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High Temporal Resolution Phase Contrast MRI With Multiecho Acquisitions

Richard B. Thompson^{*} and Elliot R. McVeigh

Laboratory of Cardiac Energetics, National Institutes of Health, Bethesda, Maryland.

Abstract

Velocity imaging with phase contrast (PC) MRI is a noninvasive tool for quantitative blood flow measurement in vivo. A shortcoming of conventional PC imaging is the reduction in temporal resolution as compared to the corresponding magnitude imaging. For the measurement of velocity in a single direction, the temporal resolution is halved because one must acquire two differentially flow-encoded images for every PC image frame to subtract out non-velocity-related image phase information. In this study, a high temporal resolution PC technique which retains both the spatial resolution and breath-hold length of conventional magnitude imaging is presented. Improvement by a factor of 2 in the temporal resolution was achieved by acquiring the differentially flow-encoded images in separate breath-holds rather than interleaved within a single breath-hold. Additionally, a multiecho readout was incorporated into the PC experiment to acquire more views per unit time than is possible with the single gradient-echo technique. A total improvement in temporal resolution by ~5 times over conventional PC imaging was achieved. A complete set of images containing velocity data in all three directions was acquired in four breath-holds, with a temporal resolution of 11.2 ms and an in-plane spatial resolution of 2 mm × 2 mm.

Keywords

MRI; phase contrast; temporal resolution; flow; cardiac

Understanding the nature of the 3D vector fields that describe the complex blood flow through large vessels and the chambers of the heart is important in numerous fields of medicine. Vascular surgeons need to model pressure gradients and flow patterns when designing bypass and graft options in the treatment of occlusive disease (1). Clinical cardiologists utilize blood flow patterns that result from material obstructions (2), valvular defects (3), and diastolic dysfunction (4) for the diagnosis of pathology. Incomplete knowledge of the relationship between cardiac mechanics and hemodynamics has led to extraordinary efforts to construct models of ventricular flow patterns using computational fluid dynamics and massive super-computing resources (5,6). To date, these models have lacked human in vivo data with sufficient spatial and temporal resolution to characterize the complex flow. This study presents a new phase contrast (PC) MRI protocol to obtain vector flow fields in the chambers of the heart with a temporal resolution that is ~5 times that achieved with commercially available sequences.

Noninvasive detection of blood velocity within the heart is most commonly reported with M-mode and 2D color Doppler echocardiography. Time-resolved PC-MRI (7,8) is an alternative to Doppler which offers many advantages for quantitative flow evaluation. In particular, MRI can be used to examine blood and tissue using arbitrary image-plane orientations without

^{*}Correspondence to: Richard B. Thompson, Laboratory of Cardiac Energetics, National Institutes of Health, Room B1D 416, Bldg. 10, 10 Center Drive, Bethesda, MD 20892-1061. E-mail: thompsonr@nih.gov

restrictions due to access windows. Additionally, PC-MRI is insensitive to velocity errors caused by source angle sensitivity (9). Most importantly, PC-MRI can provide three-component velocity information, compared to the single component from Doppler ultrasound. While PC-MRI can resolve complex spatial flow patterns in two and three dimensions, high spatial resolution must be achieved at the expense of temporal resolution in the cardiac cycle for a given data acquisition time, most commonly a breath-hold. This temporal/spatial resolution compromise is of particular importance for imaging blood flow within the cardiac chambers and great vessels due to the high accelerations and complex patterns of blood motion coupled with the large fields of view (FOVs) that are required to avoid aliasing. To date, the temporal and spatial resolutions required to capture the most complex blood flow patterns within the cardiac chambers remain to be quantified, although frame rates ranging from 15 to 30 frames per second (FPS) (temporal resolutions from 70 ms to 35 ms) are commonly reported for cardiac PC-MRI (10-13). For myocardial wall motion, Doppler echocardiographic estimates of the temporal resolution required to resolve all components of motion, at resting heart rates, are as high as 70-100 FPS (14,15). Comparable estimates for intracardiac blood motion have not been made with Doppler techniques, although frame rates reaching 90 FPS have been reported with small sector angles and small regions of interest (ROIs) with 2D color Doppler (16). In this study a high temporal resolution breath-hold 2D PC-MRI technique with frames rates approaching 100 FPS is described. All velocity components (v_x , v_y , v_z) are measured and the spatial resolution of conventional MRI is maintained. An in-plane resolution of 2.0 mm $\times$ 2.0 mm and slice thickness of 8.0 mm was used for all normal volunteers examined.

Two separate approaches were used to increase the efficiency of the PC experiment. First, an improvement by a factor of 2 in the temporal resolution was achieved by acquiring the phase-reference images in a separate breath-hold rather than interleaved with the velocity-encoding images. Additionally, a multiecho readout was incorporated into the PC experiment to acquire more views per unit time than possible with the single-gradient-echo technique (17,18). Successful application of the multiple breath-hold PC experiment required gradient first-moment nulling (flow compensation) for slice, phase, and read-encoding directions (8,17-23) to ensure that velocity phase was eliminated from the phase-reference images. Susceptibility to phase-difference artifacts caused by misalignment of slices between breath-holds is minimized with a novel phase correction method for breath-hold misregistration, in combination with an appropriate flow-encoding scheme. The multi-breath-hold, multiecho PC method is validated against a high temporal resolution single-gradient-echo PC approach using a pulsatile flow phantom. The efficacy of the multiecho first-moment nulling, and the improvement in temporal resolution vs. conventional PC-MRI, are displayed for both phantom and in vivo applications. In vivo velocity data was obtained from several normal volunteers using temporal resolutions as short as the length of a single excitation interval (TR = 11.2 ms). A complete set of images containing velocity data in all three directions is acquired in four breath-holds. Complex temporal and spatial ventricular blood flow patterns are displayed and the actual required temporal resolution is discussed.

