Velocity Measurements in Cardiac Magnetic Resonance Imaging

Rolf, M.P.

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PART I

FLOW QUANTIFICATION OF THE MITRAL VALVE: COMBINING PHASE CONTRAST WITH SSFP SEQUENCES

Chapter 2

Extrinsic multiecho phase-contrast SSFP: evaluation on cardiac output measurements

Marijn P. Rolf, Mark B.M. Hofman, Joost P.A. Kuijer, Vinay M. Pai, Andreas Greiser, Albert C. van Rossum, and Rob M. Heethaar

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Abstract
Multiecho phase-contrast steady-state free precession (PC-SSFP) is a recently introduced sequence for flow quantification. In this multiecho approach, a phase reference and a velocity-encoded readout were acquired at different echo times after a single excitation. In this study, the sequence is validated in vitro for stationary flow. Subsequently, the sequence was evaluated on cardiac output measurements in vivo for throughplane flow in comparison to regular single gradient echo velocity quantification [phase-contrast spoiled gradient echo (PC-GE)]. In vitro results agreed with regular flow meters (RMS 0.1 cm/s). Cardiac output measurements with multiecho PC-SSFP on 10 healthy subjects gave on average the same results as the standard PC-GE. However, the limits of repeatability of PC-SSFP were significantly larger than those of PC-GE (2 l/min and 0.5 l/min, respectively, P=0.001).

The multiecho approach introduced some specific problems in vivo. The difference in echo times made the velocity maps sensitive for waterfat shifts and B_0-drifts, which in turn made velocity offset correction problematic. Also, the addition of a single bipolar gradient cancelled the flow compensated nature of the SSFP sequence. In combination with the prolonged TR, this resulted in flow artifacts caused by high and pulsatile through-plane flow, affecting repeatability.

Given the significantly lower repeatability of PC-SSFP, cardiac output in turn is less reliable, thus impairing the use of multiecho PC-SSFP.

2.1 Introduction

Flow quantification is an important tool in cardiovascular magnetic resonance imaging (MRI), for example, to measure cardiac output [1–4]. The conventional approach to flow quantification utilizes spoiled gradient echo (GE) imaging technique, which inherently has a limited signal-to-noise ratio (SNR) when applied with short repetition times. With the advent of faster gradient systems flow quantification with steady-state free precession (SSFP) sequences has become feasible, three different approaches were published by Overall et al. [5], Markl et al. [6] and Pai [7]. Advantages of SSFP are shorter acquisition times and higher SNR [8, 9]. The most recently published approach to flow quantification with SSFP was using multiecho phase-contrast SSFP (PC-SSFP) by Pai [7]. The multiecho PC-SSFP sequence uses a regular SSFP scheme with a second echo and a fly-back gradient between the two readout echoes. During the flyback gradient, a bipolar gradient is applied in slice-select direction for through-plane velocity encoding (extrinsic approach). The first echo provides the phase reference while the second echo is flow-encoded.

This approach has the advantage that it is most time efficient in its acquisition of phase reference and flow encoded data, compared with the single echo approaches. Also, with a multiecho approach, the steady-state does not need to be disturbed between reference and flow-encoded readouts, which can be advantageous with respect to artifact sensitivity. The extrinsic implementation of multiecho PC-SSFP permits a wide range of encoding velocities and is slightly faster than the intrinsic implementation.

A disadvantage of SSFP is its sensitivity to artifacts from pulsatile and high through-plane flow [10–13]. In the multiecho implementation, this sensitivity is slightly increased due to the longer TR and an uncompensated bipolar gradient. Another potential complication of phasecontrast measurements with a multiecho sequence is the different TEs at which the reference and flow encoded signals are read out. This makes the phase-contrast image sensitive to offsets in resonance frequency.

In this study, multiecho PC-SSFP was first evaluated in vitro

using a flow phantom. To assess the clinical value of multiecho PC-SSFP, the accuracy and reliability of cardiac output measurements in healthy volunteers was investigated. The results of multiecho PC-SSFP were compared with the current clinical standard PC-GE.

