NUMERICAL AND EXPERIMENTAL STUDY OF THREE IMAGING
ADVANCEMENTS IN PHASE CONTRAST MAGNETIC RESONANCE IMAGING

By

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ABSTRACT

This study aimed at the numerical simulation of three imaging options in phase contrast magnetic resonance (PC-MR), developed jointly at University of Alabama at Birmingham and Allegheny Research Institute. The three methods were: 1) Fragmented Regional Interpolation Segmentation for K-space (FRISK); 2) Enhanced Temporal Resolution (ETR) technique; and 3) Self Reference (SR) PC-MR. The three methods were tested on various physiologic platforms and the data accuracy and acquisition time savings processed by these methods were directly compared to those processed by conventional (CON) PC-MR.

Computational fluid dynamics (CFD) data of: a) two-chamber orifice flow model simulating valvular regurgitation, b) a femoral artery model, and c) a U-shaped model simulating the aortic arch for simulation purposes were generated. FRISK was configured to capture either high temporal information or complexly varying spatial information with a temporal component or a mixture of both. The errors of temporal misregistration of velocity compensated (VC) and velocity encoded (VE) pairs were further eliminated or dramatically reduced by using the ETR option. CON PC-MR requires the knowledge of VC and VE data pairs at each time frame to get the true velocity informa-
tion, which inevitably introduces first-order intrinsic errors caused by the temporal misregistration of the paired data sets. SR PC-MR was conceived to allow the reference scan to be eliminated from the dynamic acquisition.

FRISK was shown to maintain or even improve data accuracy while reducing the scan time by at least 50% compared to corresponding CON PC-MR. By adapting the FRISK parameters for flowfields with different features, FRISK was capable of capturing in-plane and through-plane velocity information with excellent detail in approximately 20 heartbeats duration. Compared to the CON PC-MR processed data, the ETR processed data better represented peak velocities (101%±13% vs. 127%±28%, p<0.001) and correlated more closely with the reference (REF) data (r = 0.94±0.05 vs. r = 0.67±0.23, p<0.001).

The SR PC-MR data showed significantly better representation of the velocity-time waveform as assessed by lower root-mean-square (RMS) errors (9.0±1.0% vs. 24.0±0.2%, p<0.005). Overestimation of peak velocity was dramatically attenuated using Self Reference compared to the conventional approach (2.8±0.4% vs. 16.9±6.4%, p<0.005). An average of 119.4 ± 26.6 % (p<0.005) SNR was realized in both in vitro and in vivo SR PC-MR data compared to conventional scans.
DEDICATION

To my father, Xijiu Li, who inspired me to pursue my PhD program.
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<td>Fragmented Regional Interpolation Scheme for K-space</td>
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LITERATURE REVIEW

MRI in cardiovascular blood flow has a range of established applications, especially in assessing congenital heart disease and heart valves\(^1\-^3\) and several other interesting research applications which may soon become clinically useful\(^4\-^7\). Phase contrast magnetic resonance (PC-MR) imaging has been shown by many studies to provide accurate quantitative flow velocity information with single-pixel resolution and has wide clinical applications when imaging relatively simple flow fields\(^8\,^9\). For instance, PC-MR is capable of capturing the through plane flow in a large vessel such as the aorta with a normal flow pattern in a breath hold scan time\(^10\). However, due to its requirements for post-processing and wide applications of Doppler ultrasound units, the use of PC-MR imaging has been limited in cardiovascular imaging compared to the current clinical standard echocardiography. With the increasing power of MR imaging units and reduced post-processing time, this situation is changing rapidly and more and more applications are evolving for PC-MR flow measurements to evaluate the quantitative cardiovascular function\(^11\-^13\). Compared to the clinical gold standard echocardiography, there are some advantages of using PC-MR in cardiovascular imaging: 1) it can provide velocities at all points in the flow field resolved in three directions, as opposed to only velocity components towards or away from the probe\(^14\-^16\); 2) free selection of imaging planes is allowed in PC-MR while probe selection is limited by body habitus in echocardiography; 3) spatial resolution, temporal resolution and scan time can be interchanged to improve image
quality in PC-MR\textsuperscript{17}. The limitations of PC-MR compared to the current gold standard echocardiography usually lie in its long scan times, poor temporal resolutions and its inaccuracy in the presence of flowfields with high acceleration terms\textsuperscript{18,19}. To address these issues, three imaging advancements have been developed in our research group for improved accuracy in PC-MR. They are 1) FRISK; 2) ETR technique and 3) SR PC-MR.

**FRISK**

When imaging complex flowfields, higher spatial and temporal resolution than is generally acquired is needed, which typically requires extending the scan time well beyond a breath hold, thereby introducing disruptive respiratory artifacts, or alternatively, suffering from loss of detail of the flow field\textsuperscript{20,21}. The breath-hold PC-MR approaches that are commercially available are using different algorithms to realize breath-hold scans. Usually, gradient echo sequences with low flip angles are employed to get the shortest possible repetition time (TR) and echo time (TE), such as Turbo gradient Echo sequences\textsuperscript{22}. Some of them use segmentation concept and electrocardiographical gating (FASTCARD\textsuperscript{23}). Also, hardware improvements are required for some fast imaging techniques such as parallel imaging\textsuperscript{24,25}.

Despite the complexity of blood flow, it is usually characterized by smoothly varying gradients over time and space. This high level of signal continuity in the flow field data permits dramatic reductions in data sampling. When a high degree of interframe correlation is present, the data can be captured using a sparse sampling scheme. The sparsely sampled data can be used to generate the full data set by applying a suitable processing scheme that incorporates the correlation relationship. Based on this observa-
tion, Block Regional Interpolation Scheme for K-space (BRISK) was conceived, to realize breath-hold cardiac cine imaging\textsuperscript{26}. BRISK is a sparse sampling strategy that acquires data over the cardiac cycle at varying rates, with a high sampling rate applied to the central lines of k-space and progressively slower rates applied to the outer lines. In the BRISK reconstruction strategy, the sparsely sampled k-space lines are interpolated to generate k-space lines at intermediate points between sampled positions\textsuperscript{27}. The BRISK and turbo BRISK results compared well with conventional PC-MR and laser Doppler Velocity measurements in phantom studies\textsuperscript{28,29}. Thompson et al. used data acquisition sequences similar to BRISK to investigate intracardiac pressure differences both in phantoms and in a canine model by measuring in-plane velocities and found that there was an excellent agreement between the transducer and PC-MR results in all studies\textsuperscript{30}. A further refinement of BRISK is presented here, in which data are distributed evenly in the spatial-temporal domain for each cardiac phase. This variant, termed Fragmented Regional Interpolation Segmentation for K-space (FRISK) has several advantages over currently used breath-hold imaging sequences, including: 1) an efficient sampling algorithm, so that cardiovascular flows can be sampled with reduced segmentation to allow all three directions of velocity to be encoded in a breath-hold time; 2) flow data associated with each cardiac phase are temporally aligned during post-processing, making them less sensitive to temporal acceleration affects; and 3) spatial and temporal resolution in data sampling can be adjusted depending on the general nature of the acceleration characteristics of the flow field being studied.
Temporal Misregistration Artifacts in Jet Flow

The presence of jet flow in vivo is almost exclusively associated with pathology, and non-invasive imaging approaches have been used to quantify jet features, including maximum velocity, length and trajectory. However, despite the routine availability of quantitative PC-MR velocity-encoded cine imaging approaches for over a decade, clinical attention has largely focused on non-jet flow applications of MRI, since jet flow tended to result in extensive regions of signal loss and provided incomplete flow information. Recently, the performance level of imaging gradients in MR scanners has improved and now allows routine visualization of the jet’s laminar core from its origin up to the turbulent transition zone, permitting trajectory and laminar jet length evaluation. The potential advantages of PC imaging compared to 2D color Doppler are that visualization and characterization of flowfields is feasible in both through-plane and in-plane orientations, allowing interrogation, visualization and measurement of jet velocities, even for complex flowfields such as those in which the jet follows the curvature of a vessel lumen or impinges on a chamber wall. However, while routine visualization of the jet core is now possible using PC-MR images, concerns remain about the accuracy of velocity measurements, especially in regions of high temporal and convective acceleration.

The origin of the temporal displacement error term is illustrated in Fig 1, which shows the process by which quantitative PC data are derived. Since it is necessary to compare two data sets to derive the quantitative velocity data, the measured velocity is sensitive to the temporal alignment of the two data sets. In Fig 1, the top panel illustrates the process whereby the pixel velocity (Vel) at each time point is derived by subtracting the velocity measured using a velocity compensated (VC) reference data set from the ve-
locity encoded (VE) data. Alignment of the vertical arrows indicates that the VC and VE data sets are correctly temporally registered. The lower panel illustrates the situation whereby the VC and VE data sets are temporally misaligned (temporal displacement of arrows). In this case, the peak velocity of the calculated Vel curve dramatically overestimates the true velocity, and the Vel curve is also distorted in other regions. In this section, a post processing remedy is presented, that can be applied without knowledge of the flowfield, which improves accuracy for the widely available conventional PC data acquisition scheme. The algorithm of the remedy is shown in the Fig 2.

Figure 1  Schematic of the distribution of time resolved velocity compensated (VC) and velocity encoded (VE) data. In the top panel, the convergence of the vertical arrows indicates that the VC and VE data sets are temporally aligned. In the lower panel, the separation of the verti-
cal arrows indicates that the VC and VE data sets are temporally shifted. The corresponding Vel data exhibits a dramatic distortion compared to the Vel curve in the top panel.

Figure 2 Interleaving scheme for a typical PC-MR data acquisition. In this schematic, segmentation factor of 2 is used, and the velocity compensated (VC) and velocity encoded (VE) data are acquired at different time points. The function of the ETR algorithm is that each of the VC and VE data sets are temporally shifted to align to one reference data point (in this case the reference data point is where VE1 is sampled) within each cardiac phase. Temporal shifting is accomplished by an interpolation routine34.

