Original Research

A New Method for the Determination of Aortic Pulse Wave Velocity Using Cross-Correlation on 2D PCMR Velocity Data

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Purpose: To evaluate the reproducibility of a new multisite axial pulse wave velocity (PWV) measurement technique that makes use of 2D PCMR data and cross-correlation analysis.

Materials and Methods: PWV was estimated with MRI in 13 healthy volunteers by a transit-time technique (TT), a multisite technique utilizing 1D PCMR data in the descending aorta (FOOT), and a new multisite axial technique that uses 2D PCMR data over the ascending, transverse, and descending sections of the aorta (2D-XC).

Results: No significant difference was observed between PWV measurements values measured by the three techniques. However, 2D-XC displayed significantly better intertest reproducibility than either the TT or FOOT methodologies. Average percent difference between scans: TT: 15.8% ± 13.4%, FOOT: 21.3% ± 16.9%, 2D-XC: 7.72% ± 4.73%. $P = 0.02$ for both 2D-XC/TT comparison and 2D-XC/FOOT comparison.

Conclusion: 2D-XC is a more reproducible method than either the established TT or FOOT methods to estimate the aortic PWV.

Key Words: pulse wave velocity; aorta; cross correlation
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AORTIC STIFFNESS has been shown to correlate with age (1,2), blood pressure degree (2,3), and the presence of atherosclerosis (4). Elevated aortic stiffness has also been shown to be a predictor of mortality in patients with renal failure, hypertension, and diabetes (3,5–7). Additionally, changes in aortic stiffness may be an indicator of response to therapies aimed at modification of vascular tone or endothelial function (8).

Pulse wave velocity (PWV) can be used as a measure of arterial stiffness. The two are related through the Moens-Korteweg equation:

$$PWV = \sqrt{\frac{Eh}{2\rho r}},$$

where E is the Young's modulus (stiffness) and h is the vessel wall thickness, ρ is the blood density, and r vessel radius at end diastole. This equation assumes a large vessel diameter relative to a uniform wall thickness and that the vessel contains an ideal incompressible fluid. The PWV is most often estimated by dividing the distance between two measurement sites by the propagation time of the pressure or flow wave between the two sites. Doppler ultrasound has been extensively used to measure PWV using carotid-femoral pulse pressures (3–9). However, the ultrasound method uses surface anatomy to estimate artery length and does not take into account the often torturous route the vessels take within the body. Inaccurate measurements of the distance between transducers leads to high reported PWVs (10) and yields only moderate reproducibility. In addition, ultrasound measurements can only indirectly estimate the central aortic PWV since the recording locations result in values that include contributions from carotid and femoral arteries.

Determining PWV using magnetic resonance imaging (MRI) has the advantage of determining *central aortic* PWV and eliminating errors in length measurement. Several MRI-based methods have been used to determine PWV, including 1D MRI measurement techniques (11), flow-area methods (12–14), and correlation of second-order derivatives of the velocity waveforms (15). The most commonly used MRI method, however, is the *transit-time method*, which is similar to the technique used in ultrasound in that PWV is estimated by dividing the distance between two measurement locations by the propagation time of the pulse wave between the points. Two slices perpendicular to the aorta are most

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commonly used for recording locations. A time-marker on the flow waveform must be chosen in order to compare pulse wave arrival times at the two sites. The most common feature used as a marker for pulse wave arrival is the foot of the flow vs. time curve (14,16,17), although other features such as the half-maximum of the flow waveform have been used (17,19). As an extension of the transit-time method, the *multisite method* uses a parasagittal slice down the length of the aorta to obtain flow waveforms at multiple locations along the length of the aorta (20). A line is fit to multiple points on an arrival time vs. distance along aorta plot rather than just the two measured points used in the transit time method. The use of multiple points allows a regression line to be fit and potentially enables a more robust estimate of central aortic PWV.

In the present study we propose an extension of the multisite axial technique that contains two improvements. First, the time delay of the flow waveform at multiple locations is estimated through a cross-correlation (XC) between the flow waveforms. The cross-correlation utilizes the entire flow waveform over the cardiac cycle and thus presents a more robust estimate of the arrival time than choosing a single feature, such as the foot of the flow waveform, as a time-marker. Second, we incorporate velocity data from the ascending and transverse sections of the aorta as well as the descending aorta by acquiring 2D PCMR data and constructing a velocity image made from the two velocity components for determining the flow waveforms.

