Three-Dimensional Coronary Dark-Blood Interleaved with Gray-Blood (cDIG) Magnetic Resonance Imaging at 3 Tesla

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**Purpose:** Three-dimensional (3D) dark-blood MRI has shown great potential in coronary artery plaque evaluation. However, substantial variability in quantification could result from superficial calcification because of its low signal. To address this issue, a 3D coronary dark-blood interleaved with gray-blood (cDIG) technique was developed.

**Methods:** cDIG is based on a balanced steady-state free precession readout combined with a local re-inversion-based double-inversion-recovery (LocReInv-DIR) preparation. The LocReInv-DIR is applied every two RR intervals. Dark-blood and gray-blood contrasts are collected in the first and second RR interval, respectively. To improve the respiratory gating efficiency, two independent navigators were developed to separately gate the respiratory motion for the two interleaved acquisitions. In vivo experiments in eight healthy subjects and one patient were conducted to validate the technique.

**Results:** cDIG provided dual-contrasts without compromise in scan time. The dark-blood images with cDIG demonstrated excellent wall and lumen signal performances and morphological measurements. Advantageously, cDIG yielded a second contrast that was shown to help identify the superficial calcification in the coronary plaque of a patient.

**Conclusion:** A novel technique was developed for obtaining 3D coronary vessel wall and gray lumen images. The additional contrast may aid in identifying calcified nodules and thus potentially improve the evaluation of coronary plaque burden. *Magn Reson Med 000:000–000, 2015. © 2015 Wiley Periodicals, Inc.*

**Key words:** coronary vessel wall imaging; magnetic resonance imaging; balanced SSFP; gray-blood imaging; local re-inversion

INTRODUCTION

Coronary artery disease (CAD) has a long subclinical course with the risk of life-threatening events, such as myocardial ischemia and infarction (1,2). These events may be caused by rupture of coronary atherosclerotic plaques and subsequent thrombosis (3,4). Visualization and geometric quantification of coronary plaque can be of vital importance for the assessment of plaque vulnerability, disease diagnosis and treatment decision-making, and the evaluation of treatment outcome (5–7).

Dark-blood MRI has shown great potential in coronary plaque visualization and quantification (8–10). While two-dimensional (2D) acquisition strategies have commonly been used in previous clinical studies (8), three-dimensional (3D) coronary vessel wall imaging is advantageous in terms of spatial coverage, signal-to-noise ratio (SNR), and the flexibility of reformating and visualizing images from different views (11–13). However, several challenges are associated with 3D methods, including long scan times and suboptimal suppression of blood signals. An appealing solution dates back to 2001 when Botnar et al combined a modified double inversion recovery (DIR) magnetization preparation with a spiral sampling trajectory to achieve efficient 3D dark-blood coronary wall MRI (11). The advantage of the modified DIR preparation, compared with the typical design, lies in the second inversion pulse which only targets the segment of interest by means of 2D excitation. This technique avoids re-inversion of the blood spins in the left ventricle that will otherwise remain bright and subsequently flow into the coronary segment following an inversion delay time. Such a local re-inversion (LocReInv) approach was later adapted by Priest et al (14) where an oblique slab-selective re-inversion pulse was used in place of the 2D excitation pulse. This allows broadband adiabatic pulses to be adopted, making the inversion preparation less sensitive to B1-field inhomogeneity. In both works, the LocReInv-based DIR (LocReInv-DIR) preparation was applied every two RR intervals to obtain an optimal dark-blood contrast during the first RR interval. Thus, the second RR interval was simply used for longitudinal magnetization relaxation.

Despite the value of dark-blood MRI, studies evaluating carotid plaques with MRI have suggested that dark-blood contrast may not be adequate for accurate plaque burden assessment (15,16). An underestimation of plaque burden may result from superficial calcification that often mimics part of the lumen because of its low-signal appearance. Recently, a so-called gray-blood contrast...
was proposed that complements the dark-blood contrast by depicting the calcification as a dark region surrounded by moderate-signal-intensity lumen and other wall tissues (16). As demonstrated on carotid plaques, combined gray-blood and dark-blood images allow an improved accuracy of plaque burden assessment when a superficial calcified nodule exists (16). Coronary plaque imaging would likely benefit from such a dual-contrast methodology as well given that calcification is a major risk factor in CAD (17).

