Accelerated aortic 4D flow MRI with wave-CAIPI

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Purpose: The aim of this study was to investigate the acceleration potential of wave-CAIPI (controlled aliasing in parallel imaging) for 4D flow MRI, provided that image quality and precision of flow parameters are maintained.

Methods: The 4D flow MRIs with acceleration factor $R = 2$ were performed on 10 healthy volunteers, using both wave-CAIPI and standard Cartesian/2D-CAIPI sampling for reference. In addition, 1 patient with known aortic valve stenosis was examined. The flow rate ($Q$), net flow ($Q_{\text{net}}$), peak velocity ($v_{\text{max}}$), and net average through-plane velocity ($v_{\perp}$) were calculated in eight analysis planes in the ascending and descending aorta. The acquisitions were retrospectively undersampled ($R = 6$), and deviations of flow parameters and hemodynamic flow patterns were evaluated.

Results: Flow parameters measured with an undersampled wave-CAIPI trajectory showed considerably smaller deviations to the references than the 2D-CAIPI images. For $v_{\text{max}}$, the mean absolute differences were $6.02 \pm 2.08$ cm/s versus $14.36 \pm 5.68$ cm/s; for $Q_{\text{net}}$, the mean absolute differences were $3.67 \pm 1.40$ ml versus $5.87 \pm 1.91$ ml for wave-CAIPI versus 2D-CAIPI, respectively. Noise calculations indicate that the 2D-CAIPI sampling exhibits a $(43 \pm 38)\%$ higher average noise level than the wave-CAIPI technique. Qualitative discrepancies in hemodynamic flow patterns, visualized through streamlines, particle traces and flow velocity vectors, could be reduced by using the undersampled wave-CAIPI trajectory.

Conclusion: Use of wave-CAIPI instead of 2D-CAIPI sampling in retrospectively 6-fold accelerated 4D flow MRI enhances the precision of flow parameters. The acquisition time of 4D flow measurements could be reduced by a factor of 3, with minimal differences in flow parameters.

Key words
4D flow, aorta, phase contrast, wave-CAIPI
1 | INTRODUCTION

Dynamic 3D phase-contrast MRI (4D flow) can be used to investigate blood flow through the heart and large vessels by calculating flow parameters, such as the flow rate or the peak flow velocity.\(^1\)\(^2\) 4D flow MRI is also used to quantify and visualize flow for neuro and abdominal applications.\(^6\)\(^7\)\(^8\)\(^9\)\(^10\) One advantage of 4D flow over the conventional 2D phase-contrast methods is its flexibility to evaluate flow in arbitrary plane orientations and positions after the examination. Furthermore, complex hemodynamic flow patterns can be visualized using 4D flow MRI. Various heart diseases can be associated with flow pattern alterations, such as increased local peak flow velocities in the ascending aorta in patients with aortic valve stenosis.\(^4\)

However, the clinical application of 4D flow MRI is limited by its long acquisition time due to the intrinsic large amount of data that has to be acquired with 3D spatial coverage and four velocity encodings (three flow-encoded data sets in three orthogonal directions and one flow-compensated data set). Long acquisition time not only reduces patient comfort, but also increases the risk of involuntary patient movement, which ultimately degrades image quality. Therefore, to integrate 4D flow MRI examinations in the clinical routine, the scan times need to be reduced to an acceptable range. The image acquisition can be accelerated with parallel imaging; however, a significant noise enhancement emerges in the final images from high acceleration factors.\(^11\)\(^12\) A higher SNR in parallel imaging reconstructions can be achieved by using sampling-efficient non-Cartesian trajectories, as was demonstrated for 4D flow MRI with spiral k-space trajectories.\(^13\) Although the application of non-Cartesian k-space trajectories can have a beneficial effect on parallel imaging reconstructions, some challenges also arise. For instance, off-resonance effects in spiral trajectories cause significant blurring in image space, especially for long readout durations.\(^14\)\(^15\) Furthermore, imperfections in the gradient system of the MR scanner can lead to significant distortions of gradient waveforms.\(^16\)\(^17\)\(^18\)\(^19\) As a consequence, a gradient-correction technique is often required for non-Cartesian imaging, to avoid image artifacts.

