Computer-assisted evaluation of aortic stiffness using data acquired via magnetic resonance

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Abstract

Aortic stiffness is frequently assessed through pulse wave velocity (PWV) measurements. Based on data acquired by magnetic resonance (MR) using a one-dimensional time-of-flight technique, a new computational tool has been developed to rapidly construct flow velocity images and automatically calculate PWV. Comparison between PWV results obtained from this and a manual analysis demonstrates good agreement (correlation coefficient of 0.9951), while the new method improves the time efficiency by more than 20 times. The new method can also significantly improve flow signal quality and yield more credible results when strong interfering background signals are present.

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1. Introduction

According to the National Center for Health Statistics, cardiovascular disease is the leading cause of death in the United States [1]. Arterial stiffness is thought to be a powerful indicator of present and possibly future cardiovascular risk [2–6]. Therefore, interest in the noninvasive clinical measurement of arterial stiffness is increasing. Aortic pulse wave velocity (PWV) is widely accepted as an excellent target parameter for stiffness assessment, and magnetic resonance (MR) is regarded as one of the most accurate measurement methods.

PWV is defined by the Moens–Korteweg equation: PWV = \((Eh/(2pr))^{1/2}\), where \(E\) and \(h\) are Young’s modulus and thickness of the vessel wall, respectively, \(r\) is vessel radius at end diastole, and \(\rho\) is blood density. Physically, there are two distinct wave velocities: pressure wave velocity and flow wave velocity. However, with regard to magnitude, they are identical, and both may be referred to as PWV. In humans, aortic PWV may range upwards to 15 m/s, indicating a very stiff vessel, whereas the lowest PWV may be less than 3 m/s, indicative of a compliant vessel. Generally, aortic PWV increases with age [7].

In practice, PWV is usually obtained by measuring the time for the pulse wave to travel a certain distance along the blood vessel. Noninvasive determination of PWV can be achieved by applanation tonometry [8,9], ultrasonography [10,11] and MR imaging. For accessing aortic PWV, MR has the advantages of deep tissue penetrability and precise spatial positioning, thus potentially increasing its accuracy over other methods.

Several MR methods to measure PWV have been described, including phase contrast MRI [12,13], Fourier velocity encoding [14,15], real-time acquisition and evaluation (RACE) [16], and one-dimensional (1D) MR tagging [17,18]. Difficulties with these methods include lengthy acquisition times, the requirement of a long straight aortic segment (up to 24 cm), extensive post-processing, and/or time-consuming analysis. These difficulties have hindered their widespread clinical acceptance.

The 1D projection velocity method previously developed by our research group [7,19,20] is a novel, rapid and reliable PWV measurement with a MR acquisition time of one or two heartbeat(s). Because of the projective design of the sequence, the data are not reconstructed as standard MR images, but instead are analyzed as a time-resolved sequence of 1D spectra. However, using conventional manufacturer-supplied spectroscopy software, data analysis and PWV calculation for one measurement usually takes...
half to 1 h. Such long and tedious manual data processing is error-prone and impractical for routine use. Additionally, standard spectroscopy software allows the operator to view only one spectrum at a time. In our method, one spectrum provides velocity information at one instant of the measurement. Typically, completing one measurement requires more than 20 sequentially acquired spectra. Standard software is unable to provide an overview of the entire multi-spectra dataset. Without this overview it is difficult to determine whether acquisition parameters were correctly set and whether the data are analyzable. To address these problems, a new computational tool, which allows fast construction of flow velocity waveforms and performs automatic calculation of PWV, has been developed on a portable PC running Microsoft Windows operating system. This article presents an integrated method for PWV measurement, starting from MR data acquisition, to the implementation of this tool. The validity of the method is demonstrated by comparison of in vivo results against those evaluated using conventional manual analysis.

2. Methods

As shown in Fig. 1, the PWV measurement described herein is an integration of MR acquisition with data analysis software (called wave velocity analysis or WVA). A detailed description of each follows.

