Title
Velocity encoding with the slice select refocusing gradient for faster imaging and reduced chemical shift-induced phase errors

Permalink
https://escholarship.org/uc/item/6rj106hg

Journal
Magnetic Resonance in Medicine, 71(6)

ISSN
0740-3194

Authors
Middione, MJ
Thompson, RB
Ennis, DB

Publication Date
2014

DOI
10.1002/mrm.24861

Peer reviewed
Velocity Encoding with the Slice Select Refocusing Gradient for Faster Imaging and Reduced Chemical Shift-Induced Phase Errors

Matthew J. Middione,1,2 Richard B. Thompson,3 and Daniel B. Ennis1,2,4*

Purpose: To investigate a novel phase-contrast MRI velocity-encoding technique for faster imaging and reduced chemical shift-induced phase errors.

Methods: Velocity encoding with the slice select refocusing gradient achieves the target gradient moment by time shifting the refocusing gradient, which enables the use of the minimum in-phase echo time (TE) for faster imaging and reduced chemical shift-induced phase errors. Net forward flow was compared in 10 healthy subjects (N=10) within the ascending aorta (aAo), main pulmonary artery (PA), and right/left pulmonary arteries (RPA/LPA) using conventional flow compensated and flow encoded (401 Hz/px and TE=3.08 ms) and slice select refocused gradient velocity encoding (814 Hz/px and TE=2.46 ms) at 3 T.

Results: Improved net forward flow agreement was measured across all vessels for slice select refocused gradient compared to flow compensated and flow encoded: aAo vs. PA (1.7% ± 1.9% vs. 5.8% ± 2.8%, P = 0.002), aAo vs. RPA = LPA (2.1% ± 1.7% vs. 6.0% ± 4.3%, P = 0.03), and PA vs. RPA/LPA (2.9% ± 2.1% vs. 6.1% ± 6.3%, P = 0.04), while increasing temporal resolution (35%) and signal-to-noise ratio (35%).

Conclusion: Slice select refocused gradient phase-contrast MRI with a high receiver bandwidth and minimum in-phase TE provides more accurate and less variable flow measurements through the reduction of chemical shift-induced phase errors and a reduced TE/repetition time, which can be used to increase the temporal/spatial resolution and/or reduce breath hold durations. Magn Reson Med 71:2014–2023, 2014. © 2013 Wiley Periodicals, Inc.

Key words: phase-contrast MRI; chemical shift; velocity encoding; flow quantification

Measurement of volumetric blood flow rates using phase-contrast MRI (PC-MRI) in the cardiovascular system is a primary clinical application of magnetic resonance imaging. However, quantitative volumetric imaging of blood flow with PC-MRI is limited by systematic errors in phase (1–4) leading to clinically significant flow errors, which dampen clinical enthusiasm for the technique.

In particular, our previous work has shown that chemically shifted perivascular fat can significantly corrupt PC-MRI flow measurements (5). In that work, we characterized the impact of chemical-shifted lipid signals in PC-MRI and defined a coherent strategy to reduce chemical shift errors. Briefly, the amount of chemically shifted fat pixels that shift into the vessel can be reduced by increasing receiver bandwidth (BW) at the expense of signal-to-noise ratio (SNR). Second, an in-phase echo time (TE; TEIN) will ensure that fat and water resonances are in-phase, which minimizes the resulting errors in the calculated velocity.

Chemical shift errors are more challenging to address at 3 T, when compared with 1.5 T, because of the larger frequency difference between water and fat, which leads to a larger spatial shift of fat for a given BW. Furthermore, the shorter minimum in-phase TE (TEIN,MIN) at 3 T (2.46 ms for δ₁T₁ = 420 Hz and scanner reported B₀ = 2.89 T) is shorter than at 1.5 T (4.76 ms for δ₁T₁ = 210 Hz and scanner reported B₀ = 1.49 T), and may not be routinely achievable with standard flow-encoding methods at conventionally targeted velocity-encoding strengths (VENCs).

Herein, we describe and evaluate a method for flow encoding in PC-MRI that uses the slice select gradient and a time-shifted refocusing gradient lobe to generate the target gradient moments, which shortens the TE/repetition time (TR) (increases temporal resolution) and enables the use of TEIN,MIN at 3 T for time-efficient reduction of chemical shift-induced phase errors.