Recently, the wave-CAIPI (CAIPIRINHA [controlled aliasing in parallel imaging results in higher acceleration]) technique was shown to be an optimized sampling method for accelerated 3D MRI, enabling parallel imaging reconstructions with reduced noise enhancement. The helix-shaped readout lines of the wave-encoding technique leads to a more homogeneous distribution of missing k-space locations in the case of undersampling, compared with standard Cartesian readout lines. In contrast to the Cartesian k-space trajectory, the omission of phase-encoding lines with wave-CAIPI distributes the aliasing in all three spatial dimensions, including the frequency-encoding direction. As a result, variations in receive coil sensitivity profiles are used more efficiently in parallel imaging reconstructions, leading to a reduced noise enhancement. The wave-CAIPI technique has been predominantly used in brain application\(^20\)\(^21\)\(^22\) so far; however, it is also a promising method for efficient investigations of other organs.\(^23\)\(^24\)

In this work, the beneficial aliasing characteristics of the wave-CAIPI k-space trajectory are exploited to perform parallel imaging reconstructions of accelerated 4D flow MRI acquisitions with reduced noise enhancement. The aim of this study was to compare 4D flow MRI with wave-CAIPI encoding to Cartesian sampling for \(R = 2\) (prospective) and to 2D-CAIPI sampling for a retrospective undersampling rate of \(R = 6.\)\(^25\)\(^26\) In this context, variations in flow parameters were quantified and compared for each sampling technique, and hemodynamic flow patterns were investigated.

2 | METHODS

2.1 | Study design and setup

The wave-CAIPI k-space trajectory was integrated in a time-resolved 3D phase-contrast gradient-echo pulse sequence with 3D velocity encoding. The helically shaped readout lines of the wave-CAIPI were generated by using sinusoidal gradient waves on both phase-encoding axes during readout. A schematic pulse diagram is shown in Figure 1A. The gradient oscillations were delayed with respect to one another, to create a phase difference of \(\pi/2.\) A maximum gradient wave amplitude of \(A_{\text{wave}} = 9\) mT/m and a fixed number of complete wave cycles \(N_{\text{wave}} = 4\) was chosen. The sinusoidal gradient waves were implemented as integer multiples of half-cycles. Spoilers on the phase-encoding axis were programmed to start immediately after the wave gradients.

Images were acquired in sagittal orientation with frequency encoding in head–foot direction and a k-space matrix of \(128 \times (76-96) \times (28-36).\) For the healthy volunteers, the spatial resolution was set to \(2.5 \times 3.5 \times 3.5\) mm\(^3\), which is within the range of typical resolutions used in cardiac 4D flow MRI.\(^2\)\(^5\) For the patient examination, the resolution in slice-encoding direction was decreased to \(5.0\) mm\(^3\) for increased spatial coverage. Further pulse-sequence parameters were \(\text{FOV} = 320 \times (260-320) \times (98-180)\) mm\(^3\), flip angle = \(7^\circ, \text{TR} = 6.03\) ms, \(\text{TE} = 3.40\) ms, temporal resolution = \(48.24\) ms, readout bandwidth = \(500\) Hz/pixel, and maximum encoded flow velocity \(v_{\text{ENC}} = 200-250\) cm/s. A cardiac acquisition window of \(550-700\) ms was chosen for all examinations, and 11-14 cardiac phases were reconstructed using prospective electrocardiogram gating. All measurements were acquired with an acceleration factor of \(R = 2\) in the anterior–posterior direction. A slab-selective excitation pulse was used in the left–right direction.

Respiratory motion was accounted for by using a navigator readout at the lung/liver interface, acquiring data near expiration. To increase navigator efficiency, the ReCAR...
technique was applied to reorder the phase-encoding scheme, such that central k-space is acquired at end-expiration and peripheral k-space is acquired during inspiration.5 With the ReCAR method, the acceptance window of the navigator can be increased to 8 mm, without introducing motion artifacts.5

To evaluate the performance of the wave-CAIPI 4D flow sequence, 10 healthy volunteers (age: [25.3 ± 2.7] years, 3 male) were examined using both Cartesian/2D-CAIPI25,26 and wave-CAIPI sampling. In retrospective, the wave-CAIPI and Cartesian 4D flow data sets were undersampled, using acceleration rates of $R = 4-8$ and subjected to the reconstruction algorithm as detailed in the following section. Flow parameters were calculated from the obtained images and were compared with flow parameters that were calculated from the original data sets. Furthermore, hemodynamic flow patterns of 6-fold undersampled 4D flow MRIs were compared with the 2-fold accelerated images. The maximum possible acceleration rate was studied by calculating the error in the average through-plane velocity $v_{\perp}$ in the respective analysis planes along the aorta of the healthy volunteers. In accordance with the work of Gatehouse et al.,27 the criterion for the maximum possible acceleration rate was defined as the undersampling factor $R$, which led to mean errors in $v_{\perp}$ of below 0.6 cm/s. Although this theoretical limit warrants acceptable errors in a number of flow measures, as detailed in Gatehouse et al.,27 the maximum possible undersampling rate further depends on the specific investigation of a certain pathology, the hardware setup, and the individual patient.

