4. Diagnostic Performance of Adenosine Stress Perfusion

<table>
<thead>
<tr>
<th>Stenosis by Patient</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>25</td>
<td>2</td>
<td>3</td>
<td>11</td>
<td>0.89 (0.72–0.98)</td>
<td>0.85 (0.55–0.98)</td>
<td>0.88 (0.74–0.96)</td>
<td>0.93 (0.76–0.99)</td>
<td>0.79 (0.49–0.95)</td>
</tr>
<tr>
<td>70%</td>
<td>21</td>
<td>6</td>
<td>2</td>
<td>12</td>
<td>0.91 (0.72–0.99)</td>
<td>0.67 (0.41–0.81)</td>
<td>0.80 (0.65–0.91)</td>
<td>0.78 (0.58–0.91)</td>
<td>0.86 (0.57–0.98)</td>
</tr>
<tr>
<td>50% Stenosis by Territory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>20</td>
<td>5</td>
<td>2</td>
<td>14</td>
<td>0.80 (0.59–0.93)</td>
<td>0.88 (0.55–0.98)</td>
<td>0.83 (0.68–0.93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>11</td>
<td>6</td>
<td>2</td>
<td>22</td>
<td>0.85 (0.54–0.98)</td>
<td>0.79 (0.59–0.92)</td>
<td>0.80 (0.65–0.91)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>14</td>
<td>5</td>
<td>2</td>
<td>20</td>
<td>0.88 (0.62–0.98)</td>
<td>0.80 (0.59–0.93)</td>
<td>0.83 (0.68–0.93)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FN indicates false negatives; FP, false positives; LAD, left anterior descending; LCX, left circumflex artery; NPV, negative predictive value; PPV, positive predictive value; RCA, right coronary artery; TN, true negatives; and TP, true positives.
larger extent of k-space (higher spatial resolution) can be sampled in the same or shorter readout duration. By using a density compensation function that intentionally underweights the variable-density data, the k-space data are effectively apodized, reducing ringing (either because of motion or Gibbs ringing) and increasing SNR with only a slight loss of spatial resolution. Overall, the resolution is higher than that which could be achieved with a conventional spiral, with a 25% increase in acquisition efficiency and significantly less ringing artifacts.

The recently described radial technique by Sharif et al uses a similar approach. A higher readout bandwidth is used to achieve a higher spatial resolution with the same readout duration at the cost of a reduction in SNR. The data are apodized (in their case by a Gaussian filter) to remove residual ringing artifacts, effectively underweighting the high spatial frequencies and recovering SNR.

Spiral pulse sequences have some inherent efficiency and SNR advantages compared with radial techniques, although they may be more sensitive to off-resonance and both techniques require accurate scanner calibration and special image reconstruction techniques. Both non-Cartesian techniques show potential for improving image quality and improving acquisition efficiency for first-pass myocardial perfusion imaging.

This study has several limitations. The sample size is relatively small, and there is a high prevalence of CAD. Given the latter, we defined a positive study based on the presence of an adenosine-induced perfusion abnormality rather than using LGE or wall motion abnormalities to define a positive study. This is more consistent with the goal of trying to define the presence of ischemia rather than infarction. However, the population in this study is representative of patients undergoing CA at our institution, which increasingly includes patients with known CAD and prior percutaneous coronary intervention. Another limitation is the use of QCA as the reference standard instead of FFR. Because the patients were undergoing clinically ordered CA studies, the use of FFR was at the discretion of the operator. Although multiple studies have demonstrated the superiority of FFR-guided interventions, data from the National Cardiovascular Data Registry suggest that in the United States, even among patients who were undergoing percutaneous coronary intervention, FFR was only used in 6.1% of patients. Furthermore, we did not directly compare the spiral pulse sequence with a standard Cartesian pulse sequence because it was not feasible to have patients undergo multiple research adenosine stress perfusion studies before cardiac catheterization.

Spiral pulse sequences have several potential drawbacks that require careful consideration to create the high-quality images presented in this study. Spiral pulse sequences are more sensitive to gradient hardware fidelity and eddy current effects. We use an anisotropic gradient delay and eddy current model of the theoretical k-space trajectory to correct these effects. Spiral sequences are sensitive to off-resonance effects, which can result in image blurring. We have carefully optimized the spiral trajectory design to balance between off-resonance artifacts and SNR efficiency. Second, we obtain a field map with each image acquisition to measure field homogeneity and use a rapid conjugate reconstruction technique with a Chebychev polynomial approximation of the off-resonance phase. The image reconstruction occurs in real time on the MRI scanner during image acquisition, and no off-line processing is required. The combination of these 2 factors minimizes off-resonance artifacts. With our current readout duration, we on occasion see off-resonance artifacts in regions of prior myocardial stents or occasionally near the inferior cardiac vein, but these are confined to the epicardium and thus do not significantly affect the evaluation of ischemia. Although spiral pulse sequences seem to be relatively robust to DRA, the additional apodization produced by the density compensation function further reduces ringing artifacts from Gibbs ringing and motion.