THEORY

For a typical PC-MRI experiment, two velocity-encoded acquisitions with different first moments are necessary to encode flow along a single direction (6–8). All encoding schemes are designed to null the zero gradient moment for both encoding steps, M₀,1 = M₀,2 = 0, to refocus the position-related phase, but with a net difference in first moments to yield velocity-dependent phase with no dependence on nonvelocity background phase.

\[
\Delta \phi = \gamma v_z (M_{1,1} - M_{1,2}) = \gamma v_z M_1. \tag{1}
\]

In Eq. [1], Δϕ is the phase difference between the two velocity-encoded images, γ is the gyromagnetic ratio, v_z is the velocity in the through-plane direction, and M_{1,1}
and \( M_{1,2} \) are the first gradient moments for encoding steps 1 and 2. The VENC, defined as the velocity that produces a phase shift of \( \pm \pi \) radians, is determined by \( \Delta M_1 \) for any encoding strategy:

\[
VENC = \frac{\pi}{\gamma |\Delta M_1|} \tag{2}
\]

The target \( \Delta M_1 \) is conventionally achieved by using either bipolar velocity-encoding gradients or a set of flow compensated and flow encoded (FCFE) velocity-sensitizing gradients. For bipolar encoding, \( M_{0,1} = M_{0,2} = 0 \) and the equal and opposite gradient polarities yield \( M_{1,1} = X/2 \) and \( M_{1,2} = -X/2 \) \((7,8)\). For FCFE-encoding strategies, \( M_{0,1} = M_{0,2} = 0 \), while \( M_{1,1} = 0 \) and \( M_{1,2} = X \) \((6,9)\). Although not widely appreciated bipolar encoding is more time efficient for low VENCs and FCFE is more time efficient for mid to high VENCs. Furthermore, FCFE provides reduced signal loss owing to intravoxel coherent velocity-related phase dispersion \((10,11)\), such as in the presence of shear or complex flow, and reduced ghosting artifacts in the phase encode direction arising from large \( M_1 \)-induced velocity-related phase shifts \((8)\).

However, in the presence of perivascular fat, the chemical shift difference between water and lipids can give rise to non-velocity related phase, which can be minimized by selection of optimal timings, to keep the water and lipid signals in-phase \((5)\). The design of the flow-encoding gradients is thus further constrained by their total duration if the criteria for minimum in-phase TE are to be satisfied: \( TE_{\text{IN,MIN}} = 2.46 \text{ ms at 3 T} \). Bernstein et al. \((12)\) previously defined strategies for minimizing TE times in PC-MRI sequences for both bipolar and FCFE encoding and our proposed methods make further reductions in TE possible.

Previously, time-efficient velocity encoding without the need for time-consuming bilobe encoding gradients has been achieved by taking advantage of the intrinsic first moment of the slice-selection gradient waveform and refocusing lobe. Markl et al. \((13)\) previously developed a balanced steady-state free precession phase-contrast pulse sequence that used a slice-selection gradient with alternating polarity for each encoding step, thereby combining the velocity encoding with the slice selection and slice select refocusing gradient (SSRG). Thompson and McVeigh \((14)\) used a time shift of the refocusing lobe and bipolar flow-encoding lobe to control the VENC without altering the slice-selection gradient. Herein, we adopt similar principles to significantly reduce the time needed to achieve velocity encoding over a range of clinically useful VENCs by using a time shift of the refocusing lobe and no other flow-encoding lobes. Our proposed technique is referred to throughout as the SSRG sequence.

The most common implementations of flow-encoding gradients are shown for FCFE gradient waveforms in Figure 1a and bipolar gradient waveforms in Figure 1b, whereas our proposed SSRG velocity-encoding technique is shown in Figure 1c.

For our SSRG method, the relationship between the gradient parameters and the resulting zero, \( M_0 \), and first

\[
G_1 \quad M_{0,S} \quad G_R \quad G_S \quad t=0 \quad I_s \quad M_{0,R} \quad \Delta t \quad t_n \quad \Delta m \quad G_R \quad G_S \quad t=0
\]

\[
G_2 \quad M_{0,S} \quad G_R \quad G_S \quad t=0 \quad I_s \quad M_{0,R} \quad \Delta t \quad t_n \quad \Delta m \quad G_R \quad G_S \quad t=0
\]

FIG. 2. Slice select and refocusing gradient (SSRG) lobes for the SSRG PC-MRI sequence. The slice thickness and RF duration determine \( M_{0,S} \) of the slice select gradient lobe from \( t=0 \). A time-efficient triangular refocusing gradient lobe is constructed such that \( M_{0,R} = M_{0,S} \). The refocusing gradient lobe for the second measurement is shifted in time by \( \Delta t \) to produce the target VENC. \( M_{0,S} \) is the area of the slice select gradient; \( G_R \) is slice select gradient amplitude; \( I_s \) is the duration of the slice select gradient; \( M_{0,R} \) is the area of the refocusing gradient; \( t_n \) is the duration of the refocusing gradient ramp from 0 to \( G_R \); and \( \Delta t \) is the time shift of the refocusing gradient needed to produce the \( \Delta M_1 \) associated with the target VENC.
moments, $M_1$, and thus the VENC, can be determined analytically. Parameters characterizing a typical SSRG waveform for a symmetric radiofrequency (RF) pulse are shown in Figure 2. For any given RF pulse, the amplitude, $G_S$, is determined by the desired slice thickness, whereas the length of the slice select gradient lobe, $t_S$, is determined by the duration of the RF pulse. The $M_0$ of the slice select gradient lobe, $M_{0,S}$, and refocusing gradient lobe, $M_{0,R}$, must be equal ($M_{0,S} = M_{0,R}$) to ensure that all excited spins are refocused over the thickness of the slice after excitation:

$$M_{0,R} = G_S t_S.$$  

[3]

