Cardiac 4D phase-contrast MRI at 9.4 T using self-gated ultra-short echo time (UTE) imaging

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Abstract: In this work we present a 4D phase-contrast UTE acquisition strategy that uses the shortest possible echo-times in combination with an efficient self-gating navigator signal extracted from the oversampled center of k-space. The proposed technique was validated in both flow phantoms and healthy mouse hearts. Image quality and quantitative flow analysis results were furthermore compared with those obtained with a standard ECG-gated Cartesian 4D PC FLASH sequence on a 9.4 T small-animal MR system.

Zusammenfassung: In der vorliegenden Arbeit präsentieren wir eine 4D Phasenkontrast UTE Bildgebungssequenz mit kürzest möglichen Echozeiten und effizienter Selbsttriggerung basierend auf Daten aus dem von jedem Readout überabgetasteten k-Raum Zentrum. Die Bildgebungstechnik wurde anhand von Phantom- und in vivo Mausmessungen validiert und mit einer EKG-getriggerten Kartesischen 4D Phasenkotrast FLASH Sequenz an einem 9.4 T Kleintier MRT verglichen.

Background

Quantitative blood flow analysis using 4D time-resolved phase-contrast magnetic resonance imaging (4D PC MRI) is a valuable tool for studying the cardiovascular system in humans and animals (1). In pre clinical studies the non-invasive character of PC MRI has the potential to enable monitoring of cardiac diseases in animal models longitudinally over time. However, the technique is challenging to apply in the murine heart for several reasons. One major limitation of the currently established Cartesian 4D PC MRI techniques (2) are the relatively long echo times (TE) of 2 ms and longer (3), which are a direct consequence of the required flow encoding and three-dimensional volume encoding in Cartesian gradient echo sequences. In combination with the fast blood flow in the murine heart this often leads to signal dropouts in the images or erroneous flow velocities due to intravoxel dephasing and turbulent fluctuations. In addition, robust and reliable respiratory and cardiac triggering over extended periods of time (2) is required. External ECG gating, however, prolongs preparation time of the animals and often suffers from interferences with the magnetic and radio-frequency fields, which causes unreliable or unstable trigger signals.

To overcome the described limitations we present in this work a self-gated ultra-short echo-time (UTE) acquisition with phase-contrast for quantitative blood flow analysis in mice at 9.4 T.

Material and Methods

All measurements were performed on a 9.4 T Bruker BioSpec USR 94/20 MR scanner with a horizontal bore of 20 cm, a gradient system of 660 mT/m and ParaVision 6.0.1 operation software (Bruker BioSpin, Ettlingen). For the acquisition of data in vitro, a vendor supplied 40-mm-diameter mouse body quadrature volume coil was used. In vivo experiments were conducted in healthy mice (male, C57BL/6J, 6 months old) with a vendor supplied two-channel quadrature cryoprobe.

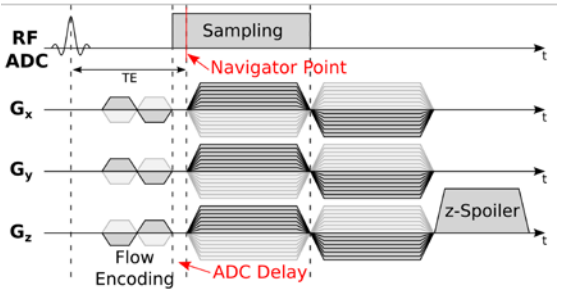

Fig. 1: Sequence diagram of the flow encoded time-resolved 4D UTE acquisition. The navigator location obtained from the center of k-space is indicated, as are the ADC delay and the constant spoiler in z-direction. To realize a cone-by-cone UTE sampling; the readout gradient strengths were modulated in the x, y and z directions according to (4).

MRI pulse sequences

A vendor supplied center-out cone by cone 3D UTE imaging sequence was modified by including a four-point Hadamard flow encoding scheme (5). To extract a stable navigator signal from the center of k-space of the entire non-selectively excited 3D volume two crucial modifications were made to the imaging sequence. First, a constant z-spoiling was added because one major source for unwanted contamination of the sensitive navigator signal is the magnetization from previous excitations. The second artifact source originates from digital filter artifacts in the first data points of the ADC (4). To allow for sufficient time for the ADC signal to stabilize, the ADC was switched on 100 µs prior to the start of the readout, discarding data points sampled during this time interval. The gradient and data sampling scheme is presented in Figure 1.

