Aortic Pulse Wave Velocities Using Real-Time Phase-Contrast MRI

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Abstract: *Purpose:* To evaluate aortic pulse wave velocities obtained by real-time phase-contrast (PC) MRI in comparison to cine PC MRI.

Methods: Real-time PC MRI of eight healthy volunteers employed highly undersampled radial FLASH sequences and phase-sensitive image reconstructions by regularized nonlinear inversion (NLINV) at 40 ms temporal resolution and 1.3 mm in-plane resolution. Pulse wave velocities were analyzed for combinations of 2, 3 and 4 locations of aortic flow using time-to-upslope and cross-correlation methods.

Results: For the time-to-upslope analysis mean pulse wave velocities ranged from 3.5 to 3.9 m s^{-1} for real-time PC MRI and from 3.5 to 3.8 m s^{-1} for cine PC MRI. A cross-correlation analysis of the same data resulted in 2.9 to 3.3 m s^{-1} and 3.3 to 3.7 m s^{-1}, respectively.

Conclusion: Real-time PC MRI determined aortic pulse wave velocities from single cardiac cycles in close correspondence to values obtained by cine PC MRI.

Keywords: Real-time MRI, Phase-contrast MRI, Pulse wave velocity, Blood flow.

INTRODUCTION

The pulse wave velocity (PWV) describes the pulse wave of blood flow through the aorta and reflects its elastic properties [1, 2]. It is considered as a biomarker or indicator of aortic stiffness [3] which is an important sequela of diseases such as artherosclerosis [4], stroke [5], and hypertension [6]. PWV is usually calculated from the distance travelled by the pulse wave between at least two locations along the aorta divided by the time needed. This transit time may be obtained from respective flow curves using different proposed analysis methods (see below). A pressure catheter is considered as gold standard for aortic PWV determination, but is not frequently applied due to its invasive nature [7]. Alternative methods determine peripheral PWV by a variety of tools such as, for example, sphygmomanometers in order to derive aortic PWV with the use of invasively validated algorithms [8-10]. Instead of these approaches, however, the focus has shifted to the use of cine phase-contrast (PC) MRI where the acquisition extends over multiple heartbeats with synchronization to the electrocardiogram (ECG), but allows for noninvasive flow velocity measurements from arbitrary positions along the aorta [11-13]. The method determines the velocity of through-plane flow in a single averaged cardiac cycle which is retrospectively reconstructed from multiple heartbeats. It may be extended to multi-dimensional PC MRI which encodes velocity in three dimensions at the expense of prolonged measuring time [14, 15]. In fact, cine 2D PC MRI and 4D PC MRI methods under free breathing conditions have typical measuring times of about 3.5 min and at least 10 min, respectively. Therefore, real-time MRI techniques using echo-planar [16], spiral [17-20] or radial encoding strategies [21, 22] in combination with data undersampling and parallel imaging [23-25] gained increasing interest for flow assessments. However, only few studies using one-dimensional MRI techniques have attempted to analyze PWV in real time [26, 27]. This situation may now be overcome by recent advances in real-time MRI which combine highly undersampled radial fast low-angle shot (FLASH) acquisitions with image reconstructions by regularized nonlinear inversion (NLINV) [28-32]. This technique has been adapted to PC MRI to obtain flow information in real time [33-36]. The aim of this study was to evaluate the performance and potential of PWV determinations based on real-time PC MRI in comparison to conventional cine PC MRI.