In this work, a 3D coronary dark-blood interleaved with gray-blood (cDIG) MR technique was proposed for dual contrast imaging of the coronary vessel wall at 3 Tesla (T). Similar to the LocReInv-DIR scheme proposed by Priest et al (14), a LocReInv-DIR preparation is applied every two RR intervals; a dark-blood contrast is collected in the first RR interval, whereas the second RR interval during which blood magnetizations have partially recovered is used for the acquisition of a gray-blood contrast. Two independent navigators, Nav1 and Nav2, were implemented to separately gate the respiratory motion for the two interleaved acquisitions. We hypothesized that cDIG would provide more information such as lumen delineation and existence of calcified nodules without incurring substantial prolongation of scans compared with the single-contrast LocReInv-DIR approach. Parameter optimization and feasibility studies were performed on healthy volunteers by comparing 3D balanced steady-state free precession (bSSFP) cDIG against two existing dark-blood methods, namely 3D LocReInv-DIR-prepared bSSFP (LocReInv-bSSFP) and 2D DIR-prepared turbo spin-echo (DIR-TSE). Additionally, preliminary results from one patient with coronary artery calcification are presented with the computed tomography (CT) imaging findings as the reference.

METHODS

Sequence Design

A schematic of the proposed cDIG technique is shown in Figure 1. An oblique slice-selective LocReInv-DIR preparation followed by a navigator restore pulse (Nav Restore) is applied every two RR intervals. In the first RR interval, a dark-blood contrast is collected during the cardiac quiescent period that approximately coincides with the nulling point of the blood. During the quiescent period of the second RR interval, a gray-blood contrast is collected as longitudinal blood magnetizations have partially recovered is used for the acquisition of a gray-blood contrast. Two independent navigators were implemented to separately gate the respiratory motion for the two contrasts. We hypothesized that cDIG would provide more information such as lumen delineation and existence of calcified nodules without incurring substantial prolongation of scans compared with the single-contrast LocReInv-DIR approach. Parameter optimization and feasibility studies were performed on healthy volunteers by comparing 3D balanced steady-state free precession (bSSFP) cDIG against two existing dark-blood methods, namely 3D LocReInv-DIR-prepared bSSFP (LocReInv-bSSFP) and 2D DIR-prepared turbo spin-echo (DIR-TSE). Additionally, preliminary results from one patient with coronary artery calcification are presented with the computed tomography (CT) imaging findings as the reference.

Respiratory Gating Scheme with Two Independent Navigators

The cDIG sequence acquires data during free breathing using a prospective respiratory navigator gating scheme.
Because the two contrasts are acquired in alternated RR intervals, scan efficiency would be prohibitively low when data acquired in the two successive RR intervals are simultaneously accepted or rejected. To address the issue, two independent navigators that separately gate the two alternated measurements were implemented. A flowchart of the proposed respiratory gating scheme is shown in Figure 2. The two navigators, Nav1 and Nav2, work independently to determine if the acquired data is accepted or not. When the acquisition of one contrast is completed before the other, the decision-making for the corresponding navigator is disabled and only dummy RF pulses applied in the corresponding RR interval. “db”: dark-blood; “gb”: gray-blood.

**Numerical Simulations of cDIG’s Signal Evolution**

Numerical simulations of the Bloch equations using a matrix formulation were performed to examine the signal and contrast properties of the proposed cDIG technique. For simplicity, the contrast between the vessel wall (T1 = 1412 ms, T2 = 50 ms) (20–22) and arterial blood (T1 = 1935 ms, T2 = 275 ms) (20–22) was determined by the signal from the central k-space line. The parameters for simulations included: repetition time/echo time (TR/TE) = 3.90/1.67 ms, flip angle = 70°, six dummy Kaiser preparation pulses (~24 ms) for bSSFP, and fixed data acquisition window of 100 ms corresponding to 20 segments per RR interval. Inversion delay time, TI, was determined by the RR interval using an empirical equation (Eq. [1]) (23). Six different heart rates, with the RR interval ranging from 700 ms to 1200 ms in increments of 100 ms, were simulated. In addition, the signal evolutions of LocReInv-bSSFP and DIR-TSE were also simulated with an RR interval of 1000 ms and an acquisition repetition time of 2 RR intervals for comparison.