As comparison data were also acquired with a vendor supplied, prospectively triggered Cartesian 4D PC FLASH.

Self-Gating and Image Reconstruction

An intrinsic navigator signal was obtained from each acquired read-out by taking the last data point sampled just before the start of the readout gradient. Depending on the measurement conditions and quality of the navigator signal either magnitude or phase information was manually selected from one of the receiver coil channels. After selection of the best navigator function a second order Savitzky-Golay smoothing filter [6] with a width of 90 ms was applied, followed by peak detection employing first-order difference information to detect cardiac cycle onsets. Regarding respiratory motion, the input navigator function was smoothed with a broader Savitzky-Golay filter with a width of 400 ms followed again by peak detection. Around each respiratory onset an asymmetric exclusion window of 250 ms duration was placed. To reconstruct consecutive cardiac cine frames a sliding-window was applied with window width of 15.5 ms and a frame-to-frame shift of 3.1 ms. A total of 48 cine frames spanning 150 ms were reconstructed. The radial trajectory was measured using a vendor supplied calibration scan.

Image reconstruction of the 3D volume was performed offline using state-of-the art regridding with iterative sampling density estimation and an optimized kernel (7).

In vitro flow measurements

For validation of the 4D UTE PC sequence phantom measurements were performed using a home-built flow phantom containing four tubes with a diameter of 3 mm placed inside a water-filled cylindrical acrylic glass body with a diameter of 30 mm [2] attached to a peristaltic pump (Medorex e.K., Hörten-Hardenberg). As gold-standard a vendor supplied Cartesian 3D FLASH based flow mapping imaging sequence (Bruker BioSpin, Ettlingen) was used. The Cartesian FLASH sequence used: a 25% readout Partial Fourier factor, 2.5 ms TE, 6.5 ms TR, 1h 25min total acquisition time (TA), 4 averages. The 4D PC UTE sequence used parameters: 0.5 ms TE, 5.0 ms TR, 1h 45min TA, 2 averages. Both imaging sequences acquired data with a 10° flip angle, FOV of 32 x 32 x 32 mm³ and an acquisition matrix size of 200 x 200 x 200 using a 40-mm-diameter quadrature volume coil. To account for the varied pump rates of 200, 400, 600 and 750 ml/min, the strength of the flow encoding gradients was adjusted to a maximum flow (venc) of 50, 90, 150, 200 cm/s in both sequences, respectively.

In vivo blood flow measurements

Measurements were performed in a group of ten healthy mice using either the Cartesian FLASH sequence with ECG- and respiratory gating as gold-standard (n = 5) or the proposed time-resolved 4D PC UTE imaging sequence with self-gated acquisition (n = 5). A mixture of 1.5% to 2.5% isoflurane and O2 was used for inhalation anesthesia. For optimum positioning of the mouse heart with respect to the tight cryoprobe the animals were positioned on their back. The total time in the MR scanner, including positioning, ECG setup, localization and shimming, was kept below 3 hours. During all experiments body temperature and respiration were monitored. All measurements were performed with a FOV of 22 x 22 x 22 mm³ to cover the whole heart and an acquisition matrix size of 96 x 96 x 96, resulting in an isotropic resolution of 230 µm. To minimize the TE of the Cartesian FLASH sequence, a 25% readout Partial Fourier acquisition with TE of 2.1 ms and TR of 5.0 ms was used with an acquisition bandwidth of 85 kHz. For the UTE acquisition both TE and TR could be shortened to 0.5 ms and 3.1 ms, respectively, while using an acquisition bandwidth of 150 kHz. Both sequences used an excitation flip angle of 10° realized with a 40 µs hard-pulse (UTE) and a 3D slab-selective sinc-pulse (FLASH). With the Cartesian FLASH sequence

20 frames of the cardiac cycle were acquired with an effective TA between 1h35min and 1h55 min, depending on the gating efficiency. For the self-gated UTE sequence a fixed TA of 1h 58min was used during which 20 repetitions, each containing 28733 radial readouts per flow encoding direction, were acquired. For all measurements in vivo the flow encoding gradients were adjusted to a venc of 120 cm/s.