2.1. MR data acquisition

The strategy behind the MR assessment of PWV is the rapid measurement of aortic blood flow, using time-of-flight principles [7]. Both slice selection and data acquisition gradients are aligned with the blood flow direction. A thin section of tissue (orthogonal to the long axis of the thoracic aorta) is excited by a radiofrequency (RF) pulse, and a gradient echo signal is elicited. The frequencies within the echo signal reflect the spatial positions of excited spins at the echo time (TE). If the aortic blood moves between RF excitation and the TE time, the echo will exhibit an altered frequency component. A 1D Fourier transform of the echo yields a spectrum of the various frequency components. The frequency shift due to blood flow is directly proportional to the distance traveled in the time TE. In this way, instantaneous blood velocity is observed. The velocity waveform can thus be sampled by rapidly repeating the sequence. By extension, the PWV measurement strategy is to simultaneously record the initial systolic flow velocity waveforms at two vessel sites separated by a known distance. In Fig. 2, which is a sagittal scout image of the descending thoracic aorta, the two anatomic sites are depicted as overlaid white lines. Since the flow propagation rate is finite, there is a distinct delay between the two velocity waveforms. This delay time can be accurately determined from a graph of these two waveforms. The separation distance between the two sites (84 mm in our method) divided by this delay time yields the PWV.

Fig. 1. Schematic overview of the aortic pulse wave velocity (PWV) measurement. It includes MR data acquisition and computer-aided data analysis. After each MR acquisition (left box), data is downloaded to a portable PC via wireless network connection in less than 10 s. The data analysis software executes the steps shown in the right box, and can complete one measurement in as little as 20 s.
To excite two sites concurrently by MR, a dual-frequency RF excitation pulse is required. This study utilizes a RF pulse described previously [7]. A timing diagram of the MR sequence is shown in Fig. 3. Compared with that used previously [7], this sequence differs only by substitution of a simplified pre-saturation scheme, while keeping the data acquisition segment unchanged. Therefore, measurement parameters such as TR (repetition time), TE and A/D conversion (ADC) time are unchanged. Typically, the RF/ADC process is repeated 22 times in rapid succession with a TR of 5.5 ms and a TE of 6.5 ms. Early systolic flow is therefore observed for a period of 121 ms (22 × 5.5). During each ADC period (one acquisition) an array of 64 sampled points is acquired, which yields one frequency spectrum after Fourier transformation.

In vivo, echo signals are returned not only from aortic blood, but also from surrounding tissue within each transverse section. This so-called static signal produces high intensity peaks at the excitation positions in the 1D spectra. The static signal is much more intense than the aortic blood signal because of the relatively great predominance of static tissue. Spatial pre-saturation is the first of two strategies for suppressing this static signal. In this study, a coronal saturation plane is positioned parallel to the aorta, and applied over the spine and adjacent muscle and skin. The second strategy for suppressing static background is by raw data subtraction, which is accomplished by subtracting a measurement during diastole from that during systole.

This study was approved by the Virginia Commonwealth University institutional review board, and all participants gave informed consent. All MR measurements were performed on a clinical 1.5 tesla (T) system (Vision, Siemens Medical Solutions) equipped with 25 mT/m gradients.

2.2. Computer-aided data analysis

The reasons for developing the new computer-aided data analysis tool on a portable PC are 2-fold. First, direct

![Fig. 2. A sagittal scout MR image. The central hyperintense vessel is the thoracic descending aorta, in which blood flows downward during cardiac systole. The two white lines perpendicular to the aorta indicate RF excitation or measurement positions separated by 84 mm.](image)

![Fig. 3. Timing diagram of MR PWV measurement sequence. After the QRS trigger, a variable delay synchronizes the measurement portion to begin just before the pulse wave arrives at the upstream measurement site. Spatial pre-saturation is applied posterior to the aorta immediately before the measurement in order to reduce static signal intensity. During the measurement period, the same physical gradient (z) is used during both RF transmission and signal reception (A/D convert). For this sequence, TR = 5.5 ms, TE = 6.5 ms, RF duration is 0.896 ms, ADC duration is 1.024 ms. Static signal is further reduced by repeating the sequence during cardiac diastole and subtracting the two measurements.](image)
development of new software on the MR host computer may be limited by operating system obsolescence. Secondly, due to the ease of upgrading hardware and software, a portable PC provides an ideal platform for development and allows easier interfacing with other MR systems.

The portable PC employed in this study is a Toshiba Satellite 2435-S255, with a 2.4 GHz Pentium 4 processor, 512 MB memory, and Microsoft XP operating system. The newly developed PWV analysis software package is called WVA (wave velocity analysis), and is based on the platform of MatLab version 6.5. Its processes are shown in the right box of Fig. 1.

2.2.1. Data format and transfer from MR system to PC

For the sequence illustrated in Fig. 3, each measurement involves 22 data acquisitions, and each acquisition generates one data file. The first 6144 bytes are for file headers that include patient information, date/time, measurement parameters and sequence name. Immediately following the header is the acquired data consisting of 64 complex numbers saved in succession with the real part ahead of the imaginary part. Each part is a 32-bit IEEE single precision floating number.