2.2 Materials and Methods

Sequence

The multiecho PC-SSFP sequence [7] was based on a regular SSFP gradient scheme extended with a second echo, where both echoes were encoded with a different velocity sensitivity (Figure 2.1). Both echoes were assigned to the same cardiac phase and phase encoding step. The fly-back gradient between the two echoes was configured to have the same net area under the gradient as the first echo but with opposite sign to give the second echo the same zero'th moment. During the fly-back gradient, flow was encoded by a bipolar gradient in the slice-select direction, and the bipolar gradient was configured such that its first moment M_1 gave a phase shift of π for a v_{enc} chosen by the user:

$$M_1 = \frac{\pi}{\gamma \cdot v_{enc}} \tag{2.1}$$

The duration of the fly-back gradient and the bipolar flow encoding gradient was kept as short as possible typically 1.0 ms. Velocity maps v were calculated from the phase difference between the phase image from the first readout, ϕ_1, and the flow-encoded image from the second readout ϕ_2:

$$v = \frac{\phi_1 - \phi_2}{\pi} v_{enc} \tag{2.2}$$

The multiecho PC-SSFP sequence was implemented on a 1.5T scanner (Magnetom Sonata, Siemens, Erlangen, Germany) with a gradient performance of 40 mT/m and 200 T/m·s.

In vitro measurements

The sequence was validated using a custom-made flow phantom. The phantom consisted of a Perspex cube with 15-cm-long edges, filled

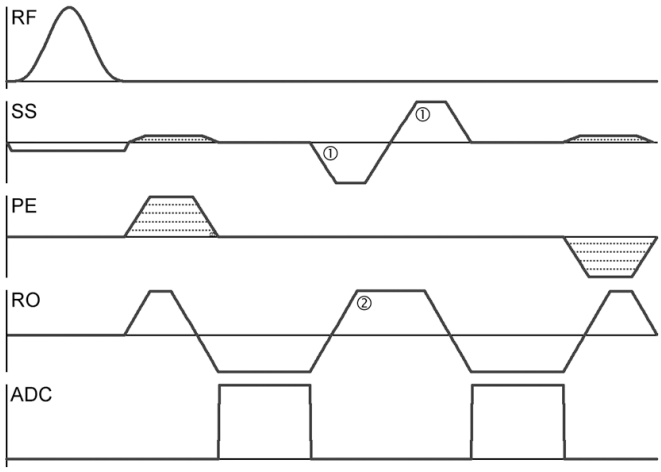

Figure 2.1: Multiecho PC-SSFP sequence. The bipolar gradient ① is placed on the slice-select axis (SS) at the time interval between the two readouts for through-plane flow encoding. The readout axis (RO) contains the gradients for the two echoes and the fly-back gradient ② is placed between them.

with stationary fluid. Inside the cube, fluid flowed through a tube of 4.15 mm in diameter. The flow circuit was driven by a rotary vane pump (Procon, Murfreesboro TN, USA), creating steady flow. A float displacement flow meter (Brooksmeter model 1307, Brooks Instrument, the Netherlands) was mounted in the flow circuit and was calibrated for the actual viscosity of the phantom fluid. This setup could generate flow velocities ranging up to 3 m/s, covering the physiologic range of flow velocities in the aorta of healthy humans. The phantom fluid consisted of 0.9% mass percent NaCl to load the coils, 0.05 mmol/l $MnCl_2$ to lower relaxation times (T1/T2/T2* 1505/204/198 ms, experimentally determined with MR). To give the fluid a viscosity comparable to blood ($\sim$3.5 mPa·s in normal population [14]), methylcellulose (4000 cP 0.2 vol%) was added, resulting in a viscosity of 4 mPa·s. Measurements were performed at 14 different flow settings. PC-SSFP sequence parameters were: spatial resolution $1 \times 1 \times 8$ mm^3, matrix 256×205, FOV 262×213 mm^2, v_{enc} 150 cm/s,

TR 6.4 ms, TE 1.9/4.5 ms, excitation angle 70°, bandwidth (BW) 1220 Hz/pix and 4 averages, using the body coil. PC-GE used TR 11 ms, TE 4.8 ms, excitation angle 15°, BW 190 Hz/pix; all other parameters were equal to those used with PC-SSFP.

The velocity assessed by a multiecho sequence is sensitive to B_0-offsets. This B_0-offset is influenced by the high gradient duty cycle of the PC-SSFP sequence; and thereby results in a velocity offset drift over time. To measure this drift in velocity offset as a function of time, subsequent measurements were performed on a stationary fluid filled phantom. The PC-SSFP sequence was played out repeatedly for 23 minutes. Sequence parameters were: TR 5.8 ms, TE 1.75/4.01 ms, v_{enc} 150 cm/s, acquisition time 50 s, and a phased-array receiver coil was used.