SR PC-MR

At present, blood flow measurements are largely performed by two-dimension phase contrast magnetic resonance (PC-MR) and a number of studies on accuracy in MR quantitative flow measurement based on both steady flows and realistic flows have been carried out35-38. For CON PC-MR, linear gradients are employed to generate a phase shift that is proportional to the velocity of the moving spins39. By adjusting a bipolar gradient,
the velocity encoded phase ($\Phi_{VE}$) and a velocity compensated phase ($\Phi_{VC}$) data are obtained; to extract the true velocity data, the data pair corresponding to each time frame are subtracted producing an image in which phase is linearly proportional to flow velocity (see the detailed information in the theory section). Typically, for cardiac flow measurement, high segmentation values (range 4-8) are usually used to shorten the scan time and reduce disruptive artifacts caused by respiration\textsuperscript{23,40}. However, there are some impediments to accurate cardiac PC-MR when the flows with high acceleration terms are presented (i.e., valve regurgitation and stenosis): 1) relatively poor temporal resolution associated with high VPS is insufficient to capture the fast jet flows; 2) The data extraction process requires comparison of $\Phi_{VE}$ and $\Phi_{VC}$ at each time point, making the CON PC-MR technique intrinsically sensitive to temporal acceleration\textsuperscript{34}.

A novel PC-MR technique termed SR PC-MR is introduced by our research group. The unique feature of this new PC-MR technique is that the VC and VE data do not have to be compared in temporally registered pairs. One extreme example of this involves the use of an average value of VC to correct each VE data set. However, other variants are possible, each with a different practical application area. Here my research will focus on the variant where the temporally averaged $\Phi_{VC}$ ($\Phi_{VC_{AVE}}$) data are used to correct the phase of the VE data ($\Phi_{VE}$) data. This implementation can be used to improve the SNR of cardiac PC-MR data, while other implementations can be used to improve temporal resolution. Due to the different method of extracting velocity employed, it will be shown that the temporal resolution of the data in the systole can be dramatically improved or even doubled by using different application algorithms; 2) data becoming less sensitive to temporal acceleration terms; Without having to compare data sets at each frame removes
a major source of distortion in the presence of high acceleration terms, thus improving the data accuracy. Combined in vitro/in vivo experiments and numerical simulations will be investigated in this study to explore the possibility and potentials of this novel PC-MR technique.

*The Theory of SR PC-MR*

The position of a group of spins moving in a gradient $G(t)$ as a function of time can be given by

$$x(t) = x_0 + v_0 \cdot t + a_0 \cdot t^2/2 + \ldots \quad (1)$$

The phase accumulation as the function of time can be written by the following expression:

$$\Phi(t) = \int \omega(t) \cdot dt = \int \gamma G(t) \cdot x(t) \cdot dt = x_0 \cdot M_0 + v_0 \cdot M_1 + a_0 \cdot M_2 + \ldots \quad (2)$$

Where $\gamma$ is the gyromagnetic ratio and $M_i$ are the moments of the gradient waveforms with respect to time$^{41}$. When bipolar gradients are used and acceleration terms ($a_0$) are omitted, two phases of the moving spins (velocity encoded phase $\Phi_{VE(i, t)}$ and velocity compensated phase $\Phi_{VC(i, t)}$) can be collected and extracted to obtain the phase of the moving spins ($\Phi_{TRUE(i, t)}$) that are proportional to the their velocity at location ($i$) and time point ($t$). Both static and moving spins will be contaminated by an inhomogeneity related phase variation ($\Phi_{in}$) and this variation is the same for $\Phi_{VC(i, t)}$ and $\Phi_{VE(i, t)}$. The relationships between them can be expressed as:

$$\Phi_{VC(i, t)} = \Phi_{TRUE(i, t)} \cdot KC + \Phi_{in} (i) \quad (3)$$

$$\Phi_{VE(i, t)} = \Phi_{TRUE(i, t)} \cdot KE + \Phi_{in} (i) \quad (4)$$

$$\Phi_{TRUE(i, t)} = \Phi_{VE(i, t)} - \Phi_{VC(i, t)} \quad (5)$$
where KC and KE are scaling parameters determined by the first moments of the velocity compensated (VC) and velocity encoded (VE) imaging gradients respectively. Conventionally, the VC and VE data sets are paired and related to each other by a constant ratio, R.

\[
KC = KE \cdot R \quad (6)
\]

Here, consider the case where the temporal average of \(\Phi_{VC}\) over a cardiac cycle, \(\Phi_{VC\_AVE}\), is used as the phase reference for \(\Phi_{VE}\) at each time point to obtain the observed phase \(\Phi_{ob}\) (as shown in Fig. 3a). In this case, the observed phase \(\Phi_{ob}\) does not directly correspond to the true velocity, but instead is linked by the following relationship:

\[
\Phi_{ob(i, t)} = \Phi_{TRUE(i, t)} + \Phi_{VC(i, t)} - \Phi_{VC\_AVE(i)}
\]

\[
= \Phi_{TRUE(i, t)} + \Phi_{TRUE(i, t)} \cdot KC - \Phi_{TRUE\_AVE(i)} \cdot KC \quad (7)
\]

Rearranging the equation (7), we obtain:

\[
\Phi_{TRUE(i, t)} = \frac{\Phi_{ob(i, t)} + \Phi_{TRUE\_AVE(i)} \cdot KC}{1 + KC} \quad (8)
\]

From this equation, it can be seen that once \(\Phi_{TRUE\_AVE}\), first moment related constant KC and observed velocity \(\Phi_{ob}\) are known, the true velocity of the moving spins \(V_{TRUE(i, t)} = \Phi_{TRUE(i, t)} \cdot VENC/\pi\), where VENC is the encoding velocity) can be easily obtained. Importantly, the extraction of the time resolved true velocity does not rely on comparing paired data sets at each time point.

The KC in the equation (8) is dependant on gradient conditions and scanner manufacturer. From the Eq.(3) and Eq.(4), it can be seen that there is always a certain dependence between \(\Phi_{VC\_AVE(i, t)}\) and \(\Phi_{VE\_AVE(i, t)}\) (2:3 when the static field inhomogeneities are not included). For the scanner (General Electric, Milwaukee WI) we used in this study, \(KC = 2\) when the encoding velocity (VENC) \(\geq 200\text{cm/s}\) and \(KC = -0.5\) when VENC <
200cm/s. Once the KC is acquired, it can be used in the equation (8) to calculate the true velocity according to their different VENC values.

The applications of the SR PC-MR in cardiac imaging are several. One of the applications that has been studied in this dissertation is shown in Fig 3b App1: only VE data (the black arrows in Fig 3b) sets are sampled during the systolic phase of the cardiac cycle, where high temporal resolution is usually required; while in the diastolic phase, the VC (the gray arrows in Fig. 3b) and VE data pairs are acquired. The VC and VE data pairs acquired in the diastolic phase are used to get $\Phi_{ob}$, $\Phi_{TRUE_AVE}$. This way, even under the condition where scan time reduction is significant and a relatively high segmentation factor is employed, the temporal resolution in the systolic part can still be diagnostically adequate to capture rapid changing flows. Another possible application of SR PC-MR is increasing the sampling ratio between VE and VC (Fig.3b, App2), i.e., sampling VE data sets two to five times more often than VC data sets, so that the temporal resolution of the complete cardiac cycle can be increased. The study on this application in vitro/in vivo is currently ongoing and the preliminary results have been published as an abstract$^{42}$. 
Figure 3  The phase relationships between $\Phi_{VC}$, $\Phi_{VE}$ and $\Phi_{VC\_AVE}$ and the two applications of SR PC-MR. In App1, only VE data are sampled in systolic part of cycle while in diastole, VC and VE pairs are sampled. In App2, the ratio of sampling VC and VE data sets is 2 or even larger than 2, so that the temporal resolution of the whole cycle can be improved.
METHODOLOGY

FRISK

Numerical simulations and validation.

The three representative flow-fields studied are shown in Figure 4. The jet flow model is representative of valvular stenosis or regurgitation, and features a dominant region of high temporal acceleration proximal to the orifice. The upper part of the femoral bifurcation model of the common femoral, extending up to the profunda and the superficial femoral arteries, is characterized by a complex flowfield with primary as well as secondary velocities associated with regions of reversed flow near the bifurcation. The 180-degree curved tube is representative of the flowfield in the aortic arch, and is characterized by a velocity profile skewed towards the outer wall with strong helical features that are characterized by high temporal and spatial gradients.

The detailed process for generating numerical jet model is depicted as follows: Automatic mesh generation software (Proam CD-Adapco Groups, Melville, NY) was used to discretize the jet model. The inlet flow was obtained directly from the PC-MR through-plane velocity data at the inlet of a phantom model that has the exact geometry as that of the numerical simulation model. The walls of the model were assumed to be rigid and a zero exit pressure at the outlet was used in the simulation. Blood in the simulation was modeled as a Newtonian fluid with a density of $1.06 \times 10^3$ kg/m$^3$ and molecular viscosity of $3.0\times10^{-3}$ Pa. Pulsatile flow model was computed for three cardiac cycles using a model with first-order accuracy in time to solve the incompressible Navier-Stokes
equations. The model was solved on 8 Linux cluster processors with 4GB RAM each by
running Star-CD (CD-Adapco Groups, Melville, NY) version 3.20. The duration of run-
ing each cycle was 1 second. The time step for the transient model was $0.25 \times 10^{-3}$ s. A
preliminary mesh independence study was carried out to ensure that the converged solu-
tion was independent of mesh density. A coarse mesh model with 0.3 million cells and a
fine mesh with 0.8 million cells were used in the simulation. The femoral artery bifurca-
tion model and the U-shape model were developed and validated in previous studies\textsuperscript{43,44}
and detailed model configurations were depicted in the papers.