\[ TI = 0.5 \times RR + 275 \text{ ms} - 60 \times (1000 \text{ ms}/RR). \]  

**In Vivo Experiments**

Eight healthy subjects (six males and two females, age range = 23–53 years, mean age = 29 ± 9 years) were studied using the proposed cDIG method, with a study approval by our institutional review board. Written informed consent was given by all subjects before MRI. Imaging was performed using a 3T clinical whole-body MR system (MAGNETOM Verio; Siemens AG, Germany). A 32-channel cardiac phased array coil was used for signal reception. Subjects were placed in a head-first supine position. Additionally, an outpatient (male, age =
65 years) with a CT-confirmed calcified coronary plaque was recruited and evaluated with the cDIG technique. A 3D gradient-echo (GRE) B0-shimming sequence was first conducted in the heart region. A four chamber cardiac cine imaging was then performed to determine the subject’s cardiac quiescent period. A bright-blood coronary MR angiogram (MRA) (1.3 × 1.3 × 1.3 mm³) was obtained to localize the coronary arteries using a 3D electrocardiogram (ECG) triggered, navigator-gated segmented bSSFP sequence. Following multiplanar reconstruction (MPR) of the 3D coronary MRA, the left anterior descending (LAD) or right coronary artery (RCA) was randomly selected from healthy subjects for subsequent coronary wall imaging. The patient underwent only one cDIG scan at the plaque site detected by both MRA and CT images. During the following scans involving the LocReInv preparation, an oblique-view MPR MRA image showing both the left ventricle and the long-axis of the coronary artery segment was used to prescribe the 30-mm-thick LocReInv slab (i.e., the effective spatial range of the LocReInv RF pulse). Care was taken to avoid the overlap between the slab and blood upstream of the coronaries, specifically the left ventricle and proximal ascending aorta, and also between the slab and crossing point of the two navigator bars at the dome of the right diaphragm. Herein, we assumed similar locations of the coronary artery between the late-diastole where the LocReInv preparation was applied (i.e. right after the R-wave) and the mid-diastole where the MRA and subsequent cDIG imaging data were acquired.

**Pilot Study for the Proposed Respiratory Gating Scheme**

A pilot study in five of eight healthy subjects was performed to determine the efficacy of the proposed respiratory gating scheme with two independent navigators (TwoNav-Independent). Two additional navigator gating schemes were conducted for scan-efficiency comparison, including two dependent navigators (TwoNav-Dependent) and one navigator (OneNav). The TwoNav-Dependent, as implemented in Andia et al (24), was used to simultaneously accept or reject data for the two successive RR intervals. The OneNav scheme was used to gate the respiratory motion for single-contrast imaging whereby a single navigator was applied every two RR intervals (10,11,25,26). For simplicity without loss of generality, the schemes were investigated with a 2D segmented bSSFP sequence to save scan times. The same imaging parameters were used in all the three scans: acquisition repetition time = 2 RR-intervals, asymmetric echo sampling with TR/TE = 3.90/1.67 ms; matrix = 320 × 304 with isotropic 0.81 × 0.81 mm² in-plane resolution; partial Fourier in the phase encoding direction = 7/8; flip angle = 70°; slice thickness = 2.0 mm; segments per heartbeat = 20; respiratory gating window = ±2.5 mm.