The purpose of this study is to compare the reproducibility of our multisite two-directional PCMR cross-correlation method (2D-XC) to: 1) a foot-identified multisite method (FOOT), and 2) a transit-time method (TT).

MATERIALS AND METHODS

Subjects And Scan Parameters

Thirteen healthy volunteers (11 male, mean age 29.4 ± 7.4 years) with no symptoms of cardiovascular disease were studied after experimental procedures had been explained and informed written consent obtained. All scans were performed on a Philips Medical Systems 1.5T Intera MRI scanner (Best, Netherlands) after 15 minutes of rest in the supine position. All subjects underwent two exams separated by 2.9 ± 7.3 days. To measure PWV using the TT method, PCMR images were obtained at two slices along the aorta, one in the ascending aorta at the level of the pulmonary artery (PA) bifurcation and the other in the descending abdominal aorta. Each slice was oriented to ensure the slice was perpendicular to the aorta. To measure PWV by the multisite methods, an oblique sagittal PCMR slice covering the length of the aorta was acquired. Two sets of images were acquired, one with velocity encoded in the foot–head direction, the other with velocity encoded in the anterior–posterior direction. For the multisite foot method (FOOT), only the descending aorta on the foot–head velocity encoded images were used to create the flow waveform. For the new 2D-XC methodology, the in-plane velocity vector was obtained by combining the vectors from the foot–head encoded images and from the anterior–posterior encoded images at each time-point. The length (magnitude) of these in-plane velocity vectors were then used to create the flow waveforms. Velocity components in the left–right direction were presumed to be negligible and were therefore not included in constructing velocity magnitude images. Thus, for the 2D-XC method we obtain the velocity magnitude at all locations in the aorta, including the arch. This allows a greater length of the aorta to be investigated since the ascending aorta and aortic arch can be included in the analysis.

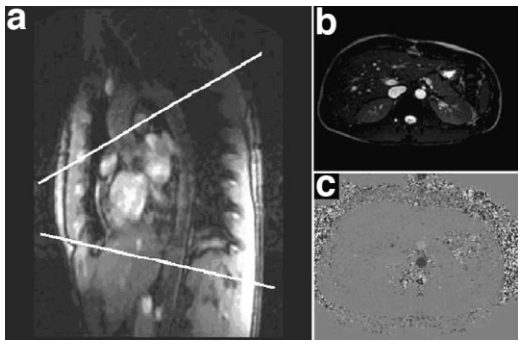

Figure 1. MR images for PWV determination using the transit-time method. **(a)** Cross-sectional slice location for through-plane velocity determination. **(b)** Anatomical image from distal slice. **(c)** Velocity data corresponding to anatomical image from (b).

A retrospectively ECG-gated, nonsegmented phase contrast sequence was used for all velocity measurements. The sequence had a repetition time 4.7 msec, echo time 2.7 msec, and flip angle 20°. The field of view (FOV) was 35 × 35 cm, matrix size 256 × 256 pixels (pixel size 1.37 × 1.37 mm^2), and slice thickness 10 mm. The velocity encoding value was 2.0 m/sec and velocity encoded and velocity compensated images were acquired in successive heart beats. The total number of velocity images acquired (for both transit-time and each multisite method) was 128 per cardiac cycle unless the subject's heart rate was too high to accommodate that number of phases, in which case the maximum number of allowable phases was acquired. This resulted in a temporal resolution of 7.6 ± 1.0 msec.

TT PWV Estimation

To compute PWV using the TT method, average through-plane velocity curves over the cardiac cycle in each volunteer were calculated in the ascending and descending aorta (Fig. 1). Data points were increased 10-fold in time with a bicubic interpolation to facilitate analysis. The wave propagation time between the basal and distal curves was determined as described by Mohiaddin et al (1). Briefly, the foot of the waveform at each recording location was identified as the intersection of the minimal value of the presystolic section of the flow waveform with a line fitted to the upslope portion of the waveform. The upslope was taken as all points between 20% and 80% of the maximal value on the increasing slope of the waveform; the number of points used was 50.9 ± 12.2. PWV was then taken as the distance be-

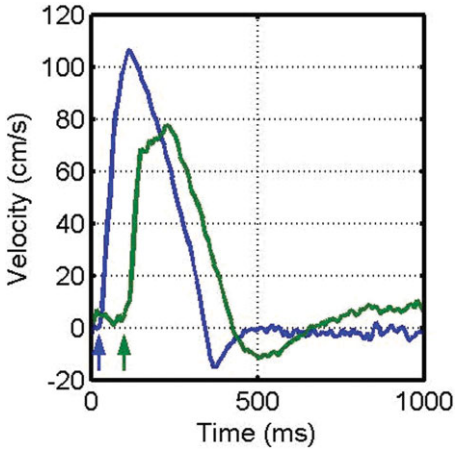

Figure 2. Representative velocity profiles from cross-sectional velocity images in Fig. 1. Blue = ascending aorta, green = descending aorta. Wave arrival times are determined by foot location (indicated by arrows) for both TT and FOOT methods.

tween measuring sites divided by the time delay of the wave between the sites (Fig. 2).