![Figure 4: The geometry of the models used in the computation fluid dynamics (CFD) and FRISK simulations. The red boxes show the position of the slices taken for the FRISK simulations.](image)
For *in vitro* PC-MR validation of simulation results, a jet flow phantom with the same geometry as the CFD simulation was used to validate numerical results. The PC-MR images were acquired using a CV/i 1.5T system with maximum gradient strength 40 mT/m (General Electric, Milwaukee WI). A PC gradient echo imaging sequence was used: TR/TE/flip 7.1ms/3.2ms/20°, matrix 256×256, field of view 240 × 240 mm, and slice thickness 6 mm. A conventional scan with a VPS of 1, 256 lines (VPS1 256L) was acquired as a reference scan, such that the PC-MR data represented the velocity accurately, without assumptions of data segmentation. The PC-MR data at slice 1 was used as the inlet boundary for the numerical simulation (Fig. 4). The PC-MR data at slice 2 was used to validate the numerical results. Jet flow was observed distal to the orifice and was imaged in an in-plane manner, with the slice aligned through the jet center and the velocity encoding (VENC) sensitivity set at 100 cm/s for the validation slice. *In vivo* PC-MR images in a normal volunteer were performed on the same MR scanner. A PC gradient echo imaging sequence was used: TR/TE/flip 8.7ms/3.2ms/20°, field of view 240 × 240 mm, pulse rate = 88 BPM and slice thickness = 6 mm. The imaging parameters for non-breath-hold conventional scan were: VPS2, number of excitations averaged (NEX) 2, scan time 154s, Phase FOV 1; The imaging parameters for breath-hold FRISK were: VPS4, NEX 1, scan time 16 s (12 s for dynamic sampling and 4 s for sampling static regions), Phase field of view 1 (phase FOV 1); The imaging parameters for breath-hold conventional scan were: VPS4, Nex 1, scan time 12s, Phase FOV 0.25.
FRISK and CON PC-MR simulations.

The CFD source data were used to simulate the PC-MR FRISK acquisitions. The CFD velocities were combined by averaging to generate 1×1×6 mm³ voxels to simulate the partial-volume effects associated with the finite slice thickness and voxel size of MR data. Flow compensated and flow encoded data sets were simulated by mapping the associated phase angles according to the following formula:

\[ \alpha = \frac{V_i \cdot VENC}{\pi} \]  

where \( \alpha \) is the output matrix in radians; VENC is the encoding velocity; \( V_i \) is the input velocity matrix. A complex image matrix was created using the formula:

\[ V_{\text{complex}} = \cos(\alpha) + i \cdot \sin(\alpha) \]  

The complex matrix was 2-D Fourier transformed and quadrant-shifted to generate time-resolved k-space data sets (Fig. 5). The FRISK data-sampling pattern in k-space and time was applied to extract the sparsely sampled data set, Fig 6. In essence, the basic FRISK sampling strategy reduces the scan time for dynamically sampled lines by a factor of 2, with additional lines sampled in a static manner. The segmentation concept that is commonly used in PC-MR blood flow measurement was superimposed on the FRISK acquisition pattern in the manner indicated in Figure 6, effectively combining a number of lines from consecutive cardiac phases to contribute to a single k-space image. A Fourier interpolation scheme written in Matlab (The Mathworks, Inc., Natick, MA) was employed to: 1) retrospectively generate the data that were not directly sampled, and 2) to temporally align the sampled and interpolated data at each cardiac phase. The schematic of the FRISK data processing is shown in Figure 5.
For triggered PC-MR, the reported sources of errors can be divided into two groups: systematic error and random error. The systematic errors mainly arise from (1) partial volume effects, (2) errors caused by data misregistration and (3) intravoxel phase dispersion. Errors caused by partial volume effects are due to the limited spatial resolution of MR flow measurements and the fact that some voxels that cover the vessel lumen contain both moving spins and stationary tissue\textsuperscript{45}. Intravoxel phase dispersion occurs due to the averaging of the phases of the moving spins with large phase differences within a voxel, thus causing signal dropout\textsuperscript{46}. By averaging the numerical data (with spatial resolution around 0.5×0.5×0.5mm\textsuperscript{3}) to generate 1×1×6mm\textsuperscript{3} voxel, both partial volume effects and intravoxel phase dispersion are simulated. Errors of data misregistration can be either mainly associated with higher order velocity components\textsuperscript{34} or/and time delay between phase encoding and phase readout\textsuperscript{41}. These errors were not incorporated in the simulations. However, another type of temporal data misregistration associated with the high temporal misregistration were considered in this dissertation by interleaving the VE and VC data in a manner similar to the way in which experimental PC-MR data are sam-
pled. More details regarding this type of error are discussed in ETR section in this dissertation.

The major source of random errors comes from the white noise. It can easily be shown that the random error of each channel, $\sigma_v$, is entirely determined by the velocity encoding value (VENC) and the SNR, when equal magnitudes of base images are assumed:

$$\sigma_v = VENC \cdot \pi/\text{SNR} \quad (11)$$

The random noise in the \textit{in vitro} data VTR2 was calculated and then used to generate random noise for the simulated data. The average SNR with the size of $50\times50\text{mm}^2$ was calculated from the magnitude images and then, white noise derived from Eq.(11) was generated and incorporated into both VE and VC channels separately. Exactly the same systematic and random errors were simulated for all the simulated jet data.

Figure 6 The FRISK data-sampling schematic. The velocity compensated data (VC) and velocity encoded data at three directions ($\text{VE}_x$, $\text{VE}_y$, $\text{VE}_z$) are grouped together per VPS. The measured velocity is obtained by subtracting the phase of $\text{VE}_{x,y,z}$ from the phase of
VC. The VPS is 2 in this figure. In this example, a total of 128 lines are sampled dynamically in each effective cardiac phase, and due to the FRISK sampling approach this is accomplished in 32 heartbeats. The scan time to obtain static lines is less than 4 heart-beats. To bring the scan to within a breath hold (~20 heartbeats), the proportion of dynamic to static lines can be altered in FRISK. In the following figures, only the sampling times for the dynamic lines are calculated and 60 heartbeats per minute assumed in all of the simulated data.

The schematic of temporal alignment of sampled VC and VE data incorporated in FRISK post processing is shown in Fig. 7. Finally, the phase-angle information of the VE and VC data sets were used to extract velocity information. The numerical data sets were simulated with a range of views per segment (VPS) and the number of k-space lines sampled dynamically by the FRISK algorithm was varied. In order to validate the efficacy of FRISK, conventional scans with same VPS and number of lines sampled in FRISK were simulated for comparison purposes. Due to its efficient sampling algorithm, FRISK should halve the sampling time compared with the corresponding conventional scans, while at the same time, maintaining comparable accuracy. The details of the simulated FRISK and conventional sequences are listed in Table 1.
Figure 7 The schematic of data alignment of three k-space lines in FRISK post-processing. VPS of 3 and one velocity encoded component. In conventional PC-MR, the temporally distributed VC and VE data in each segmentation are simply combined to form the segmented data at each time point. In FRISK post-processing, as shown in this figure, the sampled VC and VE are interpolated at a series of reference time points (in this case, the reference time points are set at the time points where VC₁ is sampled) and then the interpolated to better align prior to subtraction to obtain the velocity values.
Table 1

*The simulation parameters of FRISK and CON*

<table>
<thead>
<tr>
<th>Sampling Methods</th>
<th>FRISK parameters</th>
<th>Dynamic Sampling time (heart beats)*</th>
<th>Temporal resolution (ms)</th>
<th>Through-plane velocity component</th>
<th>All three velocity components</th>
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<tr>
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*For FRISK, when dynamic sampling time is less then 16s. The total sampling time is within a typical breath-hold duration, <20 heart beats, which includes the overhead of 4 heart beats for sampling of the data acquired in a static manner for each FRISK configuration.*
The same numerical results of the jet flow used for FRISK simulations were used for ETR simulations. Custom Matlab (Mathworks, Natick, MA) programs were written to simulate the CON PC-MR with and without ETR technique and the results were compared and analyzed.

All experimental scans used in the ETR study were acquired using a CV/i 1.5T system with slew rate 140 mT/m/s and maximum gradient strength 40 mT/m (General Electric, Milwaukee WI). The same phantom model used in FRISK validation was used to acquire in vitro data for ETR study. A PC gradient echo imaging sequence was used: TR/TE/flip 7.1ms/3.2ms/20°, matrix 256x256, field of view 240 x 240 mm, and slice thickness 6 mm. Jet flow was observed distal to the orifice and was imaged in an in-plane manner, with the slice aligned through the jet center and the velocity encoding (VENC) sensitivity set at 500 cm/s. Image reconstruction was performed using custom routines written in MATLAB. Phase-contrast imaging was implemented with the k-space data acquired using VC and up to three velocity-encoded, VE_x, VE_y and VE_z, data sets for each of the Cartesian axes, X, Y and Z, respectively. As is common practice, to reduce scan time, k-space segmentation was employed, encoding multiple lines of k-space for each nominal time position within the flow cycle. The conventional acquisition mode on the scanner was to group the VC and each of the VE scans within the k-space segmentation acquisition, e.g. the temporal ordering of data when encoding VC, VE_x, VE_y, and VE_z with a segmentation value of 2 was: VC-1, VE_x-1, VE_y-1, VE_z-1, VC-2, VE_x-2, VE_y-2, VE_z-2, where 1 and 2 indicate segmentation value 1 and 2 respectively.
The conventional mode for our scanner was to interleave velocity scans within each segment. All conventional scans were acquired using a segmentation factor of 2 and the number of velocity directions acquired was separately set at 1, 2, or 3, resulting in the number of frames per cycles of 32, 21, and 16, respectively. These options allowed the effects of frame rate, frame duration ($T_{\text{sample}}$), and data misalignment interval ($\Delta T$) to be evaluated. In each case, the scan time was constant at 2 min 10s.

