Improved Semi-automated Pulse Wave Velocity Analysis in the Thoracic Aorta using 4D flow MRI

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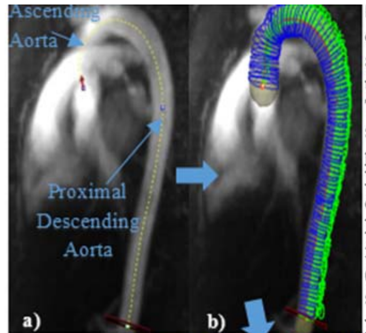
Target audience: Radiologists and researchers interested in measuring vessel stiffness as a predictor for cardiovascular disease.

Purpose: Pulse wave velocity (PWV) measures vessel compliance and can indicate atherosclerosis and vessel stiffness as well as predict cardiovascular events and all-cause mortality[1,2,3]. However, reliable estimation of PWV from MRI data has been challenging due to the need for a high temporal resolution. Recent studies have employed 4D flow MRI of the aorta coupled with a fast semi-automated segmentation technique to utilize the full volumetric coverage of the vessel and extract PWV using many analysis planes (Figure 1 a-b)[4,5]. Existing models such as time-to-foot (TTF) analysis suffer from high variability when fitting noisy data, and least-squares plane fitting[4,5] may systematically underestimate PWV because the upslope gradient varies along the vessel. The aims of this study were to (1) assess the viability of using a least-squares 2[nd]-order surface fit to derive PWV, (2) compare the new fitting method to TTF and plane fitting techniques of deriving PWV in terms of accuracy, stability, and goodness of fit, and (3) compare results to corresponding high-temporal-resolution 2D phase contrast (PC) measurements as the reference standard.



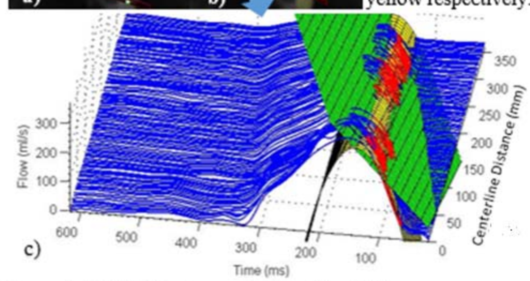
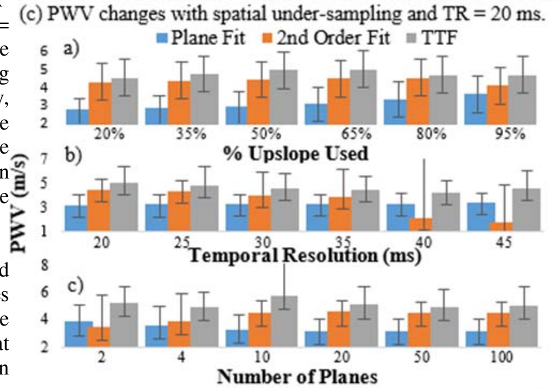


Figure 1: a) The vessel centerline is detected automatically using two user defined points. b) The lumen is auto-segmented and analysis planes are created. c) Flow waveforms are calculated and mean PWV is derived using a fit of the upslope region (red). Plane and 2[nd] order surface are green and yellow respectively.

Methods: 4D flow MRI (temporal resolution = 20 ms) and 2D PC-MR (temporal resolution = 8 ms) data was acquired for nine volunteers using a previously described sequence prototype[4]. 4D flow data were imported into an investigational 4D Flow Evaluation prototype (version 2.3)[6] (Siemens AG, Erlangen, Germany), where a semi-automated centerline extraction and aortic lumen segmentation was performed[7-8] to acquire 100 analysis planes with corresponding flow-time curves (Figure 1). An in-house MATLAB (Mathworks, Natick, MA) tool was then used to automatically calculate mean PWV from flow waveforms using three separate techniques: TTF, plane fitting, and 2[nd]-order surface fitting. All three methods rely on fitting a model to a portion of the systolic upslope of each flow waveform along the vessel (Figure 1c). TTF analysis finds the intersection of linear fits of each upslope with the foot of the upslope region. A least-squares fit plane extends this method by fitting all upslope data at once, theoretically reducing the variability inherent in fitting each waveform. The 2[nd]-order fit solves the equation $f(x,t) = A + Bx + Ct + Dx^2 + Ext + Ft^2$ in a nonlinear least-squares sense where x = centerline distance, y = time, and f(x,t) = flow rate. As with the plane, the velocities at the intersection of the surface with the foot of the upslope region (calculated with a linear fit of the intersection data) closely resembles the changing flow profile over time and can be used to calculate mean PWV. To evaluate each fit's stability, PWV and goodness of fit statistics between the data and the model (R-squared values) were calculated using progressive spatial and temporal undersampling, and varying percentages of the upslope region. Finally, each method was applied to the corresponding high-temporal-resolution 2D-PC data to determine agreement between 4D-flow-based PWV analysis and the reference standard.

