Spiral Coronary Angiography Using a Blood Pool Agent

Steffen Ringgaard, PhD,1* Michael Pedersen, PhD,1 Jonas Rickers, MD,1,2 Lars O. Johansson,3 Peter Børnert, PhD,4 and Erik M. Pedersen, DMSc1,2

Purpose: To experimentally investigate the optimum dose of an iron-oxide-based blood pool agent for spiral coronary MR angiography (MRA), and the difference between single and multiple spiral excitations in each cardiac cycle.

Materials and Methods: Images using single and triple spiral excitations in each cardiac cycle were obtained in late diastole of the left main coronary artery in eight pigs following an inversion prepulse. Measurements were obtained before and after injection of increasing doses of an iron oxide blood pool agent (Clariscan) corresponding to concentrations of 0.8, 2.2, and 3.9 mg Fe/kg BW. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were measured.

Results: For 0.8 mg Fe/kg BW relative to precontrast values, a significant increase was observed for both one (SNR: 2.3, CNR: 3.8) and three (SNR: 1.4, CNR: 2.2) excitations (P < 0.01). When the dose was increased from 0.8 mg Fe/kg BW to 2.2 mg Fe/kg BW, only the SNR (P < 0.01) increased further. Significantly higher CNR (1.6–1.8) and SNR (1.4–1.6) values were seen for one excitation relative to three excitations at all concentrations (P < 0.05).

Conclusion: At low concentrations, an iron oxide blood pool agent can increase SNR and CNR significantly with both single excitation and triple excitations using an inversion-prepared spiral acquisition scheme. At higher concentrations, T2* effects reduce image quality.

Key Words: coronary magnetic resonance angiography; spiral acquisition; intravascular contrast agent; contrast dosage; CNR


IMAGING CORONARY ARTERIES by magnetic resonance (MR) is a promising but challenging alternative to catheter and x-ray based coronary arteriography. The obstacles are mainly related to the motion of the heart due to contraction (1,2) and respiration (3), the high spatial resolution required to visualize stenoses, and the difficulty of obtaining sufficient contrast between blood and myocardium (4).

Contrast between blood and myocardium can be obtained by exploiting the inflow effect or using a T2-preparation sequence (5). Alternatively, the contrast is obtained by reducing blood T1 using paramagnetic contrast agents. Both gadolinium (Gd)-based substances (6) and intravascular blood pool agents (7) have been used. The Gd-based agents leak quickly into the interstitial space, and data acquisition in combination with such substances must be performed rapidly during the first passage of the agent. Intravascular agents, on the other hand, stay in the blood vessels for hours and are thus more suitable for coronary angiography.

When blood pool contrast agents are used, the contrast dosage should be sufficiently high to reduce the T1 of blood markedly compared to the T1 of myocardium. On the other hand, too-high concentrations may lead to a considerable reduction of T2* and subsequently reduce the image quality for sequences with long readout times, such as those based on spiral acquisition. Therefore, it is critical to determine the appropriate dosage to achieve the desired contrast.

MRI spiral acquisition inherently reduces motion and flow artifacts because it involves the use of very short echo times (TEs) and the start of data sampling in the center of k-space (8). Thus, the spiral sequence has the potential to be beneficial for coronary angiography (9).

Most coronary MRI sequences apply multiple excitations in each cardiac cycle, but the use of only one excitation per heartbeat will provide nearly full longitudinal relaxation before a subsequent excitation. This means that a large flip angle (e.g., 90°) can be used that will lead to high signal amplitude, which seems particularly advantageous for spiral data acquisition because of the extensive amount of data acquired per excitation (10). However, the use of single or multiple excitations per heartbeat has not been compared experimentally for spiral data acquisitions combined with contrast agents.

Accordingly, the purpose of the present study was to experimentally investigate the combined use of spiral acquisition and intravascular contrast agents for coronary angiography. In particular, we investigated the use of various dosages and compared contrast and im-
age quality for single and multiple excitations in each cardiac cycle.

Based on the above findings, we hypothesized that 1) increasing concentrations of iron oxide blood pool agents would increase SNR and CNR for spiral coronary MRI, but only until a certain concentration at which $T_2^*$ effects would reduce image quality; and 2) using only one excitation per heartbeat with a 90° flip angle would increase SNR compared to multiple excitations per heartbeat.