The undersampling pattern that was used in all retrospectively 6-fold accelerated scans is shown in Figure 1B. Noise was analyzed for the retrospectively 6-fold accelerated 2D-CAIPI and wave-CAIPI examinations of 1 healthy volunteer by means of the pseudo multiple replica method.12

In addition to the healthy volunteers, 1 patient (female, 84 years old) with known aortic valve stenosis was examined using only the wave-CAIPI sampling method. All measurements were performed on a 3T clinical MR scanner (MAGNETOM Prisma®; Siemens Healthcare, Erlangen, Germany). The in vivo study was approved by our institution’s ethics committee, and informed, written consent was obtained from each subject before the examination.

### 2.2 | Image reconstruction

Imperfections in the gradient system cause gradient errors,16-19 such that the gradient oscillations of the wave-CAIPI are distorted. Deviations of the output gradients from the theoretical input gradients lead to inaccuracies in the resulting k-space trajectory and finally translate to severe image artifacts. Knowledge of the scanner-specific gradient system transfer function, which is a linear model for gradient distortions, can be used to estimate the gradient errors and account for them during reconstruction. Image artifacts that arise from gradient errors can be sufficiently removed using only the self-terms of the gradient system transfer function. These self-terms describe alterations in gradient amplitude and temporal shifts for each individual gradient axis. The gradient system transfer function was characterized using additional phantom measurements before the in vivo study.18,19 Using a phantom-based approach, the phase evolution of the MR signal was measured in a pair of parallel slices, while a series of triangular gradient pulses were played out on the gradient axis perpendicular to the measured slices. From the phase evolution in the two slices, the true gradient can be calculated and compared with the nominal input gradient. Systematic comparisons of measured and nominal gradients allow for the calculation of a system transfer function to characterize the gradient system behavior.

After gradient correction, the undersampled data sets were reconstructed using an iterative conjugate gradient SENSE algorithm.28 Coil sensitivity maps were estimated from a low-resolution Cartesian scan with increased FOV in the left–right (partition-encoding) direction. The coil sensitivity

![FIGURE 1](image-url)
map scan was performed in between the Cartesian and the wave-CAIPI 4D flow scan. To this end, an ESPRIT\textsuperscript{29} calibration algorithm, as implemented in the Berkeley Advanced Reconstruction Toolbox\textsuperscript{30} on the CPU, was used. The iterative SENSE algorithm was stopped once the conjugate gradient residual was smaller than a predetermined threshold, which was proportional to the estimated image noise.

Imperfect excitation profiles of the slab-selective RF pulse lead to considerable aliasing in the outer part of the encoded FOV in the partition-encoding direction. No slice oversampling was used. The average reconstruction time of one wave-CAIPI and Cartesian/2D-CAIPI 4D flow data set with the conjugate gradient SENSE algorithm was about 1 hour, not including the sensitivity map calculation with the Berkeley Advanced Reconstruction Toolbox.

### 2.3 Calculation and comparison of flow parameters

The acquired Cartesian 2D-CAIPI and wave-CAIPI 4D flow data sets were retrospectively undersampled in the partition direction by an additional acceleration rate of 3 (total undersampling factor \( R = 2 \times 3 = 6 \)), thereby simulating a scan-time reduction from (11:55±02:01) minutes to (03:58±00:40) minutes for the healthy volunteers. The flow rate \( Q \), the net flow per cardiac cycle \( Q_{\text{net}} \), the peak velocity \( v_{\text{max}} \), and the net average through-plane velocity \( \overline{v}_\perp \) were calculated in eight analysis planes along the ascending and descending aorta. Measurements were taken in each time frame and in each plane. For a given time frame and plane, \( Q \) represents the total flow through the entire plane; \( v_{\text{max}} \) represents the maximum velocity magnitude that occurs in that plane; and \( \overline{v}_\perp \) denotes the through-plane velocity, averaged over the entire plane. The net flow \( Q_{\text{net}} \) results from the time integral over the flow rate.