A reference scan was obtained without data segmentation or interleaving. In this non-interleaved scan, data for each VC and VE set were acquired in separate cycles, allowing temporal alignment with each other. The reference scan generated PC images with a time resolution per frame of 7.1 ms. This high temporal resolution was achieved at the expense of a prolonged scan time of 17 min (256 k-space lines for each VC, VE$_X$, VE$_Y$, and VE$_Z$ data set, acquired over 1024 cycles).

**SR PC-MR**

*Numerical simulations and validation.*

The two-chamber-orifice jet model was used for the SR PC-MR numerical simulation. The jet flow model is representative of valvular stenosis or regurgitation, and features a dominant region of high temporal acceleration proximal to the orifice. The detailed process for generating numerical jet model is depicted as follows: automatic mesh generation software (Gambit, Fluent. Inc) was used to discretize the jet model with the cell number of 0.6 million. The inlet flow was taken directly from the flow rate measured by the PC-MR through-plane velocity data at the inlet of a phantom model that has the
exact geometry as that of the CFD model. As the pulsatile flow in the simulation is difficult to determine in advance whether it has become turbulent, the second-order accuracy $k-\omega$ model that has been proven capable of simulating both turbulent flow and laminar flow well was chosen \cite{48}. The walls of the model were assumed as rigid. A zero exit pressure at the outlet was used in the simulation. The fluid in the simulation was modeled as Newtonian fluid with a density of $1.06 \times 10^3$ kg/m$^3$ and molecular viscosity of $3.0 \times 10^{-3}$ Pa. Pulsatile flow model was computed for three cardiac cycles using a model with second-order accuracy in time to solve the incompressible Navier-Stokes equations. The model was solved on Linux cluster processors with 8GB RAM each (Fluent 6.2, Fluent. Inc.). The duration of running each cycle was 1 second and total CPU time was 9 hours 20 minutes. The time step for the transient model was $0.5 \times 10^{-3}$ s.

*In vitro and in vivo PC-MR data acquisitions.*

The custom made phantom of an idealized model of severe aortic regurgitation was used, consisting of a circular orifice of diameter 10mm with a concave curvature on the high-pressure side extending to the cylindrical flow chamber of diameter 76 mm. Pulsatile flow close to the aortic flow pattern was generated by a CV pump system (Shelly Medical Imaging, Vancouver, Canada) and fluid with a viscosity similar to blood was used (60% glycerin, 40% distilled water). The peak Reynolds number was approximately 4000 and the mean Reynolds number was approximately 1200, which are typical of *in vivo* conditions in patients with aortic stenosis. The flow waveform cycle time was 1000 ms (60 beats per minute) and data acquisition was synchronized to the flow waveform by an electronically generated TTL pulse. The pump is calibrated to reproduce the flow
waveform with a precision of better than 10 ms, with the standard deviation of flow volume being 0.1 ml s\(^{-1}\) (i). A PC gradient echo imaging sequence was used: TR/TE/flip 7.1ms/3.2ms/20°, matrix 256x256, field of view 240 x 240 mm, and slice thickness 6 mm.

The imaging parameters of in vitro and in vivo images used for self reference study are listed in Table 2. In vivo PC-MR images in a normal volunteer were performed on the same MR scanner. The PC gradient echo imaging sequence was used: TR/TE/flip 8.7ms/3.2ms/20°, field of view 240 x 240 mm, heart beat of 88 BPM and slice thickness 6 mm.

Table 2

*The parameters of PC-MR for self reference study*

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<tr>
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<th>VTR1</th>
<th>VTR2</th>
<th>VIV1</th>
<th>VIV2</th>
<th>RF1</th>
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<td>1</td>
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<td>500</td>
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<td>150</td>
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<tr>
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<td>2</td>
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<td>1</td>
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<tr>
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<td>2</td>
<td>-0.5</td>
<td>-0.5</td>
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</table>

Programs written in Matlab (The Mathworks, Inc., Natick, MA) were used to receive and process the raw data from the GE MR scanner according to the algorithms for CON and SR PC-MR. In order to exclude all the differences in the flow features, so that the quantitative comparisons between the CON and SR PC-MR can be straightforward, all *in vitro* and *in vivo* data were sampled only once in the conventional way but processed differently, i.e., in both conventional and self reference methods. The downside of processing the data in this manner is that no improved temporal resolution in the systolic phase in *in vitro/ in vivo* SR PC-MR data as outlined in Figure 3b App1 was possible.
ANALYSIS

Quiver plots were used to visualize the in-plane velocities of flowfields in the femoral artery and U-shape models. The correlation study between the numerical results and corresponding PC-MR data at the orifice of the jet model was carried for validation purpose. To quantify the errors generated on each CON and the other imaging options, the average temporal root-mean-square (RMS) difference was used as an index. It is defined as the square root of the mean of the squares of differences between expected values and true values divided by the temporally average true values:

$$\text{RMS}_{(i)} = \frac{1}{V_{\text{true ave}(i)}} \cdot \sqrt{\frac{1}{n} \sum_{t=1}^{n} (V_{\text{exp}(i,t)} - V_{\text{true}(i,t)})^2} \quad (12)$$

Where $V_{\text{true ave}(i)}$ is the average true velocity and $V_{\text{exp}(i,t)}$ can be either the simulated CON PC-MR data or simulated FRISK/SR/ETR data.

Peak Velocity Overestimation is used in the jet flow for evaluating the errors at the peak generated by FRISK/ETR/SR and CON PC-MR. It is defined as the absolute difference between the true velocity and FRISK/ETR/SR/CON velocity at the peak divided by the true velocity:

$$\text{Peak Velocity Overestimation} = \left| \frac{\text{CFD}_{(i,t)} - \text{MEAD}_{(i,t)}}{\text{CFD}_{(i,t)}} \right| \times 100\% \quad (13)$$

where MEAD can be either FRISK/SR/ETR or CON PC-MR data.

A single SNR acquisition method was employed to compare the SNR of the CON and SR PC-MR results. A region of interest (ROI) of 20×20 mm² was used to calculate the SNR for both in vitro and in vivo data by the following formula:
\[ \text{SNR}_{\text{mean}} = 0.655 \times \frac{S_{\text{mean}}}{\text{SD}_{\text{air}}} \]  \hfill (14)

Where \( S_{\text{mean}} \) is the average value of the signal in the ROI and \( \text{SD}_{\text{air}} \) is the standard deviation of the signals in the air. The 0.655 factor arises because the noise is derived from the different image.
RESULTS

FRISK

Jet phantom validation

Figure 8 shows comparison of the through-plane velocity of the predicted CFD results and the reference PC-MR results acquired in the phantom experiment. A very favorable agreement between MRI data and CFD data was obtained.

The velocity surface plots of the PC-MR and the CFD predicted data at four time points along one cardiac cycle were shown in Figure 9.

Figure 8 Comparison of axial velocity of MRI data and CFD predicted data at the center of the orifice. The boundary data of the CFD model is taken from PC MRI at the position slice 1 shown in the lower left figure. The correlation coefficient (R) between these two sets of data is 0.9
Figure 9 The velocity surface plots of PC-MR and CFD data at four time points. The validation location was sampled at the center of the jet orifice.

**FRISK simulation on three models**

**Jet Model.** Through-plane velocity was sampled and reconstructed in accordance with the FRISK and CON PC-MR algorithms respectively. Jet flows are characterized by predominantly axial velocities near the orifice, therefore, in plane velocities were not considered. A slice 3 cm downstream of the orifice was taken for FRISK simulation. For the scans that have the same number of lines sampled and VPS, FRISK scan requires only half of the scan time of that in CON PC-MR. Figure 10 shows the temporal RMS errors of FRISK and CON PC-MR with different VPS and number of lines. Improved accuracy
in terms of RMS were seen on all of the simulated FRISK data compared to the simulated CON PC-MR data, even though the FRISK data need only half of the scan time required by the corresponding CON PC-MR data when the same number of lines and VPS are considered. Note that the complicating influence of respiratory motion has been omitted from simulations, and thus the result of the scans that require scan time longer than a breath hold may be considered as indicative of the upper limits of performance with reference to in vivo flow measurement. In practice, respiratory artifacts can severely degrade image quality in cardiovascular flow measurements when scan time is beyond a breath hold. The peak velocity overestimation plots of the CON and FRISK PC-MR were shown in Figure 11. Severe peak velocity overestimation (> 14%) was seen in the simulated CON PC-MR data when VPS is low (1, 2). On the contrary, No or minimal peak velocity overestimation was seen in the simulated FRISK data. The reasons that the peak velocity overestimation becomes high when VPS is low are discussed in details in the discussion section. The correlation comparisons between the simulated CON and FRISK PC-MR data further prove the superior accuracy of the simulated FRISK data (Fig. 12). Only half of the scan time required, the simulated FRISK data still show similar or even better correlations in comparison to the CON PC-MR data.

To investigate the fidelity of FRISK technique at different locations across the tube phantom, the linear regressions between the CFD velocity and FRISK (VPS1, 32lines) reconstructed velocity at three different locations were compared and the results are shown in Fig 13. The results show that the correlation coefficient (R) values at these three locations did not vary significantly over the selected slice (R>0.98), indicating that
in the simulations, FRISK is capable of faithfully representing true simulated velocity over the whole cross section of the jet orifice phantom.