Recent studies have demonstrated the potential for 3-dimensional (3D) coverage of the ventricle using highly accelerated 3D k-t Principal Component Analysis techniques. 3D spiral perfusion pulse sequences are feasible and may enable 3D imaging with higher spatial coverage than that achievable with Cartesian techniques because of the increased efficiency afforded by spiral trajectories. Initial results from our group and others have demonstrated significant potential for 3D spiral techniques such as stack-of-spirals. When combined with parallel imaging techniques, 2D spiral perfusion imaging techniques can also produce images with high temporal and spatial resolution, enabling full ventricular coverage by interleaving multiple slices after each saturation pulse. With further shortening of the readout duration per interleaf, similar image quality can be obtained at 3 T. In conclusion, VDS pulse sequences represent a new avenue of research in the quest for high spatial and temporal resolution adenosine stress CMR imaging, with minimal DRA. This technique demonstrates high diagnostic accuracy in a single-center study, but further validation in a larger population in a multicenter setting will be necessary to confirm the diagnostic accuracy of this promising technique in a broader clinical setting.

Acknowledgements

The authors would like to thank Jayne Missel, RN for her help on innumerable aspects of this project, and John Christopher, RT(R) MR for his help performing the CMR imaging.

Sources of Funding

This work was supported by grants from American Heart Association (AHA 10SDG2650038) and National Institutes of Health (NIH RO1 HL079110, NIH K23 HL112910-01, NIH ST32EB003841).

Disclosures

Drs Salerno, Meyer, and Kramer received research support from Siemens Medical Solutions. The other authors report no conflicts.

References

4. Nandalur KR, Dwanena BA, Choudhri AF, Nandalur MR, Carlos RC. Diagnostic performance of stress cardiac magnetic resonance imaging...

**CLINICAL PERSPECTIVE**

There is a large body of evidence suggesting high diagnostic accuracy and potential clinical use of adenosine stress cardiovascular magnetic resonance imaging. However, adenosine stress cardiovascular magnetic resonance perfusion imaging can be limited by motion-induced dark-rim artifacts that may be mistaken for true perfusion abnormalities. Non-Cartesian MRI pulse sequences such as spiral or radial imaging are less susceptible to these artifacts and could improve the performance of adenosine stress cardiovascular magnetic resonance. We have previously demonstrated that spiral pulse sequences reduce dark-rim artifacts in first-pass perfusion imaging. In this first clinical evaluation of a spiral technique, we demonstrate that spiral adenosine stress cardiovascular magnetic resonance results in high diagnostic accuracy for the detection of obstructive coronary artery disease with excellent image quality and minimal dark-rim artifacts. Spiral pulse sequences demonstrate potential as a novel technique for reducing dark-rim artifacts in first-pass perfusion imaging. Although initial results are promising, further study is warranted in a larger clinical population.
Adenosine Stress Cardiovascular Magnetic Resonance With Variable-Density Spiral Pulse Sequences Accurately Detects Coronary Artery Disease: Initial Clinical Evaluation
Michael Salerno, Angela Taylor, Yang Yang, Sujith Kuruvilla, Michael Ragosta, Craig H. Meyer and Christopher M. Kramer

_Circ Cardiovasc Imaging_. 2014;7:639-646; originally published online April 23, 2014; doi: 10.1161/CIRCIMAGING.113.001584

_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/7/4/639

Data Supplement (unedited) at:
http://circimaging.ahajournals.org/content/suppl/2014/04/23/CIRCIMAGING.113.001584.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation: Cardiovascular Imaging* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation: Cardiovascular Imaging* is online at:
http://circimaging.ahajournals.org//subscriptions/
Supplemental Material

Video Legends

Video 1. Stress perfusion images from a subject who had normal LV function and no LGE demonstrates a reversible perfusion abnormality in the anterior wall and anteroseptum. The coronary angiogram demonstrated an 85% stenosis of his LAD. Video corresponds to figure 1 in the manuscript.

Video 2. Resting perfusion images from the same subject do not demonstrate any perfusion abnormality.