THEORY

In NMR experiments, sample motion in the presence of a magnetic field gradient will result in the accumulation of motion-dependent phase. The component of that phase which is proportional to the sample velocity can be expressed in terms of the first moment, $\mathbf{M}_1$, of that gradient:

$$\varphi = \gamma \mathbf{M}_1 \cdot \mathbf{v} = \gamma (M_{1x}v_x + M_{1y}v_y + M_{1z}v_z). \quad [1]$$

In MRI, the velocity phase that is encoded to a given pixel is proportional to the mean velocity in that pixel and the value of $\mathbf{M}_1$ at the center of k -space.

Time-resolved velocity imaging with PC-MRI (8) is now commonly carried out with segmented k -space experiments (24). The minimum experiment length, in heartbeats, is determined by the number of segments acquired. For conventional single-echo cine imaging, the maximum temporal resolution that can be achieved, which is the length of a segment, is equal to the number of views per segment (VPS) times the length of a single acquisition (TR). For a cine experiment with both PC and a multiecho acquisition scheme, the temporal resolution, in terms of TR, VPS, and echo-train length (ETL) is:

$$\Delta t = \frac{2 \cdot TR \cdot VPS}{ETL} = \frac{2 \cdot TR \cdot N_y}{ETL \cdot N_{HB}}, \quad \text{where} \quad VPS = \frac{N_y}{N_{HB}}. \quad [2]$$

The VPS is expressed in terms of the number of phase-encoding steps, N_y , which determines the spatial resolution in the phase-encoding direction, and the number of heartbeats in the experiment, N_{HB} . Because the experiment is typically carried out using breath-holds to eliminate respiratory artifacts, N_{HB} is limited, in practice, by breath-hold length. The factor of 2 in Eq. [2], which is unique to the PC experiment, is a consequence of the interleaving of two differential flow-encoded experiments (Fig. 1a) (8). Two flow-encoded experiments are required to subtract out unwanted background phase information that arises from the radiofrequency coils, off-resonance evolutions, and gradient imperfections. The factor of 2 can be eliminated, without compromising N_y or N_{HB} , by acquiring the two flow-encoding experiments in separate breath-holds, as shown in Fig. 1b, rather than interleaved in the same breath-hold. A multiecho readout is also pictured in Fig. 1b, which can be utilized to further increase the temporal resolution for a given spatial resolution and breath-hold length (25), as compared to the single-gradient-echo readout pattern. Comparing the approaches pictured in Fig. 1a and b, the multiecho, multi-breath-hold PC approach improves the temporal resolution by $2 \cdot ETL \cdot TR_{SE}/TR_{ME}$, where TR_{ME} is the multiecho repetition time and TR_{SE} is the single-echo repetition time, while maintaining the breath-hold length and spatial resolution.

Flow-Encoding Multiple Velocity Directions in Multiple Breath-Holds

The improvements in temporal resolution outlined above for the multiecho, multi-breath-hold PC experiment were for the case of a single velocity direction, and required two breath-holds to complete the exam, as shown in Fig. 1b. The same approach can be extended to acquire all three velocity components in a four-breath-hold exam that will maintain the improved temporal resolution by using a four-point flow-encoding scheme (26,27). Two standard four-point flow-encoding schemes, the simple and balanced methods, are outlined in Table 1. Both of these approaches have advantages, depending on the application (26,27). For PC exams, misalignment of image phase between the breath-hold experiments may result in residual, non-velocity-encoded phase differences which will present as velocity artifacts in the PC images. The simple method is superior to the balanced method for such multiple breath-hold exams for several reasons. With the simple four-point method, each component velocity is calculated from the phase difference of only two breath-holds, as shown in Table 1. Because only one of these experiments has velocity information, the phase error is due only to misalignment of the background phase, which contains no velocity information, and is composed primarily of low spatial frequency information (28,29). Referring again to Table 1, balanced methods encode velocity information from each direction into all four breath-holds, making all three phase difference images susceptible to errors from misalignment of any one of the four breath-holds. Furthermore, the misalignment error for balanced methods will be due to an offset of the background phase as well as the velocity-encoded phase. Because the image phase arising from velocity encoding contains relatively high spatial frequency information, due to the sharply defined vessels and cavities in which the blood flows, even relatively small slice misalignments may result in significant phase errors using balanced methods.

While the simple four-point encoding scheme minimizes the phase-difference errors from slice misalignment, there may still be residual errors due to offset of the background image phase between breath-holds. To calculate the breath-hold misalignment phase error for any pair of breath-holds with the simple flow-encoding scheme, a single segment in the velocity-encoded sequence is acquired as a first-moment nulled phase-reference segment, shown in the second breath-hold (BH-2) in Fig. 1c. Thus, one cardiac phase of the velocity-encoded cine series will contain a phase-reference image, which can be compared to the corresponding phase-reference image from BH-1 (Fig. 1c). The phase difference between these reference images is the residual nonvelocity phase that resulted from the breath-hold misalignment. The correction map is subsequently applied to all cardiac phases in the phase-contrast image series. Phase errors from both in-plane and through-plane misalignment will be represented. A phase correction can be calculated for each velocity direction if a phase-reference segment is substituted in each of the three velocity-encoded experiments. There is an unavoidable loss of temporal resolution around the cardiac phase selected for the phase correction, because velocity information is not acquired for that segment. To avoid a loss of velocity information during phases of rapid change, the replacement segment was inserted at 75% of the mean cardiac interval, in the middle of diastasis, in each heartbeat for all velocity-encoded experiments.