Figure 10 Comparisons of temporal RMS errors of FRISK and CON scans in the jet model. The sequences for a range of VPS and sampled lines were simulated. For similar VPS and number of lines sampled, the conventional scans required approximately twice the scan time compared to FRISK. The scan times required for each FRISK and CON PC-MR scan are listed in the table (unit: second). Scans that require less than 16s are considered as the breath-held scans in our simulations.
Figure 11 Comparisons of peak velocity overestimation errors of FRISK and CON scans in the jet model. The sequences for a range of VPS and sampled lines were simulated. For similar VPS and number of lines sampled, the conventional scans required approximately twice the scan time compared to FRISK.
Figure 12 Comparisons of correlation results of FRISK and CON scans in the jet model. The sequences for a range of VPS and sampled lines were simulated. For similar VPS and number of lines sampled, the conventional scans required approximately twice the scan time compared to FRISK.
Figure 13  The correlation study of FRISK at three locations in the jet model.

The diagonal lines are the lines of identity and the dashed lines are the best fit lines.

Femoral Artery Model.  In the femoral artery model, FRISK was evaluated at a position near the bifurcation. A 6 mm thick slice was simulated at the position shown in Fig 4b. The velocity-times waveforms at the center of the femoral artery model of the simulated FRISK and CON PC-MR scans are shown in Fig.14 (VPS2, Line 128). By using only half of the scan time of the CON PC-MR scan, the FRISK scan showed better fidelity than the CON PC-MR ones. For the two in-plane simulations, the FRISK data still show very favorable agreements with the CFD data due to the data interpolation and alignment incorporated in the FRISK post-processing, while the CON PC-MR scans deviate from
the true velocity severely as the time delay ($\Delta T$) between each VC and VE data pairs increases in the two in-plane velocities scans.

Figure 15 shows the comparison of temporal RMS errors of FRISK and CON scans of the femoral artery model with different VPS and number of lines. The temporal RMS results shown in Fig. 15 further confirmed what was shown in Fig. 14. As the time delay between each of the VC and VE data pairs increases for two in-plane velocities, the velocity-time waveforms of the two CON PC-MR in-plane scans are severely distorted due to the increasing temporal misregistration errors. Even considering the fact that the FRISK scans requires only half of the scan time of the CON PC-MR ones when the same VPS and number of lines are used, the FRISK PC-MR data still show much better fidelity than the CON PC-MR data, making accurate PC-MR measurement of three velocity components of blood flow possible. The correlation results in Fig. 16 clearly show that the $W$ velocity component in the CON PC-MR data is not correlated with the true velocity while that in FRISK PC-MR data is well correlated. This means that for the conventional PC-MR, without data alignment and interpolation incorporated in the FRISK data post-processing, it is very difficult or even impossible to reconstruct the complex velocities of the three components accurately.

As a breath-hold scan is not required for femoral artery model sampling, the through-plane velocity and in-plane velocities of FRISK data with VPS2, 128 lines at three time points were plotted in Figure 17. It can be seen that the FRISK reconstructed data represent the true simulated data in all three components faithfully ($r>0.95$ in all three velocity components). Detailed in-plane velocity features are also accurately captured in the FRISK simulation.
Figure 14 The velocity-time waveforms of the simulated FRISK and CON PC-MR scans in the femoral artery model. The simulation parameters are VPS2 and lines number of 128 in three velocity directions, U, V, and W (b,c,d), where U represents through-plane component, V and W represent in-plane velocity components. The scan time for CON PC-MR and FRISK are 64s, 32s respectively. The rectangle in the (a) shows the sampled area.
Figure 15 Comparisons of the temporal RMS of the FRISK and CON PC-MR scans in the femoral artery model. Different VPS and number of lines sampled in three velocity directions, U, V, and W were simulated, where U represents through-plane component, V and W represent in-plane velocity components. When the same VPS and number of lines are sampled, the conventional scans require twice the scan time compared to that of the FRISK scans. The scan time for each CON and FRISK PC-MR scan is listed in Fig. 10.
Figure 16 Comparisons of the correlations of the simulated FRISK and CON PC-MR scans in the femoral artery model. Different VPS and number of lines sampled in three velocity directions, U, V, and W were simulated, where U represents through-plane component, V and W represent in-plane velocity components. When the same VPS and number of lines are sampled, the conventional scans required twice the scan time compared to that of the FRISK.
Figure 17 Comparisons of through-plane and in-plane velocities of FRISK and CFD data in the femoral artery model. Three representative time points along a cardiac cycle were chosen (indicated in the top graphic). The sampling parameters were VPS1 128 lines, which took 64 seconds to sample the dynamic data. There are totally 25 frames for each velocity component. The maximum values of quiver arrows for each of three time points are: 0.10m/s, 0.17m/s, 0.05m/s.
**U-shaped Model.** FRISK and CON PC-MR data were evaluated at a location near the arch of the U-shaped model. A 6 mm thick slice was simulated at the position shown in Fig 4c. The velocity-times waveforms at the center of the U-shaped model of the simulated FRISK and CON PC-MR scans are shown in Fig.18 (VPS2, Line 128). FRISK results show better agreement in all of the three velocity components. For the two in-plane simulations, the agreements between FRISK and the CFD data are still favorable, while it gets worse in the two velocity components in the CON PC-MR, where the velocity-time waveforms deviate from the true velocity severely as the time delay between each VC and VE paired group increases.

The comparisons of temporal RMS errors of the FRISK and the CON scans in the U-shaped model with different VPS and number of lines are shown in Fig.19. For the through-plane velocities, FRISK data show similarly favorable agreements with the CFD data as that of the CON PC-MR, except that FRISK needs only half of the scan time required by the CON PC-MR data when the VPS and number of the lines are the same. However, when it goes to the two in-plane velocity components, it can be seen that FRISK shows much better agreements than the CON PC-MR data. The temporal RMS of the CON PC-MR data in the W velocity component reaches around 10, which means that the average deviation of the CON PC-MR velocity-time waveforms from the true velocity-time waveforms is around 10 times larger than the average velocity at that sampled location. The correlation results in Fig. 20 further show that the W velocity components in CON PC-MR data are not correlated with the true velocity while the FRISK PC-MR data are well correlated.
From the Figure 20, it can be seen that there are three FRISK scans that are within
the breath-hold range, VPS1 with 32 lines; VPS2 with 64 lines; and VPS4 with 128 lines.
Of these scans, the one with the overall best accuracy was FRISK VPS2 with 64 lines,
which is compared to the CFD data at three time points in Figure 21. It can be seen that
the breath-hold FRISK sequence VPS2, 64 lines is able to capture the original flow fea-
tures accurately in both through-plane and in-plane velocity components (Figure 21).

![Figure 18](image)

Figure 18 The velocity-time waveforms of the FRISK and CON scans in the U-shaped
model. Simulation parameters of VPS2 and lines number of 128 in three velocity direc-
tions, U, V, and W were plotted, where U and represent through-plane component, V and
W represent in-plane velocity components. The scan time for CON PC-MR and FRISK
are 64s, 32s respectively. The rectangular frame in the upper left figure shows the location of the sampled area.

Figure 19 Comparisons of the temporal RMS of the FRISK and CON PC-MR scans in the U-shaped model. Different VPS and number of lines sampled in three velocity directions, U, V, and W were simulated, where U and represent through-plane component, V and W represent in-plane velocity components. When the same VPS and number of lines are sampled, the conventional scans required twice the scan time compared to FRISK. The scan time for each CON PC-MR and FRISK is the same as those shown in Fig.10.
Figure 20 Comparisons of the correlation (R) of FRISK and CON scans in the U-shaped model. Different VPS and number of lines sampled in three velocity directions, U, V, and W were simulated, where U and represent through-plane component, V and W represent in-plane velocity components. When the same VPS and number of lines are sampled, the conventional scans required twice the scan time compared to FRISK. The scan time for CON PC-MR and FRISK are the same as those shown in Fig.10
Figure 21 Comparisons of through-plane and in-plane velocities of FRISK data and CFD data in the U-shaped model. Three representative time points along a cardiac cycle were plotted. The sampling parameter is VPS2 64 lines per k-space, which took 16 seconds to sample the data. The frame number for each velocity component is 12, therefore the temporal resolution for each velocity component is 83ms/frame. The maximum values of quiver arrows for each of three time points are: 0.07m/s, 0.07m/s, 0.06m/s.

In vivo FRISK

In vivo PC-MR images in a healthy volunteer were performed using conventional imaging and FRISK imaging. The magnitude and phase images of non breath-hold con-
ventional imaging (VPS2, 256L, 2.56min), breath-hold FRISK imaging (VPS4, 128L, 16s) and breath-hold conventional imaging (VPS4, 64L, 12s) are shown in Fig 22. For two breath-hold images, FRISK has the same temporal resolution as that of the conventional PC-MR imaging. Slight blurring in the non-breath held conventional magnitude image was observed. This is likely the result of the volunteer’s movements and respiratory artifacts. The surface plots of flow velocity distributions in the ascending aorta using non breath-hold conventional, breath-hold FRISK and breath-hold conventional methods are extracted and shown in Figure 23. Breath-hold FRISK that requires the similar scan time as the breath-hold conventional imaging provides more detailed velocity distribution in the imaged aorta. Comparison velocity-time profiles of the in vivo data are shown for three regions: 1) The center of the aorta, 2) 8mm from the center and 3) static tissue, and are plotted in Fig 24. Other studies have shown that for the ascending aorta, imaged using PC-MR with similar parameters and reconstruction of over 10 frames, that the velocity has a deviation of ±10% from the peak at maximum cardiac output, when imaged at the highest temporal resolution, which is a poorer temporal resolution than shown in our in vivo experiments (12 frames). It can be seen from the Fig 24 that the velocity-time waveforms of the two breath-hold images are very similar to that of the non breath-hold conventional image, indicating that the temporal resolution of the breath-hold scans (approximately 80 ms) is sufficient to accurately capture the flow features of the ascending aorta in our study.
Figure 22 Comparisons of magnitude and phase images of FRISK and CON PC-MR in a healthy volunteer. Non-breath hold conventional imaging, breath-hold FRISK imaging and breath-hold conventional imaging at the time point 0.16s were plotted. Blurring was observed on the magnitude image of the non breath-hold conventional image. Due to its efficient sampling and interpolation algorithm, the breath-hold FRISK scan shows comparable resolution to the longer acquisition conventional scan and superior spatial resolution compared to the corresponding breath-hold conventional obtained with a similar data acquisition time.
Figure 23 Comparison of ascending aorta flow surface plots. Non breath-hold conventional imaging, breath-hold FRISK imaging and breath-hold conventional imaging at three time points along the cardiac cycle were plotted in the figure. The breath-hold FRISK scan shows spatial resolution comparable to the non-breath hold conventional scans and has the same temporal resolution as that of the breath-hold conventional scan, which requires approximately the same acquisition time but has lower resolution.
Figure 24 The time-velocity plots of *in vivo* aortic artery and static tissue. Non-breath-hold conventional imaging, breath-hold FRISK imaging and breath-hold conventional imaging at three 3×3 pixel regions: A) the center of aorta; B) 8mm from the center of the aorta and C) the static tissue were plotted in the figure. The temporal resolution of the non breath-hold conventional scan (approximately 40ms) is twice that of the breath-hold FRISK and conventional scans (80ms). Notice in the breath-hold images that the artifact level in the background region is slightly lower than in the non breath-hold image.
ETR simulations.