Foot-Identified Multisite (FOOT) PWV Estimation

To compute the PWV using a FOOT multisite method, flow waveforms were computed at 30 evenly spaced points along a length of a user-defined centerline along the descending aorta (this methodology is similar to that described by Yu et al [20]). The foot of each waveform was identified as in the TT method and the arrival time of the flow waveform at each location was plotted against its distance from the first waveform. PWV was the inverse of the slope of a line fitted to this plot.

Two-Directional Cross-Correlation Multisite (2D-XC) PWV Estimation

To compute PWV using the 2D-XC method, a centerline was drawn down the aorta starting in the ascending aorta and continuing through the arch into the descending aorta on the combined velocity images (Fig. 3a). Bicubic interpolation on each curve was used to increase the number of timepoints available for analysis 10-fold. The waveform at each location down the centerline was then compared to the waveform at the first location using a cross-correlation function. The cross-correlation function applies a time-shift to the more distal waveform until the highest correlation value between the two waveforms is obtained. This effectively returns a time shift for each location relative to the first location. A line is then fitted to the plot of location vs. time shift and the inverse of the slope is the PWV (Fig. 3b).

Reproducibility Analysis

To evaluate intraobserver repeatability for both multisite methods, the PWV analysis in each subject was repeated 5 times by the same observer. Intraobserver repeatability for PWV from both multisite methods was evaluated by the coefficient of variation (CoV), the standard deviation of the five measurements in each subject divided by mean value from that subject, expressed as a percent. PWV from the TT method was not included in this analysis since only one estimate is obtained from a set of images. Differences in CoV of the two multisite methods (FOOT and 2D-XC) were assessed with a two-tailed unpaired *t*-test.

To assess intertest reproducibility, results from the two repeated scans were analyzed. Intertest reproducibility was evaluated by the coefficient of repeatability (CoR) of the differences between multiple scans of the same type (21), and by the absolute value of experiments' difference between scans (as a percent). Intertest reproducibility of PWV measurement methodologies (as evaluated by the percent difference) were compared using a repeated measures analysis of variance (ANOVA) with a Huynh–Feldt correction followed by a least significant difference post-hoc test. Statistical calculations were performed in SPSS v. 15.0 (Chicago, IL). A value of $P < 0.05$ was defined as statistically significant.

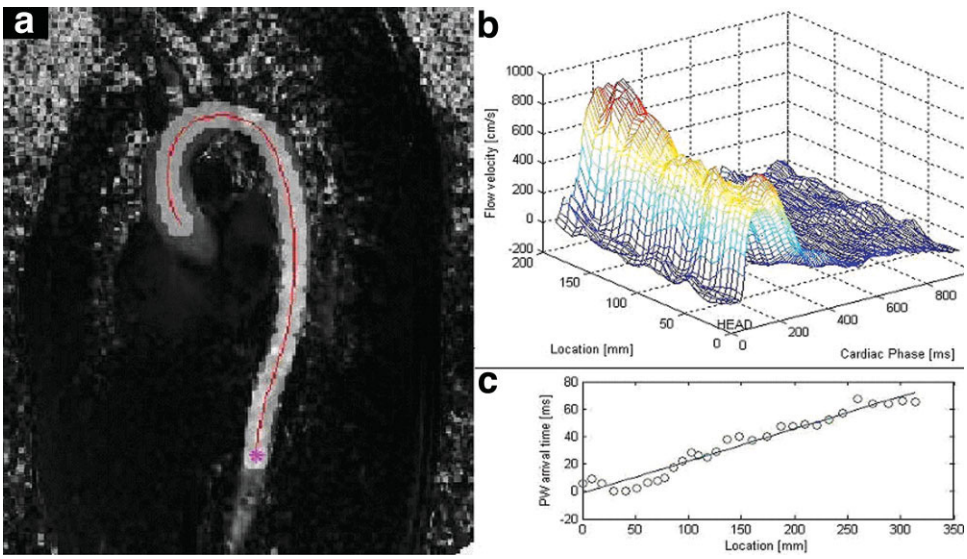

Figure 3. Multisite PWV analysis. **(a)** Centerline with inclusion area for velocity measurement. Velocity curves are determined at 30 evenly spaced points along each line. **(b)** 3D velocity curve. **(c)** Using cross-correlation, wave delay times for each location relative to the most basal location on the ascending section are plotted against the distance from the first location. PWV is the inverse of a line fitted to this plot.