Results

In vitro flow measurements

To validate the 4D PC UTE sequence we performed flow measurements on a flow phantom adjusted to different pump rates (Fig. 2). The velocity profiles across the tubes (Fig. 2, top left) showed close agreement between both sequences, with the Cartesian FLASH sequence yielding slightly higher flow velocities. This became also evident when determining the flow volume for different pump rates and averaging over all four tubes (Fig. 2, bottom). For all pump rates, the Cartesian FLASH sequence provided slightly higher flow velocities with an average deviation from the UTE sequence of 2.2 ± 1.6 %. For both sequences the flow volumes did coincide with the pump setting (gray area in Figure 2).

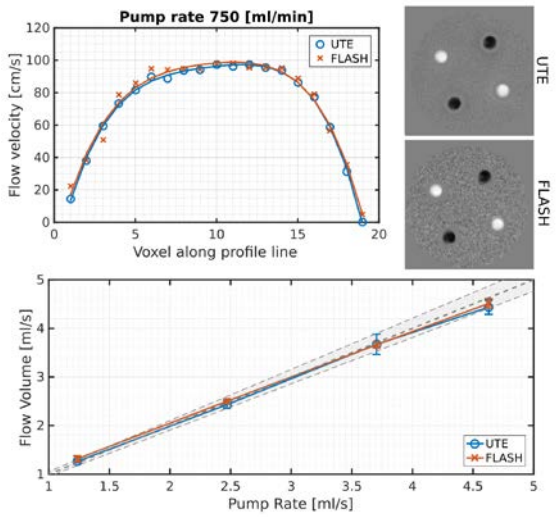

Fig. 2: Axial view of the central slice through the flow phantom acquired with the 4D PC UTE and the Cartesian PC FLASH sequence (top, right), corresponding flow profiles of one tube for a pump rate of 750 ml/min (top, left) as well as the flow volume averaged over all tubes for different pump rates (bottom).

In vivo flow self-gating

For 4D PC UTE flow measurements in vivo a reliable navigator signal was extracted from the oversampled k-space. Exemplary navigator signals from the k-space center magnitude are shown in Figure 3. A clear navigator signal showing both cardiac and respiratory motion could be extracted which was well suited for the automatic detection of both cardiac and respiratory signal modulations. The average gating efficiency of the self-gated 4D UTE sequence was 61.8 % ± 11.5 % while the Cartesian FLASH sequence showed a smaller gating efficiency of 48.5 % ± 4.9 % due to the active ECG and respiratory gating. While the actively triggered Cartesian FLASH sequence naturally had k-space coverage of 100%, the coverage was smaller with the UTE sequence as only 85.1% ± 8.4% of radial rotation angles required for full k-space coverage were measured. Over the total measurement duration of 2 hours the navigator signal was stable and showed an average error rate of wrongly detected cardiac onsets of 4.3 ± 2.4 %.

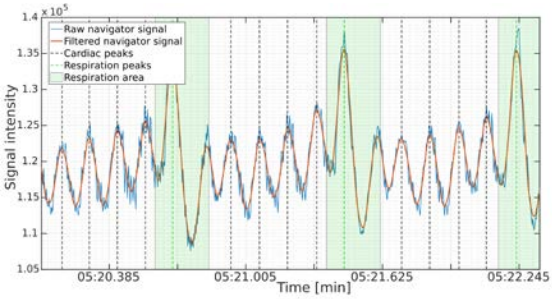

Fig. 3: Navigator signal extracted from the magnitude of the k-space center before (blue) and after (red) filtering. The black dashed lines and the green dashed line indicate the detected cardiac and respiratory onsets, respectively. Also shown are the respiration windows within which all data are discarded.

In vivo flow measurements

The peak blood flow velocities in the AAO were 132.8 ± 18.3 cm/s and 134.7 ± 13.4 cm/s for the UTE and Cartesian FLASH sequence, respectively. Results obtained for the PMA were also similar for both sequences with respective values of 78.5 ± 15.4 cm/s (UTE) and 86.6 ± 6.2 cm/s (FLASH). The averaged temporal velocity waveforms over all animals in the PMA and AAO, revealed good conformity in amplitude and temporal evolution (Fig. 4) for both sequences. A higher temporal resolution due to the shorter TR and due to a greater number of time frames that could be reconstructed retrospectively was achieved for the UTE sequence compared to the FLASH reference.