The amplitude of the refocusing gradient lobe, $G_R$, can be determined by using the minimum available gradient rise time of the system, $r_R$, and the result of Eq. 3:

$$G_R = \frac{M_{0,R}}{r_R}.$$  

[4]

The first moment for a symmetric gradient waveform (i.e., the refocusing lobe) centered at any point in time, $t$, can be determined by $M_1 = M_0 t$. Thus, for the first encoding step, with the refocusing gradient lobe centered at $t = t_S + r_R$, the first moment of the refocusing gradient lobe can be calculated as $M_{0,R}(t_S + r_R)$. The nonzero first moment of the entire gradient waveform for the first encoding step, $M_{1,1}$, is thus given by

$$M_{1,1} = M_{1,S} + M_{1,R} = M_{1,S} - M_{0,R}(t_S + r_R).$$  

[5]

For the second encoding step, the refocusing gradient lobe is shifted in time by $\Delta t$ and is thus centered at $t = t_S + r_R + \Delta t$, resulting in a first moment of $M_{0,R} (t_S + r_R + \Delta t)$. The nonzero first moment of the entire gradient waveform for the second encoding step, $M_{1,2}$, can be determined as

$$M_{1,2} = M_{1,S} + M_{1,R} = M_{1,S} - M_{0,R}(t_S + \Delta t + r_R).$$  

[6]

The slice select gradient lobe is identical for the two encoding steps and thus its first moment contribution cancels when calculating the net first moment, $\Delta M_1$

$$\Delta M_1 = M_{1,1} - M_{1,2} = M_{0,R} \Delta t.$$  

[7]

Substituting Eq. 7 in Eq. 2 above, the time shift for the target VENC is

$$\Delta t = \frac{\pi}{\gamma M_{0,R} \text{VENC}}.$$  

[8]

METHODS

Comparison of Velocity-Encoding Strategies

The minimum available TE as a function of VENC was determined for FCFE, bipolar, and SSRG sequences. The TE and VENC were determined at both low BW (LBW) = 401 Hz/px and high BW (HBW) = 814 Hz/px with all other parameters held constant (192 × 120 encoding matrix, 1.6 mm × 1.6 mm spatial resolution, 5 mm slice thickness, 30° flip angle, four views-per-segment, 500 μs RF pulse width, and a maximum slew rate of 157 mT/m/ms).

Preclinical Evaluation in Normal Volunteers

A preclinical evaluation of SSRG was performed in 10 normal volunteers (N = 10) to show that SSRG suppresses chemical shift effects while shortening the TE/TR compared to FCFE. All imaging was performed on a Siemens Trio 3 Tesla system (Siemens Medical Solutions, Erlangen, Germany) with 40 mT/m maximum gradient amplitude and 200 T/m/s maximum slew rate. Our university’s Institutional Review Board approved the study and informed consent was obtained for each subject before MRI scanning. Subjects were positioned head first in the supine position on the scanner bed and imaged using an anterior six-element body matrix coil and a posterior six-element spine matrix coil for signal reception. Blood flow was measured using PC-MRI in the ascending aorta (aAo), main pulmonary artery (PA), and right/left pulmonary arteries (RPA/LPA) of 10 (N = 10) volunteers (two females and eight males; age 27.6 ± 4.0 years) with no previous history of cardiovascular disease. High-resolution black blood turbo spin echo images were also acquired with and without fat saturation (15,16) during end systole to define the presence (or absence) of perivascular fat for the vessel of interest at the same slice location used for PC-MRI flow measurements.

The imaging plane for aAo flow was located distal to the aortic valve and coronary ostia. The imaging plane for flow in the PA was located downstream from the pulmonary valve and proximal to the first bifurcation. The imaging planes for the LPA and RPA were located ~1 cm distal to the pulmonary bifurcation. All imaging planes were prescribed on bSSFP cine images during end systole with end-expiratory breath holds.

