Accurate method for measuring pulmonary artery pulse wave velocity by magnetic resonance imaging – mathematical proof and applications

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Introduction: The flow-area (QA) method has potential importance for measuring pulse wave velocity (PWV) from MRI images, especially in the pulmonary artery (PA). Nevertheless, the QA method is highly affected by errors in measurements of the PA cross-sectional area. In this study, a modified version of the QA method is introduced for accurately measuring PWV. The new 'flow-time-area' (QTA) method is more robust to errors in area measurements than the QA method, which is mathematically proved and demonstrated in pulmonary hypertension study. PWV was correlated to gold standard non-MRI measurements in PAH in order to compare the performance of the two methods for estimating PWV. The effects of image resolution, segmentation criteria, inter-, and intra-observer variabilities were studied.

Methods: In contrast to the QA method, which calculates PWV from the ratio of flow change to area change; in QTA, an intermediate step is added to calculate the ratios of flow change to time change, and of area change to time change. PWV is calculated from the ratio of these two ratios to cancel out the common factor, time.

***Mathematical Proof*:** In QA, PWV is estimated from the slope of the line fitted to flow measurements, $\boldsymbol{q}_{m\times1}$, versus area measurements, $\boldsymbol{a}_{m\times1}$, using linear least squares. The resulting line is $\widehat{\boldsymbol{q}} = u\boldsymbol{a} + v$, where $\widehat{\boldsymbol{q}}$ is estimated flow, from which $PWV_{QA} = \Delta q/\Delta a = u$. The coefficients vector $\boldsymbol{u} = [u\ v]^T$ is obtained by solving the normal equation to reach: $\boldsymbol{u} = (\boldsymbol{A}^T\boldsymbol{A})^{-1}\boldsymbol{A}^T\boldsymbol{q}$, where $\boldsymbol{A} = [\boldsymbol{a}\ \boldsymbol{1}]$. By expanding the equation, we reach: $PWV_{QA} = (m\Sigma a_i q_i - \Sigma a_i \Sigma q_i)/(m\Sigma a_i^2 - (\Sigma a_i)^2)$, where a_i and q_i are the i^{th} components in $\boldsymbol{a}$ and $\boldsymbol{q}$, respectively. In QTA, two lines are formed: $\widehat{\boldsymbol{q}} = u_1\boldsymbol{t} + v_1$ and $\widehat{\boldsymbol{a}} = u_2\boldsymbol{t} + v_2$, where $\boldsymbol{t}$ is the set of time points at which flow and area are obtained, from which $PWV_{QTA} = (\Delta q/\Delta t)/(\Delta a/\Delta t) = u_1/u_2$. Following derivations as in QA, we reach: $PWV_{QTA} = (m\Sigma t_i q_i - \Sigma t_i \Sigma q_i)/(m\Sigma t_i a_i - \Sigma t_i \Sigma a_i)$. Under perfect linear relationship $\boldsymbol{q} = u\boldsymbol{a} + v$, it can be shown that $PWV_{QA} = PWV_{QTA} = u$. Now, we analyze the case in which there is a positive deviation (Δa) in area measurement at point j, where j is assumed > $m/2$, which results in rotating the fitting line clockwise, leading to measured pulse wave velocity $\widetilde{PWV}$ that is lower than the correct value PWV. We now show that the amount of reduction (error), $\Delta PWV = PWV - \widetilde{PWV}$, in QTA is always lower than or equal to that in QA. This can be proved by showing that the accuracy measure, $M = PWV/\Delta PWV - 1$, in QTA is always greater than or equal to that in QA, where M ranges from 0 (maximum error) to ∞ (zero error). By mathematical manipulation, where a_j is now substituted by $a_j + \Delta a$, and assuming q_j is not affected by area change (which is always the case due to the large rate of flow change during early systole), the following formulas are obtained: $M_{QA} = (u_2(m\Sigma t_i^2 - (\Sigma t_i)^2) + (mt_j - \Sigma t_i)\Delta a)/((mt_j - \Sigma t_i)\Delta a + (m-1)(\Delta a)^2/u_2) = (N1 + N2)/(D1 + D2)$, and $M_{QTA} = u_2(m\Sigma t_i^2 - (\Sigma t_i)^2)/(mt_j - \Sigma t_i)\Delta a = N1/D1$. To complete the proof, we show that: $D2/D1 \geq N2/N1$. By mathematical manipulation, we reach: $N1D2 - N2D1 = \Sigma_{i>k;i,k\neq j}(t_i - t_k)^2 \geq 0$,which proves that $M_{QTA} \geq M_{QA}$. Similar proof can be shown for $j < m/2$, which rotates the fitting line counterclockwise and increases the calculated PWV. Finally, by linearity, the proof can be generalized to any number of errors. It should be noted that the location of the error (at which frame it occurs)affects the significance of deviation in PWV.

***MRI Scans*:** Twenty five PAH patients, confirmed by right heart catheterization, and twenty five volunteers were scanned on a 3.0-Tesla Siemens Trio scanner. The imaging protocol included cine images covering the heart, and high-resolution velocity-encoding flow images perpendicular to main PA (Figure 1). In the volunteer group, an additional set of low-resolution flow images were acquired. The heart cine images were processed to calculate right ventricle (RV) cardiac index (CI). The PA boundary was manually delineated at the frames during early systole to measure PA cross-sectional area and flow from flow magnitude and phase images, respectively. The high-resolution volunteer images were processed twice, where in the second time, PA boundary was semi-automatically delineated using segmentation propagation algorithm. The images were processed by two experts, and twice by the first expert to measure inter- and intra-observer variabilities using Bland-Altman analysis. Results reported as mean ± SD. Statistical t-test and correlation analysis were conducted to compare PWV by QTA and QA, and validate against standard measurements in PAH (mean PA pressure (mPAP), PA vascular resistance (PVR), and CI). Correlations between PWV from high- and low-resolution images were calculated for both QTA and QA methods. Correlations between PWV from manually- and automatically-segmented images were calculated for both QTA and QA.