In vivo measurements

Ten healthy volunteers were scanned with multiecho PC-SSFP. The study was approved by the local ethics committee, and all subjects gave written informed consent. Throughplane velocity measurements were performed in a transverse plane in the ascending aorta at the level of bifurcation of the pulmonary artery trunk. The same measurement was also performed using a conventional phase-contrast spoiled gradient echo (PC-GE). The temporal resolution of PC-SSFP was matched as close as possible to the PC-GE. Each measurement was performed twice. All four measurements within each subject were performed in random order. Imaging parameters for both sequences were as follows: spatial resolution $1.25 \times 1.25 \times 8$ mm^3, matrix 256×205, FOV 320×260 mm^2, retrospective electrocardiographic gating [15] with 30 reconstructed phases, v_{enc} 150 cm/s, no parallel imaging, and a phased-array receiver coil was used; for PC-SSFP: TR 5.8 ms, TE 1.75/4.0 ms, five segments, excitation angle 70°, BW 1220 Hz/pix, temporal resolution 29 ms, locally adjusted shim and acquisition time 41 sec at a heart rate of 60 beats per minute; for PC-GE: TR 11 ms, TE 4.8 ms, 1 segment, excitation angle 15°, BW 190 Hz/pix, temporal resolution 22 ms, acquisition time 3.4 minutes at a heart rate of 60 beats per minute.

For the PC-GE sequence, a usual flip angle of 15° was applied. After the series of volunteers was scanned, questions rose whether the observed SNR differences between PC-SSFP and PC-GE were simply due to their difference in flip angle. To answer that question another three healthy volunteers were scanned with PC-SSFP and PC-GE with a range of flip angles (15°, 30°, 45°, 60°, and 70°), all other sequence parameters were kept similar as above.

Data analysis and statistics

Flow phantom

Cross-sectionally averaged velocities in the PC-SSFP and PC-GE images were measured using commercial software (Argus, Siemens, Erlangen, Germany). Regions of interest were drawn with an area matching the known tube diameter, to limit partial volume errors. Velocity offset was corrected using average reference region of interest in the static fluid part of the phantom. MR determined velocities were compared with velocities assessed by regular flow meters. Validity of flow measurements was tested by comparing the slope and intercept outcomes of linear regression with the line of identity.

Velocity offset drift

Average velocity was measured in the center of the phantom in all 26 scans. Linear regression of velocity offset against time since start of the measurement yielded the velocity offset drift.

SNR and SNR efficiency

SNR measurements were performed using commercial software (Mass, Medis, Leiden, The Netherlands). SNR was measured from the average signal in the ascending aorta divided by the standard deviation of noise. Noise was measured in air outside the subject and care was taken not to include any flow artifacts. A factor of 0.70 was applied to correct for noise measured in magnitude images from multiple receivers [8]. SNR was averaged over the whole cardiac cycle and the two measurements. SNR efficiency was calculated by dividing the SNR by the square root of the scan time. Differences in SNR and

SNR efficiency between the two sequences were tested with a paired Student's t-test.

Cardiac output
Aortic flow curves were determined with manually drawn contours at all cardiac phases using commercial software (Flow, Medis, Leiden, and the Netherlands). Phase offsets in PC-SSFP were corrected by defining the average velocity in the aorta in the last cardiac phase as zero. Cardiac output was determined as the average volume flow in the aorta over the complete cardiac cycle multiplied by heart rate. Repeatability of the two techniques was analyzed by mean difference plots of the cardiac outputs of PC-SSFP and PC-GE [16]. To limit physiologic variation and to focus on differences in acquisition techniques, only those subjects with a change of less than 5% in nominal heart beat interval between repeated measurements were included.

Artifacts
In order to understand the influence of through-plane flow artifacts on cardiac output measurements, two different artifact measures were assessed. First, artifacts were measured as the maximum artifact magnitude over the cardiac cycle outside the subject but within the ghosting band of artifacts originating from the aorta. The artifact intensity was expressed as percentage of the average intensity in the aorta in the same cardiac phase. Another problem was the fact that, due to artifacts, the aorta contour was at some cardiac phases difficult to draw. Therefore, a second artifact measure was introduced: the number of cardiac phases in which the aorta contour was obscured by artifacts. This was visually scored.