**Healthy Volunteer Study Comparing cDIG with LocReInv-bSSFP and DIR-TSE**

3D cDIG imaging was performed in a cross-sectional scan and, if time permitted, an in-plane scan. Relevant imaging parameters included: asymmetric acquisition echo sampling with TR/TE = 3.90/1.67 ms; matrix = 320 × 304 with isotropic 0.81 × 0.81 mm² plane resolution (interpolated to 0.41 × 0.41 mm²); partial Fourier in the phase encoding direction = 7/8; flip angle = 70°; slice thickness = 2.0 mm; 4 slices with 50% oversampling (cross-sectional scan) or 8–10 slices with 12.5% oversampling (in-plane scan) in the partition encoding direction; receiver bandwidth = 822 Hz/pixel; segments per heartbeat = 11–25 depending on the subject’s cardiac quiescent period (70–150 ms); SPAIR with a delay time of 180 ms (empirically determined based on a series of ex vivo experiments) for fat suppression; respiratory gating window = ±2.5 mm; oversampling in the phase encoding direction = 10–25%. For the in-plane scan, the slice thickness was interpolated from 2.0 mm to 1.0 mm.

In addition, 3D LocReInv-bSSFP and 2D DIR-TSE were performed for cross-sectional vessel wall imaging. The LocReInv-bSSFP scan used the same image volume and imaging parameters as in the 3D cDIG scan. The DIR-TSE scan was conducted only on one of the four slices obtained in the 3D cDIG scan, with field of view (FOV) and in-plane spatial resolution matched. Other imaging parameters for DIR-TSE included: TR/TE = 2 RR intervals /13.0 ms; echo spacing = 6.6 ms; slice thickness = 3.0 mm; bandwidth = 401 Hz/pixel; turbo factor = 9–11 depending on the duration of subject’s cardiac quiescent period; frequency-selective fat saturation pulses for fat suppression.

**Patient Study Using the Proposed cDIG Technique**

A patient with known coronary artery calcification underwent a 3D cDIG cross-sectional scan. The imaging parameters were the same as in the healthy volunteer study.

**Image Analysis**

Image analysis was primarily performed on the images acquired from the healthy volunteer study using a workstation (Leonardo; Siemens AG, Germany). The 3D images acquired by cDIG and LocReInv-bSSFP were reformatted to the same slice thickness and location as in DIR-TSE.

**Dark-Blood Image Analysis**

Dark-blood images were obtained with cDIG, LocReInv-bSSFP and DIR-TSE techniques. To determine any signal compromise in the dark-blood images with cDIG due to the additional gray-blood acquisition, mean signal intensity of the vessel wall, lumen and perivascular fat (or epicardial fat) were compared between cDIG and LocReInv-bSSFP. Regions of interest (ROIs) for each tissue were manually drawn by a radiologist on a location-matched dark-blood cDIG image and a LocReInv-bSSFP image for each subject, independently. SNR was defined as the mean signal intensity divided by the standard deviation (SD) of noise that was measured in an artifact-free air region. Wall-blood and wall-fat contrast-to-noise ratios (CNRs) were calculated as the difference between the SNRs of appropriate tissues. In addition, above quantities were also measured on DIR-TSE for a comparison between cDIG and DIR-TSE. To evaluate the morphologic quantification capability of cDIG, wall thickness and lumen area were measured on the corresponding slice for dark-blood cDIG, LocReInv-bSSFP, and DIR-TSE, respectively. The inner and outer wall boundaries were manually outlined on respective dark-blood.
Healthy subject scan using two independent navigators.

The quality (vessel wall sharpness and image artifacts) of the vessel wall delineation was scored by two radiologists in consensus on the randomized dark-blood images obtained with the three techniques using a five-point scale (0 = very poor, 1 = poor, 2 = fair, 3 = good, 4 = excellent).

Gray-blood Image Analysis

Gray-blood images were only obtained from cDIG technique. To characterize the wall-blood CNR on the gray-blood cDIG images, mean signal intensities of the vessel wall and arterial blood were also measured on the gray-blood cDIG images using the same ROIs as previously defined on corresponding dark-blood cDIG images.

To confirm whether the vessel wall was shown in the gray-blood contrast or not, the discernible outer boundary of the vessel on both dark-blood and gray-blood images from the same slice as analyzed above were independently contoured for each subject, and the resulting enclosed areas were compared.