To ensure comparability between the Cartesian/2D-CAIPI and the wave-CAIPI results, the segmentation of the aorta, as well as the placement of analysis planes, was performed identically for both sampling strategies. The segmentation was performed on the prospectively 2-fold accelerated wave-CAIPI scan and then transferred to the Cartesian/2D-CAIPI scans. The images were visually examined for segmentation errors, caused by patient motion in between the wave-CAIPI and the Cartesian scan. The 4D flow images were processed using a prototype software (4D Flow V2.4; Siemens Healthcare). Images were preprocessed with background phase correction and phase anti-aliasing, separately, for the different acceleration rates. In the prototype software, background phase error was estimated by linear regression of the phase in the stationary tissue, identified by voxels with low phase variance over time.

Deviations in the measured flow parameters (\( Q, Q_{\text{net}}, v_{\text{max}}, \) and \( \overline{v}_\perp \)) were calculated between the reference scans (no retrospective acceleration; prospective undersampling rate \( R = 2 \)) and the retrospectively 6-fold accelerated scans. Hemodynamic flow patterns, visualized using particle traces, streamlines and velocity vectors, were qualitatively compared. Qualitative evaluation of particle traces, streamlines, and velocity vectors was performed by J.A.J.R. and T.W. Flow velocity vectors were calculated in each of the eight analysis planes. Particle traces were set to originate in the analysis plane closest to the aortic root. New particles were inserted into the analysis plane in each cardiac phase, and the tracing duration of the particles was one heart phase. The seeds for the streamline calculation were evenly distributed in the entire volume of the segmented aorta. The streamlines follow the measured velocity vector field and end when the boundary of the segmentation is reached. To investigate systematic errors in flow parameters introduced by the wave-CAIPI trajectory, differences in flow parameters between wave-CAIPI and Cartesian sampling were calculated for an acceleration rate of \( R = 2 \), and a linear regression of the parameter values was performed. Systematic differences were quantified by means of the average (signed) difference of flow parameters between \( R = 2 \) and \( R = 6 \) scans. The \( L_1 \)-norm (average absolute difference) of the difference of flow parameters between \( R = 2 \) and \( R = 6 \) scans was used as a measure of precision, quantifying the average error. Furthermore, the corresponding signed mean difference was used to report on a possible bias that is introduced by the retrospective undersampling from \( R = 2 \) to \( R = 6 \). The effect of undersampling on the flow parameters was also investigated by means of correlation and Bland-Altman plots.

An estimate of image noise was calculated for a wave-CAIPI and a 2D-CAIPI examination of a healthy volunteer, using the pseudo multiple replica method.\textsuperscript{12} To this end, 500 reconstructions of the same data set were performed, each time adding artificial, properly correlated noise. From the fluctuation of pixel intensities across the set of pseudo replicas, the image noise can be estimated. To calculate accurate pseudo replica scans, noise amplitudes and correlations between different receiver elements must be accurate. The noise correlations were measured in a short scan after the MR examination. For this measurement, the same sequence parameters as for actual in vivo imaging were used, with the RF amplitude set to zero. The acquired signal therefore consists only of noise and can be used to calculate a noise covariance matrix to capture noise correlations between the different receive channels.

### 3 RESULTS

The acquisition times of the 4D flow examinations depended on the subject’s specific heart rate and respiratory motion pattern. On average, the scan time was (11:55±02:01)
minutes for the healthy volunteers. The acquisition time for the patient with aortic valve stenosis was 17:15 minutes (prospective acceleration factor \( R = 2 \)).

The investigation of the maximum possible acceleration rate is provided in Figure 2. Box plots of the error in \( v^\perp \) indicate that for wave-CAIPI, \( R = 6 \) is the highest acceptable acceleration rate (median below 0.6 cm/s), whereas for 2D-CAIPI sampling, the defined criterion is not fulfilled already at \( R = 4 \) for most of the cases. For \( R = 8 \), the criterion is violated for all wave-CAIPI and 2D-CAIPI examinations in this study.

Pixel-based velocity differences between \( R = 2 \) and \( R = 6 \) in left–right, anterior–posterior, and head–feet direction are presented in Supporting Information Figure S1 for a healthy volunteer during peak systole.

Two 4D flow examinations (with wave-CAIPI and Cartesian sampling) of a healthy volunteer with prospective acceleration factor \( R = 2 \) are presented in Figure 3 and compared with retrospectively undersampled data sets. Undersampling was performed with respect to the 2D-CAIPI pattern displayed in Figure 1B. Particle traces, originating from a plane near the aortic root, and streamlines along the aorta are displayed on top of a maximum intensity projection of the temporal mean velocity. In the Cartesian 2D-CAIPI case, considerable discrepancies of streamline representations of flow (Figure 3A) between \( R = 2 \) (prospective) and \( R = 6 \) (retrospective) are visible, especially in the descending aorta. In the ascending aorta, an underestimation of flow velocity near the aortic root can be clearly observed from the particle traces (Figure 3B). In contrast, streamlines and particle traces derived from the accelerated \( R = 6 \) wave-CAIPI 4D flow measurement show only minor deviations from the reference acquisition \( R = 2 \).