**MATERIALS AND METHODS**

**Animals and Instrumentation**

Eight Danish Landrace pigs with a mean weight of 33.2 ± 2.2 kg were examined. The pigs were anesthetized by intravenous administration of ketamine/morphine/pavulon, and incubated and ventilated with an MR-compatible respirator. The average heart rate during all scans was 98 ± 23 min⁻¹.

A Philips NT 1.5T scanner (Philips Medical Systems, Best, The Netherlands) equipped with 21 mT/m and 105 mT/m/msec gradients was used. An 18-cm surface coil was used for signal reception. Spiral acquisition software was implemented in the INCA release 5.2 research patch, and image reconstruction was performed offline with in-house-built software. The main off-resonance artifacts were corrected during reconstruction using manual offset of the demodulation frequency as assessed by image quality.

**Protocol**

Three-dimensional coronary MR angiography (MRA) was performed using a stack of spirals covering the first few centimeters of the left coronary artery in a nonanlgulated, transversal plane. Images were acquired with a field of view (FOV) of $340 \times 340$ mm², a $512 \times 512$ matrix $(0.66 \times 0.66$ mm² in-plane resolution), and 3-mm slice thickness. Forty-eight spiral interleaves were sampled with a 20-msec acquisition window using a spectral saturation prepulse for fat suppression. ECG triggering was used for cardiac synchronization and navigator gating, with a 3–4-mm window, used for respiratory control. The navigator was positioned on the right hemidiaphragm. The TE and repetition time (TR) of the spiral sequence were set to 1.3 msec and 26 msec, respectively.

**Contrast Administration**

Scans were performed at three different contrast dosages: 1) after precontrast acquisitions, 1 mg iron oxide/kg BW was administered; 2) at 30 minutes and following two different scans, an additional 2 mg Fe/kg BW was injected and the scans were repeated; and 3) at 60 minutes an additional 3 mg of iron oxide/kg BW was injected. The overall scan protocol is outlined in Table 1. The intravascular half-life of Clariscan has been measured in pigs to be 51 minutes (11). Assuming exponential decay, the true concentrations at 15 minutes after each contrast injection were 0.8, 2.2, and 3.9 mg Fe/kg BW, respectively. These concentration values were used in the subsequent analyses.

**Precontrast Acquisitions**

For precontrast acquisitions, a T2-preparation pulse (5) was used and 20 slices were acquired using a 40° flip angle and three spiral excitations placed in mid-diastole, giving an acquisition time of 78 msec for each heartbeat. This sequence was denoted T2-3exc.

**Postcontrast Acquisitions**

After the iron oxide was administered, two 3D scans were performed at each dosage level within the 30 minutes before the next dosage was administered. The first scan was similar to the precontrast acquisition except that it employed a slice-selective 180° T1-weighting prepulse with a 380-msec delay instead of the T2-preparation prepulse (denoted as T1-3exc). The second 3D scan was also performed with a 180° prepulse, but with only one spiral interleave per heartbeat and a flip angle of 90° (denoted as T1-1exc). Only 10 slices (half the volume) were acquired, resulting in only a 50% increase in scan time compared to T1-3exc.

**Data Analysis**

The SNR and contrast-to-noise ratio (CNR) were measured in the slice containing the largest part of the proximal left coronary artery. The SNR was calculated as the mean signal in the coronary artery divided by the standard deviation (SD) of signal in air, and the CNR was assessed using the SNR in the coronary artery minus the SNR in the myocardium next to the coronary artery. Correction for the reduced (halved) 3D volume in the proximal left coronary artery. The SNR was calculated as the mean signal in the coronary artery divided by the standard deviation (SD) of signal in air, and the CNR was assessed as the SNR in the coronary artery minus the SNR in the myocardium next to the coronary artery. Correction for the reduced (halved) 3D volume in the proximal left coronary artery. The SNR was calculated as the mean signal in the coronary artery divided by the standard deviation (SD) of signal in air, and the CNR was assessed as the SNR in the coronary artery minus the SNR in the myocardium next to the coronary artery. The resulting slope value was the average of these 10 values.

Potential differences in SNR and CNR between sequences and contrast concentration levels were assessed using paired Student’s $t$-tests.

**RESULTS**

The scan times were 4–6 minutes (6–9 minutes for T1-1exc scans) with an average navigator efficiency of 40–50%.