The improvements in temporal resolution outlined thus far were made with the assumption that the conventional PC approach is applied with the six-point flow-encoding scheme (26), with each velocity direction acquired in one of three separate breath-holds. This assumption was made to maintain the temporal resolution of the conventional PC exam regardless of the number of velocity directions acquired. The alternative—to acquire all three velocity directions in a single breath-hold with a four-point flow-encoding scheme—is not practical in a breath-hold exam due to the exceedingly poor temporal resolution that would result, and is not compared to the methods introduced in this study.

Multiecho Flow Compensation

Flow compensation using bipolar gradients to cancel an unwanted first moment eliminates velocity-sensitive phase from the reconstructed images. This method is commonly used for flow compensation in the slice-selection direction for both single- and multiecho experiments. Flow compensation of in-plane motion requires that the first moment is nulled at the center of k -space for both the read and phase-encoding gradient directions. For multiecho experiments, complex patterns of first moments across k -space for both read and phase-encoding directions can include nonzero values at the center of k -space (18-23). An analytic expression for the multiecho phase-encoding first moment at $k_y = 0$ (22) was used to design a compensatory bipolar gradient to null the unwanted moment. The moment-nulling bipolar pair was incorporated in the multiecho pulse sequence, as shown in Fig. 1b. The calculation of the read-encoding first moment at the center of k -space for echo-train experiments is influenced by the sharp first-moment discontinuities between sequential echoes, a consequence of the gradient reversal between each echo. To avoid discontinuities at $k_y = 0$, either center-out trajectories or top-down trajectories with odd ETLs can be used. Although the discontinuities can be altogether eliminated by using a flyback readout, this approach is less desirable due to the reduction in acquisition efficiency (31,32). In this study, a top-down trajectory with ETL = 5 was used for the multiecho experiments. For this case, the effective first moment at the center of k -space is equal to the first moment at the center of the third echo. This read-encoding first moment can be nulled with a bipolar gradient, applied prior to the readout gradients, with equal and opposite first moment. A schematic pulse sequence diagram is displayed in Fig. 1b.

Multiecho Flow Artifacts

The relationship between k -space trajectories, the associated patterns of first-moment discontinuities, and the image artifacts generated by motion, have been extensively studied for

single- and multishot echo-planar acquisitions (18-23). In this study, a gradient moment smoothing technique (22) was used for all multiecho experiments to eliminate the discontinuities in the phase-encoding direction. While there are no methods (other than the inefficient flyback readout (31,32)) to eliminate the read-encoding moment discontinuities, several precautions were found to drastically reduce image artifacts resulting from motion in the readout direction. All multiecho experiments incorporated a maximum of 160 readout points, a maximum of five echoes, and the maximum available acquisition band-width, ± 125 kHz, on the GE cv/i system. These precautions limited both the TR, which is strongly correlated to image quality for multiecho experiments (25,33), and the first-moment discontinuity between successive echoes. Second, imaging planes were oriented such that the high velocities—those along the inflow and outflow directions—were primarily in the phase-encoding direction. Echo-shifting (34) was incorporated in all multiecho experiments to eliminate phase discontinuities from off-resonance evolutions.

Residual eddy current phase is also known to contaminate PC velocity images (35,36). Fortunately, phase accumulation from eddy currents is independent of the sample, so it is insensitive to breath-hold misalignment. Correction of the residual eddy current phase in this study was done by fitting a low-order polynomial to the phase of stationary objects in the phase-difference images and subtracting the resulting phase (35,36). Stationary objects were selected based on the variation of the phase-difference values over the entire cardiac cycle. Finally, the phase sensitivity of the multiecho pulse sequences to higher-order motion was calculated and found to be negligible for the range of accelerations expected in vivo, up to 30 m/s^2 .

MATERIALS AND METHODS

All MR measurements were performed on a 1.5 T GE cv/i MRI scanner (GE Medical Systems, Waukesha, WI) with high-performance gradients (40 mT/m amplitude, 150 T/m/s slew rate) and a four-element phased array receiver coil. For all multiecho experiments scan parameters were as follows: 8-mm slice thickness, 32×24 cm FOV, 160×120 matrix, ± 125 kHz receiver bandwidth, 15° tip angle, and ETL = 5. A top-down k -space trajectory with echo-shifting (34) was used for all experiments. For these parameters, the echo-spacing (ESP) was $920 \mu\text{s}$ and the TR was 11.2 ms. For the single-gradient-echo PC experiments a GE product pulse sequence was used (Fastcard PC, GE Medical Systems, Waukesha, WI), with a TR of 6.0 ms, a ± 62.5 kHz receiver bandwidth, and a 10° tip angle. Phase-reference and velocity-encoded experiments are inter-leaved between sequential excitations with the product sequence, as illustrated in Fig. 1a.

A prospectively gated, retrospectively sorted acquisition/reconstruction method, similar to cardiac phase to order reconstruction (CAPTOR) (37), was used for all PC experiments. Data was collected for the entire R-R interval and assigned a cardiac phase based on a model of the cardiac cycle rather than on the absolute time after the R-wave. Within each heartbeat, the time series for each k_y -line was rebinned with a linear interpolation kernel to the appropriate location in the RR interval determined by the desired number of reconstructed images, typically 100 frames for the multiple breath-hold PC experiments. Note that the true time from the QRS to the acquisition of each k_y -line was incorporated to resolve the views acquired within a given segment. Reconstructing 100 frames across the RR interval for all volunteers was a matter of convenience, to allow each image frame to be 1% of the interval and allow for comparison between individuals. The true number of frames that can be reconstructed without upsampling depends on the mean heart rate, with 89 frames for a heart rate of 60 BPM using the parameters described above.

For both phantom and in vivo experiments, reduced temporal resolution data sets were extracted from high temporal resolution data to study the requirement for temporal resolution

in MR blood flow imaging without the influences of interexperiment variability. Care was taken to extract the lower resolution data from the single TR resolution data set in a pattern identical to the actual lower temporal resolution experiments. In particular, when emulating high VPS data from a lower VPS data set, all views in a given segment were extracted in a manner consistent with their sequential collection.