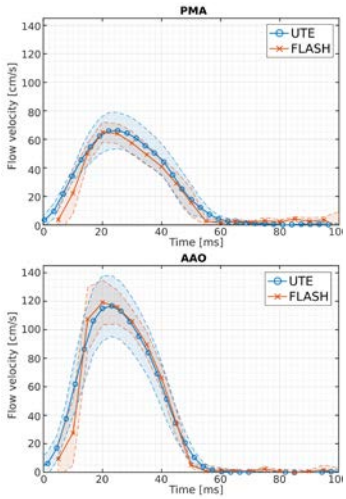

Fig. 4: Flow velocity-time course averaged over five animals in the pulmonary artery (PMA) (a) and ascending aorta (AAO) (b) for the 4D PC UTE (blue) and the Cartesian FLASH (red) sequence. The colored error bands indicate the standard deviation over all animals.

In addition substantial differences in image quality were noticed, when comparing the magnitude images (Fig. 5, left). The UTE images were free of major artifacts with SNR (left ventricular cavity: 8.9 ± 2.5, myocardium: 15.7 ± 1.9) and CNR (7.8 ± 2.4) values that were nearly a factor of two higher than the values obtained from the Cartesian FLASH reference (Tab. 1). In comparison to the UTE images, the Cartesian FLASH sequence had diffuse artifacts overlaying the images with changing shapes and positions in each time frame. This also affected the calculation of the flow velocity maps with the FLASH sequence showing more noise both in the vessels and in static areas such as the myocardium where no flow was supposed to occur. The standard deviation of the flow velocity in the myocardium exhibited a reduced flow noise of 3.2 ± 1.1 cm/s with the UTE sequence compared to 10.8 ± 6.8 cm/s of the Cartesian FLASH.

A reformatted slice of the velocity encoded 4D volumes showing the inflow of the right ventricular (Fig. 5, right) reveals again distinctly reduced artifacts in the UTE images, the tricuspid valve becaming clearly visible.

Discussion

Our proposed self-gated 4D PC UTE sequence enabled measuring flow velocities of the whole heart in all three spatial dimensions with full temporal coverage of the cardiac cycle in healthy mice. Compared to a vendor supplied Cartesian 4D PC FLASH sequence, image and flow artifacts were substantially reduced accompanied by higher SNR and CNR. In addition active external ECG gating was unnecessary. One of the reasons for the high performance of the UTE technique is the radial center-out 3D acquisition which renders the measurement very robust against motion related k-space inconsistencies which are inevitably occurring during long acquisition times in vivo.

Even though the applied center-out 3D UTE sampling technique requires more readouts by a factor of π to fill 3D k-space completely compared to the prospectively gated Cartesian FLASH sequence, the overall measurement time was the same for both sequences. The increased amount of required readouts can be compensated by shorter echo- and repetition-times in combination with an efficient retrospective gating strategy. Moreover, animal preparation and handling can be accelerated substantially, as the placing of ECG electrodes can be avoided completely. The navigator signal extracted from the center of the three-dimensional k-space turned out to be very reliable over the long measurement durations. Aside from the differences in the noise of the flow velocity maps, SNR, CNR and image quality, our results show that averaged flow velocities obtained in vivo in larger arteries closely agree between the UTE and the Cartesian FLASH sequences. This is in line with the results from phantom measurements which also revealed identical flow values for both techniques.