Figure 2: (a) PWV values calculated for all fit types as a percent of the upslope region used for fitting (100 planes) (b) PWV changes with progressive temporal under-sampling (100 planes). (c) PWV changes with spatial under-sampling and TR = 20 ms.



	Plane Fit	2[nd] Order Fit	TTF
Mean Difference (m/s)	-1.19	-1.58	-1.87
Limit of Agreement (m/s)	±0.85	±1.17	±2.61

Table 1: Bland Altman analysis of 2D PC vs. 4D flow.

Results: The mean PWV for all volunteers using 100 analysis planes, full temporal resolution, and 50% of the upslope region was 3.2±0.9 m/s, 4.5±0.8 m/s, 5.0±1.3 m/s with mean R-squared values of .75±.08, .86±.06, .74±.18 for the plane fit, second-order fit, and TTF methods, respectively. The PWV values from the 2[nd]-order fit were significantly different using a student's t-test evaluated at α=.05 from those found with plane fitting ($p = 3.76\times10^{-5}$) but not from TTF (p =.064). When fitting to a range of 20-95% of the upslope, PWV varies by 29.0%, 5.1% and 10.0% for plane fitting, 2[nd]-order fitting, and TTF, respectively (Figure 2a). During spatial under-sampling using 10-100 planes (at temporal resolution = 20 ms), the PWV values change by 4.3%, 1.4%, and 16.0%, while during temporal under-sampling from 20 - 35 ms and using 100 planes they change by 5.6%, 13.0%, and 11.0%, respectively. For these spatial and temporal variations, the range of R-squared values of the 2[nd]-order surface (.85 to .96) are higher than those for TTF or plane fitting (.73 to .81 and .71 to .93, respectively) with lower standard deviations. Compared to the reference standard high–temporal-resolution 2D-PC MR, Bland Altman analysis (Table 1) shows moderate agreement for both the plane fit and 2[nd]-order fit, although all fits of 2D PC data suffer from underestimation compared to the 4D counterparts due to insufficient spatial resolution to characterize the changing flow waveform.

Discussion: We have extended the functionality of a previously reported rapid and semi-automated technique for extracting PWV measurement from 4D flow data by developing a 2[nd]-order polynomial surface fit with reduced variability compared to the TTF method, and which more closely conforms to the data than the plane, thus correcting the underestimation with a plane fit. The proposed 2[nd]-order fit outperformed the other methods in goodness of fit and either matched or exceeded them in a stability analysis including temporal and spatial under-sampling, and varying percentages of upslope used. The surface fit is less sensitive to varying amount of upslope or spatial resolution used, but more sensitive to significant decreases in temporal resolution than both other methods. The 2[nd]-order fit can also be applied to traditional high-temporal-resolution 2D PCMR data with somewhat consistent results. The measured PWV's using the 2[nd]-order surface correspond well with the literature[1-3,5] as well as the TTF fit. In conclusion, the 2[nd]-order polynomial fit may have value in the calculation of PWV, and further work in cases of pathology is warranted.

References: 1.Circulation 1991; 83:1754–1763; 2. Br Med Bull 1989;45:968–990; 3. JACC 2010;55:1318–1327; 4. Proc. ISMRM 2013, 6398; 5. JMRI 2012; 35: 1162-1168; 6. Proc. ISMRM 2012, 4148; 7. Gulsun & Tek, MICCAI 2008; 8. Gulsun &Tek, SPIE 2010.

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