Phase corrections for slice misalignment and residual eddy current effects were automatically calculated for all experimental results with no user input using in-house software. All phase differences were calculated as the angle of the complex conjugate multiplication of the two differentially flow-encoded experiments. For phased-array experiments, care was taken to combine the multiple channel data optimally (38).

Flow Phantom

A flow phantom designed for validation of the high temporal resolution multiecho PC experiments consisted of a flexible tube system (15-mm inner diameter) driven by a constant pressure head provided by a peristaltic pump fed through a baffle (Fig. 2). The baffle consisted of a closed bath with an air cushion to absorb vibrations from the pump. The flow control was adjusted by a voltage-controlled pinch valve that was triggered by a synthetic EKG generator (60 beats/min) to produce cyclic time-dependent flow rates. The same EKG signal was used for triggering the data acquisition. The solution in the tube system was water-doped with Gd-DTPA (Magnevist, Berlex) (0.07 mMol/L) to approximate the T_1 of blood at 1.5 T (1200 ms).

For all flow validation experiments, the tube was formed into a return loop in a coronal plane (Fig. 2) to generate in-plane flow in both the read and phase-encoding directions for a coronal slice orientation, and through-plane flow for an axial slice. As a standard for high temporal resolution velocity measurements, conventional cine PC imaging with a gradient-echo sequence (Fig. 1a) was carried out for each velocity direction ($V_{enc} = 80$ cm/s) for both coronal and axial orientations. The sampling interval can be reduced to $2 \cdot TR = 12$ ms by acquiring a single VPS, which resulted in an experiment length of 120 trigger cycles (160 pts $\times$ 3/4 phase FOV) per velocity direction. The FOV was 32 cm $\times$ 24 cm. Identical slice prescriptions and flow conditions were used for the multiecho, multi-breath-hold PC protocol (Fig. 1b), with ETL = 5 and VPS = 5, for which the experiment length was 24 trigger cycles for each encoding step of the four-step experiment. The sampling interval (TR) was 11.2 ms for the multiecho sequence.

In Vivo

After informed consent was given, cine PC imaging was performed on five normal volunteers, 26-42 years old, without contraindications for MRI. Sagittal and long- and short-axis breath-hold EKG-triggered multislice localizers were used to prescribe two-, three-, and four-chamber long-axis views for the PC scans. To study the evolution of image phase and measured velocity as a function of cardiac phase, individual pixels from both the left (LV) and right (RV) ventricle were examined.

Experiments to validate the multiple breath-hold PC method consisted of a four-breath-hold PC experiment, for the measurement of all three velocity components, as well as four additional phase reference breath-hold experiments with incremented slice offsets to emulate poor breath-hold alignment. Phase-difference images were calculated using velocity-encoded data, from the original four-breath-hold PC experiment, in combination with the original phase-reference breath-hold data as well as with each of the four slice-offset experiments. The five cases were compared using magnitude and PC images as well as a velocity time series for a representative pixel. The original slice, for the four-breath-hold PC experiment, was prescribed graphically from a basal short-axis image to select a three-chamber long-axis view. The subsequent four

slices were prescribed parallel to the original slice, with offsets of +12.3 mm, +7.3 mm, - 8.5 mm, and -14.9 mm between the center of the original slice and the offset slice. For all validation experiments 10 VPS were acquired ($ETL = 5$), resulting in a temporal resolution of $2*TR = 22.4$ ms. Fifty image frames were reconstructed over the full RR interval.

RESULTS

Flow Phantom

The four-point multiecho PC experiment (Fig. 1b) was used to acquire four cine image series from the pulsatile flow phantom, with a coronal slice orientation to measure the in-plane velocities. Figure 3a displays both the duty cycle of the voltage controlled pinch valve and the resulting amplitude of the velocity from a single pixel in the flow phantom at a location indicated in Fig. 2. Figure 3b displays the phase of this image pixel from each of the four separate “breath-hold” experiments, which include the phase-reference scan and three velocity-encoded scans. The test pixel was selected to contain nonzero velocities in both the read and phase-encoding directions to validate the required first-moment nulling of the reference experiment. As can be gleaned from the time-course of the phase plots in Fig. 3b, both v_x and v_y are nonzero and vary significantly over the cycle, while the reference phase plot is constant, illustrating that the reference experiment is first-moment nulled in both read and phase-encoding directions. Note that the pixel phase from the v_z -encoded experiment is overlapping with the reference plot, indicating a negligible velocity in this direction, as expected for this coronal slice with the tube lying in a coronal plane.