In Figure 4, a velocity vector representation of flow is displayed in eight planes along the aorta for both sampling strategies at systole (same volunteer as in Figure 3). Consistent with the particle traces in Figure 3B, the vector representation reveals a noticeable underestimation of flow velocities near the aortic root (Figure 4B; plane 1) for the accelerated Cartesian 2D-CAIPI acquisition. In addition, the retrospectively 6-fold accelerated 2D-CAIPI image exhibits an overestimation of flow velocities in the descending aorta (plane 8). Calculations of flow rates reveal a partial underestimation in plane 1, and a partial overestimation in plane 8. Alterations in velocity vectors and net flow-rate calculations due to undersampling are far less pronounced in the wave-CAIPI case (Figure 4A).

The mean absolute differences (L1-norm) and the mean differences in flow rate \( Q \), net flow \( Q_{\text{net}} \), peak velocity \( v_{\text{max}} \), and net average through-plane velocity \( \overline{v}^\perp \) between the \( R = 2 \) and retrospectively accelerated \( R = 6 \) scans are summarized in Table 1, comparing both sampling techniques. Both error measures are lower for wave-CAIPI sampling. Figure 5 shows both error measures for each examined volunteer. On average, the mean absolute differences of the flow parameters for wave-CAIPI sampling was \((34.5 \pm 4.8)\% \) lower for \( Q \), \((36.4 \pm 17.0)\% \) lower for \( Q_{\text{net}} \), \((55.4 \pm 12.1)\% \) lower for \( v_{\text{max}} \), and \((37.0 \pm 6.0)\% \) lower for \( \overline{v}^\perp \), compared with the deviations of the Cartesian/2D-CAIPI scans. In most cases, the mean differences of the flow parameters are lower for wave-CAIPI sampling (Figure 5, lower row).

Figure 6 displays noise maps (with respect to magnitude images) of a wave-CAIPI and a 2D-CAIPI examination of a healthy volunteer in a sagittal slice in late diastole, for a retrospective acceleration factor of \( R = 6 \). The image noise was calculated following the pseudo multiple replica approach.\(^{12}\) On average, the noise level of the 2D-CAIPI image was 3.3 times higher than the noise level in the wave-CAIPI image. In the region of largest noise enhancement, the noise level of the 2D-CAIPI image was 3.3 times higher than the noise level of the wave-CAIPI image.

A correlation plot and a Bland-Altman plot of the calculated flow rates of the wave-CAIPI and Cartesian scans are shown in Figure 7 for \( R = 2 \). The plots show flow rates of all 10 volunteers. The two methods yield comparable values: The average difference and SD are \( \langle Q \rangle = (0.70 \pm 13.74) \) ml/s. The average difference is \( \langle Q_{\text{net}} \rangle = (0.46 \pm 3.84) \) ml for the net flow, \( \langle \Delta v_{\text{max}} \rangle = (1.93 \pm 7.11) \) cm/s for the peak velocity, and \( \langle \Delta \overline{v}^\perp \rangle = (0.18 \pm 3.35) \) cm/s for the net average through-plane velocity. The corresponding correlation and Bland-Altman plots of \( \Delta Q_{\text{net}} \), \( v_{\text{max}} \), and \( \overline{v}^\perp \) are shown in Supporting Information Figure S2.

To investigate possible systematic errors due to undersampling, Figure 8 compares the flow rates of the 2-fold accelerated reference scans to the retrospectively 6-fold accelerated data sets, for both wave-CAIPI and Cartesian/2D-CAIPI

\[ \text{FIGURE 2} \quad \text{Box plots of mean differences in the average through-plane velocity} \overline{v}^\perp \text{as a function of the acceleration factor} \ R. \text{The dashed line represents the acceptable level of variation in} \overline{v}^\perp. \]
sampling. The average difference and SD between flow parameters of accelerated and reference scans are summarized in Table 1. Correlation and Bland-Altman plots comparing $Q_{\text{net}}, v_{\text{max}},$ and $v_{\perp}$ for $R = 2$ and $R = 6$ are shown in Supporting Information Figures S3, S4, and S5, respectively.