Figure 25 shows the time-velocity waveforms of the downstream of the jet flow at five points with 15mm interval each. In the CON PC-MR processed data, no ETR technique was simulated to correct errors caused by temporal misregistration. It can be seen that CON PC-MR processed data have overestimation of accelerating flow but underestimation of decelerating flow.

Figure 25 The velocity-time curves of CON PC-MR with and without ETR option. The simulation parameters here are VPS1, Line 256.
ETR experimental results.

Expressed as a percentage of the reference data the modeled PC data, processed conventionally (CON PC-MR), demonstrated a progressive overestimation of velocity range with increasing number of VE directions encoded (i.e. as ΔT increased) Fig 26 (a). Further, from Fig 26 it can be seen that overestimation of the velocity range for the CON PC-MR data also increased with increasing temporal acceleration in the flow-field. Conversely, the same data sets processed using the ETR routine exhibited close agreement with the reference data for maximal acceleration up to 53 m/s² (4 cm from the origin), and only diverged sharply when the acceleration reached 128 m/s² (5 cm from the orifice), Fig 26 (b). When confining analysis to the laminar flow region (i.e. for the 5 velocity-time curves obtained from the jet origin and extending up to 4 cm) the CON processed data overestimated peak velocity by an average of 126%±25%, and the average correlation r-value was relatively poor at 0.83±0.12. The corresponding ETR data better represented maximal velocities (100%±9%, p<0.001) and the average correlation r-value was improved (0.97±0.03, p<0.001). Representative CON and ETR velocity-time curves are shown in Fig 27 for a point 2 cm from the jet origin. The ETR data closely match the reference flow waveform, while the CON reconstructions overestimate maximal velocity by up to 50%. Note that jet decay is well represented in the ETR data, while the CON data shows consistent underestimation of velocities.

In our MR experiments, it shows that while the VENC was set higher than the true maximal velocity (500cm/s) the conventional reconstructions exhibited increasing
regions of signal alias with increasing number of velocity directions encoded, while in the ETR reconstructions signal alias was either absent or minimal (Fig 28).

Figure 26 Plots of the maximal velocity range error measured in phase-contrast data. The results were evaluated from the jet origin and at 1 cm intervals up to 5 cm, calibrated in terms of the maximum temporal acceleration present. Results are plotted for (a) conventionally processed data (CON PC-MR) and (b) ETR processed data for acquisitions in which 1, 2, and 3 velocity directions were encoded.
Figure 27 The velocity-time curves for CON PC-MR processed data acquired with 1, 2, and 3 velocity directions encoded. The location is 2 cm from the origin of the jet flow. The panel (a) and (b) shows the corresponding plots for data processed without and with the ETR approach. In each plot, the reference scan data are plotted.
Figure 28 Experimental data processed using CON PC-MR and ETR reconstructions. Jet flow for, left to right, the reference (REF) data set and data acquired with a segmentation factor of 2 and encoding 3, 2, and 1 velocity directions. The top panel shows the data processed using conventional reconstruction and the lower panel shows data processed using enhanced temporal registration reconstruction.

SR PC-MR

Numerical simulations and validation

Figure 29 shows the comparison of the velocity-time waveforms of the predicted simulation results and the experimental reference PC-MR results at the location of the slice 2. It can be seen that the agreement of through-plane velocity values between PC-MR data and CFD data is very favorable (R = 0.98; Y = 1.1X + 0.02).
Figure 29 a) The numerical simulation results of the jet flow and its validation for SR PC-MR study. The flow rate at slice 1 measured from the reference PC-MR was used as the boundary condition for numerical simulation as shown in (a). The comparison of the velocity-time plots of the reference PC-MR and numerical results at the location of slice 2 (b).

**SR PC-MR simulations**

Five regions downstream of the jet flow with an interval of 15 mm were sampled (ROI: 3×3mm²) on both simulated CON and SR PC-MR data with VPS of 2 and the results were listed in Figure 30. The simulated CON PC-MR data have very close systematic and random noise and exactly the same temporal resolution as those of the *in vitro* phantom data VTR1. Compared with the simulated CON PC-MR data there is a twofold improvement of temporal resolution in systole of the simulated SR PC-MR. Very significant peak velocity overestimation was observed in the simulated CON PC-MR results (as
shown in Figure 3 B, C, D, Fig.31) in the area down stream of the jet flow, where high acceleration terms occur. On the contrary, the simulated SR PC-MR showed very good fidelity compared to the simulated CON PC-MR. No or minimal peak velocity overestimation was seen (Overall 2.8±0.4% vs. 16.9±6.4% Fig. 31). The quantitative evaluation of the average temporal RMS and peak velocity overestimation of the two sets of the data groups clearly show that the simulated SR PC-MR generated significantly less error than the CON PC-MR simulations under all three VPS conditions (Overall RMS: 9.0±1.0% vs. 24.0±0.2%, Fig. 31).

Figure 30 The comparison of velocity-time plots of the simulated CON and SR PC-MR.
Figure 31 The temporal RMS and peak velocity overestimation of the CON and SR PC-MR at five regions. The five points are the same as those shown in Fig. 30 with three different VPS values (VPS = 1,2,4)

After the *in vitro* phantom data and *in vivo* ascending aorta data were sampled on the GE scanner in a conventional manner, the data were reconstructed according to the SR and CON PC-MR algorithms. The same five regions were sampled on the *in vitro* VTR1 (Fig. 32). Even though our PC-MR simulation sequences shown in Figure 30 are not based on the data from the *in vitro* data VTR1 shown in Fig 32, the patterns of the errors between the simulated data and the experimental data are highly similar. As there is no gold standard velocity for our *in vitro* and *in vivo* PC-MR studies, it is difficult to
quantitatively evaluate and compare the accuracy of the CON and SR PC-MR results. However, it can easily be seen that at region B (ROI $3 \times 3 \text{ mm}^2$), the CON PC-MR data overestimated the peak velocity, as from our previous experiments in the jet phantom, the maximal velocity in the phantom should appear at the region close to the orifice area (region A). Also, when the acceleration terms are high, the overestimation of accelerating part and the underestimation of the decelerating part of the cycle predicted in the simulated CON PC-MR data (Figure 30) are also observed in the experimental data (Figure 32).

Figure 32 The comparison of velocity-time waveforms of the in vitro CON and SR PC-MR at five points.

An area (ROI $3 \times 3 \text{ mm}^2$) 20 mm downstream of the jet flow was sampled on both CON and SR PC-MR processed data and the magnified velocity-time curves were plotted
in Figure 33 a, b. The acceleration-time curves of CON PC-MR along the center line of the jet were also plotted in Figure 33c to investigate the influence of actual temporal resolution on the acceleration terms. The velocity-time curves of the simulated SR and CON PC-MR data at the same area with VPS 8 were shown in Figure 34.

The velocity-time curves of the CON and SR PC-MR in vivo data VIV1 are shown in Figure 35. As the temporal acceleration terms in the normal ascending aorta flow are smaller than that in the jet phantom used to simulate pathological flows, there is a certain comparability between CON and SR PC-MR data (R = 0.99; Y = 0.89X + 0.35).

As seen in Figure 32 the data processed by the SR algorithm have smoother velocity-time curves than those processed by the CON PC-MR method, which usually indicates a better velocity-to-noise ratio. The SNR, which is proportional to the VNR, was calculated for all four sets of experimental data and the results are listed in Table 3. Compared to CON PC-MR, a SNR of 119.4 ± 26.6 % (p<0.005) was achieved in the data processed using the SR algorithm.
Figure 33 The velocity-time plots and acceleration-time plots of CON and SR PC-MR. (a): the simulated CON PC-MR and (b): the simulated SR PC-MR 20 mm downstream of the orifice (ROI $3 \times 3$ mm$^2$) with two VPS values. (c): acceleration-time plots of CFD and CON PC-MR. It can be seen that when the VPS is low, peak velocity overestimation in CON PC-MR (due to temporal misregistration of VC and VE) is the dominant error; When the VPS becomes high, the temporal resolution of the sampled CON PC-MR data is averaged, erratically alleviating the data misregistration errors, thus making the overall RMS similar when VPS ranging from 1 to 4.
Figure 34 The velocity-time plots of the simulated SR and CON PC-MR data with VPS8. The sampled location is 20mm downstream of the jet orifice and the scan time for these two sets of simulated data is 32s.
Figure 35 The comparison of the CON and SR PC-MR in the *in vivo* data. A) the ascending aorta; B) the static tissue.