Figure 4a displays a single velocity component (v_y) measured from the flow phantom with both the multiecho, multi-breath-hold PC approach (Fig. 1b) ($ETL = 5$, $VPS = 5$) and the standard single-echo PC approach (Fig. 1a). The single-echo experiment was implemented with a single VPS to maximize the temporal resolution, resulting in an experiment length of 120 s (trigger cycles) for a single velocity direction, while the multiecho, multibreath-hold experiment is 24 s in length ($N_{HB} = N_y/VPS$). Also displayed is the same velocity component calculated with a subset of the single-echo single-VPS data, selected to emulate an acquisition equal in total length to the multiecho acquisition (i.e., $VPS = 5$). The single VPS experiment had an effective temporal resolution of 12.0 ms ($2*TR$) because the phase-reference and velocity-encoded experiments were interleaved. Likewise, the $VPS = 5$, single-echo, experiment had a temporal resolution of 60.0 ms, while the multiecho experiment, $ETL = 5$, had an effective temporal resolution of a single repetition time, $TR = 11.2$ ms. Note that temporal resolution of the single-echo experiment could be improved to ~ 50 ms by increasing the receiver bandwidth from ± 62.5 kHz to ± 125 kHz, to match the multiecho case. The higher bandwidth was not utilized in the single-echo phantom experiments due to the $\sqrt{2}$ loss in signal-to-noise ratio (SNR) for a modest improvement in temporal resolution. The cine data sets for all experiments were linearly interpolated to a temporal resolution of 10 ms (100 FPS) to allow the time series to be directly compared. The velocity curves in Fig. 4a illustrate excellent agreement between single-echo ($VPS = 1$) and multiecho experiments, while the single-echo ($VPS = 5$) experiment shows a significant loss of high temporal frequency information. Figure 4b displays the local acceleration calculated directly from the velocity curves from Fig. 4a using a central-difference approximation of the derivative with respect to time ($a_i = -v_{i+2} + 8v_{i+1} - 8v_{i-1} + v_{i-2}$). The multiecho and high-resolution single-echo accelerations are in excellent agreement, while the low-resolution single-echo experiment ($VPS = 5$) both underestimates and blurs the results. The calculated accelerations provide a useful measure of the loss of this high temporal frequency information as a function of temporal resolution. Additionally, acceleration of the blood within the cardiovascular system is valuable in itself as it is related to important physiological parameters such as pressure gradients.

In Vivo

Several standard radial long-axis slice orientations, including the two-, three-, and four-chamber views, were prescribed with the multiecho multi-breath-hold sequence for each of the normal volunteers. Figure 5 displays a typical four-chamber view image acquired with the multiecho pulse sequence. Figure 5a shows the magnitude data from the phase-reference breath-hold. This frame corresponds to peak filling, which occurs at 49% of the mean cardiac RR interval for this healthy volunteer. Figure 5b-d show PC images for the same slice prescription that displays the velocity component in the phase-encoding direction (up/down) at the onset of systole, during peak ejection, and peak filling, respectively. The time-resolved raw image phase of two representative pixels, indicated in Fig. 5a as (i) and (ii), are displayed in Fig. 6a and b, respectively. Four time-series are plotted for each pixel, which correspond to the four breath-hold experiments—namely, the phase-reference and each of the three orthogonal velocity-encoding experiments. Location (i) was selected because it is in the path of a short-lived atrial regurgitation across the closing tricuspid valve, which can be seen as the upward-directed flow (black) that reaches its peak in the pictured image frame (Fig. 5b). Small tricuspid regurgitations such as the one displayed in Fig. 5b are commonly observed with Doppler flow imaging in patients with structurally normal hearts (39). Location (ii) is in both the outflow and inflow paths of the LV, which are plainly pictured as upward (black) and downward (white) flows in Fig. 5c and d, respectively. For both locations and all breath-hold experiments, the phases displayed are those acquired from just one of the four RF coils from the phased-array. Note that for both sample locations the phase of the reference data does not vary significantly as a function of time, illustrating the velocity insensitivity (first-moment nulling) of the phase-reference experiment at the sample locations, as well as the time-independence of the background phase information. Additionally, because all data sets were acquired over the complete RR interval, there is no loss of information at the end of the cardiac cycle. This full coverage allows the velocity information to be represented continuously from diastole, through atrial systole, into ventricular systole, as is evident from the plots in Fig. 6. Note that the x -axis has been shifted to the right for display purposes.

The velocities in the phase-encoding direction (up/down) at pixel locations (i) and (ii) are displayed in Fig. 7a and b, respectively. The three plots in each figure correspond to three temporal resolutions of 11.2 ms (VPS = 5), 33.6 ms (VPS = 15), and 56.0 ms (VPS = 25)—all multiples of the actual TR = 11.2 ms and ETL = 5. The three data sets displayed in each panel were extracted from the same high temporal resolution data set to allow the results to be directly compared without errors from interexperiment variability. The local accelerations for all resolutions are displayed in Fig. 7c and d, for pixel locations (i) and (ii). The sharp appearance of the single TR resolution velocity data in Fig. 7a, and acceleration in Fig. 7c, indicates that even the 11.2-ms-resolution experiment is undersampled for this location. The underestimation of the local acceleration at location (ii) (Fig. 7d) for the 3*TR- and 5*TR-resolution cases are significant, with up to a 33% loss for the former and up to 70% for the latter, for this single representative pixel. It was found that the range of the temporal frequencies of the blood motion in the cardiac chambers, and thus the impact of undersampling, varied significantly with location.

Figure 8a displays a single three-chamber image (frame 59) from 100 frames reconstructed from a multiecho, multi-breath-hold PC acquisition. The image displayed is from the phase-reference breath-hold. Also displayed is a velocity vector plot calculated from the in-plane velocities from this frame, shown in Fig. 8b, for a 32 mm $\times$ 60 mm rectangular ROI. The vector field reveals a flow vortex that has formed behind the anterior mitral leaflet. The in-plane resolution is 2.0 mm $\times$ 2.0 mm for both the magnitude image and the vector field image. Figure 9 displays a series of eight velocity vector frames, including frame 59 from Fig. 8, that show the formation of the vortex over time and the associated movement of the anterior mitral valve

leaflet upwards toward the plane of the mitral annulus. For this normal volunteer the mean heart rate was 56 BPM, resulting in a reconstructed frame rate of 94 FPS, or ~ 10.5 ms per frame, to generate 100 frames over the mean RR interval. Approximately 21.0 ms separate the vector image frames in Fig. 9. The complex spatial flow patterns displayed in Fig. 9 are complemented by rapidly time-varying velocities. Figure 10a and b display the velocity and the corresponding calculated acceleration for the pixel of interest, which is highlighted in gray. The pixel of interest is indicated in Fig. 8, and in Fig. 9 in each vector frame. Three temporal resolutions are compared in Fig. 10, to illustrate the high temporal frequency information associated with the evolution of the flow vortex, from frames 47 and 61.