PC-MRI flow measurements were obtained using a FCFE cine gradient echo phase-contrast sequence with retrospective ECG gating: mid-phase TE (TEMID = 3.08 ms), which orients the fat vector to be approximately perpendicular to the blood vector, TR = 6.04 ms, 192 × 132 matrix, 1.6 mm × 1.6 mm × 5 mm acquisition voxel, 30° imaging flip angle, 401 Hz/pixel receiver BW (LBW), four views-per-segment (17), a total scan time of 20 heartbeats, a temporal resolution of 48.3 ms, 20–24 cardiac phases (heart rate dependent) reconstructed during one end-expiratory breath hold with retrospective ECG gating, and GRAPPA (18) parallel imaging with an acceleration factor of 2 and 24 reference (central) k-space lines. Two-dimensional through-plane velocity encoding was performed using VENC of 200 cm/s for all flow territories. Although it is possible to fine-tune the VENC for each subject and each particular vessel, this will introduce changes in the TE and TR, which can be confounding when making comparisons in a controlled study. Therefore, the VENC was kept high enough to reduce the risk of aliasing and was therefore held constant for all subjects and all vessels. Fractional echo was not used for any sequence.
Both $TE_{MIN} = 3.08$ ms and $LBW = 401$ Hz/px were found to be close approximations to commonly used values in clinical scans found in current PC-MRI literature (19–21). This combination of TE and BW sensitizes the measurements to the effects of chemical shift. Measurements were also obtained using the SSRG velocity-encoding sequence with identical parameters as described above, except for the following changes: $TE_{IN,MIN}/TR = 2.46/4.46$ ms, 814 Hz/px receiver BW (HBW), a temporal resolution of 35.65 ms, and 27–32 reconstructed cardiac phases (heart rate dependent). Additional data were also acquired using FCFE with our previously optimized chemical shift protocol: $TE_{IN}/TR = 4.92/6.91$ ms, 814 Hz/pixel receiver BW (HBW), a temporal resolution of 55.3 ms, and 17–21 reconstructed cardiac phases. Both FCFE at HBW $+ TE_{IN}$ and SSRG at HBW $+ TE_{IN,MIN}$ theoretically provide the same insensitivity to chemical shift-induced phase errors, but SSRG at HBW $+ TE_{IN,MIN}$ provides increased SNR and a shorter TR (i.e., improved temporal resolution or shorter breath-hold durations) owing to the TE/TR reduction.

### Image Processing

Data were processed offline using MATLAB (The MathWorks, Natick, MA) and a DICOM viewing tool (Osirix, www.osirix-viewer.com). Eddy current background phase errors were measured and corrected, for all sequences, using a stationary phantom (2,22,23) after each exam. For quantitative flow assessment at each vessel territory, a region-of-interest (ROI) was drawn in Osirix around the contours of each vessel boundary as indicated in the magnitude images. The same ROIs were imported into the eddy current correction images for correction of background phase errors. The resulting ROI information was then exported from Osirix to MATLAB for quantitative velocity and flow analysis. The measured net forward flow of blood was computed by scaling the mean ROI signal intensity (velocity-related phase shift) by $VENC/\pi$ (cm/s). The resulting mean ROI velocities were then multiplied by the area of the ROI (cm$^2$) to calculate the flow rate (mL/s) and finally integrated over the cardiac cycle to yield the net forward flow results (mL).

### Data Analysis

#### Chemical Shift Effects on Net Forward Flow

To analyze the effects of chemical shift on net forward flow, measurements were made in the aAo, PA, RPA, and LPA for FCFE with LBW $+ TE_{MIN}$ and HBW $+ TE_{IN}$ as well as SSRG with HBW $+ TE_{IN,MIN}$.

#### Internal Blood Flow Consistency

An analysis of the internal blood flow consistency was conducted by comparing the measured net forward flow in the aAo and PA, aAo and RPA $+ LPA$, and the PA and RPA $+ LPA$ for FCFE with LBW $+ TE_{MIN}$ and SSRG with HBW $+ TE_{IN,MIN}$. In the absence of shunts or regurgitant flow (neither of which is expected within our normal volunteer population), we expect that the blood flow in the PA = 1.05 aAo [accounting for coronary flow (24)] = RPA $+ LPA$. A two-sample $t$-test with Holm–Sidak post hoc correction was used to measure the statistical significance of the differences in the measured net forward flow between the two sequences.

#### Eddy Current Comparison

Eddy current-induced velocity offsets were measured by copying the manually contoured ROIs from each volunteer and vessel to the eddy current correction images. The eddy current-induced velocity offsets were compared by averaging the mean velocity from each ROI through time for SSRG at HBW $+ TE_{MIN}$ and FCFE at LBW $+ TE_{MIN}$ and HBW $+ TE_{IN}$.

The magnitude of chemical shift- and eddy current-induced flow errors was compared. Chemical shift-induced flow errors were obtained by calculating the mean, standard deviation, and minimum/maximum of the flow error (mL) between the aAo and PA, aAo and RPA $+ LPA$, and the PA and RPA $+ LPA$, between FCFE at HBW $+ TE_{MIN}$ and SSRG at HBW $+ TE_{IN,MIN}$. Eddy current-induced flow errors were similarly calculated as the flow difference arising from measurements with and without eddy current correction for both sequences. A two-sample $t$-test was used to measure the statistical significance of the differences in flow errors arising from eddy currents and chemical shift.

#### Pulmonary to Systemic Blood Flow Ratios

Pulmonary to systemic blood flow ratios (Qp/Qs, PA flow divided by aAo flow) were calculated for each volunteer. A two-sample $t$-test with Holm–Sidak post hoc correction was used to measure the statistical significance of the differences in the measured Qp/Qs ratios for FCFE with LBW $+ TE_{MIN}$ and SSRG with HBW $+ TE_{MIN}$.