<table>
<thead>
<tr>
<th>Time</th>
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<th>Pre</th>
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<td>T1-3exc</td>
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<td>T1-1exc</td>
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Table 1

Scanning Protocol
Examples of pre- and postcontrast images using three excitations per heartbeat at the different concentration levels are demonstrated in Fig. 2, and the corresponding images with only one excitation per heartbeat are shown in Fig. 3.

The SNR and CNR values at different contrast levels are shown in Figs. 4 and 5, respectively. For 0.8 mg Fe/kg BW relative to precontrast values, a significant increase ($P < 0.01$) was seen for both one (SNR: 2.3, CNR: 3.8) and three excitations per heartbeat (SNR: 1.4, CNR: 2.2). When the dose was increased from 0.8 to 2.2 mg Fe/kg BW for the three excitation sequence, only SNR increased further (10–20%, $P < 0.01$), while CNR had a borderline increase ($P = 0.06$). For the one-excitation sequence, no significant increase was observed. No significant increase was observed when the dosage was increased from 2.2 to 3.9 mg Fe/kg BW for either SNR or CNR. Significantly higher CNR (1.6–1.8) and SNR (1.4–1.6) values were observed for one excitation relative to three excitations at all concentrations ($P < 0.05$).

The sharpness (slope) of coronary artery edges increased at 0.8 mg Fe/kg BW relative to precontrast and then decreased with increasing contrast level (Fig. 6). This was probably due to T2* relaxation effects. However, none of these differences reached statistical significance.

DISCUSSION

The study showed that low doses of intravascular contrast agent improved the image quality, particularly in terms of SNR and CNR, compared to noncontrast scanning for coronary angiography with spiral acquisition. At higher doses the images were blurred due to T2* relaxation effects. Using only one excitation per heart cycle gave rise to improved image quality compared to three excitations, but at the expense of prolonged scan time.

Contrast in coronary MRA can be obtained by the combined use of inflow effect, fat suppression, and T2 preparation of the myocardium (14), or by the use of contrast agents. Until now, most coronary angiography studies have utilized the inflow effect, but as 3D acquisitions with thick slabs become increasingly popular, it is becoming more difficult to use the inflow effect, and hence the use of contrast agents is becoming more logical. The advantages and disadvantages of using contrast agents were extensively discussed by Lorenz et al (10). In most cases, contrast agents will improve the signal amplitude by reducing the T1 (12,15), and the blood-to-myocardium contrast by enhancing the relative T1 difference.

The reduction in blood T1 is determined by the contrast dosage. Lower T1 values provide increased signal...
in gradient-echo sequences and improved myocardium-to-blood contrast. If the myocardium is suppressed using either an inversion or a saturation prepulse, a certain difference between the blood and myocardium T1 is necessary to effectively suppress the myocardium without reducing the blood signal. Johansson et al (15) showed that, particularly for ECG-triggered acquisitions, the T1 should be on the order of 50–100 msec to obtain a substantial increase in signal amplitude. However, reducing the T1 to such low values will also lead to a reduction of T2 and T2*, which may compromise the quality in spiral sequences due to long readout times. For gradient-echo sequences with Cartesian sampling, very short T2* values will lead to signal reduction, but the readout time will usually be so short that the signal variation across a k-space profile will be negligible. For long readout spiral sequences, on the other hand, the signal will decrease during sampling, leading to reduced signal in the outer parts of k-space and subsequent blurring in the images. In the present study we observed severe blurring in the images with the highest contrast doses. The image blurring was clearly seen both directly from the images (Figs. 2 and 3) and from the vessel edge assessments (Fig. 6).

Using the information that the intravascular half-life of Clariscan in pigs is 51 minutes (11) together with known T2* values in pig blood at different contrast doses (13), we estimated the T2* at the three dose levels (15 minutes after each injection) to be 45.9 msec, 14.5 msec, and 5.1 msec, respectively. The point-spread function (PSF) of a sampling method describes how signal originating from a single point source is distributed over the reconstructed image. The width of the PSF is often used as a value for the true pixel size (i.e., the spatial resolution). We calculated the PSF for spiral sampling of signal with T2* decay by multiplying the simulated signal from a point with exponentially decaying functions with time constants corresponding to the three T2* values. This filtered signal was Fourier transformed to obtain the PSF, and the resulting pixel size was taken as the full width at half maximum (FWHM) of the PSF. We found that the pixel size increased by 7.8%, 25.7%, and 110%, respectively, compared to the values without T2* relaxation. This may partly explain the blurring at the high contrast doses.