METHODS

Subjects

Nine young volunteers (7 male, 2 female, mean age 26.8 ± 3.3 years) without known cardiovascular illness were

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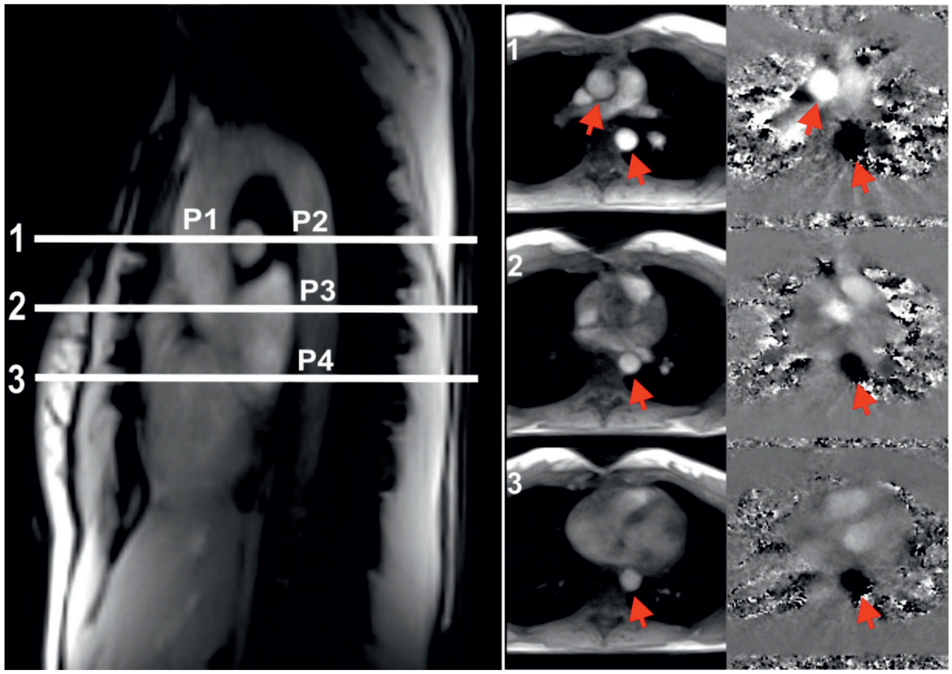

Fig. (1). MRI of aortic blood flow. (Left) Sections 1, 2 and 3 selected for measurements in positions P1, P2, P3 and P4. (Right) Corresponding magnitude images and phase-difference maps obtained from real-time phase-contrast MRI (arrows = vascular lumen of interest).

recruited for this study. One male subject had to be excluded because of abnormal high pulse wave velocities. Written informed consent, according to the recommendations of the local ethics committee, was obtained from all subjects prior to MRI.

MRI

All experiments were performed on a 3 Tesla (T) MRI system (Magnetom TIM Trio, Siemens Healthcare, Erlangen, Germany) with the use of a 16-channel anterior and 16-channel posterior body receive coil. Flow velocities in the aorta were obtained using real-time and electrocardiogram-(ECG) synchronized cine PC MRI under free breathing conditions. Real-time PC MRI was based on highly undersampled radial FLASH acquisitions with phase-sensitive NLINV reconstruction as previously described [33, 34]. The temporal accuracy of NLINV reconstructions has experimentally been confirmed [37], in particular for situations without temporal filtering as used here for real-time PC velocity maps. All PC MRI measurements were performed with an in-plane resolution of 1.3 mm, slice thickness of 6 mm, and velocity-encoding gradients corresponding to a maximum velocity of 200 cm s^{-1}. Other parameters for free-breathing cine PC MRI with Cartesian encoding and retrospective sorting (standard sequence of the vendor) were: TR = 20.05 ms, TE = 2.18 ms, flip angle = 25 degree, 3 averages, 30 cardiac phases, field of view (FOV) = 320 × 320 mm^2, base resolution 256 × 256 mm^2, measuring time 3.5 min.