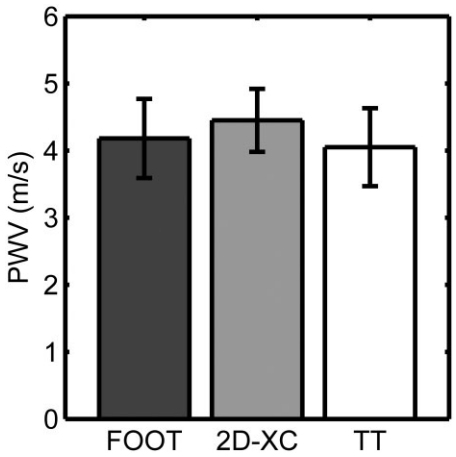

Figure 4. Pulse wave velocity measured by several methods. Error bars indicate standard deviation. No significant difference was observed between methods ($P = 0.15$).

RESULTS

PWV estimates from each of the three methods are shown in Fig. 4. No statistically significant difference was observed between the three estimates of PWV (FOOT: 4.18 ± 0.59 m/s, 2D-XC: 4.45 ± 0.47 m/s, TT: 4.07 ± 0.57 m/s, $P = 0.15$).

The 2D-XC methodology yielded significantly better intraobserver repeatability as evaluated by the CoV than the FOOT methodology (Foot: 9.2% ± 8.0%, 2D-XC: 2.8% ± 1.5%, $P = 0.01$).

The 2D-XC methodology yielded superior intertest reproducibility than the FOOT or TT methods. A CoR of 0.86 was obtained for the 2D-XC method compared to 1.90 for TT and 2.39 for FOOT. This is also seen more intuitively by the absolute value of the percent difference between the two scans averaged over all the subjects, TT: 15.8% ± 13.4%, FOOT: 21.3% ± 16.9%, 2D-XC: 7.72% ± 4.73% (Fig. 5). The percent difference between scans for the 2D-XC method and the TT and FOOT methods was significant, $P = 0.02$ for both comparisons.

DISCUSSION

In this study we present a new method to assess central aortic stiffness using MRI. The method uses 2-directional PCMR measurements and a cross-correlation function to obtain measures of PWV. The major finding of the study is that the method provides improved intraobserver repeatability and intertest reproducibility of PWV measurements. Improved reproducibility suggests that effects of pharmacologic intervention on aortic stiffness can more easily be detected when employing this new methodology.

Measures of central aortic PWV have been shown to be predictors of cardiovascular and all-cause mortality in several patient groups (6,22). In addition, pharmacologic therapies acting through the nitric oxide (NO) synthesis pathway may alter PWV (23). Therefore, PWV may provide a means for assessing early changes in vascular function due to pharmacologic intervention (8).

For young, healthy subjects, PWV values between 4–6 m/s have been reported in the literature (12,16,17,20). All three methods yielded PWV results in this range. We did not have a method to determine the true PWV, therefore accuracy could not be assessed. Further studies are needed for a comparison of the methods where the *true* PWV and compliance are known. Intraobserver repeatability values are less often reported, but Kraft et al (17) and Shao et al (18) report a range for the CoV for their methods (a TT method and a multisite flow displacement method based on tracking fluid displacement along the aorta) of 3%–13%, similar to what we obtained with both multisite methods. Intraobserver repeatability measurements using the TT method have been conducted and have shown that there is no significant difference between repeated measures (24). However, no statistical comparison of intertest reproducibility has been done in MRI studies. The large standard deviations derived from the assessment of the mean percent difference between scans for the TT method in our study may be a result of the underlying uncertainty in these type of PWV analysis methods.

The main advantage of using cross-correlation over other waveform identification methods (foot, half-maximum, etc) is that the cross-correlation calculates the time delay of the wave using *all* of the data points of the waveforms rather than identifying the arrival of the wave by a single point. In this way, errors from poor wave arrival time estimations can be minimized.