Statistical Analysis

Data are presented as means ± SD. Because of limited samples available for statistical analyses, Wilcoxon signed rank test was used to see if the quantitative measurements and qualitative scores were significantly different between the cDIG and LocReInv-bSSFP, and between cDIG and DIR-TSE. To account for above multiple comparisons, the \( P \) value was corrected using the Bonferroni method (27). Furthermore, the agreement in wall thickness and lumen area measurements obtained from cDIG and DIR-TSE was assessed through intraclass correlation analysis. A \( P \) value of \( \leq 0.05 \) (or 0.025 when the Bonferroni method was applied) was considered to indicate statistical significance. Statistical tests were performed using SPSS (version 17.0, SPSS Inc., Chicago, IL).

RESULTS

Numerical Simulations

Figure 3 shows the normalized signal of the vessel wall and arterial blood as a function of time during a TR of two RR intervals. During the quiescent period of the first RR interval, the longitudinal magnetization, \( M_z \), of the arterial blood is near the nulling point, which results in a dark-blood contrast. Similar \( M_z \) values are reached for the vessel wall and arterial blood during the quiescent period of the second RR interval. Although different periods (from 700 ms to 1200 ms) cause different TIs, similar signal and contrast behaviors were found in simulations (Figures 3 and 4). As shown in Figures 3(gkh), the cDIG technique can suppress the blood signal as efficiently as LocReInv-bSSFP and DIR-TSE. This suggests that the dark-blood and gray-blood contrasts can be robustly obtained by the cDIG technique.

In Vivo Experiment Results

Pilot Study for the Respiratory Gating Scheme

Figure 5 shows a snapshot of navigator signals from a healthy subject scan using two independent navigators in the cDIG sequence. The darker beam corresponds to the navigator for the dark-blood contrast, whereas the brighter one corresponds to the navigator for the gray-blood contrast. It is clear that the diaphragmatic positions during the two successive RR intervals may not simultaneously fall into the predefined gating window (yellow arrows). This indicates that independent navigators would be necessary for improving the scan efficiency during a dual-contrast acquisition.

Figure 6 summarizes the scan times of dual-contrast and single-contrast imaging with different respiratory gating schemes. Compared with TwoNav-dependent, the proposed respiratory gating scheme, TwoNav-independent, substantially improved the scan efficiency during dual-contrast imaging. This scan efficiency was comparable to that of OneNav as used in single-contrast imaging with a TR of 2 RR intervals, suggesting that dual contrasts may be independently acquired without compromising the scan time when using the proposed respiratory gating scheme.

Acquisition Times of cDIG and LocReInv-bSSFP in Healthy Subject Scans

All healthy subject scans were successfully completed. The average cross-sectional scan duration was 8.1 ± 3.4 min for the 3D cDIG scan and 7.0 ± 1.9 min for the 3D LocReInv-bSSFP scan (Table 1). There was no significant difference between them.

cDIG Imaging and the Dark-blood Image Analysis

Figure 7 shows representative cross-sectional images from three healthy subjects. The coronary vessel wall was clearly depicted on the dark-blood images acquired with different methods. In addition, the gray-blood images obtained by the cDIG technique depicted the coronary arterial lumen as well as the vessel wall. Figure 8 shows the in-plane imaging results by cDIG. Although the coronary blood flow direction was parallel to the imaging plane, blood signal was well suppressed in the dark-blood images using the local re-inversion pulses. The dark-blood imaging results were similar to the previous works as expected (11,13,14,26,28). There was no discernible contrast between the vessel wall and arterial blood on gray-blood images, which was similar to the cross-sectional imaging results. In both cases, dark-blood and gray-blood images were spatially co-registered due to the interleaved acquisition.

Quantitative analyses on the dark-blood image of the healthy subjects are summarized in Table 1. The SNRs of the vessel wall, lumen, and perivascular fat were not significantly different between cDIG and LocReInv-bSSFP. The same behavior was observed in the CNR of wall-to-blood and wall-to-fat. The wall thickness and lumen area measured from cDIG and DIR-TSE were in good agreement based on the intra-class correlation coefficient (0.972 and 0.967, respectively). The difference in the vessel wall thickness or lumen area between cDIG and DIR-TSE was not significant. This demonstrates that cDIG may be used as an alternative to DIR-TSE for measuring coronary vessel wall thickness and lumen area.