#### SNR Comparison

A quantitative analysis of the measured SNR for FCFE with HBW $+ TE_{MIN}$ and LBW $+ TE_{MIN}$ and SSRG with HBW $+ TE_{IN,MIN}$ was conducted by placing two ROIs within the magnitude images to produce an estimate of the signal and the noise. One set of ROIs was contoured to the aAo, PA, RPA, or LPA to obtain a measurement of the mean signal for each cardiac phase. Another set of ROIs was placed near the top left portion of the images in a region that was devoid of any artifacts as observed under window/level extremes. The mean ± standard deviation SNR for each vessel and each subject was computed as the mean of the mean signal intensity divided by the standard deviation for each cardiac phase. Another set of ROIs was placed outside the subject’s body to obtain an estimate of the background signal standard deviation (noise) for each cardiac phase. The noise ROIs were placed near the top left portion of the images in a region that was devoid of any artifacts as observed under window/level extremes. The mean ± standard deviation SNR for each vessel and each subject was computed as the mean of the mean signal intensity divided by the standard deviation for each cardiac phase. The mean ± standard deviation of the SNR for each vessel territory was compared between sequences.

### RESULTS

#### Comparison of Velocity-Encoding Strategies

Figure 3 shows the minimum available TE (ms) plotted as a function of the available VENC (cm/s) for FCFE, bipolar, and SSRG velocity-encoding strategies at both LBW (Fig. 3a) and HBW (Fig. 3b). SSRG is the only
encoding strategy that permits the use of $TE_{IN,MIN} = 2.46$ ms at HBW, which occurs for VENCs ≥ 190 cm/s. The minimum achievable TE at LBW is 2.84 ms, which can only be reached with SSRG for VENCs ≥ 190 cm/s. FCFE yields the shortest TE for all VENCs ≥ 165 cm/s. The bipolar sequence provides the use of the shortest TE for VENCs ≤ 35 cm/s. FCFE allows shorter minimum TEs compared to the bipolar sequence for the VENCs used in this study; therefore, our new SSRG velocity-encoding sequence was only compared to FCFE.

**In Vivo Studies**

**Chemical Shift Effects on Net Forward Flow**

Figure 4 shows the difference in the measured net forward flow data from the aAo, PA, RPA, and LPA for FCFE with LBW + $TE_{MIN}$ and SSRG with HBW + $TE_{IN,MIN}$, which qualitatively illustrates chemical shift-induced flow errors. The turbo spin echo images with and without fat saturation were used to detail the presence of perivascular fat for each vessel in each volunteer (Fig. 5). In the presence of perivascular fat, FCFE with LBW + $TE_{MIN}$ led to an overestimation of the net forward flow compared to SSRG with HBW + $TE_{IN,MIN}$ (aAo: 7.2% ± 1.6% vs. 1.6% ± 0.3%; PA: 8.5% ± 2.7% vs. 3.8%; RPA: 11.4% ± 2.3% vs. 3.3%; and LPA: 8.8% ± 2.8% vs. 2.3% ± 2.8%). The mean difference, across all volunteers and vessels, between the measured net flow for FCFE with HBW + $TE_{IN}$ and SSRG with HBW + $TE_{IN,MIN}$ was 1.1 mL (2.1%).

**Internal Blood Flow Consistency**

Table 1 shows an analysis of the internal consistency for net forward flow measurements made in the aAo, PA, RPA, and LPA from our preclinical evaluation of 10 normal volunteers ($N = 10$). Included in the analysis are the mean percent agreement and the minimum and maximum percent agreement (shown in brackets). In all three territory comparisons (aAo vs. PA, aAo vs. RPA, and PA vs. RPA + LPA) a statistically significant difference ($P < 0.05$) between the measured net forward flow for FCFE with LBW + $TE_{MIN}$ and SSRG with HBW + $TE_{IN,MIN}$ is observed. This indicates significant improvement in the internal consistency of flow measures through the reduction of chemical shift-induced phase errors using SSRG with HBW + $TE_{IN,MIN}$. A comparison of the measured net flow between FCFE with HBW + $TE_{IN}$ and SSRG with HBW + $TE_{IN,MIN}$ showed no significant difference.

Figure 6 shows an analysis of the internal consistency for net forward flow (aAo vs. PA, aAo vs. RPA + LPA, and PA vs. RPA + LPA) measured by FCFE with LBW + $TE_{MIN}$ and SSRG with HBW + $TE_{IN,MIN}$ with and without eddy current correction. SSRG with HBW + $TE_{IN,MIN}$ improves the intrasubject forward flow agreement for every subject. Eddy current-corrected SSRG with HBW + $TE_{IN,MIN}$ leads to better intrasubject flow agreement on average compared to FCFE with LBW + $TE_{MIN}$.