To determine the influence of artifacts on repeatability of cardiac output measurements, the correlation coefficient of each artifact score with the difference between repeated cardiac output measurements was calculated.

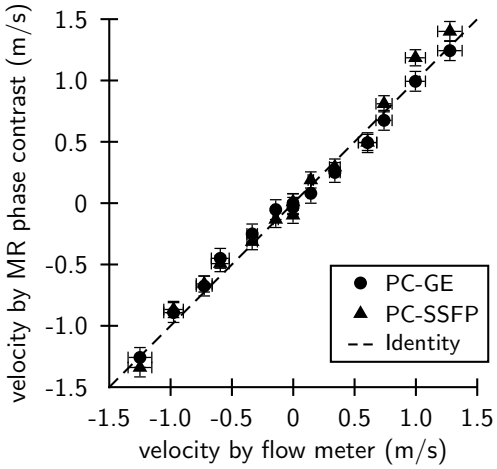

Figure 2.2: In vitro validation: cross sectional averaged velocity measured with PC-SSFP and PC-GE against flow meter readings. Error bars indicate the estimated measurement error. Data were consistent with the line of identity (PC-SSFP: slope 1.03 P=0.4, offset 0.03 m/s P=0.3, PC-GE: slope 0.94 P=0.03, offset 0.0 m/s P=0.8), and the residual errors were small (RMS 0.1 m/s for PC-SSFP and 0.05 m/s for PC-GE).

2.3 Results

In vitro measurements

Average volume flows measured in the PC-SSFP and PC-GE velocity maps were plotted against the flow meter measurements (Figure 2.2). Both measurements showed agreement with the flow meter data; data were consistent with the line of identity (PC-SSFP: slope 1.03 P=0.4, offset 0.03 m/s P=0.3, PC-GE: slope 0.94 P=0.03, offset 0.0 m/s P=0.8), and the residual errors were small (RMS 0.1 m/s for PC-SSFP and 0.05 m/s for PC-GE).

Velocity offsets showed a linear relationship with time for 23 minutes of scanning, with a squared correlation coefficient R^2 of 1.0. The velocity offset drift was 0.020 cm/s^2. Due to the small difference in TE, this had no implications in terms of image shift, as normally associated with B_0-drift [17]. For scans as used for the in vivo imaging

the resulting image shift was small relative to pixel size. However, velocity offsets between repeated scans did not reproduce because two subsequent scans had a B_0-drift induced difference in velocity offset of 1.2 cm/s.

In vivo

Figures 2.3a and b show typical magnitude images as acquired with PC-SSFP and PC-GE. PC-SSFP images suffered from artifacts during systole due to fast pulsatile through-plane flow (Figure 2.3c). A locally adjusted shim visibly reduced the artifacts but could not remove them. In all cases, artifacts remained. The difference in TE between the two echoes was minimized, given the systems gradient performance. However, the resulting difference in TE of 2.24 ms maximized the phase difference between water and fat at 1.5T. The phase shift between water and fat was clearly visible in the velocity maps (Figure 2.3d).

The results of the SNR and SNR efficiency measurements are shown in Table 2.1. The SNR efficiency improved by a factor of 1.6 (S.D. 0.4) using PC-SSFP. Average SNR ratio of PC-SSFP over PC-GE was 0.8 (S.D. 0.2).

Cardiac output was calculated for PC-GE in eight subjects and for PC-SSFP in seven subjects; subjects with large differences in heart rate between repeated scans were excluded. A typical flow curve is shown in Figure 2.4. The flow curves showed general agreement between PC-SSFP and PC-GE; however, PC-SSFP showed more differences in flow curves (see Figure 2.4 at 400 ms). The observed differences in flow curves for the PC-SSFP measurements were not systematic within and between subjects. This is confirmed by linear regression analysis, which revealed no significant difference from the line of identity (P=0.87) between PC-SSFP and PC-GE (Figure 2.5a). The observed differences for PC-SSFP curves were quantified by a Bland-Altman analysis of PC-SSFP and PC-GE, as shown in Figure 2.5b and 2.5c. The limits of repeatability of PC-SSFP, ± 2 L/min, were significantly larger (P=0.001) than those of PC-GE, ± 0.5 l/min.