The dark-blood image quality scores analyzed for cDIG, LocReInv-bSSFP, and DIR-TSE were 3.0 ± 1.0, 2.9 ± 1.4, and 2.8 ± 1.6, respectively. There was no significant
difference in image quality between cDIG and LocReInv-bSSFP ($P$ value $= 0.581$), and between cDIG and DIR-TSE ($P$ value $= 0.336$).

**Gray-Blood Image Analysis**

The SNRs of the lumen and vessel wall on gray-blood images were 28.6 ± 12.7 and 20.0 ± 8.3, respectively. The contrast between the vessel wall and arterial blood was not visually appreciable on the gray-blood images. Note that the wall signal was slightly lower than the blood signal, which disagrees with the numerical simulations shown in Figure 4. This is presumably due to the higher proton density in the blood, which was not taken into account in simulations. Nevertheless, the CNR between vessel wall and lumen was $-8.7 \pm 6.0$. Such mild contrast could potentially be useful for identification of superficial calcification in plaque. Moreover, the average area within the outer vessel boundary on the dark-blood and gray-blood images were 25.6 ± 4.8 mm² and 25.0 ± 4.8 mm², respectively, thus corroborating that the vessel wall and lumen were both depicted on the gray-blood images.

**Patient with CAD Study Results**

Proof of concept images acquired in one patient demonstrated the potential of cDIG to determine the size of a calcified plaque with high confidence. The scan targeted
the region where a calcified plaque had been identified by CT. On dark-blood vessel wall images, the calcified nodule was adjacent to the lumen and therefore difficult to visually separate from the lumen because of its dark appearance. On the gray-blood images, however, the calcified nodule was clearly depicted as a dark region surrounded by bright lumen and noncalcified wall tissue (Fig. 9). The inherent co-registration between the two contrasts facilitated discerning the interface between the dark lumen and dark calcification on the dark-blood vessel wall images (Figures 9d and e).

DISCUSSION

This work used a 3D bSSFP readout combined with a LocReInv-DIR preparation and interleaved data acquisition to simultaneously achieve dark-blood and gray-blood coronary imaging at 3T. Our numerical simulations and in vivo healthy volunteer and patient studies demonstrated the feasibility of the proposed cDIG technique to provide dual contrasts with inherent spatial co-registration for improved visualization of coronary plaques, particularly when superficial calcification is present. The technique may allow for more accurate quantification of coronary plaque burden.

The 3D coronary vessel wall imaging techniques proposed by Botnar et al (11) and Priest et al (14) require a TR equal to two RR intervals for adequate inflow of inverted blood spins as well as good wall-lumen contrast. The second RR interval is for the blood spins to recover without any data acquisition. The cDIG technique uses this period to acquire an additional contrast—gray blood. However, this would inevitably elongate the scan time if the data acquired in the first and second RR intervals are simultaneously accepted or rejected by using a two-dependent-navigators approach. To address this issue, we developed a two-independent-navigator gating scheme. Intuitively, data acquired in the first and second RR interval should have almost equal probability to be accepted or rejected. Such equality is the reason why the scan time of cDIG was comparable to that of the LocReInv-bSSFP technique with one navigator for dark-blood imaging only. The scan time was dramatically shortened in our pilot study when adopting this gating scheme. This scheme can be easily extended to other navigator-based multicontrast imaging.

FIG. 4. The contrast between the vessel wall and arterial blood on the dark-blood and gray-blood images obtained by cDIG. Note: the contrast is defined as the $M_z$ magnitudes ratio between the vessel wall and arterial blood, i.e., Contrast = $M_z_{\text{vessel}} / M_z_{\text{blood}}$.

FIG. 5. A representative snapshot to demonstrate the gating efficiency using the proposed respiratory gating scheme with two independent navigators. The darker beam corresponds to the navigator signal for dark-blood imaging in the first RR interval, and the brighter beam corresponds to the navigator signal for gray-blood imaging in the second RR interval. Yellow arrows highlight the data that were accepted for only one of the contrasts in two consecutive heartbeats.