Table 3

*The SNR of the in vitro and in vivo data*

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<tr>
<th>Data ID†</th>
<th>SNR</th>
<th>SNR Improvement (%)</th>
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<td>Self</td>
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<tr>
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<td>19.4±3.0</td>
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<td>VIV1</td>
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<td>8.8±0.6</td>
</tr>
<tr>
<td>VIV2</td>
<td>7.5±1.0</td>
<td>9.1±0.9</td>
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DISCUSSION

FRISK

Due to its flexible sampling algorithm, FRISK can be arranged to achieve an optimized balance of spatial resolution (coverage of k-space) and temporal resolution (frames per second) for any given scan time. The expected general spatial and temporal features of the flowfield should be taken into account when selecting parameters, so as to minimize the expected error function for a given scan time.

The temporal RMS surface plot shown in Figure 10 indicates that jet flow has extremely high temporal acceleration but relatively low spatial acceleration. This is apparent in the relative steepness of the error term along the VPS axis compared with the number of lines sampled axis. In this flowfield, optimization of temporal resolution is clearly indicated at the expense of spatial resolution. Thus, in this flow-field, given that the VPS sets the upper limit of accuracy, there is little to no benefit of obtaining high spatial resolution images if the temporal resolution is insufficient. The benefit of considering flow features for fast PC-MR imaging strategy is obvious: in the jet orifice model case, spatial resolution can be comfortably sacrificed to maximize temporal resolution without loosing important details of the flow, while at the same time allowing a breath-hold scan. This might provide guidance for fast cardiac imaging where complex flow features and time restrictions present major challenges for breath-hold scans.
One point clearly shown in the FRISK and CON PC-MR simulations in the femoral artery model and U-shaped models is that without the data alignment, which is part of FRISK interpolation algorithm, it is almost impossible to accurately reconstruct the velocities in three components for flow fields with complex and small in-plane velocities. This can be seen from the poor correlations between the CON PC-MR data and CFD data in the W velocity components of the two models. Generally, FRISK processed data in the W components in these two models showed very good correlation with the CFD data. However, since only limited error terms are simulated in the two models, the potentials of using FRISK to accurately reconstruct flow in three velocity components need to be further tested in *in vitro/in vivo* models where gold standards can be found to validate FRISK PC-MR data.

Of the three models studied, the U-shape model presents the most severe challenge for PC-MR for two reasons: 1) flow variations, especially in-plane flow variations, contain steep temporal and spatial velocity gradients as evidenced by the similar steepness of the error terms along the spatial and temporal axes (Fig 19 FRISKV, FRISKW). Thus, sacrificing either spatial resolution or temporal resolution is problematic when representing this kind of flowfield. As the U-shape model is designed to mimic the aortic arch, a breath hold scanning is generally required. To our knowledge, this represents the first attempt at capturing three velocity components in one scan of a breath hold duration, applied to geometry similar to the aortic arch. Depending on the fidelity required, several compromises in scan approaches might be considered: 1) the parameters chosen for Fig 19 rejected the extremes of spatial or temporal resolution in favor of the middle option.
for the given scan time; 2) consider splitting the scan to acquire only through-plane flow in one breath hold and only in-plane flow during a second breath-hold. In the latter case, increased temporal resolution is inherent in the approach, and should allow separate optimization of in-plane and through-plane components.

The previous studies on the U-shape model from our group have shown that BRISK simulation with VPS 5 achieved an excellent representation of the centerline waveform of simulated through-plane velocity, while in-plane flow was relatively poorly represented. The disagreement in in-plane velocities in our previous BRISK studies is explicable by the presence of steep temporal and spatial gradients associated with in-plane circumferential velocities, and the necessity of using higher VPS (VPS >5) to achieve breath-hold scan times.

In conclusion, FRISK, a new MRI sampling sequence that sparsely samples data temporally and spatially, and aligns interleaved and acquired data during post-processing, was numerically simulated for 3 representative physiological flowfields: A) a jet orifice model, B) a patient-specific femoral artery model, C) a U-shape model. The results showed that, spatial and temporal resolution of the sampled data in FRISK are adaptable for flows with different features to achieve optimized results. FRISK simulations agreed with the conventional scans when similar scan parameters were used, while FRISK provided a scan time advantage of approximately a factor of two, and allowed rapid or breath-hold scanning to be performed while obtaining acceptable accuracy, eliminating significant and potentially unacceptable respiratory artifacts when the scan extends beyond a breath hold duration. The clinical PC-MR experiments showed that data sampled and processed by breath-hold FRISK improved image quality compared with correspond-
ing breath-hold conventional scans. Further improvements to FRISK will be necessary in order to optimize the balance between time efficiency and diagnostic accuracy.

ETR

Failure to accommodate the temporal distribution of data in conventional PC imaging can result in gross inaccuracies in representing jet flow. It was shown that even when the time interval separating corresponding the VC and VE data is much shorter than is commonly realized (7.1ms), that dramatic overestimation of peak velocity is still possible. The inability to accurately measure peak velocity under conditions of laminar jet flow represents a severe (and possibly application limiting) restriction. Here it was shown that post processing, applied to temporally interpolate and align data, improved accuracy in representing jet flow. This approach was successfully applied without knowledge of the flowfields and is applicable to the widely implemented form of PC as well as to, faster, novel acquisition methods.

The ETR approach allows separation of two related issues: 1) the adequacy of the temporal sampling rate and 2) the degree of temporal distribution of the composite PC data sets. It is widely appreciated that high-temporal sampling rates are required to adequately represent rapidly changing flow-fields, and common approaches to accomplish this include reducing the number of velocity directions encoded and reducing the data segmentation value. These combined strategies also reduce the temporal distribution of data, and thus improvements in flowfield fidelity are necessarily derived from two sources. Here, it is noticed that data that meets or exceeds the minimum Nyquist conditions to adequately represent the temporally changing velocities does not necessarily ac-
curately represent the data. To illustrate this, consider the data sets presented here with 16 vs. 32 frames per cycle. When conventionally processed, the 16 frame set exhibited increased errors compared to the 32 frame set, and both were inaccurate compared to the reference scan. However, ETR processing was able to correct both data sets at the jet origin and in the convergent flow zone. Thus, in these regions, minimum sampling requirements were met or exceeded by each data set, but this was only apparent after applying ETR processing. Conversely, in jet flow regions where the temporal acceleration rate was higher, the minimum sampling rate was not realized for the 16 frame series, but was realized for the 32 frame series. In this case, ETR processing could not completely correct the low temporal resolution set, but was successful in improving the high temporal rate set. Thus, within the limits of applicability, ETR processing is expected to benefit PC acquisition schemes that generate temporally distributed data, allowing separation of the temporal distribution and temporal rate considerations.

The waveform distortions noted in the conventionally processed data are dependent on both acquisition and flow-field factors and may therefore be difficult to interpret. For the PC configuration shown here conventional processing resulted in overestimation of accelerating flow but underestimation of decelerating flow. Thus, measurements that incorporate time integrals (e.g. stroke volume) may to some extent be self-compensating. However, flow-field analyses that require knowledge of velocities at specific spatial and temporal locations (e.g. control volume, and proximal isovelocity surface area calculations) may be more sensitive to these distortions. A common analysis that is performed clinically uses the maximal velocity within the jet flow to estimate the maximal pressure gradient by applying the Bernoulli equation\(^5^1\). Since the formula involves the square of
velocity, even modest overestimation of maximal velocity can result in dramatic overestimation of pressure gradients. Here ETR processing was applied without prior knowledge of the flow-field, to improve conventional PC data but in principle it is applicable to any imaging approach with interleaved PC data sets.

The results presented here indicate that conventional PC scanning could possibly be improved by acquiring VC and VE data in a temporally aligned manner. This would involve acquiring VC and VE data in separate flow cycles (as implemented here for the REF acquisition). However, to void increasing the scan time compared to a conventional PC scan, a high segmentation factor would have to be used, resulting in maintaining the degree of temporal distribution of data. Thus, while this approach may eliminate the temporal mismatch between corresponding VC and VE data pairs, artifacts related to the temporal distribution of data are still expected, and it is likely that this approach would also benefit from ETR processing. Preliminary experience with this approach (results not shown) indicate that increased noise is generated, possibly related to the weaker coupling of corresponding k-space lines for VC and VE data sets.

A potential drawback of applying ETR processing is the possibility of introducing interpolation related distortions. For our implementation this can occur under the following conditions: 1) Data are acquired at too low a temporal rate compared to the minimum Nyquist conditions. This represents a fundamental limitation to accuracy of PC data and is not unique to ETR processing. In the examples shown here, applying ETR improved data agreement, but was not able to fully compensate when the temporal rate was too low. 2) Noise contamination dominates the data. In the absence of noise, use of interpolated data is as valid as use of the original data points. Excessive noise can confound this, but
the present studies have shown that under normal acquisition conditions, adequate SNR
can be obtained to allow ETR to improve accuracy. 3) The complete flow-field waveform
is not fully sampled, and the represented data is not cyclic. Distortions introduced should
primarily affect the beginning and end of the cycle, whereas most high velocity condi-
tions are realized within the middle section of the cycle. Usually, sampling can be ar-
ranged to avoid sudden transitions of high velocity data at either the start or end of the
cycle. Thus, under typical conditions, acquisitions can be accomplished with moderate
restraint to satisfy the conditions that allow ETR to provide increased accuracy.

In conclusion it was shown that severe distortions of velocity-time curves are
likely for conventional PC data sets when applied to flow-fields with high temporal ac-
celeration, such as jet flow. This situation arises because of the requirement to compare
velocity-sensitized data sets that are acquired in a temporally distributed manner. Veloci-
ty overestimation and underestimation are possible and are dependent on acquisition de-
tails and whether flow is accelerating or decelerating. A post-processing algorithm
termed ETR was applied to represent corresponding data sets at temporally aligned points,
which was able to compensate for a wide variety of flow conditions. Attention to the
principles shown here, and application of the solution, has potential to allow widespread
improvement of the accuracy of PC data in the measurement of jet flow.