To understand the lower repeatability of the PC-SSFP, the artifacts were quantified. Averaged over all 10 subjects, the maximum

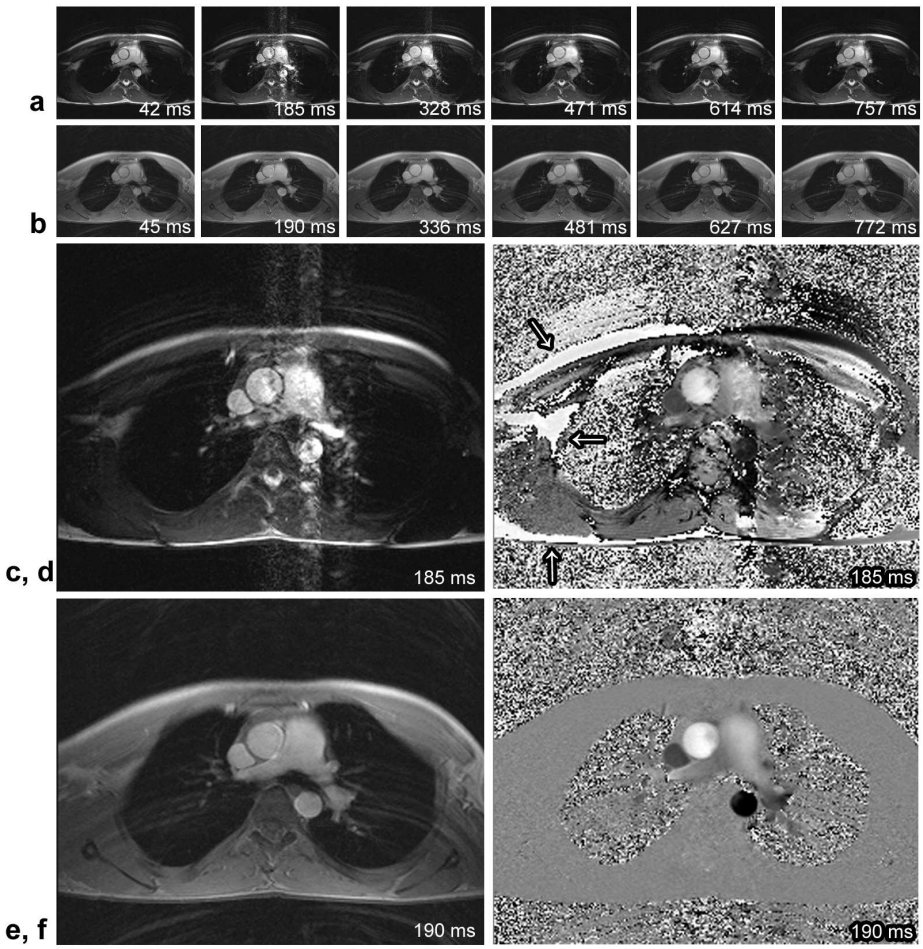

*Figure 2.3: Example of PC-SSFP (*a, c, d*) and PC-GE (*b, e, f*) images from subject 1. (*a, b*) Six images out of 30 reconstructed cardiac phases, time indicates delay after R-peak trigger. Worst artifacts of PC-SSFP were visible during systole (185 ms). (*c, d*) Magnitude and phase difference image during systole, at 185 ms. Artifacts from high through-plane flow in ascending and descending aorta were visible. The phase image also showed marked water-fat phase differences in the thorax wall (indicated by the arrows), and a spatial gradient in the offset over the image. (*e, f*) Magnitude and phase difference image of PC-GE.*

Table 2.1: SNR and SNR efficiency results at the aorta of PC-SSFP and PC-GE in ten healthy subjects; while SNR decreased with PC-SSFP (P=0.03), SNR efficiency was higher for PC-SSFP (P=0.005).

	Subject										Mean	S.D.
	1	2	3	4	5	6	7	8	9	10		
SNR												
PC-SSFP	55	46	65	48	96	51	103	55	60	37	64	21
PC-GE	89	64	75	97	84	99	91	62	68	74	80	14
Ratio	0.6	0.7	0.9	0.7	1.1	0.5	1.1	0.9	0.9	0.5	0.8	0.2
SNR efficiency ($ms^{-1/2}$)												
PC-SSFP	23	19	27	28	40	21	43	23	25	15	27	9
PC-GE	19	14	16	21	18	21	20	13	14	16	17	2.9
Ratio	1.2	1.4	1.7	1.4	2.2	1.0	2.2	1.7	1.7	1.0	1.6	0.4

These values were obtained with a 15° excitation angle of the PC-GE sequence.