FIG. 6. Pilot study on five healthy subjects with the same scan parameters for comparing the gating efficiency of different respiratory gating schemes. The gating efficiency of the proposed scheme (TwoNav-Independent) for two contrasts was comparable to that of the one navigator (OneNav) for single contrast. The TwoNav-dependent which simultaneously accepts or rejects the datasets for the two contrasts had the lowest gating efficiency.
3D bSSFP as opposed to 3D RF-spoiled GRE was used at 3T for achieving high SNR and CNR. Although bSSFP is sensitive to field inhomogeneity, the banding artifacts have been well minimized by using a 3D GRE shimming technique and using high bandwidth, asymmetric echo, and linear phase-encoding reordering. The B0-shimming technique used a quick, low resolution multislices 2D scan for B0-map estimation and then the application of compensatory shim currents to reduce the local field perturbations (29). This approach has previously been used in cardiovascular imaging and proven to be a useful technique that reduces the bSSFP banding artifacts (30). In addition, the use of high bandwidth and asymmetric echo makes the echo spacing as short as possible, helping reduce the banding artifacts (18,19). Finally, linear reordering can minimize eddy-current-induced signal discontinuity for the bSSFP acquisition and thus reduce image artifacts (19,31). Because linear reordering was used, adiabatic SPAIR pulse was applied to suppress fat signal in this technique. To optimize the SPAIR delay time, a series

<table>
<thead>
<tr>
<th>Imaging sequence</th>
<th>SNR</th>
<th>CNR</th>
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<tbody>
<tr>
<td>cDIG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LocReInv-bSSFP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIR-TSE</td>
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</table>

**Table 1** Results of Quantitative and Qualitative Analyses for Dark-Blood Images Acquired by cDIG, LocReInv-bSSFP, and DIR-TSE

<table>
<thead>
<tr>
<th>Imaging sequence</th>
<th>Vessel wall</th>
<th>Lumen</th>
<th>Epicardial fat</th>
<th>Wall-blood</th>
<th>Wall-fat</th>
<th>Wall thickness (mm)</th>
<th>Lumen area (mm²)</th>
<th>Acquisition time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cDIG</td>
<td>19.4 ± 4.9</td>
<td>6.6 ± 3.0</td>
<td>9.6 ± 2.1</td>
<td>12.8 ± 6.5</td>
<td>9.8 ± 3.8</td>
<td>1.4 ± 0.2</td>
<td>5.4 ± 1.6</td>
<td>8.1 ± 3.4</td>
</tr>
<tr>
<td>LocReInv-bSSFP</td>
<td>20.2 ± 4.4</td>
<td>6.9 ± 2.8</td>
<td>10.8 ± 2.4</td>
<td>13.3 ± 5.9</td>
<td>9.4 ± 2.9</td>
<td>1.4 ± 0.1</td>
<td>5.3 ± 1.9</td>
<td>7.0 ± 1.9</td>
</tr>
<tr>
<td>DIR-TSE</td>
<td>15.6 ± 4.1</td>
<td>7.1 ± 2.6</td>
<td>8.8 ± 4.0</td>
<td>8.5 ± 2.9</td>
<td>6.8 ± 2.7</td>
<td>1.4 ± 0.2</td>
<td>6.9 ± 2.0</td>
<td>NA</td>
</tr>
</tbody>
</table>

**P-value:** cDIG vs. LocReInv-bSSFP
- Vessel wall: ns(<0.025)
- Lumen: ns(<0.025)
- Epicardial fat: ns(<0.025)

**P-value:** cDIG vs. DIR-TSE
- Vessel wall: 0.012
- Lumen: ns(<0.025)
- Epicardial fat: ns(<0.025)

*Wilcoxon signed rank test was performed to determine the significance of the difference in quantitative measurements. ns = not significant; NA = no analyses.*

FIG. 7. Representative cross-sectional coronary wall images with different imaging techniques from three healthy subjects. The coronary vessel wall was clearly depicted on the dark-blood images acquired with different methods (DIR-TSE, LocReInv-bSSFP, and cDIG). In addition, the gray-blood images obtained by the cDIG technique depicted the coronary arterial lumen as well as the vessel wall.
of ex vivo experiments were conducted and SPAIR delay time of 180 ms was empirically determined.