Real-time PC MRI with undersampled radial encoding employed the following parameters: TR = 2.86 ms, TE = 1.93 ms, flip angle = 10 degree, 7 radial spokes per image (with and without flow-encoding gradient in a sequential acquisition mode), FOV = 192 × 192 mm^2, base resolution 144 × 144 mm^2, measuring time 40 ms for each pair of magnitude image and phase-difference map. Typically, real-time acquisitions were performed for a period of 15 s corresponding to 375 magnitude images and PC maps. Online reconstruction and display of real-time images with minimal delay was achieved by a parallelized version of the NLINV algorithm [38] and a bypass computer (sysGen/TYAN Octuple-GPU, Sysgen, Bremen, Germany) which was equipped with 8 graphical processing units (GeForce GTX, TITAN, NVIDIA, Santa Clara, CA) and fully integrated into the reconstruction pipeline of the commercial MRI system.

Three slice positions covering four locations along the aorta were chosen for flow measurements and PWV evaluations as shown in Fig. (**1**). Real-time PC MRI for the first slice was repeated three times to evaluate the reproducibility of aortic PWV determinations from just one section (or two positions). The total examination time per subject, including the long cine PC MRI acquisitions, was about 30 min.

Flow and Aortic PWV Analysis

The quantitative flow analysis of PC MRI data was performed with prototype software (Fraunhofer MEVIS, Bremen, Germany), especially modified for the automated analysis of real-time MRI acquisitions. Flow evaluations were performed for 10 consecutive cardiac cycles. As common practice for PC MRI, PWV determinations were based on the time courses of mean velocities (i.e., spatially averaged across the aortic lumen) which were fitted with in-house programs written in Matlab (Mathworks, USA). The

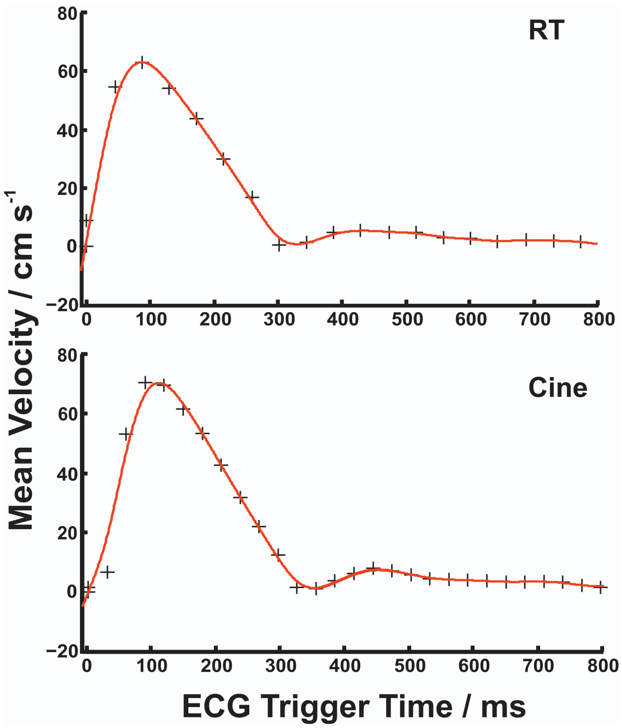

Fig. (2). Mean blood flow velocities in the ascending aorta. Real-time (RT) and cine (Cine) phase-contrast MRI data as a function of time after the R wave.

analyses were performed for two positions (P1, P2), three positions (P1, P3, P4) and four positions (P1, P2, P3, P4) as shown in Fig. (**1**). Respective distances were estimated by taking the center line along the aorta using Syngo MR (Siemens Healthcare, Erlangen, Germany).

The transit times between different regions were measured according to previously proposed methods characterized as time-to-foot, time-to-peak, time-to-upslope (TTU) and cross correlation (XCor), see [15, 39-42] for detailed definitions. However, because preliminary trials proved TTU and XCor to be much more robust than the first two approaches which rely on the correct identification of only a single data point, only TTU and XCor were chosen for the analyses presented here. TTU is defined as the midpoint of the velocity upslope to peak systole. It is obtained by fitting a straight line between data points within an interval given by 20 to 80% of the maximum velocity. The XCor method employs a cross-correlation of the velocity time courses for two locations and thereby directly determines the relative time shift.