In Figure 9, velocity vectors and streamlines are displayed for the wave-CAIPI examination of the patient with aortic valve stenosis, with prospective acceleration factor $R = 2$ and retrospective acceleration factor $R = 6$. Only small differences in vector and streamline representations of flow can be observed. The magnitude of the peak velocity at systole near the aortic root was measured to be $v_{\text{max}} = 237.2$ cm/s for the 2-fold accelerated scan and $v_{\text{max}} = 225.9$ cm/s for the 6-fold accelerated scan, which corresponds to an underestimation of 4.8%. The flow parameters of the $R = 6$ acquisition were subtracted from the parameters of the $R = 2$ acquisition, and the difference was averaged over all time frames and planes. Average absolute differences in flow parameters are $L_1(\Delta Q) = (8.5 \pm 7.4)$ ml/s, $L_1(\Delta Q_{\text{net}}) = (2.7 \pm 2.1)$ ml, $L_1(\Delta v_{\text{max}}) = (6.8 \pm 7.8)$ cm/s and $L_1(\Delta v_{\perp}) = (1.7 \pm 1.4)$ cm/s.

Raw magnitude and phase-difference images for both sampling schemes are shown in Supporting Information Figure S6.

4 | DISCUSSION

Due to the wide voxel-spreading characteristics of the wave-CAIPI k-space trajectory, variations in receive coil sensitivity profiles are exploited more efficiently during the parallel imaging reconstruction. Undersampling in the wave-CAIPI trajectory is distributed more evenly in k-space, compared with Cartesian 2D-CAIPI sampling; therefore, large voids are avoided. Furthermore, because wave-CAIPI aliasing artifacts appear incoherent in the image, residual aliasing artifacts of low amplitude may not be as disturbing as in the 2D-CAIPI images.

As proposed by Gatehouse et al., the maximum possible acceleration rate in this study was defined using flow velocity errors as a quantitative criterion. By declaring errors in calculations of stroke volumes of up to 5% as still acceptable, a mean velocity error of below 0.6 cm/s results as a theoretical limit. In Figure 2, box plots of mean errors in $v_{\perp}$ show that for wave-CAIPI, $R = 6$ is the highest undersampling factor, where the criterion is still fulfilled for most examinations. For 2D-CAIPI sampling, the defined criterion is not fulfilled at $R = 4$ and higher.

Simulation of image noise levels showed a decreased noise enhancement of the wave-CAIPI method, with respect to 2D-CAIPI sampling. As a result, accelerated phase-contrast images can be acquired with higher precision, compared with 2D-CAIPI sampling. Therefore, the calculated values of flow parameters are more stable with respect to scan-time reduction (Figure 5). The visible edges in the noise maps of Figure 6 result from aliasing of the estimated image mask, which is used to set signal outside of the object to zero. In the presented case, the image mask exhibited a vertical line at the mask boundary. The noise level is generally higher in regions of aliasing. Reconstruction of the
**FIGURE 4** Vector representation of blood flow in eight planes (labeled 1-8) along the aorta for wave-CAIPI (A) and Cartesian/2D-CAIPI (B) sampling at 2-fold and 6-fold acceleration at peak systole (time frame 3/14). Calculations of net flow rates in plane 1 and plane 8 are shown on the right for the respective sampling strategy. Both vector representation and flow-rate calculations reveal an underestimation of flow velocity in plane 1 and an overestimation of flow velocity in plane 8 in the 2D-CAIPI case. White arrows point to regions in the accelerated scans that exhibit significant deviations from the reference scans.

**TABLE 1** Average differences and average absolute differences in flow parameters between accelerated ($R = 6$) and reference ($R = 2$) wave-CAIPI and Cartesian/2D-CAIPI 4D flow acquisitions

| Parameter | Wave-CAIPI | Cartesian/2D-CAIPI |
| --- | --- | --- |
| Average Differences | | |
| Mean ± SD | 2.63 ± 12.73 | 3.51 ± 19.13 |
| Median | 2.57 | 3.65 |
| Average Absolute Differences | | |
| Mean ± SD | 9.03 ± 2.67 | 13.73 ± 3.66 |
| Median | 8.96 | 13.85 |
undersampled data with the masked sensitivity maps therefore leads to visibility of the image mask boundary in the noise map. Variations of noise amplitude can be related to the ill-conditioning of the SENSE reconstruction and are affected, for instance, by sensitivity maps. The reduced noise level in undersampled wave-CAIPI reconstructions can be noted in the phase-contrast difference images in Supporting Information Figure S1. The wave-CAIPI technique exhibits