Validation of the Multiple Breath-Hold Method

To evaluate the impact of breath-hold misregistration between the phase reference and the velocity-encoded experiments, a four-breath-hold PC acquisition was supplemented with four additional phase reference experiments, with varying slice offsets. Each additional phase reference data set was acquired in a separate breath-hold. The top row in Fig. 11 displays magnitude images from the five phase reference experiments, for image frame 29 of 50 reconstructed cardiac phases. The slice offsets and the locations of the slice centers are provided in the figure. The PC images in the lower row were calculated using a single-velocity sensitized experiment (breath-hold) in combination with each of the five phase-reference breath-hold experiments. These velocity images are sensitized to flow in the phase-encoding (up/down) direction, and correspond to a cardiac phase late in diastolic filling (frame 29 of 50). In spite of the significant offset of the five phase-reference images, as seen by comparing the magnitude images, the calculated PC images remain consistent, particularly within the chambers. The appearance of noise speckling at tissue edges in the PC images in Fig. 11 is caused by overlap of myocardium and air due to the poor slice alignment between the velocity-encoded and phase-reference images. The velocity at the location of a single pixel, indicated in both the magnitude and PC images in Fig. 11, is plotted for all five cases in Fig. 12. The pixel is in both the outflow and inflow paths and in the upwardly directed flow (apex to base) in the vortex that forms late in filling. Note that the complex velocity waveform is maintained for the complete cardiac cycle for all five cases.

DISCUSSION

We have implemented a high-temporal-resolution PC-MRI technique that is appropriate for imaging blood flow within the cardiac chambers. Parameters of interest include the velocities themselves, patterns of flow, the relative timings of velocity events, rates of volumetric flow, effectiveness of blood mixing, and pressure gradients, all of which can be determined from blood velocity information. The temporal resolutions required to reliably quantify any of these parameters have not previously been presented, save for non-breath-hold studies which were limited in application to blood flow in vessels (40). Conventional gradient-echo PC-MRI does not have sufficient temporal resolution to identify the loss of fundamental or diagnostic information due to temporal undersampling of the blood motion. We have incorporated two improvements in the conventional PC experiment to increase the acquisition efficiency, which can be utilized to increase temporal resolution. First, improvement by a factor of 2 was made, without compromising spatial resolution or breath-hold length, by acquiring the phase-reference information in a separate breath-hold, rather than interleaved with the velocity-encoded images. An additional improvement in temporal resolution was achieved by incorporating a multiecho readout, which improved the acquisition duty cycle as compared to the single gradient-echo acquisition. We obtained an increase in temporal resolution over the available product PC sequence by a factor of $5.36 = 2 \cdot \text{ETL} \cdot \text{TR}_{\text{SE}}/\text{TR}_{\text{ME}} = 2 \cdot 5 \cdot (6 \text{ ms})/(11.2 \text{ ms})$, if both time-saving measures are incorporated. For cases in which both multiple breath-holds and multiecho acquisitions are not appropriate, either one of the two methods can

be applied with a still significant improvement in temporal resolution. For example, an important clinical application for PC-MRI is the characterization of stenotic flows, which can reach velocities of 5-6 m/s for severe restrictions. The multi-breath-hold approach can be used to double the temporal resolution of a conventional PC experiment for such an application, although in the presence of such extreme velocities a multiecho acquisition may generate artifacts due to spin displacement between the sequential readouts.

The acquisition of PC image information for a single slice over multiple breath-holds has not previously been reported, most likely because of the susceptibility of the resulting phase differences to breath-hold misalignment. We have found that these errors can be minimized with an encoding scheme that ensures the misalignment is between only the background image-phase, which comprises primarily low spatial frequency information. The simple four-point flow-encoding scheme is ideal for this purpose, as each velocity direction was encoded in a separate breath-hold, as were the flow-compensated phase-reference images. Thus, the phase error in a given velocity (phase difference) image is due to misalignment of only two images. Moreover, because the velocity information for each direction is encoded entirely in the velocity-encoded breath-hold, only the low spatial frequency background phase is misaligned, which results in low spatial frequency phase errors. This residual error was calculated at a single cardiac phase for each velocity direction and subtracted from the corresponding phase difference images for all cardiac phases. Employing these methods, we have shown that even for significant slice offsets (up to 15 mm) between the velocity-encoded and phase-reference breath-holds, the calculated velocity fields within the cardiac chambers are maintained. The extreme slice offsets examined in this validation were selected as they are at the limits of the expected displacement of the heart during free breathing (41), which should far exceed the breath-hold alignment offsets for multi-breath-hold examinations. While these methods were successfully applied for regions of space within the cardiac chambers, the multi-breath-hold PC experiments are less appropriate in regions of large susceptibility differences. In particular, if such regions deform over the cardiac cycle, the background phase from the off-resonance evolutions will also vary significantly over time. For such cases, the phase reference and velocity-encoding information for each k_y -line should be acquired sequentially, at the expense of temporal resolution, to allow the background phase to be subtracted reliably.

The increase in temporal resolution achieved with the efficient multiecho acquisition must be applied judiciously due to potential motion artifacts from first-moment discontinuities in k -space. Phase errors generated by motion sensitivity to the multiecho acquisition were minimized by the appropriate choice of image orientation and acquisition parameters. First, the phase-encoding direction was oriented along the direction of the inflow/outflow tracts for long-axis images. Gradient-moment smoothing was used to eliminate first-moment discontinuities in the phase-encoding direction. Additionally, a maximum of 160 points were acquired with a maximum of five echoes, always with the maximum receiver bandwidth (± 125 kHz), which limits both the total acquisition length and the first-moment discontinuity between successive readouts. It would also be possible to acquire only the even echoes to eliminate the first-moment discontinuities, although at the expense of efficiency. While either a reduction in the number of readout points below 160 or the use of a single-echo acquisition will reduce or eliminate flow artifacts induced by the readout first-moment discontinuities, such precautions were not required for the normal volunteers studied.