Table 2 shows the importance of comparing relative and absolute blood flow comparisons for both SSRG with HBW + $TE_{IN,MIN}$ and FCFE with LBW + $TE_{MIN}$ from a single volunteer with observed perivascular fat.

**Eddy Current Comparison**

Eddy current-induced velocity offsets for SSRG with HBW + $TE_{IN,MIN}$, FCFE with LBW + $TE_{MIN}$, and FCFE with HBW + $TE_{IN}$ were 0.6 ± 0.37, 0.4 ± 0.19, and 0.52 ± 0.27 cm/s, respectively. The average magnitude of chemical shift-induced flow errors was 2.9 ± 1.6 mL [0.0.
6.4 mL (mean ± SD [min, max]). The average magnitude of eddy current-induced flow errors was 1.56 ± 1.16 mL [0.03, 4.6 mL].

**Pulmonary to Systemic Blood Flow Ratios**

The Qp/Qs ratios for SSRG with HBW + TEIN,MIN were lower and significantly different than FCFE with LBW + TEMID (1.00 ± 0.02 vs. 1.05 ± 0.04, P < 0.005).

**SNR Comparison**

The average measured SNR for SSRG with HBW + TEIN,MIN, FCFE with HBW + TEMID was 58.5 ± 24.8, 87.7 ± 40.8, and 116.8 ± 54.4, respectively.

**Sequence Timing Comparison**

Table 3 shows a comparison of the timing parameters for FCFE with LBW + TEMIN and HBW + TEIN as well as SSRG with LBW + TE_MIN and HBW + TE_IN,MIN for a VENC of 200 cm/s.

**DISCUSSION**

**Comparison of Velocity-Encoding Strategies**

In Figure 3, as the VENC increases, a theoretical minimum TE is reached because of limitations associated with the plateau of the readout gradient overlapping with the refocusing gradient. SSRG can encode larger velocities within this time, compared to the other encoding strategies, thus permitting the use of a shorter TE. For a fixed slice select gradient and RF pulse, smaller VENC values require a Δt that causes the refocusing gradient lobe to overlap with the readout gradient plateau for TEIN,MIN, thus causing an increase in the minimum achievable TE.

**In Vivo Studies**

**Chemical Shift Effects on Net Forward Flow**

In Figure 4, it can be seen that chemical shift-induced phase errors are largest in the PA, RPA, and LPA.
compared to the aAo. For low-pressure vessels (PA, RPA, and LPA) the vessel wall is thicker, thus limiting the complex signal from perivascular fat from spatially shifting into the vessel lumen. In the presence of minimal perivascular fat, the difference between the two sequences is much lower. Only one volunteer lacked perivascular fat in the PA and another volunteer lacked perivascular fat in the RPA. Only once did FCFE with LBW + TEMID lead to an underestimation of the net forward flow compared to SSRG with HBW + TEIN_MIN.

Internal Blood Flow Consistency

Table 1 shows a statistically significant difference ($P < 0.05$) between the measured net forward flow for FCFE with LBW + TEMID and SSRG with HBW + TEIN_MIN in all three territory comparisons (aAo vs. PA, aAo vs. RPA + LPA, and PA vs. RPA + LPA). This indicates significant improvement in the internal consistency of flow measures through the reduction of chemical shift-induced phase errors using SSRG with HBW + TEIN_MIN.

Internal consistency measures can only reflect a relative agreement in net forward flow, whereas for PC-MRI to provide the most clinically useful results, absolute flow measurements are preferred. In Table 2, FCFE with LBW + TEMID shows a small intrasequence difference of ~1 mL (1.4%). Importantly, SSRG with HBW + TEIN_MIN shows a similar result ($\Delta$ intraflow < 1 mL). However, when the intersequence flow differences are compared FCFE with LBW + TEMID shows an overestimation of blood flow by ~8 mL (9.3%). In this work, FCFE with LBW + TEMID led to an overestimation of blood flow in all but one vessel territory (39 of 40) in 10 volunteers, which is also consistent with our previous results (5). Although this study reports a consistent overestimation of flow when using LBW + TEMID, the magnitude and sign of the flow discrepancy depend on the superposition of the complex fat and water vectors. For this work, the use of LBW causes more fat pixels to partial volume

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapatient Percent Flow difference from the Preclinical Evaluation of 10 Normal Volunteers ($N = 10$) Expressed as a Mean ± Standard Deviation [Minimum, Maximum]</td>
</tr>
<tr>
<td>FCFE LBW + TEMID</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>aAo vs. PA</td>
</tr>
<tr>
<td>aAo vs. RPA + LPA</td>
</tr>
<tr>
<td>PA vs. RPA + LPA</td>
</tr>
</tbody>
</table>

$^aP < 0.05$ showing a statistical significant difference compared with SSRG HBW + TEIN_MIN. No significant difference was measured between SSRG HBW + TEIN_MIN and FCFE HBW + TEIN.
HBW + Eddy current-induced velocity offsets for SSRG with Eddy Current Comparison PC-MRI measurements. Score an important source of variability in clinical lute method for quantifying blood flow and also under- improvements need to be made to make PC-MRI an abso- known (data not shown). These examples highlight why flow phantom experiments, where the measured flow is from the presence of perivascular fat surrounding these vessels for this volunteer. Similar results are observed in flow phantom experiments, where the measured flow is known (data not shown). These examples highlight why improvements need to be made to make PC-MRI an absolute method for quantifying blood flow and also underscore an important source of variability in clinical PC-MRI measurements.