The wireless network protocol 802.11 is employed to establish a connection between the PC and MR system. After each MR acquisition, one downloads the MR generated files to the portable PC using a FTP tool. On the PC, WVA extracts patient information, MR measurement parameters and raw data from these files for the construction of flow velocity images and PWV calculation.

2.2.2. Complex Fourier transforms and image construction

The raw data is a time domain signal. To obtain the frequency domain signal, a complex FFT with zero-insertion is employed.

\[ X(k) = \sum_{n=1}^{N} x(n)e^{-j2\pi(k-1)(n-1)/N}, \quad 1 \leq k \leq N \]  

(1)

Here, \( X(k) \) is the transformed signal in frequency domain, \( N \) is the total number of sampling points (4096), \( x(n) \) is an array of length 4096 from the zero-filled time domain raw data. The sampling frequency used is 62.5 kHz in this study and \( X(1 \leq k < N/2) \) represents the positive frequency domain (0 ≤ \( f \) < 31.25 KHz); \( X(N/2 \leq k < N) \) the negative frequency domain (−31.25 KHz ≤ \( f \) < 0). The resulting frequency resolution is 15.26 Hz.

An aortic blood velocity image is constructed by 'stacking' all 22 1D spectra into a 2D color map. In the map, the vertical and horizontal axes represent time and frequency, respectively. The frequency spectrum at each time interval TR is presented as a horizontal line with the spectral intensity represented by color. Aortic blood motion within the time interval TE results in spectral peaks shifted from the excitation position. Because the excitation position is fixed and TE is constant, the horizontal axis on the map can be easily converted to velocity at the corresponding time. Therefore, the color map may equivalently be interpreted as a velocity waveform with respect to time.

2.2.3. Static background suppression

It is sometimes found that static signal suppression performed during MR acquisition is insufficient. When background signal is unusually strong, it may obscure the flow signal. The WVA software offers additional time-domain static signal subtraction as a post-processing option. Because blood flow ideally commences only after several acquisitions in this MR sequence, the first time domain acquisition, \( s_1 \), only contains static signal. Suppose the \( n \)th time domain acquisition is \( s_n \). By the linear properties of the Fourier transform, if \( \text{FT}(s_1) = f_1, \text{FT}(s_i) = f_i \) then \( \text{FT}(s_i - s_1) = f_i - f_1 \), where \( \text{FT} \) represents Fourier transform, and \( f_i \) and \( f_1 \) are frequency domain signals. Thus the operation \( (s_i - s_1) \) will reduce frequency components existing in \( s_1 \) from \( s_i \).

To compensate for the decay in overall signal with time, the WVA program modifies the time domain subtraction as

\[ S_i = s_i - s_1 \cdot \frac{\text{max}(s_i)}{\text{max}(s_1)} \]  

(2)

where max\((s_1)\) and max\((s_i)\) are the maximum values of \( s_1 \) and \( s_i \), respectively, and \( S_i \) is the signal remaining after static signal cancellation for the acquisition. In the program, the operation repeats \( i \) times, as \( i \) is incremented from 2 to the total number of acquisitions.

2.2.4. Automatic flow signal detection

WVA provides two choices for flow signal detection: automatic and manual. Automatic detection saves considerable time and enables near real-time analysis. The software carries out a search for spectral intensity peaks that may represent aortic blood flow. The frequency difference between flow signal and the excitation position represents blood velocity. To accommodate various flow waveforms and occasional strong background interference, the automatic detection algorithm is designed based on the following signal characteristics. (1) Within the range of 1800–5000 Hz from the static peak position, which corresponds to a flow velocity of 0.43–1.19 m/s, the largest spectral peak is generally the true aortic flow signal. (2) The earliest flow signals (velocities less than 0.43 m/s) may be less reliably identified because of their proximity to the static background signal. (3) There should be no abrupt changes in flow velocity between adjacent spectra.

Fig. 4 is a flow chart demonstrating the algorithm for automatic flow signal detection. The algorithm consists of two stages. In stage one, the peak flow velocity is identified by gradually reducing the intensity threshold and finding the strongest intensity peak (within the target velocity range) from all acquisitions. When this peak is found, the corresponding time and the velocity are identified.
Starting from this identified spectrum, the second stage of the algorithm seeks to trace the flow signal bi-directionally in time toward the first and last spectra or until the velocity is near zero.