Results: PWV_{QTA} and PWV_{QA} showed significant differences, but had better agreement in volunteers than patients (Figure 2). In high-resolution, manually-segmented images (best segmentation), PWV_{QTA}/PWV_{QA}=1.77±0.68 / 1.39±0.56 m/s and 1.36±0.53 / 1.08±0.36 m/s in patients (p=0.003) and volunteers (p=0.016), respectively. The normalized fitting-errors were 0.16/0.31for QTA/QA. There were weak correlations between PWV_{QTA} and PWV_{QA} in patients (r=0.59) and volunteers (r=0.71). QTA showed better correlations with standard measurements in PAH than did QA. The correlation coefficients between PWV (QTA/QA) versus mPAP, PVR, and CI were 0.93/0.61, 0.86/0.65, -0.71/-0.62. In the low-resolution images (volunteers), QTA outperformed QA: PWV_{QTA}/PWV_{QA}=1.33±0.53 / 0.95±0.26 m/s; p=0.001. Correlation coefficients between high- and low-resolution PWV (QTA/QA) were 0.96/0.53. QTA outperformed QA in the automatically-segmented images (volunteers), PWV_{QTA}/PWV_{QA} = 1.32±0.54 / 0.93±0.24 m/s; p=0.001. Correlation coefficients between manually- and automatically-segmented PWV (QTA/QA) were 0.95/0.47. Bland-Altman showed no bias between inter- and intra-observer measurements in both methods. However, lower variabilities were observed in QTA than in QA. In the patient group, inter- and intra-observer measurement differences (QTA/QA)=0.003±0.07 / 0.002±0.13m/s and -0.008±0.05 / -0.009±0.12m/s, respectively. In the volunteer group, inter- and intra-observer measurement differences (QTA/QA)=-0.006±0.08 / 0.00±0.11m/s and -0.004±0.07 / -0.01±0.12m/s, respectively.

Discussion: Calculating PWV from the direct relation between flow and area in the QA method results in error magnification, where errors in area measurements affect the flow data. The proposed QTA method avoids this source of error by manipulating the area and flow measurements separately before calculating PWV. The mathematical analysis showed that the QTA method always results in smaller or (at most) equal PWV errors than the QA method. The experimental results showed significant differences between PWV measurements by the two methods. QTA outperforms QA most when the range of measured areas is small, as in PAH; or when large area measurement errors occur due to low image quality (e.g. low spatial resolution) or inaccurate segmentation (e.g. automatically-segmented images). As the QTA method does not require additional scan or processing time, it should be always implemented instead of the QA method for accurate PWV estimation.

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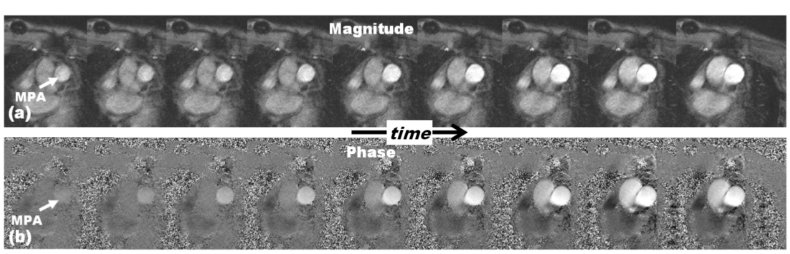

Figure 1. Succession of magnitude (a) and velocity-encoded phase (b) images showing main pulmonary artery (MPA) during early systole. The images show increase in the vessel cross-sectional area (a) and flow (b) with time.

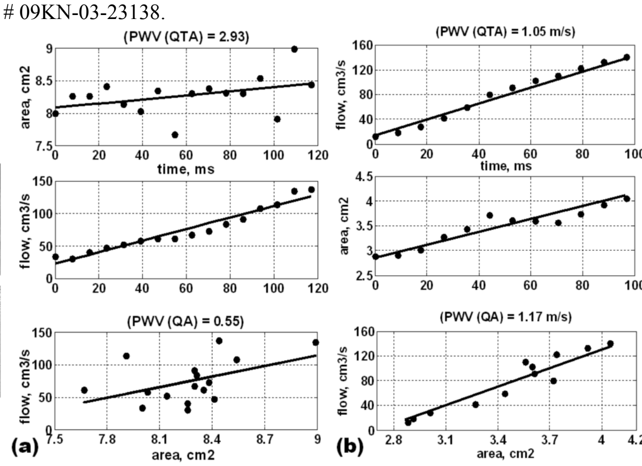

Figure 2. QTA and QA methods for measuring PWV in the pulmonary artery (PA). (a) Data from PA hypertension patient showing large difference between QTA and QA due to large errors in area measurements (lower panel, QA method). The two upper panels show separate estimations of area and flow changes in the QTA method. (b) Data from volunteer showing little differences between the two methods due to artery compliance.