**FIGURE 5** Mean absolute differences (top row) and mean signed difference (lower row) of flow parameters between retrospectively accelerated ($R = 6$) and reference ($R = 2$) 4D flow MRIs, using Cartesian/2D-CAIPI and wave-CAIPI sampling

**FIGURE 6** Noise levels in $R = 6$ accelerated wave-CAIPI (left) and 2D-CAIPI (right) magnitude images. The noise levels were normalized to the range of $[0, 1]$. The lower row of images presents the magnitude images for both sampling; the upper row presents the corresponding noise maps.
FIGURE 7  Correlation plot (A) and Bland-Altman plot (B) comparing the flow rate $Q$ of Cartesian and wave-CAIPI acquisitions of 10 healthy volunteers for an acceleration rate of $R = 2$. In each volunteer, eight planes along the aortic arch are used for flow quantification during each cardiac phase.

FIGURE 8  Correlation plot (A) and Bland-Altman plot (B) comparing the flow rate $Q$ of wave-CAIPI scans with acceleration rate $R = 2$ and $R = 6$. The correlation plot in (C) and the Bland-Altman plot in (D) compare the flow rate of a Cartesian acquisition with $R = 2$ to a 2D-CAIPI scan with $R = 6$. 
Table 1 demonstrates that using the wave-CAIPI sampling technique in 6-fold undersampled 4D flow MRI, errors in the calculated flow parameters can be reduced, taking the 2-fold accelerated scan as a reference. Average and median values of flow-parameter differences are consistently comparable to those of previous reports on undersampled ranges of variability in the measured flow parameters. For 6-fold accelerated wave-CAIPI, the observed differences in flow parameters between \( R = 2 \) and \( R = 6 \) serve to quantify a bias that is introduced by this retrospective acceleration. This bias can, however, not be interpreted as a measure of accuracy of the flow parameters, as such a measure requires a ground truth for comparison, which is not available in this in vivo study.

As it is typical for patients with aortic valve stenosis, the streamline representation of aortic flow in Figure 9B displays localized flow acceleration near the outer wall of the aorta during systole. In addition, the flow velocity vectors in Figure 9A near the aortic root exhibit an uneven cross-sectional velocity distribution. The retrospectively 6-fold accelerated wave-CAIPI scan is able to reproduce the complex flow patterns from the 2-fold accelerated reference. Mean absolute differences in flow parameters (quantified by the L1-norm of the difference between the \( R = 2 \) and the \( R = 6 \) flow parameters) lie within the expected range of variability, as estimated from the volunteer examinations (Figure 5).

For different target applications, previous works on parallel imaging reconstructions with wave-CAIPI sampling report acceleration factors ranging from \( R = 6 \) to \( R = 16 \). In the present work, the acceleration factor was limited to \( R = 6 \), as additional aliasing from the imperfect RF excitation pulse further reduced the size of the fully encoded FOV, therefore adding to the degree of undersampling. This effect could theoretically be mitigated by using moderate slice oversampling, although at the expense of additional scan time. The acceleration in this work was done in retrospective; as in all cases, the results from the reference scan with \( R = 2 \) were needed for comparison and accurate error estimation.

The scan time of the presented pulse sequence depended on the subject’s specific breathing pattern as well as the heart rate, and was therefore unpredictable. Interesting approaches toward predictable scan times in 4D flow MRI were previously investigated and are based on retrospective respiratory and cardiac self-gating. Such an approach can allow for retrospective adjustment of navigator efficiency and temporal resolution, and could be combined with the wave-CAIPI technique.

In this work, the 4D flow data sets were reconstructed with SENSE. An interesting reconstruction technique, which includes temporal correlations in the reconstruction, is k-t GRAPPA and could be used for the acceleration of 4D flow MRI. Other approaches used compressed sensing to make use of the correlations in the temporal and flow-encoding direction. Especially in dynamic phase-contrast MRI, the appropriate choice of regularization parameters for the best compromise among temporal fidelity, image noise, and residual undersampling artifacts is challenging. In a previous study by Ma et al., 4D flow measurements could be reconstructed using compressed sensing for acquisition

![Velocity Vectors](image1)

![Streamlines](image2)

**FIGURE 9** A, Flow velocity vectors in the aortic arch of a patient with aortic valve stenosis during late diastole (frame 7/14), at an angulated view, for acceleration factors \( R = 2 \) and \( R = 6 \). B, Streamlines in the same patient during systole (frame 4/14), in coronal orientation. Along the outer wall of the aorta, increased flow velocities can be observed.
times as short as 2 minutes. However, highly accelerated acquisitions came at the cost of reduced temporal fidelity, resulting in an underestimation of peak flow velocities. A promising extension of the presented work would be the reconstruction of wave-CAIPI 4D flow data sets with compressed sensing, exploiting correlations in the temporal and flow-encoding direction. For this purpose, the sampling pattern in the individual cardiac phases would have to be varied from frame to frame, to yield temporal incoherence for the undersampling artifacts.