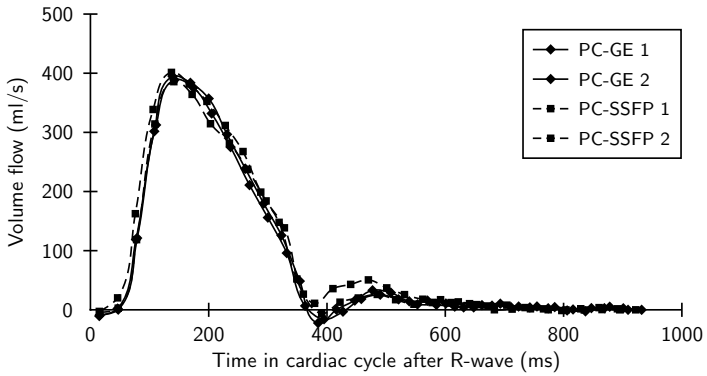

Figure 2.4: Typical aortic flow curves from PC-SSFP and PC-GE in one healthy subject (subj. 9). Flow curves showed general agreement between the two methods.

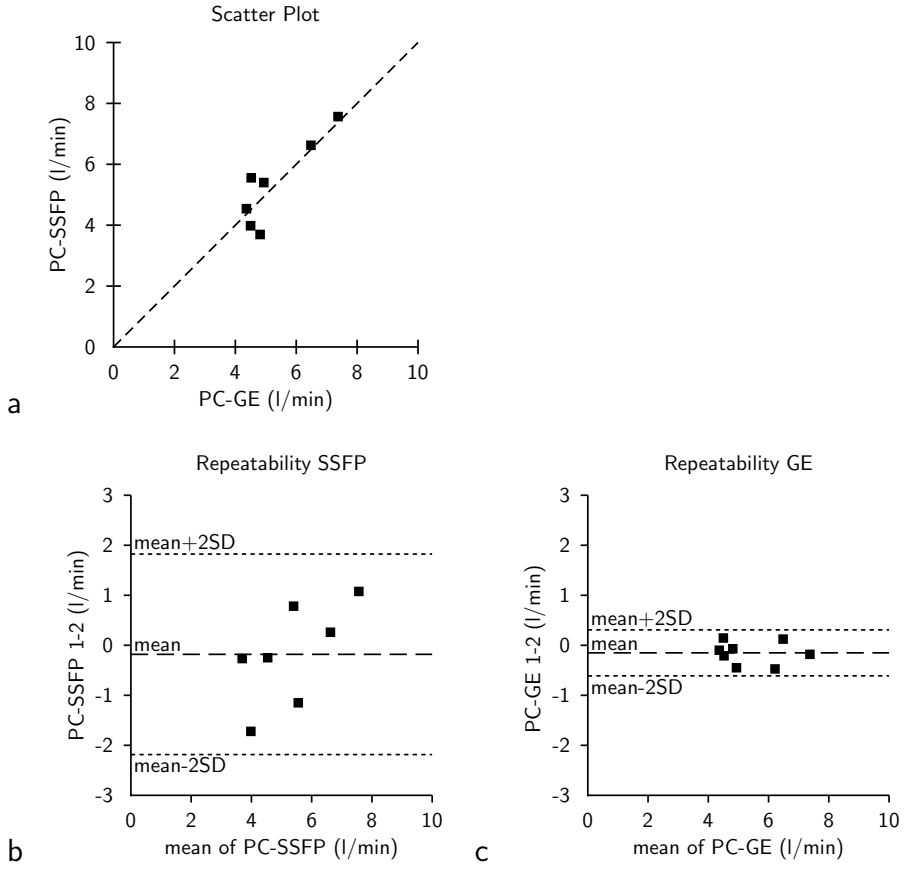

Figure 2.5: Results of cardiac output measurements. (a) Scatter plot of averaged cardiac output of PC-SSFP plotted against PC-GE. There was no significant difference from the line of identity (P=0.87). (b, c) Bland-Altman meandifference plot of PC-SSFP and PC-GE repeatability. PC-SSFP limits of repeatability of 2 l/min were significantly larger than those of 0.5 l/min of PC-GE (P=0.001).