RESULTS

Fig. (**2**) depicts the mean velocities in the ascending aorta as a function of time after the R wave for real-time PC MRI (single cycle) and cine PC MRI. The resulting absolute velocities as well as the overall time courses and respective fits are very similar in all cases. The aortic PWV values obtained for real-time PC MRI in a single section (2 positions) are summarized in Table **1** for three consecutive measurements per subject and both TTU and XCor analysis. The values correspond to the mean and standard deviation obtained for 10 consecutive cardiac cycles. It turns out that the XCor analysis results in systematically lower PWV values than the TTU method. In any case, in most subjects real-time PC MRI is characterized by a high intrasubject reproducibility. Nevertheless, physiological variations such as an initial excitement or arousal during the first measurement cannot be excluded as, for example, seen in subjects #6 and #8.

Table **2** compares corresponding mean values averaged across subjects for real-time PC MRI and cine PC MRI for both analysis methods and 2, 3 and 4 locations. In particular for the TTU method, PWV values are in close agreement for both techniques. It should be noted that the standard deviations for real-time PWV values predominantly reflect beat-to-beat variations in response to true physiological influences. These effects include the aforementioned differences

Table 1. Aortic pulse wave velocities using real-time phase-contrast MRI.

Subject	Time To Upslope			Cross Correlation		
	1	2	3	1	2	3
# 1	4.0 ± 1.2	4.3 ± 1.1	4.2 ± 1.2	3.0 ± 0.6	3.5 ± 0.7	3.3 ± 0.8
# 2	3.1 ± 0.2	2.9 ± 0.3	2.9 ± 0.2	2.5 ± 0.2	2.4 ± 0.3	2.4 ± 0.2
# 3	4.1 ± 0.6	3.8 ± 0.5	3.6 ± 0.5	3.8 ± 0.6	3.6 ± 0.5	3.5 ± 0.3
# 4	3.8 ± 0.7	4.0 ± 0.9	3.8 ± 0.7	3.5 ± 0.7	3.4 ± 0.7	3.3 ± 0.5
# 5	3.7 ± 0.6	3.4 ± 0.5	3.2 ± 0.6	2.8 ± 0.3	2.7 ± 0.2	2.6 ± 0.3
# 6	3.7 ± 0.6	3.2 ± 0.5	2.8 ± 0.5	2.6 ± 0.3	2.5 ± 0.3	2.3 ± 0.3
# 7	3.7 ± 1.4	3.6 ± 1.1	3.4 ± 1.3	2.9 ± 0.5	2.6 ± 0.4	2.4 ± 0.3
# 8	5.1 ± 1.1	3.9 ± 0.5	4.2 ± 0.5	3.7 ± 0.5	3.3 ± 0.3	3.4 ± 0.4

Values are given in m s^{-1} (mean ± SD for 10 cardiac cycles) for three repetitive measurements (1 to 3) per subject and 2 positions (i.e., one section covering the ascending and descending aorta).

Table 2. Mean aortic pulse wave velocities using real-time and cine phase-contrast MRI.

Acquisition	Analysis	2 Positions	3 Positions	4 Positions
Real-time	TTU	3.9 ± 0.6 3.6 ± 0.5 3.5 ± 0.5	3.9 ± 0.4	3.8 ± 0.4
	XCor	3.1 ± 0.5 3.0 ± 0.5 2.9 ± 0.5	3.3 ± 0.4	3.2 ± 0.4
Cine	TTU	3.5 ± 0.5	3.8 ± 0.6	3.7 ± 0.5
	XCor	3.3 ± 0.5	3.7 ± 0.7	3.6 ± 0.6

Values are given in m s^{-1} (mean ± SD) for 8 subjects and 10 cardiac cycles (real-time data). The real-time data for 2 positions represent 3 repetitions (compare Table **1**).

between repetitive measurements as well as breathing-induced changes between inspiration and expiration. This underlying sensitivity of real-time PC MRI to respiration is demonstrated in Fig. (**3**) for a single subject (single section) and 10 consecutive cardiac cycles. The traces represent mean velocities in the ascending and descending aorta together with the resulting PWV values as a function of time for a period covering about two respiratory cycles. Quantitative differences (i.e., maximum to minimum PWV values) are on the order of 1 m s^{-1}.