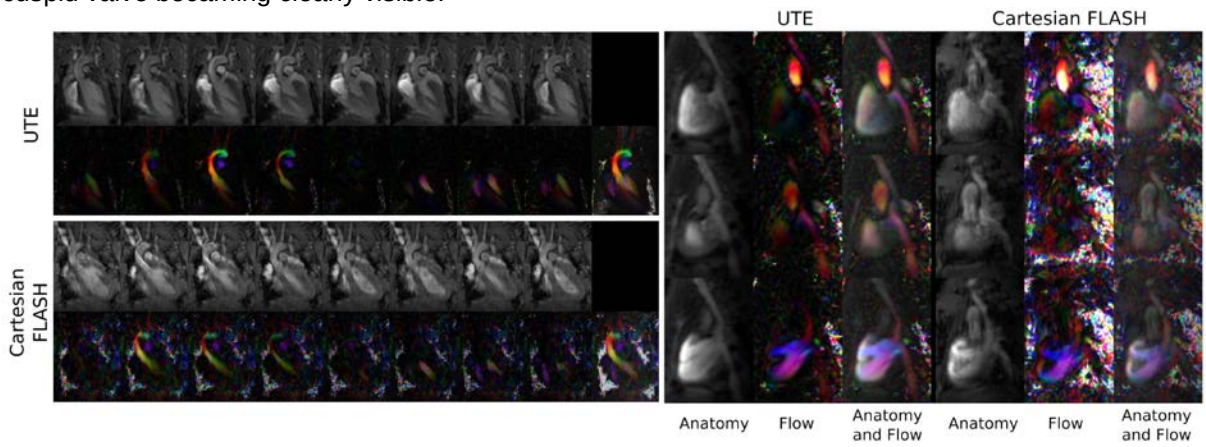

Fig. 5: Anatomic magnitude images and color-coded flow velocity images of a coronal single slice through the left ventricle (left) and right ventricle (right). On the left: 8 frames of the cardiac cycle and a maximum intensity projection over all frames are shown from left to right, respectively. On the right: 3 frames from top to bottom are shown. The flow velocity maps are color encoded and are scaled between the velocities of 0 and 120 cm/s (left) and 0 and 60 cm/s (right). Note that images all were obtained from different measurement sessions and mice.

	SNR LV	SNR MC	CNR	Flow velocity noise [cm/s]	Peak flow velocity AAO [cm/s]	Peak flow velocity PMA [cm/s]
UTE (n=5)	8.9 ± 2.5	15.7 ± 1.9	7.8 ± 2.4	3.2 ± 1.1	132.8 ± 18.3	78.5 ± 15.4
FLASH (n=5)	5.6 ± 1.2	10.1 ± 1.4	4.5 ± 2.2	10.8 ± 6.8	134.7 ± 13.4	86.6 ± 6.2

Table 1: Quality parameters of images and flow velocity maps averaged over all performed measurements: signal-to-noise ratio (SNR), left ventricular cavity (LV), myocardium (MC), contrast to noise ratio (CNR), pulmonary artery (PMA) and ascending aorta (AAO).

Although more cine frames could be reconstructed with the UTE PC sequence one has to keep in mind that the used sliding-window-reconstruction will cause a slight broadening of the temporal flow velocity profile due to its effect as a moving average filter. With respect to the measured peak velocities, the broadening should, however, have only a small effect since the temporal evolution of the peak flow in mice has a peak width of about 25 to 40 ms which is much larger than the 15.5 ms width of the sliding-window. Moreover, the width of the sliding-window can potentially also be reduced to 9.1 ms if a very accurate evaluation of the temporal flow velocity profile is desired.

In the present study, experiments were performed on healthy mice and it has not yet been investigated if the proposed self-gating based on the oversampled signal of the 3D k-space center will also provide reliable results in mice with altered hemodynamics. However, it has previously been shown that cardiac k-zero self-gated 2D UTE imaging can be performed in mice with myocardial infarction (8) and arrhythmia (9). With an appropriate modification of our proposed self-gating analysis, e.g. by excluding self-gating signal abnormalities from image reconstruction, detection of arrhythmia is expected to be feasible.

Conclusion

We have shown that the proposed self-gated 4D PC UTE sequence enables robust and accurate flow velocity mapping of the mouse heart in vivo at high magnetic fields. Due to the radial nature of the acquisition, artifacts in the anatomic magnitude images as well as in the calculated flow velocity maps are reduced when compared to a well-established, ECG-triggered, 4D PC FLASH sequence. In comparison to the Cartesian reference both anatomic SNR and CNR as well as flow velocity SNR are improved at the same time. The used self-gating, based on information obtained from the oversampled k-space center, was very reliable over several hours of measurement time and resulted in an improved gating efficiency when compared to active ECG gating.

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