In general, multisite velocity profile methods rely on fewer assumptions about the underlying mechanics of the vessel wall than the flow-area methods, and they may be more robust than the transit-time methods since they utilize more than two recording locations to estimate the PWV. While it would be possible to make other comparisons with the data available (ie, using the FOOT method on waveforms made from the 2D velocity vectors), our goal in this study was to examine the

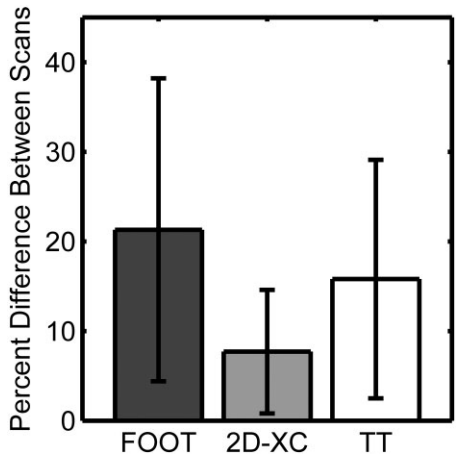

Figure 5. Mean percent difference between scans. Percent difference calculated as percent of mean PWV. Error bars indicate standard deviation. Significant differences between Foot and 2D-XC and between TT and 2D-XC methods was observed.

reproducibility of a method that incorporates both the longer aortic section and the use of cross-correlation by comparison with existing methods. Indeed, our study shows that the inclusion of ascending and arch data points along with cross-correlation to determine delay times yields a more reproducible method of determining PWV than using only points from the descending aorta.

While a larger set of measurements from a longer section of the aorta improves accuracy, possible regional differences in PWV are averaged out. The compliance in the ascending and descending aortas of young, healthy subjects is comparable; however, there is evidence that stiffness changes nonuniformly along the length of the aorta as one gets older (24,25). In this study, compliance is assumed to be similar in all sections of the aorta such that a single line may be fitted to the waveform time shifts. The extension of this method to older subjects may require modification of the fitting technique (ie, a higher-order polynomial fit rather than a simple linear fit or obtaining separate estimates of the PWV in different sections of the aorta). In using PWV for assessing effects of treatment, the difference in ascending vs. descending PWV may be less important. Since the multisite methods are essentially a 1D model, a single average value is given over the aorta and changes due to therapy would be expected to affect all regions of the aorta equally.

Limitations

As a consequence of achieving an adequate temporal resolution in this study, spatial resolution must be sacrificed in the PC-MRI scans. However, a high spatial resolution is not required since the aortic diameter is large. A limitation of using a long section of aorta is that reflections of pulse waves (which augment the pressure wave) from more distal bifurcations may differ by location along the aorta. This means that the pulse wave at each location is affected uniquely by both arrival time and reflection amplitude causing changes in the waveform shape along the length of the aorta (8). This may introduce inconsistency in our cross-correlation analyses since the waveforms from the ascending aorta and lower descending aorta have dissimilar shapes. A possible solution to this would be to compare waveforms at adjacent locations rather than comparing the waveform at each location to the first. However, this method is more prone to error since small errors in point-to-point transit-time values would result in large overall PWV estimation error. Furthermore, in younger subjects these reflections arrive in diastole so they have a smaller effect on the waveform shape. Another limitation to any multisite method of determining aortic PWV measurement is that the centerline of the aorta must stay mostly within the imaging plane. If the aorta is torturous and passes out of the imaging plane, or if the aorta is not situated well within the imaging plane due to poor slice alignment, the length of the vessel used to determine PWV will be decreased and a concomitant decrease in reproducibility can be expected. The use of 3D PCMRI and centerline tracking would be beneficial in this case, but at the expense of significantly increased scan time. Additionally, if the centerline of the aorta is not in the imaging plane, or if the user poorly traced the centerline, the average velocity of the blood will be underestimated and the height of the waveform shape will be altered (although the timing should not be affected). This effect could be lessened by automatic centerline detection and slice alignment, taking multiple contiguous slices and averaging them, or choosing the maximum velocity at each level of the aorta, but again at the cost of increased scan time (26).

In conclusion, we have presented a new method for the estimation of PWV that uses 2-directional PCMR data and processes flow waveform data using a cross-correlation function. We have demonstrated that using this method along the full length of the aorta is a more repeatable and reproducible method than either the established transit-time or multisite methods which utilize data only from the descending aorta and use a single feature of the wave (the foot) to determine arrival times.

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