DISCUSSION

As shown in Table **1** individual real-time PWV values for our group of healthy young volunteers are highly reproducible on an individual basis and regardless of the analysis method. Beat-to-beat variations suggest a pronounced sensitivity to physiological alterations. The resulting aortic PWW values compare well with literature data which nevertheless are rather diverse and cover a broad range, also because PWV values tend to increase linearly with age even in healthy subjects [1, 2]. For example, while early cine PC MRI studies [15, 33, 39] mainly used the time-to-foot method abandoned here, a more recent cine PC MRI study [42] introduced TTU and XCor analyses and reported 5.1 to 5.3 m s^{-1} for 2D PC MRI as well as 3.8 to 4.8 m s^{-1} for 4D PC MRI and middle-aged subjects.

Here, consistent PWV values in the range from 3.5 to 3.9 m s^{-1} were obtained for both real-time and cine PC MRI in conjunction with a TTU analysis. For the XCor method, the PWV values for real-time PC MRI are up to 10% lower than for cine PC MRI. However, in the absence of a true gold standard, it seems impossible to decide about the “best” or most reliable analysis technique. Moreover, this discussion is outside the scope of the present study which emphasizes real-time vs cine PC MRI.

Previous PWV work [15] suggested the measurement of flow velocities from multiple locations along the aorta for a more accurate analysis which, for example, minimizes the putative influence of turbulent blood flow close to the aortic arch. Most remarkably, however, for any chosen acquisition and analysis technique the PWV values obtained in the present study for 2, 3 or 4 positions were very consistent and comparable. This also includes a very reproducible determination of mean PWV values from real-time PC MRI measurements of only a single slice covering the ascending and descending aorta. While such a strategy might also be preferable because the data for the two analyzed positions stem from the same cardiac cycles, its successfulness depends on the shape of the aorta and the ability to place a section for measuring through-plane flow in both locations within the acceptable limits of 10 to 15º angulation [43].

A limitation of the present and previous 2D PC MRI studies is the manual determination of aortic distances from a single sagittal plane. Although simple and performed with consensus, the approach may be prone to errors because of the complex anatomy of the aorta and variations during breathing. However, when analyzing the distance for specific breathing conditions (i.e., during breathhold after inhalation or exhalation), the differences between two locations in the ascending and descending aorta (same section) turned out to be surprisingly small (about 3%, data not shown) and unable to account for the PWV modulations during free breathing. The latter effect has to be ascribed to the lowered intrathoracic pressure during inspiration which causes increased flow velocities in the ascending aorta [35].

CONCLUSION

Aortic PWV values may be obtained for single cardiac cycles by real-time PC MRI with sufficiently high spatial and temporal resolution. Respective analyses were performed for two different analysis methods and up to 4 locations along the aorta. While mean PWV values averaged across multiple cardiac cycles were found to be reproducible and consistent for 2, 3 and 4 locations, the beat-to-beat variability of PWV values from individual cardiac cycles revealed a remarkable sensitivity to breathing with highest values during inspiration, i.e. lowest intrathoracic pressure. In future, real-time PC MRI determinations of PWV are expected to markedly reduce examination times. Moreover,