For all normal volunteers examined, the multi-breath-hold PC experiments had a temporal resolution of 11.2 ms, and an in-plane spatial resolution of $2.0 \text{ mm} \times 2.0 \text{ mm}$. These parameters are not crucial, and depending on the temporal and spatial rates of change of the targeted flow, the acquisition parameters can be adjusted appropriately. If a reduction in spatial resolution from the previously outlined protocol is acceptable, for example, to $4.0 \text{ mm} \times 4.0 \text{ mm}$, the temporal resolution can be improved to as short as 7.0 ms for $\text{ETL} = 5$, with a 50% reduction

in breath-hold length, from 24 to 12 heartbeats. On the other hand, if improved spatial resolution is desired, spatial-encoding gradients with increased amplitude are required, which generate larger first-moment discontinuities between echoes in multiecho acquisitions. For this reason, multiecho acquisitions are not compatible with very high spatial resolution experiments in the presence of high velocities, although we found that for moderate in-plane resolutions (2.0 mm $\times$ 2.0 mm) motion-related image artifacts were not seen in normal volunteers or flow phantoms.

Time-resolved PC-MRI experiments can be carried out with both 2D and 3D protocols, both of which have a number of strengths and weaknesses, depending on the targeted anatomy and function. While time-resolved 3D (volume) experiments allow tortuous vessel geometries or complete volumes to be imaged, the acquisitions are too lengthy for a breath-hold exam, and thus require respiratory gating to correct for breathing motion if spatial resolution is not to be compromised. Respiratory-compensated 3D PC experiments with high temporal resolution have not previously been reported. 2D (slice) imaging experiments can typically be completed within a breath-hold examination, and thus do not suffer from respiratory motion artifacts. Also, the relatively large spherical and cylindrical geometries of the cardiac chambers and large vessels are well visualized with slices. Perhaps, in the future, efficient acquisition schemes such as the multiecho approach, in combination with robust respiratory gating techniques, will make 3D velocity imaging with PC-MRI more practical.

The flow patterns and accelerations of the blood within the chambers, which are associated with such events as valve opening and closure, and filling and ejection pressure gradients, contain a wealth of information that has historically been examined using Doppler techniques. PC imaging with both high temporal resolution and high spatial resolution can offer quantifiable noninvasive velocity information without bias due to limited source access or source angle variability. The velocity and acceleration results presented in this study indicate that both normal and pathological flow features will be underestimated or altogether missed with temporal resolutions commonly available for PC-MRI. A temporal resolution of 50 ms was shown to be inadequate for quantitative blood velocimetry within the cardiac chambers for normal volunteers, particularly if accelerations are required. On the other hand, qualitative flow mapping has previously been shown to be of value with relatively low temporal resolution. For such cases, the increases in efficiency displayed in this study can be used to reduce the acquisition time rather than to increase the temporal resolution.

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FIG. 1.

a: A schematic of a conventional, time-resolved, segmented, gradient-echo PC pulse sequence. For each line of k -space acquired, both a velocity-encoded and a phase-reference line are acquired. This two-step experiment is repeated a number of times equal to the VPS (five in this example). For the pulse sequence displayed, the velocity in the phase-encoding direction will be encoded, as indicated by the solid bipolar gradient pair. **b:** A schematic of a multiecho, multi-breath-hold PC pulse sequence. The velocity-encoded and phase-reference information is acquired in separate breath-holds (BH-1 and BH-2). For this example, the VPS is equal to the echo-train length, so only a single excitation is required per segment. For the pulse sequence displayed, the velocity in the phase-encoding direction will be encoded, as indicated by the solid bipolar gradient pair. **c:** The acquisition scheme for correction of phase error from breath-hold misalignment in multi-breath-hold experiments. A single segment in the velocity-encoded breath-hold is replaced with a phase-reference segment. The phase difference calculated at this cardiac phase is the phase error due to misalignment of the background image phase between the two breath-holds, BH-1 and BH-2. The phase-reference experiment in BH-2 occurs at a segment that corresponds to 75% of the mean RR interval of the subject.

FIG. 2.

A cartoon of the pulsatile flow phantom used for validation studies. A flexible tube system (15-mm inner diameter) is driven by a constant pressure head provided by a peristaltic pump fed through a baffle. The baffle consisted of a closed bath with an air cushion to absorb vibrations from the pump. The flow control was adjusted by a voltage-controlled pinch valve that was triggered by a synthetic EKG generator. The same EKG signal was used for triggering the data acquisition.

FIG. 3.

a: The duty cycle of the flow phantom control valve and the resulting velocity magnitude at a point in the tube system down-stream from the valve measured with the multi-breath-hold, multiecho PC pulse sequence. The approximate location of the measurement image pixel is indicated in Fig. 2. **b:** Time-resolved raw image phase from each of the four separate “breath-hold” experiments at a pixel indicated in Fig. 2, which include the phase-reference scan and three orthogonal velocity-encoded scans.

FIG. 4.

a: A single measured velocity component (v_y) for a single pixel from the pulsatile flow phantom (see Fig. 2) is displayed for three cases: the multiecho multi-breath-hold PC approach, and the standard single-echo PC approach with both one and five VPSs. For all cases, the time series were interpolated to 100 frames over the cardiac cycle. **b:** The accelerations ($a_i = -v_{i+2} + 8v_{i+1} - 8v_{i-1} + v_{i-2}$) calculated from the velocity values in **a** are displayed for all three experimental protocols.