According to the statistical results (Table 1), adding the second contrast to the conventional LocReInv-bSSFP sequence incurs essentially no penalty in the wall SNR, wall-lumen CNR, and morphological measurements. The SNR of the vessel wall obtained by cDIG was significantly higher than that by DIR-TSE. One reason is that cDIG is a 3D imaging sequence whereas DIR-TSE is a 2D sequence. The SNR of 3D imaging is intrinsically higher than that of 2D imaging. The other reason is that the scan parameters, including bandwidth and segments per heartbeat, are different between bSSFP and TSE. Different parameters would result in different image quality and signal performance. Nevertheless, the wall thickness and lumen area measurements from cDIG and DIR-TSE were in good agreement. This demonstrates that the coronary vessel wall can be well quantified by the cDIG technique.

In contrast to the previous coronary vessel wall imaging techniques, cDIG provides an additional gray-blood contrast that may improve plaque assessment. In general, vulnerable plaque morphology includes fibrous cap, large lipid-rich necrotic core, increased plaque inflammation, positive vascular remodeling and intra-plaque hemorrhage (3,32). Identification of vulnerable plaque types is an important outcome predictor and may guide the clinical management of patients with CAD. In addition to these vulnerable plaque features, recent studies have shown that superficial calcified coronary plaque is intimately related to the unstable lesions responsible for myocardial infarction (15). Identifying the superficial calcified coronary plaque is therefore important for CAD assessment. CT is a sensitive modality to detect plaque calcification; however, CT often produces beam hardening artifacts which would lead to overestimating the plaque burden (33). In addition, CT involves large radiation doses that would increase cancer risk (34). It is not a suitable modality for screening patients without CAD symptoms. Because of the low intrinsic signal of calcification, the calcified plaque cannot be identified by conventional dark-blood MRI. However, with the assistance of the gray-blood contrast, the calcified nodule may be readily distinguished from dark lumen (Figures 9b and c).

The cDIG technique does possess several limitations that are similar to the previous techniques for coronary vessel wall imaging. First, long imaging time is required with the need for ECG-triggering, respiratory gating, and high spatial resolution. If the subject’s quiescent period

FIG. 8. Representative images with in-plane cDIG imaging from two healthy subjects. Blood signal was successfully suppressed and the vessel wall (yellow arrows) depicted clearly on dark-blood images. The vessel wall and arterial blood had no visually different signal intensity on gray blood images.
is short or respiration is inconsistent, the imaging time would be even longer. Some acceleration methods with parallel imaging or sparse sampling can be used to speed up data sampling in future. Second, the spatial resolution for coronary vessel wall imaging is $0.81 \times 0.81 \times 2.00 \text{ mm}^3$ in this work. Because of the anisotropic resolution, the images cannot be optimally reformatted for detailed plaque evaluation. However, isotropic spatial resolution imaging requires more partitions, and thus needs a longer scan time for the same coverage. Third, cDIG requires subjects have a reasonable cardiac quiescent period for data acquisition. However, this is challenging on some subjects with abnormally high heart rates. In this case, Beta blocker can be administered to the subjects to slow the heart rate. Fourth, the re-inversion pulse of the cDIG technique as well as LocReInv-bSSFP is placed on the imaged artery to avoid re-inversion of the blood spins in the left ventricle. This requires operator skills and may not be effective with certain patient geometry. In addition, very limited patient data is a limitation in this work. The goal of the present work was to elaborate the technical aspects of cDIG. To elucidate the clinical value of the method, a large-scale patient study is necessary and will be our future focus.

**CONCLUSIONS**

In summary, a novel technique for simultaneously obtaining coronary vessel wall and gray lumen images was developed and validated on healthy volunteers. Dual contrasts can be acquired without compromising the dark-blood contrast and scan time offered by the existing 3D LocReInv-based coronary wall MRI techniques. A preliminary study on a patient with a calcified coronary plaque demonstrated that cDIG may provide additional information that assists in identifying calcified nodules and thus improves the evaluation of coronary plaque burden. Nevertheless, the technique warrants further technical improvements and systematic clinical studies to establish its diagnostic value.

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**REFERENCES**

3D cDIG MRI at 3 Tesla