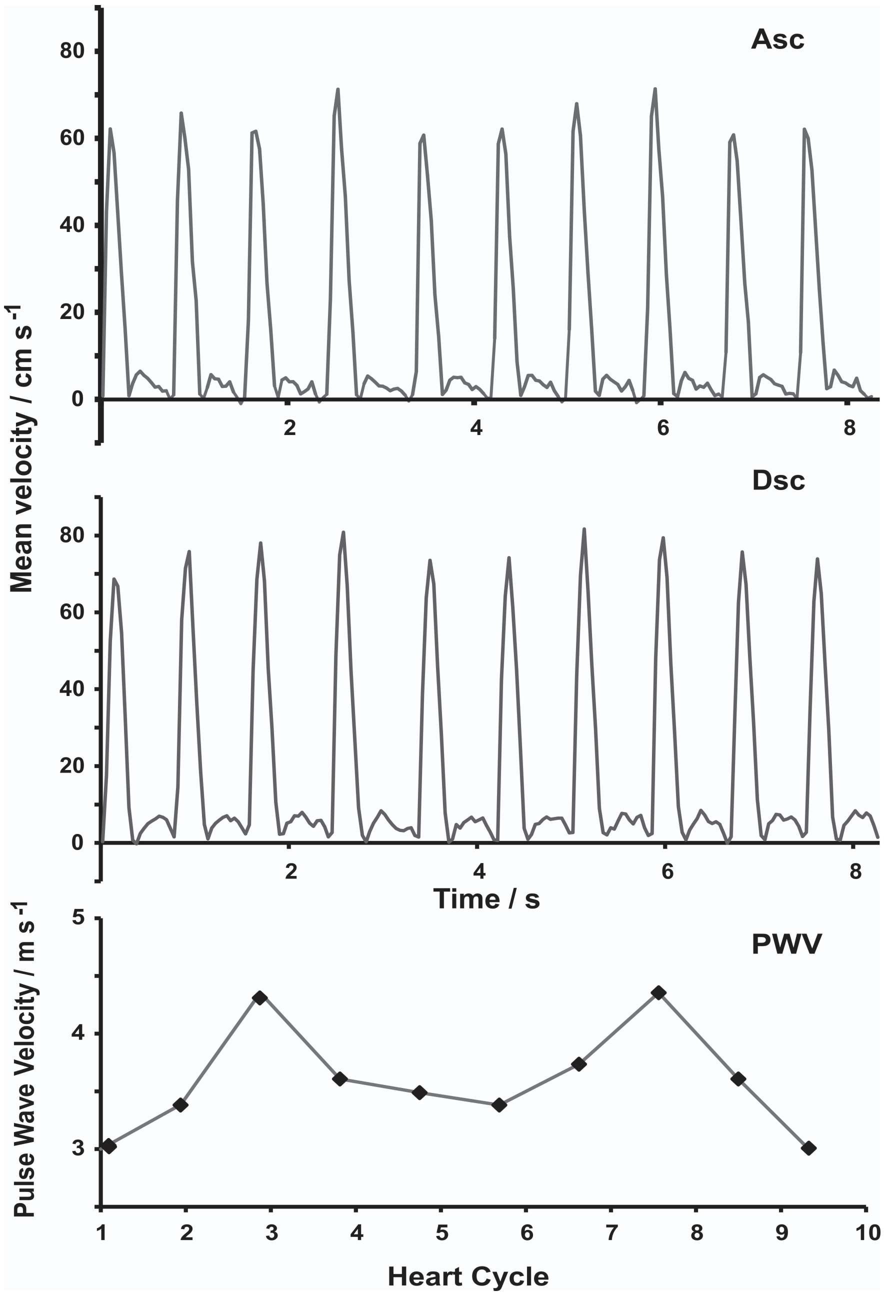

Fig. (3). Mean blood flow velocities obtained from real-time phase-contrast MRI (single subject, single section) in the ascending (Asc) and descending aorta (Dsc) as well as resulting pulse wave velocities (PWV) as a function of time for 10 cardiac cycles.

real-time PC MRI will allow for studying PWV variations in response to breathing maneuvers [27, 35, 36] or protocols of physical exercise which may aid in the diagnosis of patients with suspected aortic stiffness.

CONFLICT OF INTEREST

JF holds a patent on the NLINV reconstruction method.

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