FIG. 5.

a: A typical four-chamber view image frame acquired with the multiecho pulse sequence (five echoes, 160 pts $\times$ 120 pts, 32 cm $\times$ 24 cm FOV, $\pm$ 125 kHz). The image displayed is from the phase-reference breath-hold. This frame corresponds to peak filling, which occurs at 49% of the mean cardiac RR interval for this healthy volunteer. Velocities and accelerations at pixel locations (i) and (ii) are plotted in Figs. 6 and 7. PC images for the same slice prescription shown in **a**, which display the velocity component in the phase-encoding direction (up (black)/down (white)), are shown at: **(b)** the onset of systole, **(c)** during peak ejection, and **(d)** during peak filling. The velocity-encoding sensitivity was 100 cm/s per π radians.

FIG. 6.

a: The time-resolved raw image phase is displayed for a single pixel, location (i) in Fig. 5a, from the RV of a healthy volunteer, at the level of the tricuspid valve. Results are from the phase-reference experiment and each of the three orthogonal velocity-encoding experiments. The pixel is in the path of short-lived regurgitation across the closing tricuspid valve. **b:** The time-resolved raw image phase is displayed for a single pixel from the LV from the same volunteer, from location (ii) from Fig. 5a, which falls in the path of both the LV inflow and outflow tracts. The time-axis has been shifted to the right for display purposes. The velocity-encoding sensitivity was 100 cm/s per π radians.

FIG. 7.

a: The calculated velocity in the phase-encoding (up/down) direction, at pixel location (i) from Fig. 5a, is displayed for three temporal resolutions: 11.2 ms, 33.6 ms, and 56.0 ms. The corresponding accelerations are shown in **c**. **b:** The calculated velocity in the phase-encoding direction, at pixel location (ii) from Fig. 5a, is displayed for three temporal resolutions: 11.2 ms, 33.6 ms, and 56.0 ms. The corresponding accelerations are shown in **d**.

FIG. 8.

a: A single three-chamber image (frame 59) from 100 frames reconstructed from a multiecho, multi-breath-hold PC acquisition from a healthy volunteer. **b:** A velocity vector plot calculated from the in-plane velocities, from the image plane shown in **a**, for a 32 mm $\times$ 60 mm rectangular ROI. The in-plane resolution is 2.0 mm $\times$ 2.0 mm for both the magnitude image and the vector field image. The velocity scale for the vector plot is displayed in the lower left corner of the magnitude image. The velocity at the location of the highlighted vector is followed throughout the cardiac cycle in Figs. 9 and 10.

FIG. 9.

A series of eight velocity vector frames, including frame 59 from Fig. 8, show the formation of a flow vortex over time, as well as the associated movement of the anterior mitral valve leaflet upwards toward the plane of the mitral annulus. Approximately 21.0 ms separate each of the vector image frames. The in-plane resolution is 2.0 mm $\times$ 2.0 mm. The progress of a single vector from the velocity field, which is highlighted with a gray circle, is followed throughout the eight sample frames. The velocity at this sample location is considered in detail in Fig. 10.

FIG. 10.

a: The calculated velocity in the phase-encoding (up/down) direction, at a pixel location indicated in Figs. 8 and 9, is displayed for three temporal resolutions: 11.2 ms, 33.6 ms, and 56.0 ms. The high velocity that occurs near the end of the rapid filling phase (57% of the cardiac cycle) corresponds to the retrograde flow behind the anterior mitral valve leaflet towards the outflow tract. The corresponding accelerations are shown in **b**.

FIG. 11.

The top row displays magnitude images from five phase reference experiments, all acquired in separate breath-holds, with incremented slice offsets. The location of center of each slice and the corresponding magnitude of the offset are provided in the figure. The PC images in the lower row were evaluated using a single velocity-encoded experiment (up/down motion sensitivity), acquired at the location of slice 1, in combination with each of the five different phase-reference experiments. The velocity-encoding strength was 1.20 m/s per pi radians, but a velocity range of only ± 0.6 m/s is displayed. All images displayed are at a cardiac phase late in diastolic filling (frame 29 of 50). The dashed outline, which was traced around slice 1, is included to provide a measure of the slice offset between the five breath-hold experiments. The white square indicates the location of the measurement of a velocity component within the LV chamber.

FIG. 12.

The calculated velocity, in the phase-encoding direction (up/down), is displayed for a single pixel, whose location in the LV is indicated in Fig. 11. The five time-resolved velocity plots shown were calculated using each of the five separate phase-reference experiments.

Table 1
Flow Encoding Schemes for the Simple and Balanced Four-Point Methods

Experiment	Simple four-point method encoding direction			Balanced four-point method encoding direction		
	Read (x)	Phase (y)	Slice (z)	Read (x)	Phase (y)	Slice (z)
1	0	0	0	-M ₁	-M ₁	-M ₁
2	M ₁	0	0	+M ₁	+M ₁	-M ₁
3	0	M ₁	0	+M ₁	-M ₁	+M ₁
4	0	0	M ₁	-M ₁	+M ₁	+M ₁
$v_x = (\phi_2 - \phi_1)/(\gamma M_1)$ $v_x = (\phi_3 - \phi_1)/(\gamma M_1)$ $v_z = (\phi_4 - \phi_1)/(\gamma M_1)$ $v_x = (-\phi_4 + \phi_3 + \phi_2 - \phi_1)/(4\gamma M_1)$ $v_x = (+\phi_4 - \phi_3 + \phi_2 - \phi_1)/(4\gamma M_1)$ $v_z = (+\phi_4 + \phi_3 - \phi_2 - \phi_1)/(4\gamma M_1)$						

ϕ_1 , ϕ_2 , ϕ_3 and ϕ_4 are the phase images generated from experiments 1, 2, 3 and 4. M_1 is the first moment amplitude used to encode velocity to phase.