SR PC-MR

There have been a number of studies concerning the influence of acceleration
terms on the accuracy of the quantitative PC-MR flow measurements reported\cite{18,19,52}, due
to the common presence of acceleration in \textit{in vivo} flows either in the form of pulsatile
flow or in the form of convective acceleration. Marc et. al.,\textsuperscript{53} carried a thorough theoretical study analyzing the flow sensitivity to acceleration and concluded that it is a result of the misinterpretation of the net phase shifts at a certain Taylor expansion time point. This acceleration sensitivity can be corrected if the phase shifts are interpreted at the ‘gravity’ center of the encoding bipolar gradient function instead. However, the ‘gravity’ center is generally difficult to determine and no feasible solution was proposed in the study to eliminate the acceleration terms with currently available gradients.

However, our research group proposed another type of acceleration related error that cannot be corrected by simply interpreting the data at the ‘gravity’ center\textsuperscript{34}. From our simulated results and experiments, this type of error should be the major reason of the peak velocity overestimation in the jet flows seen both in our simulated and experimental data. For CON PC-MR data processing, a net phase shift at each time point is obtained by subtracting VC data sets from VE data sets. However, \(\Phi_{VC}\) and \(\Phi_{VE}\) data cannot be sampled at the same time point experimentally and there should be a time delay (\(\Delta t = TR\)) between the sampling time points of the VC and VE data sets: 

\[
\Phi_{MEAD(i, t)} = \Phi_{VE(i, t+\Delta t)} - \Phi_{VC(i, t)}
\]

For the sequence that samples the paired data in the order of VC-VE-VC-VE..., \(\Phi_{MEAD(i, t)} > \Phi_{TRUE(i, t)}\) when the flow is accelerating, causing overestimation of the velocity. In the same way, when flow is decelerating, \(\Phi_{MEAD(i, t)} < \Phi_{TRUE(i, t)}\), causing underestimation of the velocity (Fig 3). This manner of extracting data in the CON PC-MR makes it intrinsically sensitive to acceleration terms (Fig.36).
Figure 36 The illustration of temporal misregistration errors by using an *in vitro* reference data. An *in vitro* phantom data sampled by using a special sequence in which VE and VC were acquired in separate cycles and used as *in vitro* reference data in the literature (Table.3, RF1) \(^{34}\). In this way, the errors caused by the temporal misregistration should be minimized. A peak velocity overestimation of 21.4% was observed when VE and VC were temporally misregistered with 8ms (TR) 30mm downstream of the orifice. Vtrue: true velocity without temporal misregistration effect; Vmreg: temporally misregistered data.

The reason for the relatively constant RMS of the CON PC-MR data with varying VPS becomes more apparent when one observes the peak velocity overestimation plots (Fig. 31). Here there are actually two sources of error contributing to the overall RMS: temporal misregistration of VC and VE data, as well as peak velocity underestimation associated with insufficient temporal resolution. The combined errors produced by these two sources make the overall RMS similar when low to moderately high VPS are chosen.
(VPS1:25% vs.VPS4:23%). The fact that the temporal misregistration errors are largest in the CON PC-MR when VPS is low (e.g., VPS = 1) can be explained by Fig 33a, c, i.e. the local acceleration terms in the data are temporally averaged when only limited points are sampled with high VPS sequence, erratically alleviating the errors introduced by temporal misregistration of VC and VE. This implies that when high acceleration terms are presented in the flow studied, simply relying on the reduction of VPS in the CON PC-MR to improve the PC-MR accuracy may cause severe overestimation of peak velocity and therefore should be performed with caution.

The SR PC-MR, on the contrary, extracts the time resolved true velocity without relying on comparing paired data sets. Two static sets of data: the average velocity ($V_{\text{TRUE,AVE}}$) and the average VC velocity ($V_{\text{VC,AVE}}$) are used to correct VE data sets, making the PC-MR data less sensitive to local acceleration terms.. From Fig.33a, b, it can be seen that by using the unique data extraction method that relies on the relationship between VC and VE imaging gradients, the SR PC-MR processed data showed better agreement compared to the CON PC-MR processed data ranging from low VPS (RMS: 8.1% vs. 16.0%) to high VPS (RMS: 9.0% vs. 21.2%). A significant peak velocity overestimation is observed in CON PC-MR processed data in Fig 33b with VPS1 sequence, but is minimized in SR PC-MR processed data (Peak Velocity Overestimation: 18.4% vs. 0.7%).

Besides the advantages brought by its unique data processing manner, another advantage brought by the SR PC-MR algorithm is its improved temporal resolution. In the application (App1, Fig.3) that was investigated in this study, there is a twofold gain of temporal resolution in the systolic part of the cardiac cycle. The advantage of the im-
proved temporal resolution in systole is especially helpful when a high VPS is used for fast data sampling (Fig. 34). With a simulation sequence of VPS 8 showing in the Figure 8, the CON PC-MR processed data deviate severely from the true velocity waveform while SR PC-MR processed data still maintain relatively high fidelity (RMS: 40.6% vs. 17.0%). Severe peak velocity underestimation is also observed in CON PC-MR because of its insufficient temporal resolution (128ms), not high enough to capture the sharp velocity transitions in systole. However, due to its doubled temporal resolution in systole (64ms), the SR PC-MR maintains sufficient fidelity even when the VPS is as high as 8 (Peak velocity underestimation: 16.0% vs. 1.7%). This feature of SR PC-MR, can be readily combined with FRISK, a fast imaging technique developed in our research group that can at least half the scan time with comparable accuracy compared to CON PC-MR, to realize breath-hold data sampling for cardiovascular flows with high fidelity, where breath hold data acquisition is preferred to eliminate respiratory artifacts \(^{29,43}\).

In conclusion, SR PC-MR, a novel PC-MR technique that is able to 1) reduce the sensitivity of the PC-MR data to temporal acceleration; 2) improve temporal resolution and 3) SNR, was investigated by using numerical and experimental approach. The simulated results show that significant improvements in accuracy were generated in the SR PC-MR data compared to the CON PC-MR technique under low or moderately high VPS (Overall RMS 9.0±1.0% vs. 24.0±0.2%). No or minimal peak velocity overestimation was observed in the SR PC-MR processed data where significant peak velocity overestimation was seen in the CON PC-MR data (Overall Peak Velocity overestimation: 2.8±0.4% vs. 16.9±6.4%).). Highly similar error patterns in the velocity-time plots between the \textit{in vitro} experimental data and the simulated data were observed. An average
SNR improvement of 18.6±6.7% was acquired in both *in vitro* and *in vivo* SR PC-MR data compared to the conventional scans. A new type of acceleration related error in CON PC-MR was proposed and the advantages of SR PC-MR were analyzed at the end of the dissertation.
CLINICAL SIGNIFICANCE

Phase-contrast MR imaging goes beyond morphological imaging by allowing direct quantitative evaluation of flow dynamics. Accurate measurement of both through-plane and in-plane flow quantification in MRI offers the potential for assessing vessel patency, volume flow rate and flow velocity, representing advancements of great clinical significance. However, to our knowledge, none of the currently available PC-MR fast imaging sequences is able to provide enough temporal and spatial resolution for three velocity components. The simulation results represented here demonstrate that the accuracy of current conventional PC-MR with three velocity components encoded is very poor and can be improved by implementing the following features in FRISK: 1) efficient sampling algorithm and post-temporal alignment of data, which make the data less sensitive to acceleration, while reducing scan time by a factor of two; 2) the balance between spatial and temporal resolution should be biased towards one or the other based on the general flow features of the flow field to obtain optimized results. These features of FRISK allow superior PC-MR quality compared to corresponding conventional PC-MR scans, showing the clinical potential of FRISK to acquire three dimensional flow velocity information within a breath hold in cardiac imaging, where both accurate measurement and short scan time are favored.

Compared to CON PC-MR, SR PC-MR eliminates the need to compare paired VC and VE data sets to extract the velocity information, therefore fundamentally corrects the errors introduced by temporal misregistration between VC and VE data sets, which
has been proven to be the major error source in the simulations that disrupts the velocity-time waveforms severely in either high acceleration jet flow or complex flow-fields where three velocity components are encoded. Also, the benefits of improved temporal resolution brought by SR PC-MR algorithm can be especially useful where short scan time is clinically preferred: by improving temporal resolutions almost two folds, SR PC-MR processed data can have the similar temporal resolutions as those of the CON PC-MR processed data which require twice as much time. It can also be predicted that data sampled within a breath-held time with three velocity components accurately encoded can be obtained by combining FRISK and SR PC-MR imaging options.
LIMITATIONS

One of the limitations of our simulations is that the simulated velocity data used in this study were taken from one simulated cardiac cycle; while in a real PC-MR scan, flow data are usually not strictly cyclic and are obtained from multiple cardiac cycles. This might be able to partly explain the noisier velocity-time curves observed in the in vitro results than in the simulated ones (Fig.30, Fig.32). The jet flows used in CFD simulation and MRI phantom study are a simplification of the clinical situation. For example, the orifice in our study is circular and no wall is presented which would otherwise alter the properties of jets. In in vivo cases, jets may be eccentric instead of well-aligned to arterial walls. Other errors like through-plane motion during the excitation and in-plane motion during readouts on velocity measurement were also not included in the simulations as they are considered minor compared to the errors that were addressed in the dissertation. Currently, one limitation for the SR PC-MR technique is that it shows accuracy superior to that of CON PC-MR only under the situation in which flow has to be essentially directional, such as the jet flow. In the case where flow is distributed between three axes, the knowledge of the total velocity, i.e. sum of the velocities in all three directions, is needed to extract the true velocity in the SR PC-MR. In combination with accumulated noise, the total velocity calculation increases error, thus limiting the applications of the SR PC-MR with three velocity encoded scan.
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