artifacts had an intensity of 20% (range 10–40%) of the aorta intensity, and in three (range 0-7) out of 30 cardiac phases, the aorta contour was difficult to recognize. Correlation of the maximum artifact intensity with the repeatability of cardiac output measurements by PC-SSFP (n=7) was not significant (R^2=0.35, P=0.16), but the correlation of the number of contours affected with repeatability of cardiac output measurements was significant (R^2=0.82, P=0.01). The residual repeatability limits (not explained by the contours) were ±0.55 L/min, which was not significantly different from PC-GE (P= 0.49).

The relation between SNR and flip angle was different for the two sequences, as illustrated in Figure 2.6a. The SNR for PC-SSFP steadily increased with increasing flip angle, probably a result of the steady-state not being fully developed. As expected, PC-GE showed an optimum; however, the optimum was not at the Ernst angle but at an increased angle (45°) probably due to inflow effects. In addition, the sensitivity to high through-plane flow artifacts was different. PC-GE had only minor artifacts independent of the flip angle used, whereas PC-SSFP showed a strong decrease in artifacts with increasing flip angle (Figure 2.6b).

2.4 Discussion

This study shows that multiecho PC-SSFP is capable of measuring through-plane flow; accurate in vitro velocity quantification was performed, and in vivo cardiac output measurements showed no systematic difference with the standard technique (PC-GE). With the used parameters, the SNR efficiency was higher for PC-SSFP. However, the technique was hampered by two issues: velocity offsets were hard to correct for, and through-plane flow caused severe artifacts. These issues limited the clinical utility of this technique.

In this study SNR efficiency of PC-SSFP was higher than PC-GE SNR efficiency. Even though a low flip angle is normally applied in PC-GE [18–20], our measurements showed that a higher flip angle would have improved the SNR for PC-GE. Considering the data from

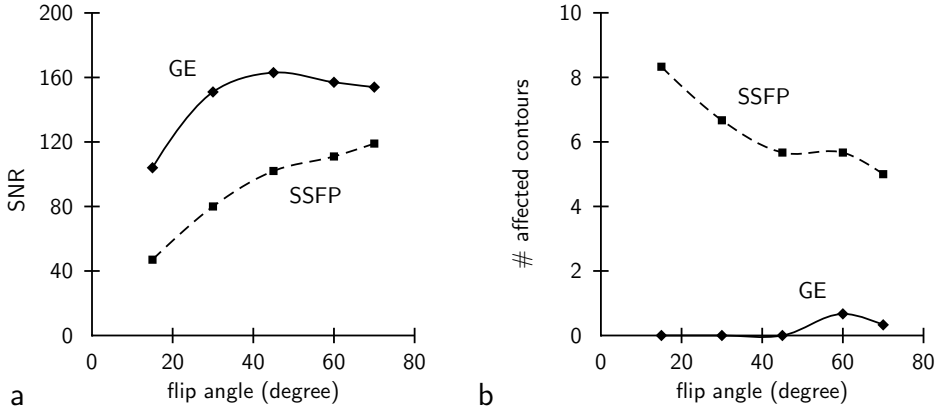

Figure 2.6: Flip angle dependency of PC-GE and PC-SSFP. (a) SNR as function of flip angle, PC-SSFP showed a steady increase, whereas PC-GE showed more complex behavior. (b) Artifacts as function of flip angle, PC-GE showed almost no dependency, whereas PC-SSFP showed a strong decrease with increasing flip angle.

Figure 2.6, the optimal excitation angle of the PC-GE could cancel the observed SNR efficiency difference. SNR efficiency was expected to be better for PC-SSFP than for PC-GE. However, a high-receiver bandwidth (to achieve a short TR) and incomplete development of the steady-state due to high through-plane flow resulted in a SNR efficiency comparable to PC-GE.