### 2.2.5. Calculation of PWV

Once the flow signal peaks are detected, fourth-order polynomial fits (95% confidence interval) are applied to the upstream and downstream signals, respectively. The resulting fitted curves represent the flow velocity waveforms at the two sites. The maximum of a velocity waveform is termed peak blood velocity (PBV). The propagation delay $t$ is determined as the temporal separation between the two polynomial curves, measured at one-half of their respective PBVs. PWV is calculated as:

$$PWV = \frac{s}{t} - \frac{v}{2}$$  \hspace{1cm} (3)

where $s$ is the distance between upstream and downstream sites (84 mm), $t$ is the observed propagation delay between the two sites, and $v$ in this instance is one-half the average peak blood velocity. The rationale for subtracting this $v$ is...
based on the observation that PWV is elevated by the motion of the fluid itself [19].

2.2.6. Statistical reports from multiple measurements

To assess the reproducibility of PWV measurements, several (e.g. 7) trials are conducted for each subject. After analysis, WVA can output statistical results including mean PWV, PWV standard deviation, PBV, patient information and MR acquisition parameters in Microsoft Excel file format.

3. Results

The aortic PWV data analysis software package (WVA) developed for this study includes implemented functions listed in the flow chart of Fig. 1. A screen shot of the WVA graphical user interface is shown in Fig. 5. The top panel in the figure is the flow velocity image, which is the stack plot of all 1D spectra comprising a single PWV measurement. The middle panel depicts one selected spectrum from the stack. The bottom panel contains user controls.

In the top panel, the horizontal axis is in units of frequency and the vertical axis represents time (increasing from bottom to top). The map style colors indicates strength of various frequency components. The frequency axis can equivalently be viewed as spatial position. Its orientation from right to left corresponds to the anatomical orientation from head to foot. Thoracic aortic blood flow, therefore, is from right to left. The vertical time axis starts at 80 ms after the subject’s R-wave, extends until approximately 200 ms, and includes 22 time points from 22 successive MR acquisitions. The middle panel displays one spectrum at the time corresponding to the yellow dashed line in the top panel. The horizontal axis is identical to that of the top panel. The bottom panel is a collection of the most frequently used controls and message boxes. Some extra tools can be found in pull-down menus.

The flow image comprising the top panel of Fig. 5 is from a 48-year-old male subject. The right and left ‘Y’-shaped traces represent upstream and downstream aortic tagging sites, respectively. For both traces, the relatively straight vertical line of intensity represents static signal, with the theoretical excitation position indicated by blue diamond-shaped markers. The leftmost intensity branches (marked by

![Image of WVA user interface](image-url)
white crosses) represent aortic flow. By simple inspection, a delay between onsets of blood flow at the two sites is apparent.

Automatic flow signal peak detection was applied to this flow image with results identical to manual detection. If manual detection or correction is desired, one can use the middle panel to select flow signals by placing the mouse cursor to the position selected. The software automatically locates the peak nearest the selected point. Circled peaks in the middle panel indicate aortic flow signals.

One can next apply polynomial curve fitting to the detected flow signals to yield aortic flow waveforms as shown in Fig. 6. The time delay \( t \) in Eq. (3) is the temporal separation between the respective half-maxima of the upstream and downstream waveforms. In this case, WVA determined \( t = 15.65 \text{ ms} \) and \( \text{PWV} = 4.92 \text{ m/s} \). WVA also reports the statistical results from 5 consecutive measurements on this subject (not shown) to be \( \text{PWV} = 4.92 \pm 0.25 \text{ m/s} \), \( \text{PBV} = 0.88 \pm 0.02 \text{ m/s} \). These values are typical for a healthy 48-year-old subject. On the other hand, manual analysis by a different observer using spectroscopy tools as described in Ref. [7] gave results of \( \text{PWV} = 4.86 \pm 0.27 \text{ m/s} \), and \( \text{PBV} = 0.87 \pm 0.02 \text{ m/s} \).

To conduct a more thorough comparison between WVA and manual data analysis, 20 measurements were chosen. These data were acquired from 4 subjects (ages 30, 37, 52 and 56) with 5 measurements of each. Every measurement was observed to exhibit clear flow signals using the WVA graphical interface. A single observer analyzed these datasets using both methods. When using WVA, the automatic flow signal detection algorithm yielded an accuracy of 95%. That is, user intervention was required only once for every 20 automatically detected flow peaks, on average. Manual analysis followed the traditional method [7] and required a total of about 12 h, compared to 30 min for computer-assisted analysis. Fig. 7 plots the results from both methods. Excellent agreement was obtained with a high correlation coefficient \( r = 0.9951 \). A paired sample test also showed these two methods to have no significant difference within the 95% confidence interval. Consequently, we conclude that WVA offers a beneficial alternative to manual data analysis.