### Eddy Current Comparison

Eddy current-induced velocity offsets for SSRG with HBW + TE_{MIN,MIN} were greater than both FCFE with LBW + TE_{MIN} and HBW + TE_{IN}, but importantly just within the 0.6 cm/s threshold of acceptable eddy current-induced velocity offsets (19). Eddy current background phase error corrections significantly improve the flow accuracy of PC-MRI (2,25,26). In this study, we have shown that the average magnitude of chemical shift-induced flow errors are almost two times larger and statistically different ($P < 5 \times 10^{-5}$) than eddy current effects. Therefore, for studies in which flow accuracy is important both eddy currents and chemical shift-induced phases error need to be minimized.

### Pulmonary to Systemic Blood Flow Ratios

Relative to SSRG, FCFE measurements of Qp/Qs are higher on average by 0.05. Chemical shift effects primarily account for the 0.05 difference between SSRG and FCFE. Our Qp/Qs results for SSRG at HBW TE_{MIN,MIN}- however, do not match the expected result of 1.05 when a 5% coronary flow contribution is assumed (24). Uncorrected phase errors could be influencing the measurements made with either SSRG or FCFE. Uncorrected phase errors that differentially contribute ~0.3 cm/s, for example, to the aAo and PA measures could give rise to an error of ±0.05 in Qp/Qs (19), for either SSRG or FCFE, and could account for the deviation of the reported results from the expected value. The source of this error is incompletely understood.

### SNR Comparison

A quantitative analysis of the measured SNR shows that the SNR for SSRG with HBW + TE_{MIN,MIN} is reduced by 50% compared to FCFE with LBW + TE_{MIN} and 33% higher than in our previous chemical shift-optimized FCFE velocity-encoding sequence with HBW + TE_{IN}. Both of these values are in good agreement with our theoretical expectation of 46 and 35%, respectively, determined based on the steady-state gradient echo signal equation and the applied flip angle, TE/TR, receiver BW, and estimates of $T_1/T_2^*$ (1400/50 ms).

### Sequence Timing Comparison

Table 3 shows that with chemical shift-optimized sequences, SSRG offers a 35% increase in temporal resolution compared with FCFE (35.65 vs. 55.3 ms). When chemical shift effects are not of a concern, the minimum available TE/TR for SSRG offers a 12% increase in temporal resolution compared with FCFE (41.95 vs. 47.85 ms). Regardless of chemical shift-induced errors, SSRG always provides the shortest TE/TR (highest temporal resolution) compared with FCFE for the previously described VENC range.

#### Table 2

<table>
<thead>
<tr>
<th></th>
<th>FCFE LBW + TE_{MIN}</th>
<th>SSRG HBW + TE_{MIN,MIN}</th>
<th>Δ Interflow</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>99.3</td>
<td>90.7</td>
<td>8.6</td>
</tr>
<tr>
<td>RPA + LPA</td>
<td>98.0</td>
<td>89.9</td>
<td>8.1</td>
</tr>
<tr>
<td>Δ Intraflow</td>
<td>1.3</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>

The SSRG technique is known theoretically and empirically to produce more accurate flow measurements. Δ Interflow = FCFE LBW + TE_{MIN} - SSRG HBW + TE_{MIN,MIN} for each flow territory. Δ Intraflow = PA – (RPA + LPA) for each sequence. All vessels contained perivascular fat.
Flow compensated images from a FCFE sequence have reduced flow-related ghosting artifacts in the phase-encode direction. However, FCFE always has one encoding step that is not flow compensated; therefore, flow-related ghosting artifacts cannot be avoided within this encoding step. The SSRG sequence has no flow compensated waveforms, but the moment distribution compared with FCFE is similar and consequently flow-related ghosting artifacts were nearly identical to FCFE. For example, when using SSRG with a VENC of 200 cm/s, $M_{1,1} = 2.3$ (mT ms$^2$/m) and $M_{1,2} = 8.17$ (mT ms$^2$/m), whereas for FCFE $M_{1,1} = 0$ and $M_{1,2} = 5.87$ (mT ms$^2$/m).

SSRG can also be combined with the shared velocity-encoding (SVE) technique proposed by Lin et al. (27) to offer an even greater increase in the effective temporal resolution. The SVE concept shares velocity-encoding k-space data between adjacent frames. As a result, the SVE technique cannot be combined with FCFE-encoding strategies because adjacent frames sharing the same velocity-encoded k-space data would not provide any new information. Thus, an SSRG sequence combined with SVE image reconstruction would represent an important and significant increase in temporal resolution compared with conventional FCFE approaches.