The used study population included predominantly healthy volunteers with an average age of 25.3 years. Challenges can arise when applying the presented method to patients. Patients may be uncomfortable in the MR scanner, and therefore could be more prone to motion. Furthermore, different body habitus may require adjustment of pulse sequence parameters. Finally, complex hemodynamic flow patterns of patients with cardiac diseases differ from those of healthy volunteers and may be more difficult to capture with 4D flow MRI. In patients with aortic valve stenosis, for example, increased flow velocities may require an increased encoded flow velocity, leading to increased overall noise in flow quantification.

Limitations of this study comprise the offline image reconstruction and the necessity for gradient correction. For a clinically acceptable workflow, an automatic image reconstruction would have to be implemented directly on the MR scanner. Furthermore, the used gradient correction, based on the system-specific gradient system transfer function, requires characterization of the gradient system by means of additional phantom scans. In addition, parallel imaging reconstructions with wave-CAIPI may, in general, require more computation time than standard Cartesian imaging. Finally, flow quantification should be available at the scanner, to include 4D flow examinations in the clinical routine.

5 | CONCLUSIONS

Using wave-CAIPI instead of 2D-CAIPI sampling in accelerated 4D flow MRI, the precision of measured flow parameters could be enhanced. Due to a reduced noise enhancement in parallel imaging reconstructions with wave-CAIPI, 6-fold acceleration of the acquisition could be achieved, with only minor deviations in the visualization of complex hemodynamic patterns.

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CONFLICT OF INTEREST

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found online in the Supporting Information section.

**FIGURE S1** Pixel-level velocity differences ([R = 2]−[R = 6]) for wave-CAIPI (controlled aliasing in parallel imaging) and Cartesian/2D-CAIPI sampling in left–right, anterior–posterior, and head–feet direction.

**FIGURE S2** Correlation plots and Bland-Altman plots comparing net-flow $Q_{\text{net}}$ (A,B), peak velocity $v_{\text{max}}$ (C,D), and net average through-plane velocity $\bar{v}_x$ (E,F) in Cartesian and wave-CAIPI acquisitions of 10 healthy volunteers with $R = 2$. In each volunteer, eight planes along the aortic arch are used for flow quantification.

**FIGURE S3** Correlation plot (A) and Bland-Altman plot (B) comparing the net-flow $Q_{\text{net}}$ of wave-CAIPI scans with acceleration rate $R = 2$ and $R = 6$. The correlation plot in (C) and the Bland-Altman plot in (D) compare $Q_{\text{net}}$ of a Cartesian acquisition with $R = 2$ to a 2D-CAIPI scan with $R = 6$. In the Cartesian case, the values of $Q_{\text{net}}$ exhibit a larger spread.

**FIGURE S4** Correlation plot (A) and Bland-Altman plot (B) comparing the peak velocity $v_{\text{max}}$ of wave-CAIPI scans with acceleration rate $R = 2$ and $R = 6$. The correlation plot in (C)
and the Bland-Altman plot in (D) compare $v_{\text{max}}$ of a Cartesian acquisition with $R = 2$ to a 2D-CAIPI scan with $R = 6$. In the Cartesian case, the values of $v_{\text{max}}$ exhibit a larger spread.

**FIGURE S5** Correlation plot (A) and Bland-Altman plot (B) comparing the net-average through-plane velocity $v^\perp$ of wave-CAIPI scans with acceleration rate $R = 2$ and $R = 6$. The correlation plot in (C) and the Bland-Altman plot in (D) compare $v^\perp$ of a Cartesian acquisition with $R = 2$ to a 2D-CAIPI scan with $R = 6$. In the Cartesian case, the values of $v^\perp$ exhibit a larger spread.

**FIGURE S6** Magnitude and phase-difference images of a healthy volunteer examination, comparing wave-CAIPI and Cartesian/2D-CAIPI sampling for 2-fold and 6-fold acceleration.

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