In coronary angiography, data are usually acquired in mid-diastole or end-diastole, where the heart is relatively steady (2). However, with the high heart rate of these pigs (98 min⁻¹ on average) there were almost no steady periods. This could explain the motion artifacts seen in some of the images, and may also explain why there were no significant differences in vessel sharpness at different contrast levels. The measured SNR and CNR are, however, still valid.

Most coronary angiography studies have used a segmented k-space approach (9,16) with multiple excitations in each heart cycle to reduce scan time; however, this also reduces signal because there is less available longitudinal magnetization in subsequent excitations. Because of the long readout trains often used in spiral sequences, the segmented k-space approach is less rational. The single excitation sequence evaluated in this study therefore could be an attractive alternative to the segmented k-space approach. To reduce the total examination time, the scan time at each contrast level was kept below 30 minutes. To comply with this time limit, the number of 3D slices in the single excitation scan was halved relatively to the three-excitation scans, and in the SNR and CNR calculations all values were multiplied by \( \sqrt{2} \) so that the SNR and CNR of the two sequences could be compared. To shorten the total scan time of the single excitation sequence, it would be tempting and logical to increase the sampling number per spiral interleave even further. However, in practice this is not feasible due to T2* relaxation and magnetic

![Figure 3](image3.png)

**Figure 3.** Example of pre- and postcontrast images using one excitation per heartbeat (the T1-1exc sequence). a–c: Postcontrast images at concentrations of 0.8, 2.2, and 3.9 mg Clariscan/kg BW, respectively. Notice the increasing level of image blurring with increasing contrast agent concentration.

![Figure 4](image4.png)

**Figure 4.** The SNR was calculated from the images by dividing the mean signal in the coronary artery by the SD of the background noise. The values shown are averages from all pigs. The SNR increased up to the 3.9 mg Fe/kg BW level.
field inhomogeneity, and thus we used the same read-out time as used for the triple excitation sequence.

The spiral sequence is rapid and has an effective sampling scheme, but unfortunately it also has some inherent disadvantages that complicate its practical use. The sequence is more sensitive to some intrinsic problems of MRI compared to Cartesian sampling, such as undersampling (foldover), field inhomogeneity, and susceptibility variations. All of these factors lead to more severe image degradation than that observed with Cartesian data acquisition. This is probably why the sequence (until now) has been used rarely in routine MRI.

In a previous study, Clariscan was evaluated in a coronary angiography patient study using a multislice 2D spiral sequence (17). In that study, three contrast doses of 0.25, 0.5, and 0.75 mg Fe/kg BW were used. Low doses were deliberately chosen to avoid the T2* effect, and it was found that both SNR and CNR peaked at the 0.5 mg Fe/kg BW concentration. This is in contrast to the SNR increase up to the highest concentration, and the CNR peak at 2 mg Fe/kg BW observed in our study. However, in the patient study no myocardium nulling prepulse was used, and therefore a large difference between myocardium T1 and blood T1 was not as important as it was in the present study.

In another study, by Klein et al (18), Clariscan contrast agent was used in a patient study with a 3D T1-weighted standard gradient-echo sequence. Five different dosages (of 1–5 mg Fe/kg BW) were used. The main conclusions of that study were that no improvement in SNR or CNR was observed in the proximal branches; however, improvement was noted in the distal branches, which peaked at 2–3 mg Fe/kg BW. At higher dosages, susceptibility artifacts were observed. These conclusions are in accordance with our observations. In a study by Bunce et al (19), 2 mg Fe/kg BW was injected and imaging was performed with both 2D and 3D standard Cartesian sampling. They found significant improvements in both SNR and CNR for the 3D sequence, but not for the 2D images, which is also in accordance with our results.

In conclusion, the present study shows that Clariscan in combination with an inversion prepulse improves both SNR and CNR up to a concentration of 2–3 mg Fe/kg BW, and that a single excitation per heartbeat is superior to triple excitations (albeit at the cost of increased scan time).

**ACKNOWLEDGMENT**

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**REFERENCES**