Conventional wisdom for PC-MRI parameter selection has always been to pick a LBW for improved SNR and the corresponding minimum TE to further improve SNR and reduce the TR. Although this approach has advantages, a judicious choice of BW and TE can lead to increased measurement accuracy by reducing the effects of chemical shift. Additionally, the 50% decrease in SNR with SSRG at HBW + TE$_{\text{MIN}}$ compared with FCFE at LBW + TE$_{\text{MIN}}$ should not negatively impact measurement accuracy. For example, Westenberg et al. previously reported that a 55% reduction in SNR (187 ± 116 vs. 84 ± 60) did not lead to flow inaccuracies in measurements across the mitral valve (28).

SSRG enables the use of TE$_{\text{MIN}}$, but under the conditions evaluated the use of FCFE at HBW + TE$_{\text{MIN}}$ results in a TE that is close to TE$_{\text{MIN}}$ ($\Delta = 0.14$ ms), but this TE would orient the fat vector at $\sim 21^\circ$ relative to stationary blood (water) for the 3-T scanner (scanner reported $B_0 = 2.89$ T used in this study). Using our previous numerical simulations at 3 T (5) indicates that FCFE at HBW + TE$_{\text{MIN}}$ (2.6 ms) can result in a forward flow error from chemical shift as large as 5% in the RPA/LPA (data not shown); a 2% reduction in SNR; and a 3% decrease in temporal resolution compared with SSRG at HBW + TE$_{\text{MIN}}$. As a result, SSRG offers reduced chemical shift effects, faster scanning, and increased SNR for VENCs $\geq 190$ cm/s.

### Limitations

SSRG permits the use of a range of VENCs that are within the range of typical blood flow velocities for imaging the aAo, PA, RPA, and LPA. Smaller VENCs lead to a large time shift, $\Delta t$, for the refocusing gradient lobe during the second encoding step. Under these low VENC regimes, SSRG loses its velocity-encoding time efficiency compared with the FCFE or bipolar sequences, which are more time efficient at encoding lower velocities. Therefore, SSRG is not well suited for measuring myocardial motion, CSF flow measurements, and other studies that require low VENCs (see Fig. 3). Furthermore, in this study, the VENC was prospectively chosen to accommodate easily the maximum expected velocity in these subjects. Reducing the VENC requires increasing $\Delta M_0$, which necessitates an increased $M_1$ for the time-shifted SSRG in SSRG. Consequently, this leads to increased intravoxel spin dephasing and potential ghosting artifacts (29). Furthermore, if the VENC had been more closely matched to the peak velocity, the impact of the higher $M_1$ values in SSRG compared with FCFE may have been more apparent (8,29).

The SSRG velocity-encoding sequence allows the use of a shorter, previously unachievable TE$_{\text{MIN}}$ of 2.46 ms at 3 T. At 1.5 T, TE$_{\text{MIN}} = 4.76$ ms (assuming $\sim 210$ Hz/px) and there is no shorter available TE$_{\text{MIN}}$ at this field strength. As a result, if chemical shift reduction strategies are to be used at 1.5 T, SSRG does not hold an advantage over FCFE. However, even if reducing the effects from chemical shift is not of interest, SSRG can still afford the use of a shorter TE/TR combination (Table 3), resulting in increased temporal resolution, breath hold duration, and/or spatial resolution compared with FCFE.

We have assumed that the use of TE$_{\text{MIN}}$ aligns the complex fat vector with slow-flowing blood at the vessel periphery, but this assumption is not always valid. For example, if the flow velocity is high as may occur for complex flow patterns, then the phase of fat may no longer closely align with the phase accorded by the local velocity. This highlights the importance of using HBW to minimize the contribution of perivascular fat.

When comparing our measured total flow results between the SSRG and FCFE techniques, the temporal resolution was not held constant. Instead, the minimum available TR was chosen for each technique to provide sequence efficiency. Despite the nonmatched temporal resolutions, improvements in total flow agreement are considered to be a result of chemical shift effects and not temporal resolution as shown in our
previous work (5) where the temporal resolution was held constant.

CONCLUSION

PC-MRI with SSRG velocity encoding is a more time-efficient velocity-encoding strategy for medium to large VENCs when used in conjunction with HBW. SSRG leads to more accurate and less variable flow measurements through the reduction of chemical shift-induced phase errors in addition to shortening the TE/TR, thus permitting the use of better temporal/spatial resolution and/or reduced breath hold duration.

ACKNOWLEDGMENTS

The authors thank Gerhard Laub, Yutaka Natsuaki, and Ning Jin for their support and discussion. This work was enabled by NIH/NHLBI K99/R00 HL087614, Siemens Medical Solutions, and the Department of Radiological Sciences research support to D.B.E.

REFERENCES