Due to the high duty cycle of the gradients, the velocity offset showed a strong drift over time. In fact, using readouts with different echo times is an established method to measure B_0-drifts [21]. The velocity drift of 0.020 cm/s^2 corresponded to a B_0-drift of 1.80 Hz/min. This was relatively high compared to values reported earlier in literature for echo-planar imaging sequences [17]. Although the drift is strongly dependent on the actual scanner model used, the drift is probably an issue on most systems. As shown in the Results section, the image shift within scans associated with B_0-drifts was negligibly small, but the difference in velocity offset between scans was substantial. This prohibited offset determination by a separate reference scan

in a phantom as can normally be done for PC-GE. The only option left for PC-SSFP offset correction was by setting the velocity of the last cardiac phase to zero. This is a less preferable solution because there can still be a low velocity due to compliance of the vessel wall, and it will not work in patients with aortic insufficiency and in vessels at other locations further away from the heart.

Multiecho PC-SSFP proved to be sensitive to throughplane flow artifacts. The uncompensated bipolar gradient and the long TR made the sequence sensitive to fast flowing and pulsatile blood [12, 13]. To illustrate the effect of the uncompensated gradient, we additionally turned the velocity encoding gradient off. The resulting images (Figure 2.7) confirm that the uncompensated gradient generated artifacts. Averaged over three subjects and two measurements per subject, the number of obscured contours reduced from 6.3 to 0.6. A locally adjusted shim and a high receiver bandwidth to obtain a short TR could reduce, but not avoid, the artifacts from fast pulsatile blood flow. Interestingly, the number of obscured contours due to artifacts proved to be a better estimator of differences between repeated PC-SSFP measurements than the relative artifact intensity. This implied that errors in region of interest placement contributed more to the total variance of cardiac output than errors in the velocity maps caused directly by the artifacts.

Even though the results from this study show that multiecho PC-SSFP cannot replace PC-GE for cardiac output measurements, there are some options for improvement. Phase offsets should be less of a problem using a 3T scanner; at 3T, the water-fat shift is minimized at the applied echo time differences of 2.24 ms. This would make it possible to perform an offset estimation by interpolation between stationary tissue in the chest wall [22]. Another option would be to expand to a three-echo sequence and determine the velocity map as Nielsen and Nayak [23] did; however, this would require an even longer TR. The sensitivity to artifacts from through-plane flow might be reduced using a second bipolar gradient after the second readout to make the sequence flow compensated again [12, 13]. The multiecho PC-SSFP sequence, as was described in this paper, might be better suitable for cerebrospinal fluid flow measurements in the

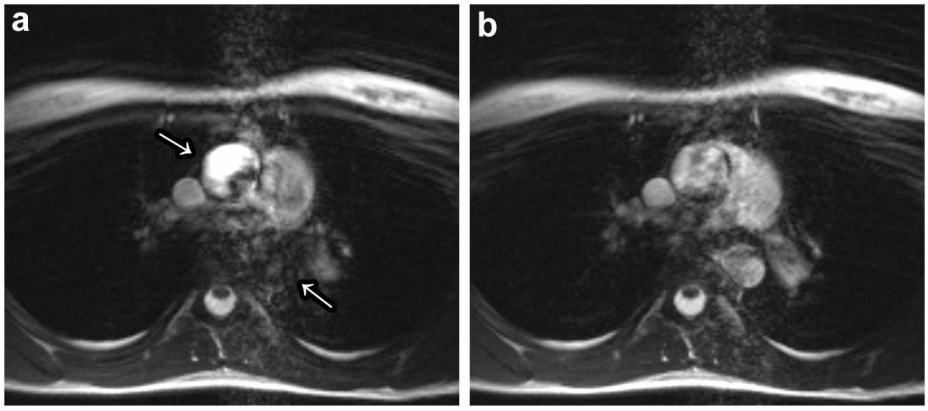

Figure 2.7: Typical example of PC-SSFP artifacts during systole (200 ms) with the bipolar gradient turned on (a) and off (b). Areas of signal saturation (ascending aorta, upper arrow) and signal loss (descending aorta, lower arrow) due to artifacts showed major improvements when the unbalanced gradient was turned off.

brain, as velocities are lower, pulsatility is less and uniform surrounding tissue is present for phase offset measurement. For cardiac output measurements, the PC-SSFP approach of Markl et al. [6] might be interesting for further investigation. Phase offset estimation should not be a problem with a single echo readout, less severe flow artifacts are expected because the sequence is flow-compensated, and TR is less prolonged.

In conclusion, multiecho PC-SSFP had a similar SNR efficiency as PC-GE, but phase offset correction was problematic and the sequence was prone to artifacts from fast and pulsatile blood flow, preventing reliable cardiac output measurements.

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