4. Discussion

The successful measurement of PWV is dependent on acquiring clear aortic flow signal. In our experience, younger subjects generally exhibit better flow signal than older subjects, due partly to the decline in PBV with age. Likewise, male subjects tend to have larger aortas and therefore typically display stronger signals than females. Another factor affecting signal quality is subject positioning, specifically the measurement sites within the aorta. Preferably, both tagging sites should be placed anatomically superior to the diaphragm (to minimize static signal) but inferior to the aortic arch. A third factor is the choice of time delay between the QRS trigger and the start of MR measurement. Ideally, aortic flow should commence after just a few applied RF pulses, in order to minimize saturation of blood. Since the arrival time of the pulse wave after QRS trigger is quite variable among different individuals and perhaps dependent on breath hold duration [17], it is helpful to perform one or two initial test measurements. The WVA software can display aortic flow waveforms within seconds of a MR measurement, making selection of the optimal delay quick and easy. Even for a given subject, the signal quality may vary from one measurement to another. Having rapid feedback concerning the quality of the MR data allows the operator to repeat acquisitions as necessary or avoid needless data redundancy when signal quality is good.

Because of the projective nature of our MR sequence, efficient suppression of signal arising from outside
the thoracic aorta is crucial. Static background signal suppression during MR acquisition relies mainly on two techniques: pre-saturation of tissue near the aorta and subtraction of a diastolic measurement. As seen in Fig. 2, when using a spine array receiver coil and supine subject position, the strongest static signals arise from tissues proximal to the coil. Consequently, applying conventional slab pre-saturation to the spine and superficial muscle and skin is approximately as effective as the cylindrical pre-saturation method described in Ref. [7]. The advantages of conventional pre-saturation are that it does not require positioning the aorta at the center of the field of view (FOV), and it can better accommodate curvature of the aorta. Spatial pre-saturation alone does not suppress static signal sufficiently, however. This is demonstrated in Fig. 8 (panel A), which shows upstream data from a 35-year-old male subject in which only spatial pre-saturation was applied. Clearly, the flow signal is buried within the high-intensity static background signal. Only after subtraction of MR data acquired during cardiac diastole is the aortic flow signal revealed, as shown in panel B.

In some cases, additional cancellation of static background signal is helpful, using the time domain subtraction feature of the WVA software. In panel B of Fig. 8, for example, the initial aortic flow signal is still partially obscured by residual static signal, probably arising from RF excitation side lobes. Panel C shows the result after WVA software processing, in which several additional early flow peaks are revealed. The recalculated PWV of 4.05 m/s after time-domain subtraction is closer to expectations for this subject than the value of 6.32 m/s obtained without post-processing.

Panels D and E of Fig. 8 illustrate another example in which WVA post-processing is advantageous. These maps reveal downstream aortic flow in a 62-year-old female subject. Panel D is before software static background subtraction. The aortic flow profile appears to step discontinuously from zero to a fixed velocity, which is physiologically unlikely. Panel E is after software cancellation, which reveals several early flow peaks and a more natural waveform. The PWV calculated after correction is 5.20 m/s, in contrast with 3.71 m/s before correction.

Other options within WVA may assist in the analysis of PWV. These options include inserting or eliminating leading zero velocity points, adjusting gain to visualize weak signals, and curve fitting only a subset of the acquired data. Future improvements are possible, such as automatic correction of the distance between RF excitations when the aorta is curved, and automatically batch processing all measurements to generate final statistical results without human intervention.

5. Summary

We present an efficient and reliable method for evaluating aortic stiffness with the assistance of a software package, WVA, which has been implemented on a portable PC. WVA yields aortic PWV results comparable to manual analysis with an approximate 24-fold reduction in time. The major advantages offered by WVA are 3-fold. First, by automatically analyzing MR data with minimal user intervention, it enables a near real-time measurement of PWV. Second, the fast PWV analysis gives immediate feedback to guide succeeding MR acquisitions more appropriately, thus improving measurement accuracy. Third, WVA provides several tools to intensify weak signals, thus improving measurement precision.

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References


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